4th Edition

Self Assessment & Review

MICROBIOLOGY
Immunology

Topicwise explanatory series of AIPGMEE, AIIMS, PGI 1993-2008
Review series from other PGMEE 1993-2008

Revision at a Glance

Bacteriology
Parasitology
Virology
Immunology
Mycology
Miscellaneous

Rachna Chaurasia
Anshul Jain

Self Assessment & Review

MICROBIOLOGY IMMUNOLOGY

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Dedication

This book is dedicated to
Our family members, teachers
and above all God
who created us

Preface

"First of all we want to thank all of the readers for their immense support—the key of success."

The overwhelming success of the previous edition has encouraged us to carry this 4th edition a step ahead to revise and update the book, so as to match the pace of present PGMEE requirement of this difficult subject.

PGMEE is a battle field in which everyone fights for success but only few succeed because only few know the correct use of weapon of "Knowledge, hard work and guidance".

So, guys learn the golden words :

Success comes when, we do things right;
When we learn how to make the best use of our time,
and how to deal with adversities

Why this book is different?

Beside adding new questions, we have taken account of all mistakes to provide an error free text.

This book provides important points of each topic in continuous manner not in parts as given in previous guides.

This book consists of theory of each topic followed by its questions so theory portion helps you to solve new questions.

This pattern of book allows you to revise whole infectious disease very clearly and quickly.

This book provides sufficient matter which can be revised without any problem.

How to use this book?

Read the theory first then do questions. You realize that this way of learning makes topic easy to understand and easy to grasp for long-term memory. Try to complete each topic in one sitting.

In the last we would like to say all the best for your PGMEE preparation and hope you will work hard with positive attitude in your mind.

Always keep one thing in your mind:

There's one thing, we cannot recycle and that's wasted time, so guys !
"Schedule a daily time for relaxing, reflecting, planning and brainstorming."


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– Anshul Jain

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In this edition Ananthnarayan refers to Ananthanarayan and Panicker's Textbook of Microbiology 7/e and Panicker refers to Panickers Textbook of Medical Parasitology 6/e.

SECTION – A

REVISION AT A GLANCE

1 Basics of Bacteriology

CATALASE POSITIVE BACTERIA	HEMOLYTIC ORGANISM
• Staphylococci	• Strep. pyogenes - β
• N. Meningitidis	• S. Aureus - β
• Atypical mycobacteria	• Vibrio Eltor
• Pseudomonas	• Clostridium perfringes
• Coliform	• Bacillus subtilis
• H.influenza	• E. coli (pathogenic strain)
• H. pylori	• Mycoplasma
• Yersinia, pasteurella	• Cornybact. mitis
• Shigella except S. dysenteriae type I	• B. cereus
• L. monocytogenes	• L. monocytogens - β
• Nocardia	• Strep. viridans, Pneumococci, Strep. sanguis, Strep. mutans, Enterococcus — **α hemolysis**
• Legionella	
• Brucella except B.neotomae, B. ovis	

Transport media	Organism
Pike's media	S.pyogenes
Stuart's	Gonococci
Cary blair	V. cholera
Sach's Buffered Glycerol saline	- Shigella

CAPSULATED BACTERIA	TYPES OF MOTILITY
• **P**neumococcus	• *Darting* – V. cholera
• Bacillus **a**nthrax	• *Tumbling* – Listeria at 20-25^{0}C
• **K**leibsella	• *Stately* – Clostridia
• H. **i**nfluenza	• *Cork screw* – T. pallidum
• **Y**ersinia	• *Lashing* – Borrelia
• **B**ordetella	• *Gliding* – Mycoplasma
• N. **m**eningococci	• *Swarming* – Proteus mirabilis, P. vulgaris, Cl. tetani, Bacillus cereus
• **C**l. perfringes and butyricum	
• **V**. parahemolyticus	
Mnemonic = **PAKIYB. M.C.V.**	

MOTILE BACTERIA

Peritrichous flagella

- All clostridia except Cl. perfringes and Cl. tetani VI
- Bacillus except B. anthrax
- Listeria monocytogens
- E. coli
- Proteus
- Salmonella except S. gallinarum - pullorum

Polar flagella

- Vibrio
- Pseudomonas
- H. pylori
- Campylobacter
- Spirochetes
- Legionella

ACID - FAST ORGANISM

- **N**ocardia
- **L**egionella micoadie
- **S**megma bacilli
- **B**acterial spores
- **R**hodococcus
- **I**sospora
- **M**ycobacterium
- **S**permatic head
- **C**ryptococcus cyst

No **L**onger **S**eparate **B**ooking for **RIM** **S**im **C**ard

SHAPE OF BACTERIA

- *Club shape* — Corynebacteria
- *Lanceolate* (flame shaped) — Pneumococci
- *Half moon* (Lens) — Meningococci
- *Kidney* — Gonococci
- *Comma* — V. cholera, Campylobacter

PIGMENT PRODUCING BACTERIA

- Pseudomonas - Green (by Ps aeroginosa)
- S. aureus - Golden yellow
- Rhodococcus - Red
- Bacteroides melanogenicus - Black
- Nocardia - Yellow to red
- Pepto and peptostreptococcus
- Photo and Scotochromogen - Yellow orange
- Atypical mycobacteria
- Hafnia, Serratia marcescens

AEROBIC BACTERIA

- **B**acillus anthrax
- **B**ordetella pertusis
- **B**rucella
- **K**leibsella
- **L**isteria monocytogenes
- **M**ycobacteria
- **N**ocardia
- **N**eiserria
- **P**seudomonas
- **P**roteus
- **P**asteurella group except Y. pseudo TB, Y. enterocolitica
- **V**ibrio cholera

Mnemonic B_3 KLMN_2 P_3V

ANAEROBES

I. Cocci

- Gram positive : Peptococcus, Peptostreptococcus
- Gram negative : Veilonella

II. Bacilli

- Endospores forming : Clostridia
- Non sporing :
  - *Gram positive* – Eubacterium, – Propionibacterium, – Lactobacillus, – Mobiluncus, – Bifidobacterium, – Actinomyces
  - *Gram negative* – Bacteroides, – Prevotella, – Fusobacteirum, – Leptotrichia

III. Spirochetes – Treponema, – Borrelia

SPORE PRODUCING BACTERIA

- **B.** anthrax and subtilis
- **S**porosarcina
- **C**lostridia
- **C**oxiella Burnetti

Mnemonic = **BSc C**hemistry

BACTERIA IN PAIR

- Neiserria
- Branhemella (N.catarrhalis) and other Neiserria
- Pneumococcus
- Kleibsella

PLEOMORPHIC ORGANISM

- Mycoplasma
- Clostridium
- H. influenza
- V. cholera
- V. parahemolyticus
- Proteus

DEAD END INFECTION

- Leptospirosis
- Legionella
- Endemic typhus
- Tetanus
- Human rabies
- Japanese Encephalitis.
- T. solium
- Echinococcus granulosus and Trichinella spiralis

BIPOLAR STAINING = SAFETY PIN APPEARANCE

- H ducreyi
- V. parahemolyticus
- Y. pestis
- Calymmatobacterium or Donovani granulomatis
- Pseudomonas mallei
- Pseudomonas pseudomallei

INTRACELLULAR BACTERIA

- Brucella and Bordetella
- Mycobacteria tuberculosis, leprae
- Legionella
- Rickettsia and Chlamydia
- Listeria monocytogenes
- Yersinia pestis
- Pneumococci
- Salmonella, Shigella
- D. granulomatis
- N. meningococci, gonococci

CASTANEDA'S STAINS

- Rickettsiae
- Chlamydiae

GIEMSA STAIN

- Rickettsiae
- Chlamydiae
- Mycoplasma
- T. pallidum
- H. pylori and Malarial parasite

UREASE POSITIVE

- **P**roteus
- **S**. aureus
- **M**organella
- **K**leibsella
- **N**ocardia
- **Y**ersinia pseudotuberculosis, Y.enterocolitica
- **C**ryptococcus
- **D**iphtheroids
- **M**ycobacteria except MAC
- **H**. pylori

Mnemonic **= PSM K**y **N**a**Y**i **CD M**eri **H**ai

ORGANISM NOT GROW IN ARTIFICIAL MEDIA

- M. Leprae
- Rickettsiae
- Chlamydia
- Pathogenic treponemas
- Virus

DESCENDING PARALYSIS	TOXINS INHIBITING PROTEIN SYNTHESIS
• Polio • Tetanus • Botulism • Diphtheria	• Sh. dysenteriae I • Diptheria • Pseudomonas • Verotoxin = Shiga like toxin of E.coli

ACUTE PHASE REACTANT (APR)	CAUSES OF TRAVELLER'S DIARRHEA
• C - Reactive protein (CRP) • Mannose binding protein • Alpha - 1 - acid glycoprotein • Serum amyloid P component • ESR • Platelets • Ferritin • I L-1 • TNF • Coagulation protein • Complement • α1 Antitrypsin • Fibrinogen • Haptoglobin	• ***Enterotoxigenic Escherichia coli (MC)*** • *Enteroaggregative E. coli* • *Shigella and enteroinvasive E. coli* • *Salmonella* • *Campylobacter jejuni* • *Vibrio cholerae* • *Rotavirus and Norwalk-like virus* • *Entamoeba histolytica* • *Giardia lamblia* • *Cryptosporidium* • *Cyclospora*

PULMONARY INFILTRATES IN IMMUNOCOMPROMISED PATIENTS

Infiltrate	*Causative organism*
Localized	Bacteria, *Legionella,* Mycobacteria
Nodular	Fungi (e.g., *Aspergillus or Mucor), Nocardia*
Diffuse	Viruses (especially CMV), *Chlamydia, Pneumocystis, Toxoplasma gondii, mycobacteria*

ONCOGENIC VIRUSES

RNA VIRUSES	**Retroviruses** • Avian leukosis viruses • Murine mammary tumour viruses • Human T cell leukemia viruses • Murine leukosis viruses • Leukosis-sarcoma viruses of various animals
DNA VIRUSES	**I. Papovavirus** • Papillomaviruses of human beings, rabbits and other animals • BK and JV viruses • Polyomavirus • Simian virus 40 **II. Poxvirus** • Molluscum contagiosum • Shope fibroma • Yaba virus **III. Adenovirus - *Not associated with human cancer*** **IV. Herpes virus** • Marek's disease virus • Epstein-Barr virus • Herpes virus pan, papio, ateles and saimiri • Lucke's frog tumour virus • Herpes simplex virus types 1 and 2 • Cytomegalovirus **V. Hepatitis B and C viruses**

INFECTIONS AFTER BONE MARROW TRANSPLANTATION

	Period after transplantation		
Infection site	***Early (<1Month)***	***Middle (1-4 Months)***	***Late (>6months)***
Disseminated	Bacteria (aerobic gram-negative, gram-positive)	Bacteria (*Nocardia,* agents of actinomycosis) Fungi *(Candida, Aspergillus)*	Encapsulated bacteria *(Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitidis)*
Skin and mucous membranes	Herpes simplex virus	Human herpesvirus type 6	Varicella-zoster virus
Lungs	Herpes simplex virus	Viruses (cytomegalovirus, human herpesvirus type 6) Parasites *(Toxoplasma gondii)* Fungi *(Pneumocystis)*	
Kidneys			Viruses (BK)
Brain			Parasites *(T. gondii)* Viruses (JC)

INFECTIONS AFTER KIDNEY TRANSPLANTATION

	Period after transplantation		
Infection site	***Early (<1month)***	***Middle (1-4months)***	***Late (>6months)***
Urinary tract	Bacteria *(Escherichia coli, Kleibsella, Enterobacteriacea, Pseudomonas.)* associated with bacteremia and pyelonephritis, *Candida*	Cytomegalovirus (fever alone is common)	Bacteria; late infections usually not associated with bacteremia
Lungs	Bacteria – *Legionella*	CMV diffuse interstitial pneumonitis, *Pneumocystis, Aspergillus, Legionella*	*Nocardia, Aspergillus, Mucor*
Central nervous system		*Listeria* meningitis, CMV encephalitis, Toxoplasma gondii	CMV retinitis, *Listeria* Cryptococcal meningitis, *Aspergillus, Nocardia*

SEXUALLY TRANSMITTED MICROORGANISMS

Bacteria	Viruses	Other
TRANSMITTED IN ADULTS PREDOMINANTLY BY SEXUAL INTERCOURSE		
Neisseria gonorrhoeae	HIV (types 1 and 2)	*Trichomonas vaginalis*
Chlamydia trachomatis	Human T-cell lymphotropic virus type I	*Phthirus pubis*
Treponema pallidum	Herpes simplex virus type 2	
Calymmatobacterium granulomatis	Human papillomavirus	
Ureaplasma urealyticum	Hepatitis B virus	
	Molluscum contagiosum virus	

Continue .....

SEXUAL TRANSMISSION REPEATEDLY DESCRIBED BUT NOT WELL DEFINED OR NOT PREDOMINANT MODE		
Mycoplasma hominis	Cytomegalovirus	*Candida albicans*
Mycoplasma genitalium	Human T-cell lymphotropic virus type II	*Sarcoptes scabiei*
Gardenerella vaginalis and other vaginal bacteria	Epstein-Barr virus	
	Kaposi's sarcoma - associated herpesvirus	
Group B *Streptococcus*	Transfusion - transmitted virus	
Mobiluncus spp.		

GASTROINTESTINAL PATHOGENS CAUSING ACUTE DIARRHEA

Mechanism	Location	Illness	Stool findings	Examples of pathogens involved
Noninflammatory *(enterotoxin)*	Proximal small bowel	Watery diarrhea	No fecal leukocytes; mild or no increase in fecal lactoferrin	Vibrio cholerae, enterotoxigenic *Escherichia coli* (LT and ST), *Clostridium perfringens, Bacillus cereus, Staphylococcus aureus, Shigelloides, Rotavirus,* Norwalk-like viruses, Enteric adenoviruses, Giardia lamblia, Cryptosporidium spp., Microsporidia
Inflammatory *(invasion or cytotoxin)*	Colon or distal small bowel	Dysentery or infla-mmatory diarrhea	Fecal Polymorphonuclear leukocytes; substantial increase *in fecal* lactoferrin	*Shigella spp., Salmonella* spp., *Campylobacter jejuni, Enterohemorrhagic E. coli, Enteroinv-*asive E. coli, *Yersinia enterocolitica, Vibrio parahaemolyticus, Clostridium difficile, Entamoeba histolytica*
Penetrating	Distal small bowel	Enteric fever	Fecal mononuclear leukocytes	*Salmonella typhi, Y. enterocolitica, Campylobacter fetus*

NORMAL BACTERIAL FLORA

Skin	– *Staphylococcus epidermidis* – *Staphylococcus aureus* – Micrococcus species – Nonpathogenic neisseria species – Alpha-hemolytic and nonhemolytic streptococci – Diphtheroids – Propoinibacterium species – Peptostreptococcus species – Candida species, acinetobacter species
Nasopharynx	– Diphtheroids, Nonpathogenic neisseria species, α- hemolytic streptococci; – *S.epidermidis,* Nonhemolytic streptococci, Anaerobes – Yeasts, Haemophilus species, pneumococci, S aureus, Gram-negative rods, *Neisseria meningitidis*
Gastrointestinal tract and rectum	– Various Enterobacteriaceae ***except*** Salmonella, shigella; yersinia; Vibrio, and Campylobacter species – Enterococci – Alpha-hemolytic and nonhemolytic streptococci

Continue .....

	– Diphtheroids – S.aureus in small numbers – Yeasts in small numbers – Anaerobes in large numbers (***MC*** Bacteroides)
Genitalia	*Any amount of the following :* Corynebacterium species, Lactobacillus species, α-hemolytic and nonhemolytic streptococci, nonpathogenic Neisseria species. *The following when mixed and not predominant :* Enterococci, Enterobacteriaceae and other gram-negative rods, S epidermidis, Candida albicans and other yeasts. Anaerobes especially prevotella, clostridium and peptostreptococcus species.

TRANSPLACENTAL INFECTION

- Toxoplasmosis
- HSV
- Parvo B-19
- HIV
- West Nile virus
- HCV
- Rubella
- Syphilis
- Plasmodium
- Coxsackie virus
- Measles
- TB
- CMV (***MC***)
- Varicella ZV
- T.cruzi
- Enteroviruses
- Hepatitis B
- Lymphocytic choriomeningitis virus

ONCOGENIC MICROBES AND PARASITES

Organism	*Neoplasm*
Human papilloma virus (papovaviridae)	Cervical, vulvar, penile cancers, squamous cell carcinoma, oropharyngeal carcinoma
HSV type 2	Cervical carcinoma, B cell lymphoma
Hepatitis B virus (Hepadnaviridae)	Hepatocellular carcinoma
Hepatitis C virus (Flaviviridae)	Hepatocellular carcinoma, Lymphoplasmacytic lymphoma
HTLV - I (Retroviridae)	Adult T cell leukemia / lymphoma
HTLV - II (Retroviridae)	T cell variant of hairy cell leukemia
HTLV - III (Retroviridae)	AIDS related malignancies, NHL, Kaposi sarcoma, SCC (esp of UG tract), Diffuse large B cell lymphoma, Burkitt's lymphoma
Epstein barr virus (Herpesviridae)	Mixed cellularity Hodgkin's, Nasopharyngeal carcinoma (anaplastic), African Burkitt's lymphoma, Post organ transplant lymphoma, Primary CNS diffuse large B cell lymphoma, Extranodal NK/T cell lymphoma (nasal type)
H. Pylori	Gastric Malt lymphoma, Gastric cancer
Human Herpes virus 8	Primary effusion lymphoma, Multicentric castleman's disease
Schistosoma hematobium	Bladder cancer (squamous cell)
Clonorchis	Cholongiocarcinoma
Opisthorchis	Cholongiocarcinoma

2 Basics of Virology

DEFINITIONS

Virion	– Extracellular infectious virus particle.
Capsid	– Protein coat that protects nucleic acid.
Envelope	– Lipoprotein coat which surrounds some virus particles. Lipid is of host cell origin while protein in the form of peplomers is virus coded.
Viroids	– Subviral infectious agent which is protein free and consist of low molecular weight RNA ***(mostly double stranded, small RNA).*** It is resistant to heat and organic solvents but sensitive to nucleases.
Prion	– Proteinaceous infectious particles causing chronic neurological degenerative disease of human.

- Virus is ***obligate intracellular parasite,*** without cellular organisation and contain only one type of nucleic acid either DNA or RNA but never both. So classified as :

	CAPSID	VIRION	NUCLEIC ACID	VIRUS FAMILY	MEMBERS
DNA VIRUS					
I.	Icosahedral	Naked	SS(-ve)	Parvoviridae	B-19 parvovirus
II.	Icosahedral	Naked	ds circular (±)	Papovaviridae	Papilloma virus, JC, BK virus, polyomavirus
III.	Icosahedral	Naked	ds (±)	Adenoviridae	Human adenovirus
IV.	Icosahedral	Enveloped	ds with ss (±) circular	Hepadenoviridae	HBV
V.	Icosahedral	Enveloped	ds (±)	Herpesviridae	VZ; HSV I, II; CMV; EBV
VI.	Complex	Complex coats	ds (±)	Poxviridae	Variola (small pox) Molluscum contagiosum
RNA VIRUS					
I.	Icosahedral or (cubical)	Naked	SS (+)	Picornaviridae	Polio, coxsackie,entero, rhino, HAV
II.	Icosahedral	Naked	SS	Astroviridae	
III.	Icosahedral	Naked	SS(+)	Calcivridae	HEV, Norwalk
IV.	Icosahedral	Naked	ds segmented (±)	Reoviridae	Rota, Reo, Orbivirus
V.	Icosahedral	Enveloped	SS (+)	Togaviridae	Rubella virus
VI.	Unknown or complex	Enveloped	SS (+)	Flaviviridae	HCV, HGV, yellow fever, Dengue virus

Continue .....

VII. Unknown or complex	Enveloped	SS (-) segmented	Arenaviridae (sandy appearance)	Lassa fever virus
VIII. Unkonwn or complex	Enveloped	SS (+)	Coronaviridae	
IX. Unknown or complex	Enveloped	SS diploid (+)	Retroviridae	HIV 1, 2; HTLV I, II; slow virus group
X. Helical	Enveloped	SS (-) segmented	Orthomyxoviridae	Influenza A, B, C
XI. Helical		SS (-) segmented	Bunyaviridae	Hantavirus, sandfly fever virus
XII. Helical	Enveloped	SS	Bornaviridae	
XIII. Helical	Enveloped	SS (-)	Rhabdoviridae	Rabies virus, Vesicular stomatitis virus
XIV. Helical	Enveloped	SS (-)	Paramyxoviridae	Parainfluenza, RSV, Mumps, rubeola New castle virus
XV. Helical	Enveloped	SS (-)	Filoviridae	Marburg virus Ebola virus

Mnemonics

- Segmented Nucleic acid = **'PARBO virus'**
  = **P**icornaviruses, **A**rena, **R**eo, **B**unya, **O**rthomyxovirus
- Enveloped virus are sensitive to ether, chloroform, bile salts while non-enveloped are resistant
- All RNA virus are enveloped except **'PARC'**
  = **P**icorna, **A**stro, **R**eo, **C**alciviridae

- **Viruses with both DNA and RNA** – Retrovirus
  – Lentivirus
  – HBV
- **Complex capsid** – Pox
  – Bacteriophage
- **Shapes**
  - *Bullet shaped* – Rabies virus
  - *Brick shaped* – Pox virus
  - *Rod shaped* – Tobacco mosaic virus
  - *Space vehicle* – Adenovirus
- Smallest size virus – Parvovirus
- Largest size virus – Filoviridae > Pox viridae

HEMATAGGLUTINATION (HA) - Is agglutination of erythrocytes by virus.

- It is unstable in myxovirus because *Neuraminidase (RDE- receptor destroying enzyme)* cause reversal of hemagglutination called as ***Elution.*** RDE also produced by cholera vibrios and many verterbrate cells.
- In other viruses HA is stable.
- In arbovirus, it is reversible by variation in pH and temperature.
- HA measures total quantity of virus.
- HA of *human* RBC is seen in - **R**eo, **I**nfluenza, **P**ara-influenza, **E**ntero and some cox and ECHO, **M**umps.

Mnemonic **– RIPE Mango**

- HA also seen in measles, toga, rhino, rabies, pox, adenovirus.

POCK ASSAY

Used for quantitative infectivity assay of viruses [also by plaque assay] since each infectious virus particle can form one pock eg. variola, vaccinia, HSV, Pox (Monkey, Cow, Camel).

PHAGE ASSAY

Used for titrating number of viable bacteriophage and for purification of phages.

PHAGE TYPING

- Used for typing and identification of bacteria eg.

  Intraspecies typing of S. typhi (by using Vi antigen) and S. aureus; species specific bacteriophage of B.anthracis, MukerJee's phage IV for classical V. cholerae.

VIRUS MULTIPLICATION

- Critical step in viral biosynthesis is transcription of mRNA from viral nucleic acid.
- **DNA virus** synthesize nucleic acid in host cell **nucleus** except pox which synthesis all their components in host cell cytoplasm.
- **RNA virus** synthesize nucleic acid in **cytoplasm** except orthomyxo, some paramyxo and retrovirus which synthesize partly in nucleus.
- **Viral protein** is synthesized only in cytoplasm.
- Herpes and adeno assembled in nucleus while picoma and pox are assembled in cytoplasm.

ABNORMAL REPLICATIVE CYCLE

Von Magnus Phenomenon : High hemagglutinin but low infectivity due to defective assembly or incomplete virus Eg. *Influenza virus.*

Abortive Infection : Defect in the type of cell (non-permissive cell) not in the parental viruses lead to defective maturation or assembly.

Defective virus : Genetically defective virus which are incapable of producing infectious daughter virions without the helper activity of another virus Eg. Rous sarcoma virus, HDV, adeno associated satellite virus (dependovirus), Measles virus from SSPE etc.

VIRAL INTERACTION

- ***Genetic Interaction*** – occur in virus by :
  1. *Mutation* – Occur during every viral infection.

     Most mutation are lethal.
  2. *Recombination* – occur when two different but related viruses (both active or both inactive or one active and one inactive) infect a cell simultaneously. It leads to cross reactivation / marker rescue; multiplicity reactivation and formation of pseudovirion.
- **Non-Genetic Interaction**
  1. *Phenotyping mixing* – transcapsidation occurs
  2. *Genotyping mixing*

3. *Complementation*
4. *Interference* – Infection of a cell by one virus inhibits simultaneous or subsequent infection by other virus. Most important mediator is Interferon, a soluble cellular product.
   - It is applied in controlling polio outbreaks by introducing live attenuated polio vaccine.
   - It can be produced by receptor destruction as in myxo and enterovirus or by autointerference.

INCLUSION BODIES

It is the most charcateristic histological feature in virus infected cells. It is of following types :

a. Intracytoplasmic eosinophilic inclusions :

Negri bodies	–	rabies
Guarnieri bodies	–	variola (small pox), vaccinia
Bollinger bodies	–	fowlpox
Henderson - peterson bodies	–	molluscum contagiosum

b. Intranuclear acidophilic inclusion bodies :

Cowdry type A	–	herpes, chicken pox, CMV, yellow fever
Torres bodies	–	yellow fever
Cowdry type B	–	polio virus

c. Both Nuclear and cytoplasmic :

Warthin Finkeldey	–	measles

d. Intranuclear basophilic inclusion bodies :

Cowdry type B	–	adenovirus

RESPIRATORY VIRUSES

Viruses	***Most frequent illness***
Rhinoviruses	Common cold
Coronaviruses	Common cold
Respiratory syncytial virus	Pneumonia and bronchiolitis in young children
Parainfluenza viruses	Croup and lower respiratory tract disease in young children
Adenoviruses	Common cold and pharyngitis in children
Influenza A, B viruses	Influenza
Enteroviruses	Acute undifferentiated febrile illnesses
Herpes simplex viruses	Gingivostomatitis in children; pharyngotonsillitis in adults

VIRUS CAUSING LATENT INFECTION

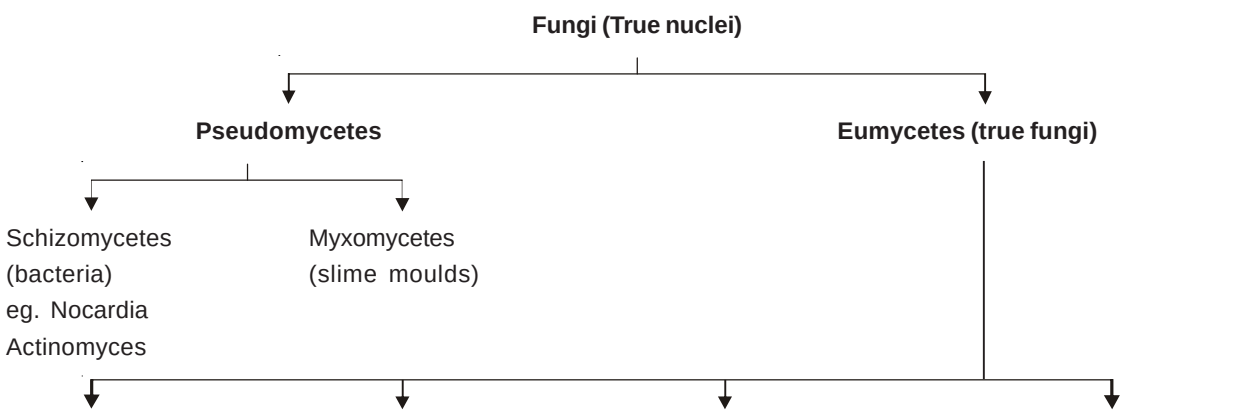
- Measles
- Human T-lymphotrophic virus
- Scrapie
- Hepatitis B virus
- Herpes virus
- Human immuno deficiency virus
- Hepatitis C virus
- Kuru
- Rabies virus
- Oncogenic virus

REACTION TO PHYSICAL AND CHEMICAL AGENTS :

- Stable at low temperature so for long term storage. They are kept by frozing at 70^0c, lyophilization or freeze drying but poliovirus do not stand freeeze drying.
- All virus are disrupted under alkaline pH. Enterovirus are very resistant to acid pH while rhinovirus are very susceptible.
- Most active antiviral disinfectants are oxidising agents such as H_2O_2, $KMno_4$ and hypochlorides.
- Chlorination kill most viruses except hepatitis virus, polio virus.

3 Basics of Mycology

CLASSIFICATION OF FUNGI

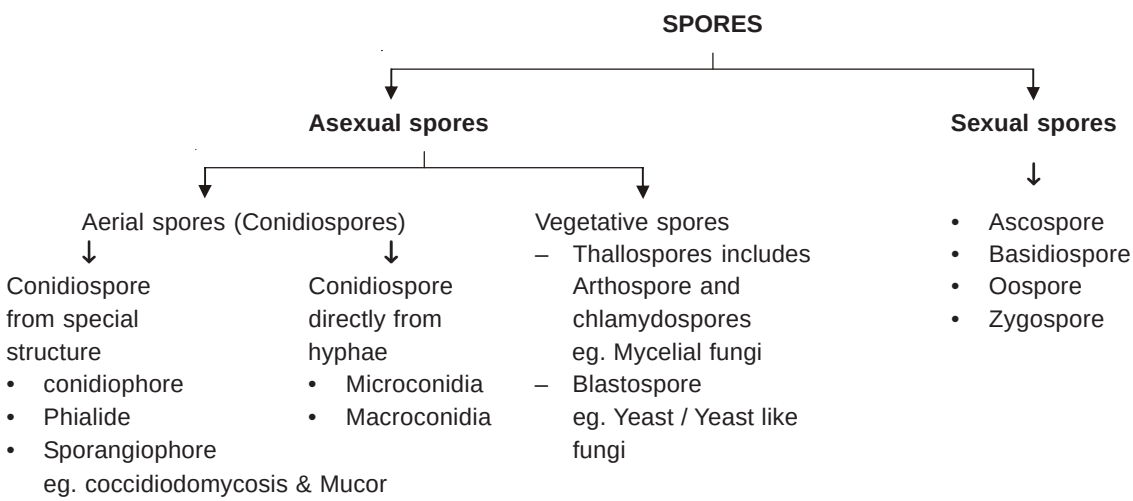


* Endogenous Asexual spores called as **'Sporangiospores'** while exogeneous asexual spores called as **'Conidia'.**

Morphological classification

Yeast	Yeast like fungi	Moulds / filamentous or Mycelial fungi	Dimorphic fungi
(No hyphae no mycelium) – Cryptococcus neoformans	*Only hyphae in the form of pseudomycelium* – Candida (forms blastopores) – Torulopsis (oppurtunistic)	*Hyphae + mycelium forms* – Dermatophytes (form arthospores) – Oppurtunistic eg. Aspergillus Zygomycetes (Phycomycetes) Fusarium Cephalosoporium Geotrichum Scopulariopsis	– Candida albicans (not other candida) – Blastomyces dermatitidis – Paracoccidiodes brasiliensis – Coccidiodes immitis – Histoplasma capsulatum – Sporothrix schenckii – Penicillium marneffi

- **Most** fungi are soil saprophytes and human infection are mainly opportunistic.
- **Most** fungi causing *systemic infections* - Belong to Dimorphic fungi.
- **Most** fungi of medical importance belong to Fungi imperfecti group (Deuteromycetes or hyphomycetes).
- Aseptate fungi are called *Coenocytic fungi.*



FUNGAL DISEASE IN MAN

Superficial mycoses
- Pityriasis versicolor
- Tinea nigra
- White piedra
- Black piedra

Cutaneous mycoses
- Dermatophytes (Microsporum, epidermophyton)
- Candidiasis of skin, mucosa nails

Sub-cutaneous mycoses
- Mycotic mycetoma
- Sporotrichosis
- Chromoblastomycosis
- Rhinosporidiosis
- Subcutaneous phycomycosis
- Phaeohyphomycosis

Endemic (primary, systemic)
- Coccidioidomycosis
- Histoplasmosis
- Blastomycosis
- Paracoccidiomycosis

Opportunistic
Systemic candidiasis
Cryptococcosis
Aspergillosis
Mucormycosis (Zygomycosis)
Penicillosis

4 Basic of Clinical Microbiology

MENINGITIS

Etiology :

Age	Most common organism
< 1 month	E. coli
1 month - 18 years	N. meningitides
> 20 years	S. pneumoniae

Classification :

Streptococcus agalactiae	Gram+ Cocci
Streptococcus pneumoniae	Gram+ Cocci
Neisseria meningitidis	Gram - Cocci
Listeria monocytogenes	Gram + Bacilli
Hemophilus influenzae	Gram - Cocco Bacilli

Common Complaints

Headache

Fever

Chills

Nausea & Vomiting

Photophobia

Neisseria meningitidis

- MC cause in 2-20 years age group. Transmission is via respiratory droplets. Pili allow the attachment to the nasopharyngeal mucosa from where it enters the the blood stream causing meningococcemia. If it crosses the blood-brain barrier, it can infect the meninges, causing an acute inflammatory response that results in a purulent meningitis.
- Presence of petechiae or purpurial rash provide an important clue.

Streptococcus pneumoniae

- MC cause in > 20 years of age. It is carried in the nasopharynx of many healthy individuals. Infection can be either *endogenous* (in a carrier who develops impaired resistance to the organism) or *exogenous* (by droplets from the airway of a carrier).
- S. pneumoniae infection can result in a bacteremia leading to infection of several sites in the human body, including the central nervous system. This meningitis has a high mortality rate.

Listeria monocytogenes

- It is common in neonates, pregnant women, elderly and in immunocompromised individuals for whom Listeria is one of the common causes of meningitis. Listeria infections are usually food borne, with the organism entering the body via the GI tract.
- Newborns can become infected during birth, resulting in meningitis with a significant mortality rate, intrauterine infections can cause the fetus to spontaneously abort or be stillborn.

Haemophilus influenzae

- It is a normal resident of the human upper respiratory tract. Transmission is by respiratory droplets.
- After attaching to the respiratory mucosa, the infection become systemic, with bacteria spreading via the blood to the central nervous system. It has been a leading cause of bacterial meningitis, especially in infants and very young children.

Streptococcus agalactiae

- It causes meningitis and septicemia in neonates. It is found normally in the vagino-cervical tract of female carriers, and the urethral mucous membranes of male carriers, as well as in the GI tract (especially the rectum). Trans-mission occurs during birth, and venereally among adults.
- Infection of an infant occurs as it traverses the birth canal. Its infection is a leading cause of neonatal meningitis, and has a high mortality rate.

URINARY TRACT INFECTION

Etiology

- *Non catheter associated (community acquired) :* E.coli, proteus, klebsiella.
- *Obstruction or calculi associated :* E.coli, proteus, klebsiella, serratia and pseudomonas.
- *Catheter associated (nosocomial) :* E.coli, proteus, pseudomonas, serratia, staphylococcus saprophyticus.

Common Complains

Escherichia coli

- E.coli is the most common cause of urinary tract infections (UTI), including cystitis and pyelonephritis. Women are particularly at risk for infection. Transmission is frequently from the patient's own flora.
- Uncomplicated cystitis (the most commonly encountered UTI) is caused by uropathogenic strains of E.coli characterized by P fimbriae (an adherence factor). Complicated UTI (pyelonephritis) often occurs in settings of obstructed urinary flow, and may be caused by non-uropathogenic strains of E.coli.

Pseudomonas aeruginosa

- It is a major cause of hospital-acquired (nosocomial) infections such as UTI, particularly in patients who have been subjected to catheterization, instrumentation, surgery or renal transplantation, or to prior antibiotic therapy.
- Disease begins with attachment and colonization of host tissue. Pili on the bacteria mediate adherence, and glycocalyx capsule reduces the effectiveness of normal clearance mechanisms. Host tissue damage facilitates adherence ad colonization.

Staphylococcus saprophyticus

- It is a frequent cause of cystitis in young sexually active women, probably due to its occurrence as part of normal vaginal flora. It is also an important agent of hospital-acquired infections associated with the use of catheters.
- It is a coagulase-negative staphylococcal species. It is distinguished from other coagulase negative staphylococci by its *resistance to novobiocin.*

Dysuria
Lumbar Pain
Fever
Chills
Hematuria

Proteus and Klebsiella

- Proteus spp. by virtue of urease production, and Klebsiella spp. through the production of extracellular slime and polysaccharides, predispose to stone formation and are isolated more frequently from patients with calculi.

Other enterobacteria

- Other genera of Enterobacteriaceae, such as Enterobacter and Serratia, which can be found as normal inhabitants of the large intestine, are primarily opportunistic and often nosocomial pathogens. They all frequently colonize hospitalized patients, especially in association with antibiotic treatment, indwelling catheters, or invasive procedures, causing extra-intestinal infections such as those of the urinary tract.
- These organisms produce exotoxins. Wide spread antibiotic resistance among these organisms necessitates sensitivity testing to determine the appropriate antibiotic treatment.

Diagnosis

UTI is said when there is :

- Bacteriuria $\geq 10^5$ /ml in *asymptomatic*
- Bacteriuria of $> 10^4$/ml in *symptomatic*
- Bacteriuria of $\geq 10^2$/ml in *catheterized* sample
- Bacteriuria of *any degree* in *suprapubic* aspirate.

Pyuria in the absence of bacteriuria *(sterile pyuria)* may indicate infection with C. trachomatis, U. urealyticum, and Mycobacterium tuberculosis or with fungi.

FOOD POISONING

Etiology		
Onset : 1 - 6 hours	***Onset : 8 - 16 hours***	***Onset : > 16 hours***
• Bacillus cereus (vomiting) • Staphylococcus aureus	• Clostridium perfringens • Bacillus cereus (diarrhea)	• Campylobacter jejuni • Clostridium botulinium • Escherichia coli • Salmonella species • Shigella species • Vibrio parahaemolyticus

Common Complains

Staphylococcus aureus

- ***MC*** cause of food poisoning in west.
- It is caused by ingestion of food containing the bacterial enterotoxin. Often contaminated by a food-handler, these foods tend to be protein-rich (eg., egg, salad, cream, pastry).
- The toxin stimulates ANS by binding to neural receptors in the upper GI tract.

Campylobacter jejuni

- Second MC cause of food poisoning in west. It also causes *traveler's diarrhea* and *pseudoappendicits.*
- Transmitted to humans through exposure to contaminated meat (especially poultry).
- It typically causes an acute enteritis following IP of 1-7 days. Symptoms may be both systemic (fever, headache, myalgia) and intestinal (abdominal cramping and diarrhea, which may or may not be bloody).

Clostridium species

- Cl. perfringens food poisoning is caused by meat, chicken, fish. Typical episode involves cooking that fails to inactivate spores, followed by holding the food that allow bacterial germination and several cycles of growth.
- It secretes a cytotoxin which acts on SI brush border altering its permeability.
- Symptoms includes diarrhea, abdominal cramp, nausea, fever is absent and vomiting is rare.
- Cl. botulinum causes food poisoning without diarrhea. It produces a neurotoxin that results in flaccid paralysis. Contact with the organism itself is not required.

Diarrhea

Nausea & Vomiting

GI Disturbances

Fever

Myalgia & Paralysis (in few cases)

Escherichia coli

- It is part of the normal flora of the colon, but can be pathogenic both inside and outside of the GI tract. Transmission is by contaminated food (such as beef and unpasteurized milk) and water serving as the vehicles.
- Several types of intestinal infections with E.coli have been identified.
  - *Enteropathogenic E. coli*
    - Diarrhoea in infants and children
  - *Enterotoxigenic E. coli*
    - Traveller's diarrhea
  - *Enteroinvasive E. coli*
    - Diarrhoea to dysentery similar to Shigellosis
  - *Enterohemorrhagic E. Coli*
    - Hemorrhagic colitis
  - *Entero aggregative E. coli*
    - Persistent diarrhea

Shigella species

- It causes shigellosis that occurs most commonly among young children.
- It invade and destroy the mucosa of the LI resulting in bacillary dysentery which is characterized by diarrhea with blood, mucus, and painful abdominal cramping.

Salmonella species

- Non-typhoidal Salmonella, particularly S. typhimurium and S. enteritidis, cause a localized gastroenteritis where the symptoms result from the causative bacteria proliferating in the intestine of affected individuals. Transmission is usually via food, especially chickens, eggs, and egg products.

5 Culture & Sterilisation

CULTURE MEDIAS

Type of medium	Name of medium	Laboratory use
Liquid Media		
A. Basal (simple)	1. Peptone water	Routine culture, basal medium for sugar fermentation test
	2. Nutrient broth	Routine culture
B. Special (Complex)		
a. Enriched	1. Glucose broth	Blood culture
b. Enrichment	1. Robertson's cooked meat medium	Culture of anaerobic bacteria
	2. Tetrathionate broth	Enrichment culture for Salmonellae
	3. Selenite F broth	Enrichment culture for Salmonella & shigellae
	4. Thioglycollate broth	Culture of anaerobic bacteria
	5. Alkaline peptone water	Enrichment culture for vibrio
Solid media		
A. Simple	Nutrient agar (2-3%agar)	Routine culture
B. Special		
a. Enriched	1. Blood agar (Also indicator media)	General culture, Streptococcus; **Most widely used medium**
	2. Chocolate agar	Culture of H. influenzae, N. gonorrhoeae
	3. Loeffler's serum	Culture of C. diptheriae
	4. Dorsett's egg	Culture of Mycobacteria
b. Selective (contains inhibitory substance)	1. MacConkey agar (also indicator and differential medium)	Enterobacteria (Lactose fermenters produce pink colonies)
	2. Deoxycholate citrate agar (DCA)	Selecitve medium for Salmonella and Shigella
	3. Lowenstein Jensen (LJ)	Culture of Myco. tuberculosis

Indicator Media

- Wilson and Blair medium for S.typhi.
- Potassium tellurite in Mcleod's medium for diphtheria bacilli.
- Agar is used in solid media due to its jellyfying property and it has no nutrient value.

STERILIZATION

Sterilization is the process by which article or medium is freed of all living microorganism either in the vegetative or spore state. Sterilizing agents are :

- Heat
- Filtration
- Sterilant liquids.
- Radiation
- Sterilant gases eg. ethylene oxide

Disinfection **–** Means destruction or removal of all pathogenic organism. Disinfecting agent (germicide) are :

a. Substance interfere with membrane functions :
   – Surface active agents eg. quaternary ammonium compounds, tween - 80
   – Phenols eg. phenol, cresol
   – Organic solvents eg. chloroform, alcohols.

b. Substance denaturing protein : eg. organic acid, HCl etc.

c. Agents that destroy or modify functional group of proteins :
   – Heavy metals
   – Oxidising agents eg. H_2O_2, Chlorine, Iodine
   – Dyes eg. acriflovin, acridine
   – Alkylating agents eg. formaldehyde.

Heat :
- Most reliable method of sterilization.
- It should be the method of choice unless contraindicated. It is of 2 types :

	Dry Heat	Moist Heat
Mechanism	Protein denaturation, oxidative damage and toxic effects of elevated levels of electrolytes	Denaturation and coagulation of proteins
Types	1. **Flaming –** for sterlizing inoculating loop or wire tip of forceps and searing spatulas 2. **Burning or Incineration –** for contaminated cloth, animal carcasses and pathological materials, PVC and polythene (Polystyrene should autoclave) 3. **Hot air oven –** *Most widely used* method of sterilization by dry heat • Holding period of 160^{0}C for one hour is used to sterilize glassware, scalpels, all glass syringes, swabs, liquid paraffins, dusting powder, fats and grease • Sterilization control is done by spore of non-toxigenic strain of **Cl. tetani** • For cutting instruments temperature of 150^{0}C for 2 hours is required • ***Drawback*** - It has no penetrating power so not used for bulky articles such as mattresses	1. **Temperature below 100^{0}C (for pasteurization of milk)** – ***Holder method*** (63^{0}C for 30 min) or ***flash process*** (72^{0}C for 15 sec) destroy all nonsporing pathogens. Coxiella burnetii is relatively heat resistant and may survive holder method. Also used for vaccines of non-sporing bacteria, serum or body fluids containing coagulable proteins. 2. **Temperature at 100^{0}C (Boiling) –** Rolling boil (boiling for 5 - 10 minutes) will kill bacteria, but not spores or viruses 3. **Steam at atmospheric pressure 100^{0}C -** Koch or Arnold steamer is usually used container and culture media are simultaneously sterilized. Single exposure of 20 min usually ensures sterilization; but for media containing sugars or gelatin an exposure of 100^{0}C for 20 minutes on three successive days is used known as ***Tyndallization*** 4. **Steam under pressure = autoclave or steam sterlizer** (>100^{0}C) **-** Most effective sterilizing agent for dressing, instruments, laboratory wares, media and pharmaceutical products; aqueous solutions. Sterlization control by ***bacillus sterothermophilus***

Filtration : Used to remove bacteria; virus isolation; testing water samples for vibrio cholera or typhoid bacilli; and obtaining bacterial toxins. Membrane filters is routinely used in water purification and analysis, sterlization and sterility testing and for preparations of solutions for parenteral use. Most widely used pore diameter is 0.22 µm.

Radiation

Non ionization	Ionizing radiation
1. Infrared radiation - Form of *hot air sterlization* used for rapid mass sterlization of prepacked items such as syringes and catheters	– X-rays, gamma rays (Commonly used) and cosmic rays referred to *as cold Sterlization* – Used for plastics, syringes, swabs, catheters, animals feeds, cardboard, oils grease, fabrics, metal foils
2. Ultraviolet radiation - For entryways, operation theaters and laboratories	– Most effective but very costly

Alcohols

- ***MC*** used are ethanol and isopropyl alcohol *(better)*.
- Both used as skin disinfectant in 70% concentration.
- Not sporicidal but active against non sporing bacteria and viruses.
- Isopropyl alcohol is used for disinfection of clinical thermometers.
- Methyl alcohol effective against fungal spores and is used for treating cabinets and incubators.
- Most effective skin antiseptic is alcoholic solution of chlorhexidine and iodine.

Aldehydes

- *Formaldehyde :* Sporicidal (Slow activity), bactericidal, virucidal. Used for sterlising instruments and heat sensitive catheters and for fumigating wards, sick rooms and laboratories.
- *Glutarldehyde :* Specially effective for tubercle bacilli, viruses and fungi.
  - 2% solution called *Cidex* used for cystoscope and bronchoscopes.

Dyes

- Acridine and aniline dyes used as skin and wound antiseptic.
- More active against Gram positive organism.

Halogens

- Iodine in aqueous and alcoholic solution is used widely as skin disinfectant.
- Active against tubercle bacteria, viruses, spores (moderately).
- Iodophores are compounds of iodine with non ionic wetting or surface active agents. They are more active.
- Chlorine is used commonly as hypochlorites.

Ethylene oxide

- Highly penetrating and highly active against all microorganism including viruses and spores.
- Specially used for sterilizing heart lung machine.

Formaldehyde gas

- For fumigation of operation theatres and other rooms.
- Betapropiolactone is more efficient for fumigation than formaldehyde.

Surface Active Agents

- Most important antibacterial agents are cationic surface active agents.
- No action on spores, tubercle bacilli and most viruses.
- Most active at alkalines pH.
- Soaps prepared from saturated fatty acids are more effective against G-ve bacilli while those prepared from unsaturated fatty acids are more active against G+ve and neisseria group.

QUESTIONS

1. Which of the following is most resistant to anticeptics? [AI 08]

a) Spore b) Prion
c) Cyst d) Fungus

2. Which of the following statement is true :

a) Solid media are enrichment media **[AI 07]**
b) Nutrient broth is basal media
c) Agar adds nutrient to media
d) Chocolate agar is selective media

3. A chest physician performs bronchoscopy in the procedure room of the out patient department. To make the instrument safe for use in the next patient waiting outside, the most appropriate method to disinfect the endoscope is by :

a) 70% alcohol for 5 min **[AI 03]**
b) 2% glutaraldehyde for 20 min
c) 2% formaldheyde for 10 min
d) 1% sodium hypochlorite for 15 min

4. Heat labile instruments for use in surgical procedure can be best sterlized by : [AI 03]

a) Absolute alcohol
b) Ultra violet rays
c) Chlorine releasing compounds
d) Ethylene oxide gas

5. Out of the following the true statement regarding sterlization is : [AI 97]

a) Dry heat is the best method of sterilization of liquid paraffin
b) All glass syringes are best sterilized by boiling at 100^0C
c) Bacterial vacines are best sterilized by ethylene oxide
d) Pasteurization of milk by flash method is done by heating at 63^0C for 30 minutes

6. The operating temperature in an ethylene oxide sterilization during warm cycle is : [AIIMS 04]

a) 20-35^0C
b) 49-63^0C
c) 68-88^0C
d) 92-110^0C

7. The sterilization method for the instruments which are damaged by dry heat is : [AIIMS 95]

a) Steam
b) Radiation
c) Boiling
d) Burning

8. Choose the correct ones for the decreasing order of resistance to sterilization : [PGI Dec. 07]

a) Prions, bacterial spores, bacteria
b) Bacterial spores, Bacteria, Prions
c) Bacteria, Prions, Bacterial spores
d) Prions, Bacteria, Bacterial spores
e) Bacterial spores, prions, bacteria

9. Decreasing order of resistance to sterilization :

a) Spores, prions, non-lipid of smll virus
b) Prions, spores, enveloped viruses **[PGI 07]**
c) Spores, mycobacteria, lipid or medium size virus

10. Sterilising agents include : [PGI 02]

a) Dry heat
b) Ethylene oxide
c) Ether
d) Alcohol
e) Chlorohexidine

11. Which of the following can be reliably used for hand washing : [PGI 00]

a) Chlorhexidine
b) Isopropyl alcohol
c) Lysol
d) Cresol
e) Glutaraldehyde

12. Sporocidal disinfectant is following except :

a) Glutaraldehyde **[PGI 99]**
b) Formaldehyde
c) Ethylene oxide
d) Benzalkonium chloride

13. All are sporicidal except : [PGI 99]

a) Lysol
b) Glutaraldehyde
c) Ethylene dioxide
d) Formaldehyde

14. Sterlization of culture media containing serum is by : [PGI 98]

a) Autoclaving
b) Micropore filter
c) Gamma radiation
d) Centrifugation

Answer

1. b) Prion... 2. b) Nutrient ... 3. b) 2% ... 4. d) Ultra violet ... 5. a) Dry heat is ...
6. b) 49-63^0C 7. b) Radiation 8. a) Prion ... 9. b and c 10. a and b
11. a, b and d 12. d) Benzalkoni ... 13. a) Lysol 14. a) Autoclaving

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b i.e. Prion *See below*

Resistance of organism to antiseptics in decreasing order is as follows :

- Prions
- Coccidia
- Spores
- Mycobacteria
- Cysts
- Small non-enveloped virus
- Trophozoites
- Gram negative bacteria (non-sporulating)
- Fungi
- Large non-enveloped virus
- Gram positive bacteria
- Lipid enveloped / medium size virus (HIV, HBV)

2. Ans. is b i.e. Nutrient broth is basal media *Ref. Ananthnarayan 7/e, p 37*

Media			
Simple media (basal media)	***Complex media***	***Synthetic or defined media***	***Special media***
– Nutrient broth	– Added ingredient	– Prepared from chemicals with defined composition e.g., simple peptone water medium	– Enriched media – Enrichment media – Selective media – Indicator media – Sugar media – Transport media

- **Enriched media :** Substance such as blood serum on egg are added to basal medium to promote growth e.g., blood agar, chocolate agar and egg media.
- **Enrichment media :** In mixed culture usually the nonpathogenic or commensal bacteria tends to overgrow than pathogenic ones. In such conditions, substances which has stimulating effect on pathogenic one or inhibitory effect on unwanted one. These media are called enrichment media e.g., tetrathionate.
- **Selective media :** If the inhibitory substance is added to solid medium so as to supress the growth of unwanted one; the media is called *selective media* e.g., desoxycholate citrate medium.
- **Indicator media :** Changes colour on growth of bacteria e.g., wilson blair media; ***Mc*** loed medium.
- **Differential media :** To differntiate different bacteria on the basis of characteristics. Eg. Mac Conkey's medium.
- **Sugar media :** – Here sugar means any fermentable substance.
  – Usual sugar media consist of 1% of the sugar in peptone water along with an appropriate indicator.
- **Transport media :** For delicate organism e.g., stuart media.

3. Ans. is b i.e. 2% gluteraldehyde for 20 min *Ref. Ananth. 7/e, p 31; Chakorvarty 2/e, p 46*

- 2% Glutarldehyde is knows as cidex (Aldehyde disinfectant) specially effective against tubercle bacilli, fungi and viruses. It is *most commonly* used for cystoscope, endoscope, bronchoscopes etc which can't be disinfected by heat.
- Also used to treat corrugated rubber anesthetic tubes and face masks, plastic endotracheal tubes, metal instruments and polythene tubing.

Other choice		
• 70% alcohol is used as skin antiseptic • It acts by denaturing bacterial proteins • Methylated ethyl alcohol is MC alcohol used for skin disinfection and hand washing	• 2 - 3 percent formaldehyde (20 - 30 ml of 40% formalin in one litre of water) is used for spraying rooms, walls, furniture and disinfecting blankets, beds, books • It is most effective at high temperature and relative humidity of 80-90%	• Sodium hypochlorite is recommended for sterilizing infant's feeding bottles • It acts in the same way as bleaching powder and is more strong.

4. Ans. is d i.e. Ethylene oxide *Ref. Park 18/e, p 108; 19/e, p 110; Ananthnarayan 7/e, p 32*

"***Heat sensitive articles may be sterilized at 55-60^{0}C by ethylene oxide which kills bacteria, spores, viruses.***"

- It is highly penetrating and highly explosive.
- CO_2 or N2 decrease its explosive tendency and water vapour increase its efficacy.
- It acts as alkylating agent.
- It is specially used for sterlizing heart - lung machines, sutures, dental equipment, books, fabrics, plastic equipment, cardiac catheters, clothing, glass, plastics, metal and paper surfaces.
- It is unsuitable for fumigating room since it is explosive.

Other choices		
Absolute alcohol	**UV rays**	**Chlorine releasing compounds**
– No action against spores – Recommended as rapidly drying disinfectant for skin and surface disinfection of clinical thermometers	– Used for disinfecting enclosed areas such as entry ways, hospital wards, operation theatres and laboratories	– ***MC*** used chlorine is hypochlorites – Used as antiseptics for dressing wound and for disinfection of water supplies, swimming pools, food / dairy industries – They are bactericidal, virucidal

5. Ans. is a i.e. Dry heat is the best method of sterilization of liquid paraffin

Ref. Ananthnarayan 7/e, p 25 - 26

- **Hot air oven :** It is the *most widely* used method of sterilization by dry heat.
- **Holding period of** 160^{0}C for 1 hour is used to sterilize glasswares, forceps, scissors, scalpel, all glass syringes, swabs, liquid paraffin, dusting powder, fat and grease.
- Bacterial vaccines are best sterilized by 'Filters'.
- Flash method involves heating at 73^{0}C for 15 seconds.
- Holding method involves heating at 63 - 66^{0}C for 30 minutes.

6. Ans. is b i.e. 49 - 63^{0}C *Ref. Park 18/e, p 108; 19/e, p 110*

Already explained, please see answer no. 4

7. Ans. is b i.e. Radiation *Ref. Ananthanrayan 7/e, p 30; Chakraborty 2/e, p 45-46*

Procedures of sterlisation of some important materials.

Materials	Methods of sterilisation and disinfection
1. Glasswares - syringes, petridishes, test tubes, flasks, surgical instrument, oily fluids and powders	Hot air oven
2. Serum, body fluids, bacterial vaccines	Waterbath, vaccine bath
3. Milk	Pasteurisation, 63^{0}C x 30 min. or 72^{0}C x 20 sec.
4. Cystoscope and endoscope	Glutaraldehyde (Cidex-2%) or ethylene oxide
5. Most of the culture media	Autoclaving
6. Culture media containing egg, serum or sugar	Tyndallisation
7. Rubber, plastic and polythene tubes, disposable syringes	Glutaradehyde, Ethylene oxide gas
8. Dressings, aprons, gloves, catheters surgical instruments except sharp instruments.	Autoclaving
9. Sharp instruments	5% cresol
10. Suture materials except catgut	Autoclaving
11. Catgut	Ionising radiation
12. Rubber or plastic disposable goods, disposable syringes, bone and tissue graft, adhesive dressings	Ionising radiation
13. Faeces and urine, vomitus Sputum	Bleaching powder, cresols, formalin, Burning, autoclaving
14. Sterilisation of operation theatre	Formaldehyde gas
15. Wards and Laboratory or Operation theatre floor space	Formaldehyde gas and cresols (Lysol)
16. Skin	Tincture iodine, spirit (70% ethanol), savlon (phenol derivative)

8. Ans. is a i.e. Prions, bacterial spores, bacteria

Already explained in Answer no. 1

9. Ans. is b and c i.e. Prions, spores, enveloped viruses; and Spores, mycobacteria, lipid or medium size

Already explained in ans. no. 1

10. Ans. is a and b i.e. Dry heat; and Ethylene oxide *Ref. Chakraoborty 2/e, p 35*

Sterilization is the process by which an article, surface or medium is *freed of all living microorganism* either in vegetative or spore state.

Sterlization agents are :

- Heat
- Ionization radiations
- Sterilant liquids
- Filteration
- Gases (ethylene oxide, formaldehyde gas)

Disinfection means destruction or removal of ***all pathogenic organism*** which are capable of producing infection. Disinfecting agents are :

- Alcohols (ethyl and isopropyl alcohol)
- Halogens (Iodine, chlorine)
- Biguanides (Chlohexidine)
- Quaternary ammonium compounds (cetrimide)
- Acids
- Metallic salts
- Dyes
- Phenol derivatives (Hexachlorophene, Lysol, cresol)
- Oxidising agents ($KMnO_4$, H_2O_2)
- Soaps
- Aldehydes

– Ether is used as anaesthetic agent not as disinfectant or sterilizing agents.

11. Ans. is a, b and d i.e. Chlorhexidine; Iso propylalcohol; and Cresol

Ref. KDT 6/e, p 858-861; Ananthnarayan 7/e, p 30 - 31; Chakarvarty 2/e, p 46

Skin disinfectants are :

i. Chlorhexidine (Savlon)
ii. Alcohols (as spirit) - Isopropylalcohol (preferred), ethyl alcohol
iii. Iodine
iv. Cresol
v. Chloroxylenol (Dettol)
vi. Hexachlorophene
vii. Tincture iodine

12. Ans. is d i.e. Benzalkonium chloride *Ref. Ananthnarayan 7/e, p 32, Park 18/e, p 108; 19/e, p 110*

Sporocidal agents are :

E – **E**thylene oxide
F – **F**ormaldehyde
G – **G**lutaraldehyde
H – **H**alogens (moderate action on spores)

- Benzalkonium chloride is Quaternary ammonium (cationic) antiseptic which are not sporicidal.

..... KDT 6/e, p 860

- Phenol and Hexachlorophene are poor sporicidal

13. Ans. is a i.e. Lysol

Already explained, please see answer no. 12

14. Ans. is a i.e. Autoclaving *Ref. Ananthnarayan 7/e, p 28*

Most of culture media are sterilized by Autoclaving at 121^{0}C for 15 min at 15 lb pressure / inch^2.

..... Chakorvarty 2/e, p 46

Steam under pressure *(Autoclaving or steam sterlizer)*

Used for sterilizing dressings, instruments, laboratory ware, media, pharmaceutical products and aqueous solution. *..... Ananthnarayan 7/e, p 28*

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. The disposable plaastic syringes are best sterlized by : **[Kar 02]**

a) Formaldehyde
b) Ethylene oxide
c) Hexachloride
d) UV radiation

[Ref. Chakarborty 2/e, p 46]

2. Auto claving is done in : **[Kolkata 02]**

a) Dry air at 121^{0}C and 15 1b pressure
b) Steam at 100^{0}C for 30 minutes
c) Steam at 121^{0}C for 30 minutes
d) Dry air at 160^{0}C for 30 minutes

[Ref. Chakraborty 2/e, p 38]

3. Culture media are sterilized by : **[Bihar 03]**

a) Autoclaving
b) B–radiation
c) Hot air oven
d) Tyndallisation

[See the list from this book]

4. Glassware and syringes are sterilized by :

a) Autoclave **[Kolkata 03]**
b) Hot air oven
c) Ethylene oxide
d) Irradiation

[Ref. Chakarborty 2/e, p 45]

5. pH of sabourauds dextrose agar is adjusted to :

a) 4-6 **[Kar 04]**
b) 1-2
c) 6-8
d). 8-10

[Ref. Jawetz Microbiology, p 29]

6. Asepsis means : **[Kolkata 04]**

a) Absence of pathogenic microbes
b) Disinfection of the surface
c) Prevention of infection
d) Destroying all forms of microorganism

[Ref. Jawetz 24/e, p 57]

7. Mac-conkeys Agar medium is : **[UP 06]**

a) Enriched medium
b) Enrichment medium
c) Differential medium
d) Synthetic medium

[Ref. Ananthnarayan 7/e, p 37]

8. Gamma radiations are used for sterlizing :

a) Syringes **[UP 06]**
b) Cystoscopes
c) Dressing aprons
d) Metal instruments

[See list of our book]

9. The process of destroying all microbes including spores is called : **[Kar 03]**

a) Disinfection
b) Antisepsis
c) Disinfestation
d) Sterlization

[Ref. Jawetz 24/e, p 57]

Answer 1. b) Ethylene oxide 2. c) Steam at ... 3. a) Autoclaving 4. b) Hot air oven 5. a) 4-6
6. a) Absence of . 7. c) Differential ... 8. a) Syringes 9. d) Sterlization

NOTES

SECTION – B

Explanatory Series of Questions 1995 - 2008 "ALL INDIA, AIIMS & PGI"

UNIT – I BACTERIOLOGY

Gram Positive Cocci

1. Staphylococci 31 – 44
2. Streptococci 45 – 67

Gram Negative Cocci

3. Neisseria 68 – 78

Gram Positive Bacilli

4. Clostridium 79 – 93
5. Corynebacterium 94 – 105
6. Actinomycetes & Bacillus 106 – 118
7. Listeria Monocytogenes 119 – 125
8. Mycobacteria 126 – 146

Gram Negative Bacilli

9. Enterobacteriaceae 147 – 171
10. Vibrio 172 – 186
11. Pseudomonas & Yersinia 187 – 195

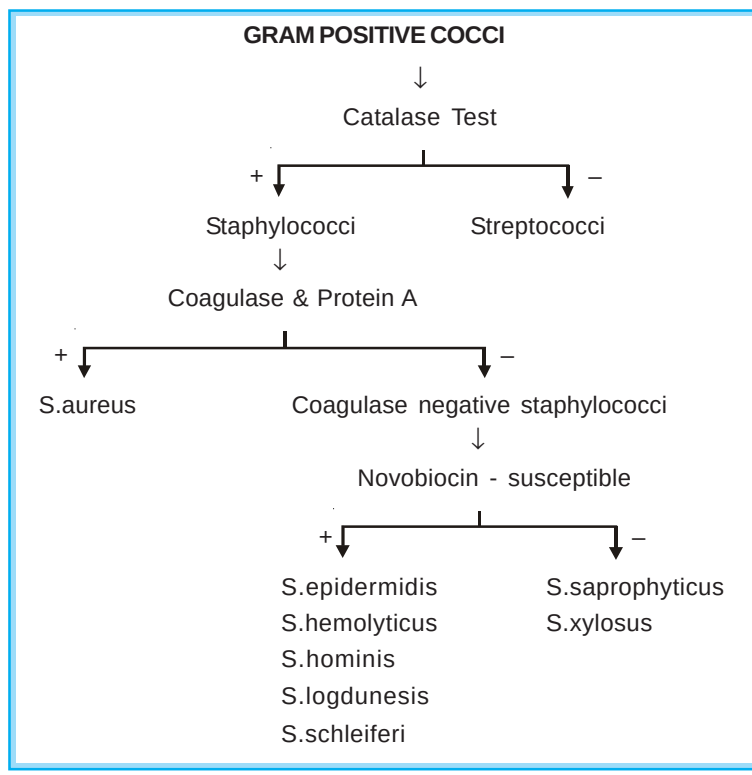
Gram Negative Cocco - Bacilli

12. Hemophilus, Bordetella & Brucella 196 – 206
13. Campylobacter & Helicobacter 207 – 214
14. Legionella 215 – 220
15. Rickettsiaceae & Chlamydiae 221 – 238
16. Spirochetes 239 – 253
17. Mycoplasma 254 – 260

1 Staphylococci

Catalase positive, nonmotile, aerobic and facultatively anerobic organism.

CLASSIFICATION



Classification of Staphylococci

Coagulase+ve / Protein A+ve	*Coagulase-ve*
• More virulent • Form golden yellow colonies on solid media • Usually pathogenic	• Less virulent • Form white colonies • Usually not pathogenic

STAPHYLOCOCCI AUREUS

- ***MC*** source of infection - Human patient and Carrier.
- ***MC*** route of infection - Skin.
- **It is the *MC* cause of :**

Acute endocarditis	Acute osteomyelitis
Spinal epidural abscess	Nosocomial pneumonia
Septic intracranial thrombophlebitis	Paronychia
Skin, soft tissue infections	Surgical wound infection

..... Harrison 16/e, p 1539

- *S.aureus is **MC** cause of acute endocarditis except early and late prosthetic valve endocarditis which are caused by Coagulase-ve staph. and Streptococci viridans respectively.*
- Recently methicillin resistant MRSA have been reported as primary cause of community acquired pneumonia.

.... Harrison 17/e, p 1621

Remember : Subacute Endocarditis is typically caused by Strep. viridans.

Culture

- On nutrient agar, show characteristic *oil paint appearance.*
- *Show β hemolysis which is marked on rabbit or sheep blood and weak on horse blood agar.*

Biochemical Reaction

- **Mannitol fermenter** anaerobically *(not by other species of Staphylococci)*
- **Phosphatase reaction** : – Gives prompt phosphatase reaction.
  – Useful screening procedure as *S.epidermidis is usually negative or only weakly positive.*

Virulence Factors

- Most constant association of *virulence* is production of enzyme *coagulase* and to a lesser extent with *mannitol fermentation.*

a. Cell associated polymers :

- *Cell wall polysaccharide peptidoglycan* - Activates complement system. Induce release of cytokines.
- *Techoic acid* - For adhesion and protection against complement mediated opsonization.
- *Capsular polysaccharide* - Decrease opsonization.

b. Cell surface proteins :

- *Protein A* - Responsible for coagglutination. Acts as an Fc receptor. Binds to Fc terminal of IgG 1, 2 and 4, preventing opsonophagocytosis by PMNs.
  – Chemotactic, anticomplementory, antiphagocytic and B-cell mitogen.
  – Responsible for Co-agglutination.
- *Clumping factor* - Surface compound that is responsible for adherance of the organism to fibrinogen and fibrin. It is distinct from coagulase detected by slides test. *... Jawetz 24/e, p 226*

c. Extracellular enzymes :

1. *Coagulase* - Sufrace enzyme which converts fibrinogen to fibrin.
   - It is a enzyme which requires presence of coagulase releasing factor (CRF) for its action.
   - Detected by tube test
   - It is of 8 types
   - Most human strain form type - A coagulase.
   - Coagulase test is standard criterion for S.aureus identification. In case of confusion tube test will be deciding factor.

Caution : Initially clumping factor is supposed to be bound form of coagulase. Now it is clear that it is totally different, so, the concept of slide test for bound cogulase is wrong.

2. Nuclease - A heat stable nuclease (DNAse) is **characteristic** of S.aureus
3. Protein receptor - For mammalian proteins eg. fibronectin, fibrinogen, IgG, C1q. Facilitates adhesion.
4. Lipase : Helps in infecting skin and subuctaneous tissue
5. Hyaluronidase.
6. Protease ⎫
   ⎬ Helps in spread of infection
7. Fibrinolysin (Staphylokinase) ⎭

α hemolysin

- Most important hemolysin
- Protein inactivated at 70^0C, but reactivated aradoxically at 100^0C.
- Lyses rabbit erythrocyte but is less active against human erythrocytes.
- Leucocidal, cytotoxic, dermonecrotic, neurotoxic and lethal.

Toxin

A. Cytolytic Toxins :

- α *Hemolysin :*
  - Most important hemolysin
  - Protein inactivated at 70^0C, but reactivated aradoxically at 100^0C.
  - Lyses rabbit erythrocyte but is less active against human erythrocytes.
  - Leucocidal, cytotoxic, dermonecrotic, neurotoxic and lethal.
- β *Hemolysin* - Shows 'hot cold phenomenon'. Sphingomyelinase, hemolytic for sheep cells.
- γ *Hemolysin* - Bi component protein.
- δ *Hemolysin* - Detergent like effect on cell membranes.
- *Leucocidin* (Panton valentine Toxin) - Bi component toxin associated with farunculosis.
- *Synergohymenotropic toxin* : Bi component toxin such as Leucocidin and γ Hemolysin.

B. Enterotoxin : (A, B, C_{1-3}, D, E and H)

- Preformed, heat stable toxin, responsible for staphylococcal food poisoning which occur 2-6 hrs after consuming meat and fish, milk or milk products.
- *Source* - usually food handler which is carrier.
- *Mechanism* - Toxin acts directly on autonomic nervous system *(Vagal stimulation)* and vomiting centre.
- *Type A* toxin is responsible for *most* cases.

C. Toxic shock syndrome toxin (TSST) :

Toxic shock syndrome is multisystem disease presenting with fever, hypotension, myalgia, vomiting, diarrhea, mucosal hyperemia, erythematous sunburn, rash, Disorientation or altered conciousness seen mostly in menstruating women using highly absorbent vaginal tampons.

- TSST-1 = Enterotoxin F = Pyrogenic Exotoxin C is responsible for most cases.
- *Vomiting is due to direct stimulation of ANS rather than local action.*
- Staph. Enterotoxin and TSST are *super antigen* leading to an excessive and non regulated immune response.

D. Exfoliative / Epidermatolytic Toxin / ET / Exfoliatin

- Cause staphylococcal scalded skin syndrome (SSS).
- Severe form is called Ritter's disease *in* ***neonate*** and *toxic epidermal necrolysis* in ***elderly.***
- Milder form are pemphigus neonatorum and bullous impetigo.
- There are two type : ETA and ETB, toxin possess serine protease activity which triggers exfoliation.

Typing

- Staphylococci are typed on basis of their susceptibility to bacteriophage.
- Phage typing is done by pattern method.

Lab diagnosis

- Diagnosis is made by *culture,* specimen is plated on blood agar.
- Smears are examined from culture and coagulase test is done.
- *Serological Test* : Helpful in diagnosis of hidden deep infection.
  - Antistaphylolysin (antialphalysin) titre of more than two unit is important specially when rising.
- Polymerase chain raction *(PCR)* based assays have been applied for rapid diagnosis of S.aureus infection.

... Harrison 17/e, p 875

Treatment

• If sensitive to penicillin	→	Penicillin G
• Penicillinase producing but sensitive to methicillin	→	Naficillin or Oxacillin
• Methicillin resistant Staph. Aureus (MRSA)	→	Vancomycin
• Vancomycin resistant Staph. Aureus (VRSA)	→	Quinopristin, dalfopristin, linezolid
• Emperical therapy	→	Vancomycin

Special Cases :

• TSS	→	Clindamycin (reduces toxin synthesis)
• Food poisioning	→	*No antibiotic* (as caused by preformed toxin)

COAGULASE (-) VE STAPHYLOCOCCI (CoNS)

- ***MC*** pathogen complicating use of I.V. catheters, shunts and grafts, pacemaker wires, prosthetic valves, vascular grafts, CSF shunts, dialyser.
- ***Mnemonic*** - CoNS are ***MC*** source of infection on any exogenous implant.

Staph.epidermidis / albus

- Normally present on human skin. Not pathogenic ordinarily.
- Predilection for growth on implanted foreign bodies.
- Common source of stich abscess.
- S. sepidermidis is adapted to colonize these devices by its capacity to elaborate the extracellular polysaccharide (glycocalyx or slime) that facilitates formation of protective biofilm on the device surface. This biofilm protects bacteria from antibiotics and host defence.
- The attachment is also facilitated by autolysis (AtlE), fibrinogen binding protein, and accumulation-associated protein (AAP).

Staph. saprophyticus

- Present on normal human skin and periurethral area.
- Cause UTI in sexually active young women. This is due to its enhanced capacity to adhere to uroepithelial cells.

S. lugdunesis and S. schleiferi

- Produces serious infections (native value endocarditis and osteomyelitis) than do other CoNS.

QUESTIONS

1. A diabetic patient developed cellulitis due to S.aureus, which was found to be methicillin resistant on the antibiotic sensitivity testing. All the following antibiotics will be appropriate except: **[AI 06]**

a) Vancomycin
b) Imipenem
c) Teichoplanin
d) Linezolid

2. Staphylococcus aureus differs from staphylococcus epidermidis by : **[AI 02]**

a) Is coagulase positive
b) Forms white colonies
c) A common cause of UTI
d) Causes endocarditis of prosthetic valve

3. True statement regarding non-coagulase staphylococci is : **[AI 99]**

a) They are non-pathogenic
b) They commonly infect indwelling prosthesis
c) They may cause scarlet fever
d) They are separated by gram's staining

4. All of the following statement are true about Staphylococci except : **[AIIMS 04]**

a) A majority of infection caused by coagulase (-) ve Staph. are due to staph epidermidis
b) β-Lactmase production is under plasmid control
c) Expression of methicillin resistance in Staphylococcus aureus increases when it is incubated at 37^0C on blood agar
d) Methicillin resistance in Staph. aureus is independent of b-Lactmase production

5. Which one of the following Gram positive organism is most common cause of UTI among sexually active women : **[AIIMS 04]**

a) Staphylococcus epidermidis
b) Staphylococcus aureus
c) Staphylococcus saprophyticus
d) Enterococcus

6. The following is characteristic feature of staphylococcus food poisoning except : **[AIIMS 04]**

a) Optimum temprature for toxin production is 37^0C
b) Intradietic toxin are responsible for intestinal symptoms
c) Toxin can be destroyed by boiling for 30 minutes
d) Incubation period is 1-6 hours

7. A patient in an ICCU is on CVP line. His blood culture shows growth of Gram (+) ve cocci which are catalase positive and coagulase negative. The most likely etiological agent is : **[AIIMS 03]**

a) Staph. aureus
b) Staph. epidermidis
c) Streptococcus pyogenes
d) Enterococcus faecalis

8. Staph. aureus causes vomiting in 6-8 hours. The mechanism of action is : **[AIIMS 02]**

a) Stimulation of CAMP
b) Vagal stimulation
c) Stimulation of CGMP
d) Acts through ganglioside GM receptor

9. A cook prepares sandwitches for 10 people going for picnic. Eight out of them develop severe gastroenteritis within 4-6 hrs of consumption of the sandwitches. It is likely that on investigations the cook is found to be carrier of : **[AIIMS 02]**

a) Salmonella typhi
b) Vibrio cholerae
c) Entamoeba histolytica
d) Staphylococcus aureus

10. A child after consuming food in a party complains of diarrhea within 1-5 hours. The diagnosis is :

a) S. aureus **[AIIMS 01, 96, 95]**
b) Streptococcus
c) Clostridium perfringens
d) Clostridium botulinum

11. A 30 year old female is on antibiotics with prolonged IV cannulation, has spike of fever, the likely cause is : **[AIIMS 99]**

a) Pseudomonas aerugenosa
b) Coagulase negative staphylococcus
c) Streptococcus agalactiae
d) E. coli

12. All are true regarding staphylococcal toxin except : **[AIIMS 97]**

a) Beta hemolysin shows hot cold phenomenon
b) Mainly endotoxin
c) Enterotoxin causes food poisoning
d) Exfoliative toxin causes Ritter's syndrome

Answer

1. b) Imipenem
2. a) Is coagul ...
3. b) They commonly ...
4. c) Expression ...
5. c) Staphyloc ...
6. c) Toxin can ...
7. b) Staph. ...
8. d) Staphyloco ...
9. b) Vagal ...
10. a) S. aureus
11. b) Coagulase ...
12. b) Mainly ...

13. Which of the following organisms is implicated in the causation of botryomycosis : [PGI 01]

a) Staphylococcus aureus
b) Staphylococcus albus
c) Pseudomonas aeruginosa
d) Streptococcus pneumonia
e) Streptococcus pyogenes

14. Staphylococcus in stool occurs in : [PGI 01, 00]

a) Staphylococcal food poisoning
b) Ischiorectal abscess
c) Toxic shock syndrome
d) May be a normal finding
e) Pseudomembranous colitis

15. Staphyloccus can cause : [PGI 01]

a) Ecthyma
b) Erytharsma
c) Furuncle
d) Impetigo contagioa
e) Sycosis barbae

16. Common source of staph in hospital : [PGI 99]

a) IV fluids
b) Infective wounds
c) Hands of hospital personnel
d) Bed linen
e) Instruments

17. Transfer of drug resistance in staphylococcus is by : [PGI 98]

a) Transduction
b) Transformation
c) Conjugation
d) Transfection

18. Pathogenicity of staphylococci is because of :

a) Lecithinase **[PGI 98]**
b) M-protein
c) Coagulase
d) Hyaluronidase

19. Incubation period of staphylococcal food poisoning is : [PGI 95]

a) 4-6 hrs
b) 6-12 hrs
c) 12-18 nrs
d) 18-24 hrs

Answer 13. a) Staphyloco ... 14. a) Staphyloco ... 15. a, c and e 16. b and c 17. a and c 18. c and d 19. a) 4-6 hrs

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b i.e. Imipenam *Ref. Harrison 17/e, p 879-880; Katzung 9/e, p 768*

"Imipenam is not effective against Enterococcus faecium, MRSA, Clostridium difficle, Burkholderia cepacia as they produce metallobetalactmases."

Treatment of MRSA

Drug of choice	Alternative	Investigatory
Vancomycin	TMP - SMX	Oritavancin
	Minocyclline	Tigecycline
	Ciprofloxacine, Levofloxacin	
	Quinupristin/dalfopristin	
	Linezolid	
	Daptomycin	

Agent	Mechanism of resistance	Site
Penicillins	β-lactamase	Plasmid
Methicilin, Cephalosporin	Altered binding protein	Chromosome
Chloramphenicol	Acetyl transferase	Plasmid
Erythromycin	Methylation of Ribosome	Plasmid
Streptomycin	Altered ribosomal protein	Chromosome
Vancomycin	Van A gene	Chromosome
Quinolones	Mutation in topoisomerase IV	

Remember

Teicloplanin is glycopeptide which is similar to vancomycin in both mechanism and spectrum of activity.

Drugs for **VRSA :** – Quinupristin / dalfopristin
– Linezolid.

2. Ans. is a i.e. Is coagualse positive *Ref. Ananthnarayan 7/e, p 192*

Property	*Staphylococcus aureus*	*Staphylococus epidermidis*
Coagulase	Positive	Negative
Mannitol	Ferments	Not ferment
Pathogenicity	Pathogenic	Not pathogenic
Colony	Golden	White
Hemolysis	*Show*	Not show
Cause Endocaritis	In normal native valve	In prosthetic valve

3. Ans. is b i.e. They commonly infect indeweling prosthesis *Ref. Ananthnarayan 7/e, p 200*

Cogulase (-)ve Staphylococcus	
S. Epidermidis	***S. Saprophyticus***
• Novobiocin sensitive • Predilection for growth on implanted foreign bodies • *Most common* cause of *prosthetic valve endocarditis*	• Novobiocin resistant • Not so • Cause *UTI in sexually active young women*

Remember :
- Both are present on normal skin and are not usually pathogenic.
- Scarlet fever is caused by strep. pyogenes.

4. Ans. is c i.e. Expression of methicillin resistance in Staphylococcus aureus increases when it is incubated at 37^0C on blood agar

Ref. Ananthnarayan 7/e, p 194

"Methicillin resistance is expressed more when Staph. is incubated at 30^0C than at 37^0C."

Penicillin resistance in Staphylococcus is by following ways :

1. *Production of β lactmase :*
   - Plasmid mediated inducible enzyme which is transmitted by transduction (more commonly) or conjugation. Now only <5% of strains of staph are sensitive to penicillin.
   - Hospital strains mostly form type A penicillinase.
   - Same plasmid carry genes for resistance to tetracycline, Erythromycin, Aminolgycoside too.
2. *Altered penicillin binding protein :*
   - Due to production of novel penicillin binding protein PBP2a. The protein is synthesized by mecAgene.
   - Chromosomally mediated expressed *more at 30^0C than at 37^0C.*
   - Responsible for resistance against penicillinase resistant penicillin such as methicilin, cloxacillin. Strains are called ***MRSA*** (Methicillin resistant Staph. aureus).
3. *Tolerance to pencillin :*
   - Bacteria only inhibited not killed.

5. Ans. is c i.e. Staph. Saprophyticus *Ref. Harrison 16/e, p 1717; Ananthnarayan 7/e, p 200*

Remember :
- ***MC*** cause of UTI - E. coli
- ***MC*** cause of nosocomial UTI - E. coli
- ***MC*** nosocomial infection - UTI
- S. saprophyticus produce ***UTI*** characteristically in sexually active young woman
- Enterococci and S.aureus cause infections in patients with renal stones or previous instrumentation or surgery.

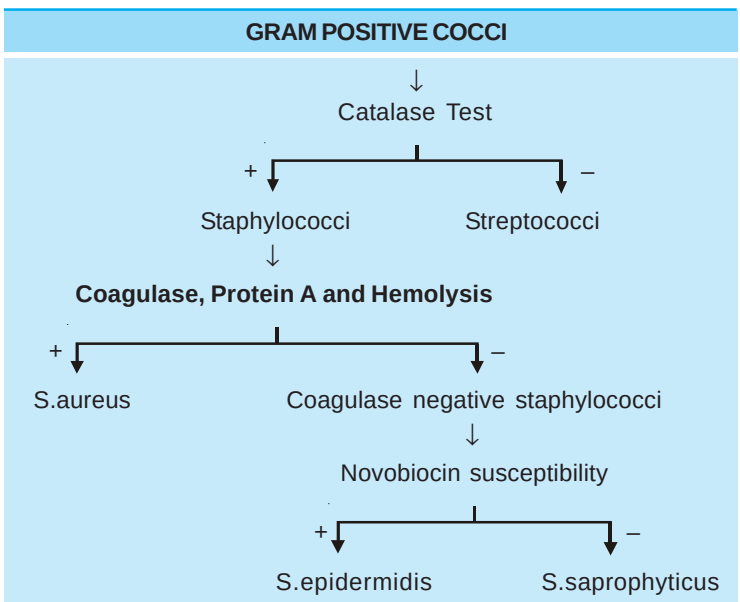
6. Ans. is c i.e. Toxin can be destroyed by boiling for 30 minutes *Ref. Harrison 17/e, p 877-878*

Staphylococcal food poisoning :

- Staphylococcal food poisoning is due to *heat stable preformed toxin* mostly after consuming milk products.
- Toxin is produced optimally at 35^0C to 37^0C.
- *IP-* 1-6 hours.
- *Mechanism -* Acts by **stimulating vagus nerve and vomiting centre of brain**
- *No antibiotics* are given for Staphylococcal food posioning.

7. Ans. is b i.e. Staph epidermidis *Ref. Ananthnarayan 7/e, p 192; Harrison 17/e, p 873*

This descrpition makes the thing clear to you.



So, *Gram (+)ve, catalse (+)ve, coagulase (-)ve bacteria* is **Coagulase negative Staph.**

- S. epidermidis infections are difficult to cure because they occurs on prosthetic valve where bacteria can sequester themselves in a biofilm by slime production.

8. Ans. is b i.e. Vagal stimulation *Ref. Harrison 17/e, p 875*

Following line from ***Harrison*** makes the answer clear to you.

"Staph. food poisoning result from heat stable preformed enterotoxin. Due to preformed nature incubation period is short. Toxin stimulates the vagus nerve and vomiting centre of brain. It also appears to stimulate intestinal persistaltic activity".

9. Ans. is d i.e. Staphylococcus aureus *Ref. Harrison 17/e, p 816*

Learn this table by heart, every year there is question on food posioning.

Bacterial food posioning		
Incubation Period, Organism	**Symptoms**	**Common food source**
1 to 6 H		
Staphylococcus aureus	Nausea, vomiting, diarrhea	Ham, poultry, potato or egg, salad, mayonniase, cream pastries
Bacillus cereus	Nausea, vomiting	Fried rice
8 to 16 H		
Clostridium perfringens	Abdominal cramps, diarrhea *(vomiting rare)*	Beef, poultry, legumes, gravies
B. cereus	Abdominal cramps, diarrhea vomiting	Meats, vegetables, dried beans,
>16 H		
Vibrio cholerae	Watery diarrhea	Shellfish
Enterotoxigenic Escherichia coli	Watery diarrhea	Salads, cheese
Enterohemorrhagic E. coli	Bloody diarrhea	Ground beef, raw vegetables
Salmonella spp.	*Inflammatory diarrhea*	Beef, poultry, eggs, dairy products
Campylobacter jejuni	*Inflammatory diarrhea*	Poultry, raw milk
Shigella spp.	*Dysentery*	Potato or egg salad, lettuce, raw vegetables
Vibrio parachaemolyticus	*Dysentery*	Mollusks, crustaceans

- S. aureus is ***MC*** cause of food poisoning in west.

10. Ans. is a i.e. S. aureus *Ref. Harrison 17/e, p 816*

Incubation period in food poisoning of S.aureus is 1-6hours.

11. Ans. is b i.e. Coagulase negative Staphylococci *Ref. Ananthnarayan 7/e, p 200*

I dont think anyone need explanation for this. *Staph. epidermidis is **MC** cause of infection on implanted foreign bodies.*

12. Ans. is b i.e.Mainly Endotoxin *Ref. Ananthnarayan 7/e, p 195 - 197*

"Staphylococci produce exotoxin not endotoxin."

Important points about staph. aureus toxin

- Beta hemolysin (sphingomyelinase) exhibits hot cold phenomenon i.e. hemolysis intiated at 37^0C but become evident only after chilling.
- Enterotoxin (***MC type A)*** produce food poisoning (even cause some cases of post antibiotic diarrhea).
- *Enterotoxin F or pyrogenic exotoxin C* cause Toxic shock syndrome (also caused by enterotoxin B or C).
- *Exfoliative (epidermolytic) toxin* cause staphylococcal scalded skin syndrome (SSSS), Ritter's disease and toxic epidermal necrolysis.

Remember **:** Only Gram postive organism which produce endotoxin is Listeria.

13. Ans. is a i.e. Staphylococcus aureus *Ref. Ananthnarayan 7/e, p 402*

Botyromycosis is a chronic granulomatous condition similar to mycetoma, usually involves the skin and characterized by granules in the pus, consisting of masses of bacteria generally staphylococcus aureus.

14. Ans. is a i.e. Staphylococcal food poisoning *Ref. Ananthnarayan 7/e, p 198*

- In case of staphylococcal food poisoning food remnant and faeces are inoculated on ***selective medium*** like **ludlam's or salt milk agar** or **Roberson cooked meat medium** *containing 10% NaCl.*
- TSS is due to systemic effect of absorbed toxin from site such as vagina, so no possibility of finding Staph. in case of TSS.
- Ischiorectal abscess is mostly due to E. coli.
- Normal intestinal flora usually don't contain Staph. aureus. So it is *not* a normal finding.
- Pseudomembranous colitis is caused by clostridium difficle.

15. Ans. is a, c and e i.e. Ecthyma; Faruncle; and Sycobis barbae

Ref. Harrison 17/e, p 875, 885; Dashore 'Manual of skin disease' 13-17; CMDT' 08, p 119

Skin and soft tissue infection of S. aureus

- ***Folliculitis*** – Superficial infection of ostia of hair follicle.
- ***Faruncles (boils)*** – More extensive painful lesions that tends to occur in hairy moist region of body and extend from hair follicle to become a true abscess, eg. buttock.
- ***Carbuncle*** – Mostly located in lower neck and are even more severe and painful.
- ***Acute paronychia – MC*** cause is S.aureus.
- ***Bullous impetigo –*** Impetigo is *most frequently diagnosed bacterial infection.*
- ***Ecthyma –*** *It is deeper form of impetigo caused by Staph or Strep.*
- ***Cellulitis***
- ***Hiradenitis suppurativa -*** Recurrent follicular infections in region such as axilla.
- **Sycosis barbae** is *chronic folliculitis of beard hair follicle.*

Remember :

- S. aureus is ***MC*** cause of surgical wound infection. *..... Harrison 17/e, p 873*
- Non - bullous impetigo, cellulitis and erysipelas is caused by Strep. pyogenes *more commonly* than S.aureus.
- Ecthyma gangreosum is caused by Ps. aeruginosa.
- Erythma migrans is caused by Borrelia burgordeferi (Tick transmission).
- Erythrasma is caused by corynebacterium minutissimus.
- Impetigo contagiosa is usually caused by streptococci or mixed infections.
  - *Most cases* of impetigo is caused by S.aureus.

16. Ans. is b and c i.e. Infective wounds; Hands of hospital personel *Ref. Harrison 17/e, p 878*

- ***MC mode*** of spread of S. aureus infection is via hands of health care workers.
- S. aureus is ***MC*** cause of surgical wound infection and can cross infect wound of other patient too.
- ***Most effective*** mode of prevention of nosocomial S. aureus infection is **hand washing.**

17. Ans. is a and c i.e. Transduction; and Conjugation *Ref. Ananthnarayan 7/e, p 194*

β lactamase mediated penicillin resistance is transmitted by transduction *(more commonly)* and conjugation.

18. Ans. is c and d i.e. Coagulase; and Hyaluronidase *Ref. Ananthnarayan 7/e, p 195*

- **M protein**, Lecithinase are not produced by Staphylococci.
- Most important virulence factor is coagulase positivity.

Remember : **Hyaluronidase** - Helps in initiation and spread of infection.

19. Ans. is a i.e. 4 - 6 hours *Ref. Harrison 17/e, p 816*

Already explained, refer answer no. 8

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Phage typing is widely used for the intraspecies classification of one of the following bacteria :
a) Staphylococci **[Kar. 95]**
b) E. coli
c) Klebsiella pneumoniae
d) Pseudomonas aeruginosa
[Ref. Ananthnarayan 7/e, p 197]

2. The antibody marker in serum for staphylococal endocarditis is : **[AIIMS 90]**
a) ASLO
b) Antitechoic acid
c) Anti Lipopolysaccharide
d) Anti-M-protein
[Ref. Ananthnarayan 7/e, p 195]

3. Toxic shock syndrome was first discovered in :
a) Tampoon users **[JIPMER 91]**
b) Diabetic septicemia
c) Drug addicts
d) None
[Ref. Ananthnarayan 7/e, p 196]

4. Phage typing is widely used for the intraspecies classification of one of the following bacteria :
a) Staphylococci **[Karn 95]**
b) Escherichia coli
c) Klebsiella pneumoniae
d) Pseudomonas aeruginosa
[Ref. Ananthnarayan 7/e, p 197]

5. All are capsulated Bacteria except : **[AP 96]**
a) Step. Pneumonia
b) Kleb. Pneunonia
c) Vibriocholera
d) H. influenza
[Ref. List of our book]

6. Pantone-valentine leucocidin is seen in infection with : **[Kerala 97]**
a) Streptococci
b) Staphylococci
c) Gonococci
d) Pnemococci
[Ref. Ananthnarayan 7/e, p 196]

7. Bacteria is not shed in : **[MP 98]**
a) Carrier state
b) Latent injection
c) Incubation period
d) Subclinical infection
[Ref. Park 19/e, p 90]

8. Gram positive cocci are : **[UP 98]**
a) Staphylococcus
b) Streptococcus
c) Pneumococcus
d) All of the above
[Ref. Ananthnarayan 7/e, p 192, 202]

9. Staphylococcal toxic syndrome is due to :
a) Enterotoxin A **[Orrisa 2K]**
b) Enterbtoxin B
c) Enterotoxin C
d) Enterotoxin D
[Ref. Ananthnarayan 7/e, p 196]

10. Staphylococcus Aureus remains in the skin for : longer period because of : **[MAHE 01]**
a) Catalase
b) Coagulase
c) Hyaluronidase
d) None
[Ref. Ananthnarayan 7/e, p 195]

Answer

1. a) Staphylococci
2. b) Antitechoic ..
3. a) Tampoon ...
4. a) Staphylococci
5. c) Vibriocholera
6. b) Staphylococci
7. b) Latent injection
8. d) All of the ...
9. b and c
10. c) Hyaluronidase

11. Post operative parotitis is caused by : [Delhi 00]

a) Staph aureus
b) Streptococcus
c) E. coli
d) Pneumococcus

[Ref. CSDT '12/e, p 28]

12. Mohan comes from dinner he compain of diarrhoea, vomiting after 4 hours of meal. Most likely causative agent : [UP 02]

a) Stap aureus
b) V. cholerae
c) Streptococcus
d) E) coli

[Ref. Harrison, 17/e, p 816; Ananthnarayan, 7/e, p 196]

13. Quikest food poisoning (1-6) hour is :

a) Staphylococcus **[Kolkata 02]**
b) B. cereus
c) Salmonella
d) Vibrio cholera

[Ref. Harrison 17/e, p 816]

14. Cutaneous mainfestation of staphylococci are all except : [St Johns 02]

a) Faruncle
b) Follicular impetigo
c) TSS
d) TEN

[Ref. Ananthnarayan 7/e, p 197]

15. Toxin of staphylococcus : [Bihar 03]

a) Hemolysin
b) Leucocidin
c) Enterotoxins
d) All

[Ref. Ananthnarayan 7/e, p 195]

16. Toxic shock syndrome is due to :

a) Streptococcus pyogenes **[Bihar 04]**
b) Staphylococcus aureus
c) Strept albicans
d) E. durans

[Ref. Ananthnarayan 7/e, p 196]

17. Staphylococcus secrete all, except :

a) Lipase **[Bihar 04]**
b) Cellulose
c) Coagulase
d) Lecithinase

[Ref. Ananthnarayan 7/e, p 195]

18. The most common mechanism of drug resistance in staphylococcus is : [M.P. 04]

a) Conjugation
b) Plasmids
c) Transduction
d) Translation

[Ref. Ananthnarayan 7/e, p 194]

19. Hot cold phenomenon is seen due to which toxin of staphylococci : [UP 04]

a) Alpha lysin
b) Beta lysin
c) Gamma lysin
d) Theta lysin

[Ref. Ananthnarayan 7/e, p 196]

20. Staphalococcus is differ from stretpococcus is by

a) Coagulase test **[Jharkhand 05]**
b) Catalse test
c) Phosphatease
d) Gram negative

[Ref. Harrison 17/e, p 873]

21. Novobiocin susceptible staph is : [UP 06]

a) S. aureus
b) S. epidermidis
c) S. hemolyticus
d) S. saprophyticus

[Ref. Harrison 17/e, p 873]

22. Coagulase negative staphylococci includes all of the following except : [UP 07]

a) Staph. epidermidis
b) Staph. haemolyticus
c) Staph. intermedius
d) Staph. saprophyticus

[Ref. Ananthnarayan 7/e, p 200]

Answer

11. a) Staph aureus
12. a) Stap aureus
13. a) Staphylococcus
14. c) TSS
15. d) All
16. b) Staphyloco ...
17. b) Cellulose
18. c) Transduction
19. b) Beta lysin
20. a) Coagulase ...
21. d) S. saprophy ...
22. c) Staph. ...

2 Streptococci

Important Streptococci and their characteristics

Species or common name	*Lancefield* group	*Hemolysis*	*Laboratory test*	*Common diseases* caused
Str. pyogenes	A	beta	***Bacitracin sensitive;*** PYR test positive; Ribose not fermented	Upper respiratory tract infections;pyoderma; rheumatic fever; glomerulonephritis
Str. agalactiae	B	beta	***CAMP test,*** hippurate hydrolysis	Neonatal meningitis, septicemia
Str. equisimilis	C	beta	Ribose and trehalose fermentation	Pharyngitis, endocarditis
Str. anginosus	A, C, F, G, untypable	beta (alpha, gamma)	Group A strains bacitracin resistant, PYR negative	Pyogenic infections
Enterococcus sp. (E. faecalis and E. faecium E. durans)	D	Gamma (alpha, beta)	***Growth in 6.5% NaCl; PYR positive***	Urinary tract infections, endocarditis, suppurative infections
Nonenterococcal Group D species (Str. bovis, Str equinus)	D	gamma	***No growth in 6.5% NaCl.***	Endocarditis
Viridans streptococi	Not typed	alpha (gamma)	***Optochin resistant***	Endocarditis *(Str. sanguis);* dental caries *(Str. mutans)*

Classification

O_2 requirement

- Aerobes and facultative anaerobes
- Obligate anaerobes eg. Peptostreptococci

Hemolysis on 5% horse blood agar

- Alpha or partial hemolysis = greenish discoloration } Normal commensal in throat
- β or complete hemolysis = Colourless zone = hemolytic streptococci • Most pathogenic
- γ hemolysis or Non hemolytic or indifferent streptococci = Enterococcus +Non enterococcus • Usually non hemolytic or sometimes α, β hemolysis

optochin sensitivity *(ethyl hydrocuprin)*

- \+ Strep. pneumococci *(Harrison 16/e, p 823)*
- – Viridians group (may show γ hemolysis) Str. sanguis : SABE Str. mutans : Dental caries

Based on 'C' carbohydrate Ag of middle layer of cell wall

20 Lancefield Group (A to V except I and J) *MC* pathogenic hemolytic Strepto is Group A = Strep. pyogens

Based on M protein Ag of outer layer of cell wall of Group A

80 Griffith types (1, 2, 3 ....)

Mnemonic

α hemolysis = **SPM**

S - **S**anguis

P - **P**neumococci

M - **M**utans

STREP PYOGENES = LANCEFIELD GROUP A

- Can form chain as divide in one plane (S. aureus form grape like cluster as it divide into three planes).
- ***Longest chain*** is produced by non pathogenic Str. salivarius.

Cultural Characteristic : Growth occur only in media containing fermentable carbohydrate or enriched with blood or serum. Growth and hemolysis are promoted by 10% CO_2.

• Virulent strain	=	Matt finely granular colonies
• Avirulent strain	=	***Glossy*** colonies
• Capsulated (virulent)	=	***Mucoid*** colonies

Antigenic structure :

a. Cell Wall :

- Inner layer made of peptidoglycan.
- Middle layer made of carbohydrate (basis ***of Lancefield classification***).
- Outer layer made of protein and lipoteochoic acid. Eg. M Protein, T, R.

– **M protein is basis** of **Griffith typing**. *Act as virulence factor* by inhibiting phagocytosis. Antibody to M is protective.
– T and R protein has no relation to virulence.

b. Hair like pilli (fimbria) : Important for attachment to epithelial cells.

Antigenic Similarity

Some antigens of streptococci are similar to normal human cells, because of which streptococal infection is associated with autoimmune disease like rheumatic fever.

Capsular Hyaluronic Acid	→	Synovial fluid
Cell wall protein	→	Myocardium
Gp A carbohydrates	→	Cardiac Valves
Cytoplasmic membrane	→	Vascular intima
Peptidoglycan (mucoprotein)	→	Skin antigen

Toxins and Virulence factors

a. Hemolysin - Streptolysin

O [Oxygen labile]	S [Oxygen stable and serum soluble]
• Activity only on pour plate • Antigenic specific • Cardiotoxic	Hemolysis on surface Non antigenic

- **ASO titre** → Anti Streptolysin O titre used in retrospective diagnosis; > 200 units is significant; inhibited by cholesterol (but not by Normal sera).

b. **Pyrogenic Exotoxin = Erythrogenic = Dick = Scarlatinal Toxin :**
- This is superantigen causing **TSS.**
- Used to identify children susceptible to scarlet fever by intradermal injection (=Dick test) and Schultz Charlton Reaction.
- Type **A** toxin is ***MC***

c. **Streptokinase (Fibrinolysin) :** Facilitates spread of infection.
d. **Deoxyribo nuclease (Streptodornase;** DNAase) - Responsible for thin serous character of strep exudates.
e. **Nictoniamide Adenine Dinucleotidase** (***NAD-ase).***
f. **Hyaluronidase :** Favour spread of infection.
g. **Serum Opacity Factor -** Lipoproteinase.

Infection

1. Respiratory :
- ***Sore throat is MC*** streptococcal infection.

2. Scarlet fever : Streptococcal pharyngitis, accompanied by rash made up of minute papules giving a characteristic *"Sand paper"* feel to skin.
- Associated with circumoral pallor, straw berry tongue.
- Rash reflect hypersentivity reaction to toxin.

3. Skin and Soft tissue infection :
- ***Impetigo*** - Superficial infection of skin mainly by group A streptococci. Face and leg are *MC site.*
  Bullous impetigo is caused by staph.

- ***Cellulitis*** - Diffuse spreading infection of skin and subcutaneous tissue especially of leg. Caused by Str. pyogenes (***MC***), Staph, Cl. perfringens, E.coli.
- ***Erysipelas*** - Superficial form of celluititis with bright red appearance of involved skin, seen classically on cheek. Skin assumes peau-d-orange texture due to involvement of superficial lymphatics.
- ***Necrotizing fascitis*** **-** Caused by Group A streptococci called as *Hemolytic Streptococcal gangrene.*
- *In skin infection ASO titre is not high and so ASO estimation has not much clinical significance.*

4. ***Genital infection :***
   - **Anaerobic streptococci** are most important cause of **puerperal sepsis.**
5. **Bacteremia, pneumonia, toxic shock syndrome.**
6. ***Non suppurative complication :*** Develop 1-3 weeks after acute infection.

Acute Rheumatic fever	*Acute glomerulonephritis*
• Develop after throat infection by any serotype of S. pyogenes • Repeated attacks common • Penicilin prophylaxis indicated • Course is progressive or static • ASO titre always raised • Marked immune response with no change in complement level	• Develop after either sore throat or skin infection by serotype 49, 53-55, 59-64, 1 and 12 • No repeated attacks • Not indicated • Spontaneous resolution • May or May not (after skin infection) raised • Moderate immune response with decrease in complement level.

Lab Diagnosis

- In acute infection diagnosis is established by throat swab culture (diagnostic).
  - *Pike's medium* is used as *transport media.*
  - Sheep blood agar is recommended for isolation as it is inhibitory for H. hemolyticus.
- In Rheumatic fever and Glomerulonephritis retrospective diagnosis is needed.
  - ***ASO titre*** > 200 is indicative of prior streptococcal disease. After skin infection ASO titre is usually low. So useful only in retrospective diagnosis of Rheumatic fever.
  - *In acute glomerulonephritis and pyoderma, Anti DNAse and antihyaluronidase are used for retrospective diagnosis.*
- Streptozyme test - *Passive slide haemagglutination* test. Sensitive and specific test for all types of streptococcal infection.

Treatment of Group A Streptococci	
• *Pharyngitis, impetigo, erysipelas,* cellulitis	– **Penicillin (Pn)**
• *Necrotizing fascitis / myositis*	– **Surgical debridement + Pn + Clindamycin**
• *Pneumonia / Empyema*	– **Pn + empyema drainage**
• *Streptococcal TSS*	– **Penicillin + Clindamycin + iv Ig**

OTHER HEMOLYTIC STREPTOCOCCI

(= Lancefield β Hemolytic Streptococci)

Group B (Strep. agalactiae) : *Virulence factor* is ***polysaccharide capsule.*** *(Group A have hyaluronic acid capsule).*

– S. agalactiae is the ***MC*** cause of neonatal meningitis in west.

– It does not hydrolyse bile esculin agar, however hydrolyse sodium hippurate and are bacitracin resistant.

– Identified by **CAMP** *(Christie, Atkins and Munch - Peterson)* **reaction.**

– In infant it cause 2 type of infection :
  - ***Early Onset*** **:** More common, acquired from maternal vagina during birth.
    – Essentially all infants are bacteremic presenting with lethargy respiratory distress and hypotension.

- ***Late Onset Infection*** *:* Infection more often obtained from environment.
  - Meningitis is *the* ***MC*** manifestation and in most cases is associated with strain of *capsular type III.*

– ***Treatment***

Penicillin is ***DOC*** for all group B streptococcal infection.

Group C - Strep. equisimilis

- Predominant animal pathogen and is the source of streptokinase used for thrombolytic therapy.

Group D - Streptococci

Includes :
- Fecal streptococci / Enterococcus.
- Non enterococcal group D streptococci.
- Enterococci are now considered as separate genus on the basis of DNA homologus studies..

... Harrison 17/e, p 881

Distinctive features of Enterococcus :

– Grow in 40% bile
– Grow in 6.5% NaCl at pH 9.6, 45^{0}C and in 0.1% methylene blue milk
– Heat resistant, surviving 60^{0}C for 30 minutes
– Present in intestine, genital tract and saliva
– Cause wound infection, UTI nosocomal bacterimia in patient with IV catheters, endocarditis.
– Usually resistant to Penicillin, cephalosporin etc
– In case of Vancomycin and β lactam resistance - Linezolid (*against all enterococci*) or quinupristin dalfopristin (*against E.faecium* only) are given.

Non Enterococcal Group D Streptococci

– Grow in bile *..... Jawetz 23/e, p 235*
– Unable to grow in 6.5% NaCl and PYR negative
– Penicillin susceptible.
– Main species causing infection is S.bovis. S.bovis endocarditis is often associated with neoplasm of GIT, most commonly colon.

Group F - Streptococci

- Called as minute streptococci.
- Includes Streptococcus MG.
- Isolated from cases of atypical pneumonia.

Viridans streptococci

- Heterogenous group of organism that are important agent of bacterial endocarditis. These are part of normal flora of mouth.
- Species include :
  - S.sanguis : *MC* viridans streptococcus associated with endocarditis
  - S.mutans : Imporant in the causation of dental caries.
  - S.salivarus

PNEUMOCOCCUS

- Gram positive Lanceolate diplococci.
- It is ***MC*** cause of *Lobar pneumonia, sinusitis, otitis media.*

- It is ***MC*** cause of *bacterial meningitis* in adults.

Pneumococci	Streptococci viridans
Capsulated lanceolate diplococci	Non capsulated, oval or round cells in chains
Bile soluble	Not soluble
Optochin sensitive	Not sensitive
Posses specific polysaccharide capsule	May or may not have capsule
Shows ***quellung*** reaction	Not show
Ferments inulin	Unable to ferment inulin

Morphology and Culture

- Capsule enclose a pair of flame shaped Lanceolate bacteria.
- Grow only in enriched media.
- On blood agar they are α hemolytic and on prolong incubation colonies show *draughtsman or carrom coin appearance*. Under anaerobic conditions produce β hemolysis.
- Strains with abundant capsular material (3,7) form large, mucoid colonies.
- Pneumococci readily undergo autolysis in culture due to presence of autolytic amidase which is activated by bile salts; hence *they are bile soluble.*
- *Bile solubility* is of *diagnostic importance.*
- *Inulin fermenter (useful test for differentiating from streptococci as they are unable to do so).*

Virulence factors

1. Capsular polysaccharide = specific soluble substance *:* ***MC*** antigen and virulent factor.
   - Protects against phagocytosis.
   - *Type 3* pneumococci has abundant capsular material, *so more virulent.*
2. Unique to penumococci is C substance ("cell wall" substance) a polysaccharide consisting of teichoic acid with a phosphoryl choline residue. These choline residue provide attachment to potential virulence factors such as pneumococcal surface protein A (PspA) and pneumococcal surface adhesin A (psaA). *... Harrison 17/e, p 865*
3. *Penumolysin :* Membrane damaging toxin which has cytotoxic and complement activating properties.
4. Autolysin

Quellung reaction

On mixing pneumococci with specific or polyvalent antipolysaccharide serum the capsule becomes apparently swollen, sharply delineated and refractile. This reaction is used for ***rapid identification.***

Manifestations

- *Commonest* pneumococcal infection are **otitis media** and **sinusitis.**
- *Meningitis* is ***most serious*** pneumococcal infection.
- Pneumonia : Mostly due to types 1 to type 8 strains.
- *Type 3 strain is* ***most virulent.***
- ***MC*** complication of pneumococcal pneumonia - ***Empyema***
- S. pneumoniae are ***MC*** cause of sepsis in splenectomized patient.
- Austrain syndrome : Concurrence of pneumococcal pneumonia, endocarditis and meningitis.

Diagnosis

- Gram's staining and culture of sputum or CSF.

Treatment

- *Otitis media/Sinusitis/ Pneumonia* - **Amoxicillin.**
- *Meningitis* - **Ceftriaxone plus vancomycin.**
- *Endocarditis* - **Ceftriaxone or cefotaxime + vancomycin.**
- *Penicillin resistance is not due to production of β lactmase but alteration in penicillin binding protein.*

Pneumococcal Vaccine

Polyvalent polysaccharide vaccine containing capsular antigen of ***23 most prevalent serotypes.***

Protection rate - 80 - 90%

Indication	*Contraindication*

• In pateint with absent or dyfunctional spleen
• Sickle cell disease
• Coeliac disease
• Chronic renal, lung, heart and liver disease
• Diabetes mellitus
• Immunodeficiencies including HIV
	• < 2yr child and > 65 yr
	• Lymphoreticular malignancies and immunosuppressive therapy
	• CSF leak
	  • Alcoholic cirrhosis
	  • Multiple myeloma
	• Chronic glucocorticoid therapy
	• 'Hodgkin's'disease
	• Organ transplant recepient

QUESTIONS

1. Which is false regarding Gram positive cocci ?
a. Staph. saprophyticus causes UTI in females
b. Micrococci are oxidase positive **[AI 08]**
c. Most enterococci are sensitive to penicillin
d. Pneumococci are capsulated

2. Which component of St. pyogenes has cross reactivity with synovium of human ? **[AI 08]**
a. Capsular hyaluronic acid
b. Cell proteins
c. Group A carbohydrate antigens
d. Peptidoglycan

3. Which of the following is not true regarding enterococcus ? **[AI 08]**
a. Common species are E.faecalis and E.faecium
b. It is a cause for peritonitis
c. It is universally susceptible to penicillins
d. Can cause intra-abdominal abscess

4. A patient admitted to an ICUs is on central venous line for the last one week; he is on ceftazidine and amikacin. After 7 days of antibiotics he develops a spike of fever and his blood culture is positive for gram positive cocci in chains, which are catalase negative. Following this, vancomycin was restarted but the culture remained positive for same organisms even after 2 weeks of therapy. The most likely organism causing infection is :
a) Staph aureus **[AI 07; AIIMS Nov. 06]**
b) Viridans streptococci
c) Enterococus fecalis
d) Coagulase positive staphylococcus
d) Bile solubility

5. An infant had high grade fever and respiratory distress at the time of presentation to the emergency room. The sample collected for blood culture was subsequently positive showing growth of α-haemolytic colonies. On Gram staining these were gram positive cocci. In the screening test for identification, the suspected pathogen is likely to be susceptible to the following agent :
a) Bacitracin **[AI 07]**
b) Novobiocin
c) Optochin
d) Cloxacillin

6. A person from village is complaining of development of pustules. Extract from pus has shown gram positive cocci, showing hemolysis, catalase –ve, identified as a group of streptococci. Following test is used : **[AI 07; AIIMS Nov. 06]**
a) Bacitracin sensitivity
b) Novobiocin sensitivity
c) Optochin sensitivity

7. All are true about streptococcus except : **[AI 01]**
a) M-protein is responsible for production of mucoid colonies
b) M- protein is responsible for virulence
c) Mucoid colonies are virulent
d) No resistance to penicillin has been reported

8. A beta hemolytic bacteria is resistant to vancomycin, shows growth in 6.5% NaCl, is non bile sensitive. It is likely to be : **[AI 01]**
a) Strep. agalactiae
b) Strep. pneumonia
c) Enterococcus
d) Strep. Bovis

9. Toxin involved in the streptococcal toxic shock syndrome is : **[AI 01]**
a) Pyrogenic toxin
b) Streptokinase
c) Hemolysin
d) Neurotoxin

10. In a patient of orbital cellulitis, micro organism on culture show greenish colonies and optochin sensitivity. The most likely organism is : **[AI 00]**
a) Strep. viridans
b) Staphylococcus
c) Pseudomonas
d) Pneumococcus

11. True statement regarding Pneumococcus is :
a) Virulence is due to polysaccharide capsule
b) Capsule is protein in nature **[AI 99]**
c) Antibodies against capsule are not protective
d) Resistance to penicillin has not yet been reported

Answer
1. c) Most enterococci 2. a) Capsular... 3. c) It is universally... 4. c) Enterococus ... 5. c) Optochin ...
6. a) Bacitracin ... 7. a) M-protein ... 8. c) Enterococcus 9. a) Pyrogenic ... 10. d) Pneumoco ...
11. a) Virulence ...

12. True statements about Pneumococcus are all except : [AI 99]

a) Pneumolysin a thiolactivated toxin, exerts a variety of effects on ciliary and PMN's action

b) Autolysin may contribute to the pathogenesis of pneumococcal disease by lysing bacteria

c) Anticapsular 'antibodies are serotype specific

d) The virulence of pneumococci is dependent only on the production of the capsular polysaccharide

13. True statement about Antistreptolysin 'O' titre is:

a) In normal people the titre is <200 **[AI 97]**

b) In acute glomerulonephritis the titre is low

c) ASO titre >200 indicate rheumatic fever

d) Streptozyme test is an active haemagglutination test

14. One of the following infections is caused by anaerobic gram positive cocci : [AI 95]

a) Puerperal infection

b) Food poisoning

c) Endocarditis

d) Septicemia

15. Lance field grouping of streptococci is done by using : [AIIMS 07]

a. M protein

b. Group C peptidoglycan cell wall

c. Group C carbohydrate antigen

d. M antigen

16. An infant had high grade fever and respiratory distress at the time of presentation to the emergency room. The sample collected for blood culture was subsequently positive showing growth of α-hemolytic colonies. On Gram staining these were gram positive cocci. In the screening test for identification, the suspected pathogen is likely to be susceptible to the following agent :

a) Bacitracin **[AIIMS 07, 06]**

b) Novobiocin

c) Optochin

d) Oxacillin

17. A patient admitted to an ICU is on central venous line for the last one week. He is on Ceftazidime and amikacin. After 7 days of antibiotics he develops a spike of fever and his blood culture is positive for gram positive cocci in chains which are catalase - negative. Following this vancomycin was started but the culture remained positive for same organism even after 2 weeks of therapy. The most likely organism causing infection is : [AIIMS 06]

a) Staphylococci aureus

b) Viridans streptococci

c) Enterococcus faecalis

d) Coagulase negative staphylococcus

18. The sputum specimen of a 70 year old male was cultured on a 5% blood agar. The culture showed the presence of a-haemolytic colonies next day. The further processing of this organism is most likely to yield : [AIIMS 05]

a) Gram positive cocci in short chains, catalase negative and bile resistant

b) Gram positive cocci in pairs, catalase negative and bile soluble

c) Gram positive cocci in clusters, catalase positive and coagulase positive

d) Gram negative coccobacilli, catalase positive and oxidase positive

19. Which of the following organism, when isolated in the blood, requires the synergistic activity of penicillin + amino glycoside for appropriate therapy : [AIIMS 04]

a) Enterococcus faecalis

b) Staph. aureus

c) Streptococcus pneumoniae

d) Bacteriodes fragilis

20. Most common causative organism for lobar pneumonia is : [AIIMS 04]

a) Staphylococcus aureus

b) Streptococcus pyogenes

c) Streptococcus pneumoniae

d) Haemophilus influenzae

21. An outbreak of Streptococcal pharyngitis has occured in a remote village. In order to carry out the epidemiological investigations it is necessory to perform the culture of the throat swab of the patient suffering from the disease. The transport media of choice would be : [AIIMS 02]

a) Asalt manntol media

b) Pike's media

c) Stuart media

d) Carry Blair media

22. Streptococcal toxic shock syndrome is due to the following virulence factor : [AIIMS 03]

a) M protein

b) Pyrogenic exotoxin

c) Streptolysin O

d) Carbohydrate cell wall

Answer 12. d) The virulence ... 13. b) In acute ... 14. a) Puerperal ... 15. c) Group c 16. c) Optochin
17. c) Enterococcus ... 18. b) Gram ... 19. a) Enteroco ... 20. c) Streptoco ... 21. b) Pike's ...
22. b) Pyrogenic ...

23. The commonest organism causing cellulitis is :
a) Streptococcus pyogenes **[AIIMS 02]**
b) Streptococcus faecalis
c) Streptococcus viridans
d) Microaerophilic streptococci

24. 45 years old Ramlal has intra abdominal sepsis. The causative organism was found to be vancomycin, gentamycin and amplicillin resistant. It grows well in presence of 6.5% NaCl and arginine. Bile esculin hydrolysis is positive. Which of the following is this organsim ? [AIIMS 01]
a) Strept. agalactae
b) Enterococcus fecalis
c) Streptococcus bovis
d) Streptococcus pneumoneae

25. A patient of RHD developed infective endocarditis after dental extraction. Most likely organism causing this is : [AIIMS 01]
a) Streptococcus viridans
b) Streptococcus pneumoneae
c) Streptococcus pyogenes
d) S. aureus

26. Risk of Pneumococcal meningitis is seen in :
a) Post splenectomy patient **[AIIMS 99]**
b) Patient undergone neurosurgical intervention
c) Patient following cardiac surgery
d) Patient with hypoplasia of lung

27. C-Carbohydrate in Streptococcus hemolyticus is important for : [AIIMS 98]
a) Lancefield classification
b) Phagocytic inhibition
c) Toxin production
d) Haemolysis

28. Causative organism of late prosthetic valve endocarditis is : [AIIMS 97]
a) Streptococcus viridians
b) Proteus mirabilis
c) Beta haemolytic streptococci
d) Staphylococci

29. Lymphangitis is caused by : [AIIMS 95]
a) Staphylococcus
b) Streptococci
c) Pneumococci
d) Neisseria

30. Which of the following factor is mainly responsible for virulence in Streptococcus : [AIIMS 95]
a) Carbohydrate
b) Streptokinase
c) Streptodornase
d) M protein

31. True about streptococcus : [PGI 03]
a) Lancefield classification is based on M protein
b) Group 'G' not found in human
c) Group 'B' causes neonatal meningitis
d) Group 'C' can be isolated from vaginal flora
e) Group 'D' causes urinary tract infection

32. After Splenectomy, most common infection :
a) Pneumococcal **[PGI 00]**
b) E. coli
c) Klebsiella
d) Streptococcus

33. Streptococcal GN is best diagnosed by :
a) ASO titre **[PGI 99]**
b) Anti DNAse
c) Anti hyaluronidase
d) Culture

34. Which toxin of streptococcus causes hemolysis:
a) Streptolysin O **[PGI 97]**
b) Sterptolysin S
c) Streptokinase
d) Sterptodornase

35. Streptococcus and pneumococcus are differentiated by : [PGI 97]
a) Bile salt solubility
b) Growth charcteristic
c) Gram staining
d) Inulin fermentation

36. Streptococci causing dental caries : [PGI 96]
a) Streptococci equisimilis
b) Streptococci mutans
c) Streptococci pneumoniae
d) Streptococci bovis

Answer

23. a) Streptoco ... 24. b) Enteroco ... 25. a) Streptoco ... 26. a) Post ... 27. a) Lancefield ...
28. a) Streptoco ... 29. b) Streptococci 30. d) M protein 31. c and e 32. a) Pneumococcal
33. b and c 34. b) Sterptolysin ... 35. a, b and d 36. b) Streptococci ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is c i.e. Most Enterococci are sensitive to penicillin

Ref. Harrison 17/e, p 888-889; Ananthnarayan 7/e, p 200

- Unlike streptococci enterococci are not reliably killed by penicillin or ampicillin alone at concentration acheived clinically in the blood or tissues.
- Antimicrobial susceptibility testing should be performed routinely on enterococcal isolates.

Enterococci resistance to penicillin is via two mechanism :

Penicillin Resistance	
Penicilase production	**Altered penicillin binxling protein**
• Seen in E. faecalis • Vancomycin, ampicillin / sulbactum, amoxicillin / clavulanate, imipenam may be used in combinatioin with gentamycin	• Common in E.faecum • Vancomycin plus gentamycin is used.

Other options

Option 'a' • Staph. saprophyiticus specially causes UTI in sexually active young women.

Option 'b' • Micrococci are catalase and oxidase positive Gr (+ve) cocci. They are strict aerobes and are non pathogenic.

• Micrococci are differentiated from Staphylococci by *Hugh and deifson oxidation fermentation* test in which micrococci shows oxidative pattern while staphylococci show fermentive pattern.

2. Ans. is a i.e. Capsular hyaluronic acid *Ref. Ananthnarayan 7/e, p 206; Harsh Mohan 5/e, p 330*

Bacterial antigen	Cross reacting human component
Capsular hyaluronic acid	Human synovial fluid
Group A carbohydrate antigen	Cardiac valves
Cytoplasmic membrane antigen	Vascular intima
Cell wall protein	Myocardium
Peptidoglycan	Skin antigen
Membrane antigens	Sarcolemma of smooth and cardiac muscle, dermal fibroblasts and neurons of caudate nucleus

3. Ans. is c i.e. It is universally succeptible to penicillins *Ref. Harrison 17/e, p 888*

Disease caused by Enterococci

- UTI (particularly who are on antibiotic treatment)
- Bacterial endocarditis
- Liver abscess, intrabdominal abscess
- Surgical wound infection.

For more details, refer answer no. 1

4. Ans. is c i.e. Enterococcus fecalis *Ref. Harrison 17/e, p 888; Ananthnarayan 7/e, p 204*

Enterococci are resistant to all cephalosporins, aminoglycosides and resistant to vancomycin is also becoming quite common with it.

Treatment of antibiotic resistant enterococcal infection

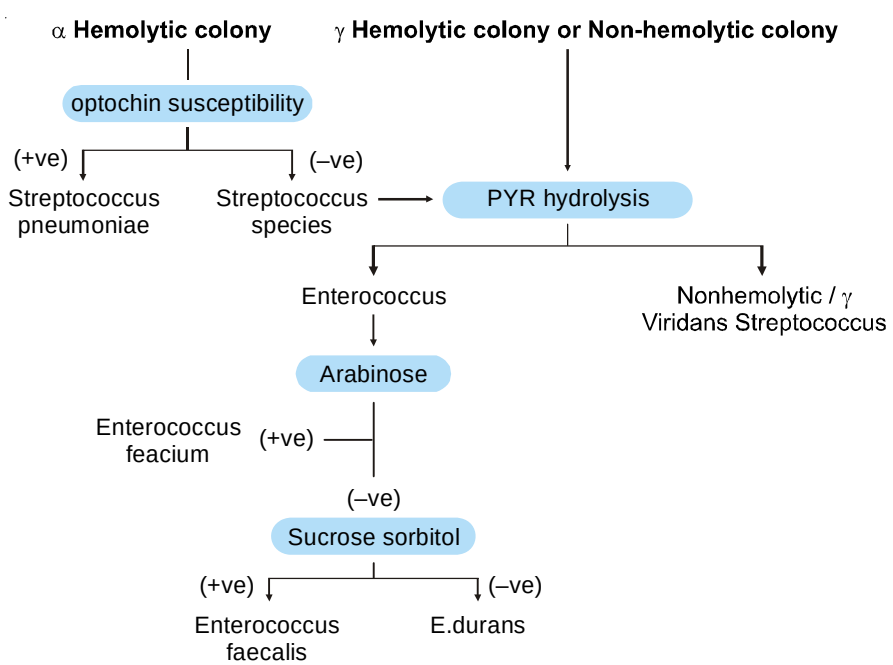
Resistance pattern	Recommended therapy
β-lactamase production	Gentamicin plus ampicillin/sulbactam, amoxicillin/clavulanate, imipenem, or vancomycin
β-lactam resistance, but no β-lactamase production	Gentamicin plus vancomycin
High-level gentamicin resistance	***Streptomycin-sensitive isolate :*** Streptomycin plus ampicillin, or vancomycin ***Streptomycin-resistant isolate :*** Continuous-infusion ampicillin
Vancomycin resistance	Ampicillin plus gentamicin
Vancomycin and β-lactam resistance	No uniformly bactericidal drugs; linezolid (all enterococci) or quinupristin/dalfopristin (E. faecium only)

Remember : Three phenotypes of vancomycin resistant Enterococci have been identified viz. Van A; Van B; Van C. Van A is associated with high grade resistance to vancomycin and teicoplanin. Van B and Van C are susceptible to teicoplanin.

5. Ans. is c i.e. Optochin *Ref. Ananthnarayan 7/e, p 217*

Infant is suffering from pneumococcal pneumonia *(Gram positive α-hemolytic cocci).*

Pneumococci is differentiated from other α hemolytic Gram positive cocci by its susceptibility to optochin and bile solubility.



6. Ans. is a i.e. Bacitracin sensitivity *Ref. Ananthnarayan 7/e, p 205*

"Sensitivity to bacitracin is employed as a convenient method for differentiating Str. pyogenes from other hemolytic streptococci."

Pustule – A vesicle filled with leukocyte. MC cause is virus. MC bacterial cause is Strep. pyogenes.

Remember :
- Str. pyogenes is the etiologic agent in most of the streptococcal skin infection.
- Vancomycin is the drug of choice.
- Optochin senstivity and bile solubility is used to differentiate pneumococci from Strep. viridans group.

7. Ans. is a i.e. M-protein is responsible for production of mucoid colonies

Ref. Ananthnarayan 7/e, p 205; Jawetz p 23/e, p 231

"Mucoid colonies are due to production of capsule of hyaluronic acid not due to M protein."

..... Harrison 17/e, p 882

Growth characteristic of Strep. pyogenes :

- On blood agar *virulent stains* forms **matt or mucoid colonies** while *avirulent* form **glossy colonies.**
- M, T, R are proteins found on outer part of cell wall and forms the basis of **Griffith classification.**
  - **M protein** - Acts as virulence factor and antibody against it are protective.
  - **T and R protein** - No relation to virulence
- Streptococci (Except enterococci) are usually susceptible to penicillin so *option "d"* is not completely wrong. As *option "a"* is completely wrong, that would be the answer.

8. Ans. is c i.e. Enterococcus *Ref. Ananthnarayan 7/e, p 204; Jawetz 24/e, p 243-244*

Group D Streptococci	
Enterococci	**Non enterococci**
(E. faecalis, E, faecium) • Able to grow in 6.5% NaCl • PYR positive • May shows α hemolysis • Penicilin resistant	(Strep. bovis) • Not able • PYR negative • Non hemolytic • Penicillin suscepitble

- Both enterococci and non enterococi group D sterptococci can grow in presence of bile and hydrolyze esculin (bile esculin positive). *... Jawetz 24/e, p 243, 240*
- Don't confuse with *Ananthnarayan 7/e, p 212* that non enterococci are inhibited with bile. If question comes go with *Jawetz.*

9. Ans. is a i.e. Pyrogenic toxin *Ref. Jawetz 24/e, p 238*

"Streptococcal TSS is caused by pyrogenic exotoxin."

Pyrogenic Exotoxin = Erythrogenic toxin = Dick = Scarlatinal Toxin

- Produced by group A streptococci (type 1, 2, 3, 12 and 28)
- There are 3 type of pyrogenic exotoxin : A, B, and C
- A (***MC*** cause of Streptococcal TSS) and C are coded by bacteriophage gene, while B is chromosomal

- Acts as superantigen
- Associated with Streptococcal toxic shock syndrome and Scarlet fever
- ***DOC*** for Streptococcal TSS is - **Clindamycin** *..... Harrison 17/e, p 886*

10. Ans. is d i.e. Pneumococcus *Ref. Ananthnarayan 7/e, p 216 - 217*

"***Pneumococci is optochin sensitive and forms green colonies on blood agar due to α hemolysis."***

Characteristic features of Pneumococci :

- Bile soluble, optochin sensitive
- Inulin fermenter
- Capsulated, shows quellung reaction
- Colonies show central umbonation, appear as *draughtsmann* or *carrom coin*
- ***MC*** causative agent *of lobar Pneumonia, Adult meningitis, otitis media, sinusitis (orbital cellulitis is complication of sinusitis)*.

11. Ans. is a i.e. Virulence is due to polysaccharide capsule *Ref. Ananthnarayan 7/e, p 219*

Virulence of Pneumococci depends on its capsule, toxin called pneumolysin and autolysin.

Virulence factors of Pneumococci
Capsule :
• Polysaccharide in nature • Protects against phagocytosis • Type 3 pneumococci has abundant capsular material and is more virulent • Antibody against capsule are type specific and protective.
Pneumolysin :
• Thial activated toxin, exterts variety of effects on ciliary cells and PMN *..... Harrison 16/e, p 807* • Complement activating and cytotoxic properties • Immunogenic.
Autolysin :
• By lysing the bacteria and releasing bacterial components contributes to virulence.
IgA1 protease
• Cleaves IgA1 and hence decreases the function of this immunoglobulin.
C-substance and peptidoglycans.

12. Ans. is d i.e. The virulence of pneumococci is dependent only on the production of the capsular polysaccharide *Ref. Ananthnarayan 7/e, p 219*

Already explained, refer just above to find answer.

13. Ans. is b i.e. Acute glomerulonephritis titre is low *Ref. Ananthnarayan 7/e, p 210*

Retrospective Diagnosis of Streptococcal infection

- ***ASO (Anti Streptolysin 'O') titre :***
  - Estimation of antibody aganist streptolysin is a standard serological test for retrospective diagnosis of streptococcal infection.
  - ASO titre > 200 are indicative of prior streptococcal infection.
  - Raised after throat infection only
  - ***Acute rheumatic fever :***
    - High level of ASO titre are usually found
    - Titres > 300 or 350 are taken as significant.
  - ***Acute glomerulonephirits :***
    - ASO titres are often low.
- ***Streptozyme test*** – **Passive slide hemaglutination test**
  Becomes positive after nearly all types of streptococcal infection whether of throat or skin.
- ***Anti DNA ase B and Antihyaluronidase*** – Useful for retrospective diagnosis of Streptococcal Pyoderma or for acute glomerulogephritis for which ASO titre is of much less value.

14. Ans. is a i.e. Puerperal infection *Ref. Ananthnarayan 7/e, p 267*

Anaerobic Cocci		
Features	**Gram (+)ve**	**Gram (–)ve**
Organism	– ***Peptostreptococci*** – ***Peptococcus***	***Veillonellae***
Inhabitation	– Intestine, vagina and mouth	Mouth, intestine and genital tract
Diseases	– ***Puerperal sepsis*** – Visceral abscess – UTI, wound infection – Gangrenous apendicitis	No disease is identified till now.
Treatment	– Sensitive to penicillin, chloramphenicol and metronidazole	

15. Ans. is c i.e. Group C carbohydrate antigen *Ref. Ananthnarayan 7/e, p 203*

Lancefield classification

Classification of β hemolytic streptococci into Group A to V (except I, J) on the ***basis*** of **group specific C carbohydrate.**

Griffith classification

Serological typing of Group A Streptococcus pyogenes on the ***basis*** of **M proteins into types 1, 2, 3 etc.**

Group C Carohydrate

- Present in middle layer of cell wall.
- This antigen is an integral part of cell wall.
- Serological grouping of streptococci depend on C carbohydrate for which it has to be extracted from cell wall.

- **Method for extraction are :**
  - Lancefield's acid extraction method (organism are grown in Todd Hewitt broth)
  - Fuller's method
  - Maxted's method
  - Rantz and Randall's method (Autoclaving).

16. Ans. is c i.e. Optochin *Ref. Ananthnarayan 7/e, p 216 - 217*

Already explained, please see answer no. 6

17. Ans. is c i.e. Enterococcus faecalis *Ref. Harrison 17/e, p 888*

- Enterococci are catalase negative and grow in chains and above all resistant to cephalosporins.
- Enterococci is a frequent cause of nosocomial bacteremias and many of these enterococci are resistant to vancomycin.
- Enterococcal bacteremis is characterstically seen in ICU in patient taking cephalosporin as antibiotic.

Other options :
- Staph. aureus and coagulase negative staph. are catalase positive.
- Streptococci viridans are sensitive to vancomycin.

Remember : Whole streptococci group forms chains while Staphylococci group forms bunch similar to grapes.

18. Ans. is b i.e. Gram positive cocci in pairs, catalase negative and bile soluble
Ref. Ananthnarayan 7/e, p 204, 221; Jawetz 24/e, p 237

Bacteria which shows α or partial hemolysis includes :

Species	Common disease caused
a. Strep. viridans including	
S. sanguis	SABE
S. mutans	Dental caries
b. Pneumococci	Lobar pneumonia, otitis media
c. S. anginosus	Pyogenic infections
d. Enterococcus including S.faecalis	UTI, endocarditis

- As in quesion, sputum specimen is taken which is required in the diagnosis of respiratory tract infection (eg. pneumonia).
- *So, it is clear that most probable* answer is Pneumococci which is : diplococci; bile soluble; catalase negative.

Remember : All streptococci is catalase negative while staphylococci is catalase positive :
- ***Choice 'a'*** points towards S. viridans but it rarely cause pneumonia.
- ***Choice 'c'*** points towards S. aureus which shows β hemolysis not α hemolysis.
- ***Choice 'd'*** points towards Legionella. Though it cause pneumonia but it doesn't shows hemolysis.

19. Ans. is a i.e. Enterococcus faecalis *Ref. Harrison 17/e, p 888*

See the following line.

"Unlike streptococci, enterococci are not reliably killed by penicillin or ampicillin alone. Because in vitro testing has shown evidence of synergistic killing by combination of penicillin or ampicillin with an amminoglycoside, combined therapy is recommended for enterococcal endocarditis and meningitis."

- *Enterococci are resistant to all cephalosporins*

20. Ans. is c i.e. Streptococcus Pneumononiae *Ref. Robbins 7/e, p 748*

Remember :
- ***MC*** - infection of pneumococci - Otitis media
- Pneumococci is ***MC*** cause of Lobar Pneumonia, Acute sinusitis, Adult meningitis
- ***MC*** cause of bronchopneumonia : Staphylococci
- ***MC*** cause of atypical pneumonia : Mycoplasma pneumoniae.

21. Ans. is b i.e. Pike's media *Ref. Ananthnarayan 7/e, p 210*

"Pike's media is transport media for Streptococci."

Diagnosis of Streptococcal infection	
Acute infection	**Non-suppurative complication**
• Gram's staining • Culture	• By detection of antibody through : – Streptozyme test – Anti DNAase and anti hyaluronidase – ASO titre

Culture
- Throat culture is diagnostic gold standard for pharyngitis.
- Swab are either plated immmediately or sent to laboratory in *Pike's medium* (*used as transport media*).
- Specimen is plated on blood agar and incubated at 37^0C anaerobically or under 5-10% CO_2.
- *Sheep blood agar* is recommeded for primary isolation because it is *inhibitory for Haemophilus.*

Remember :
- Stuart's medium is transport media for Gonococci.
- Cary - blair medium is transport media for V. cholera.

22. Ans. is b i.e. Pyrogenic extoxin *Ref. Jawetz 24/e, p 238*

Remember :
- ***MC*** cause of Toxic shock syndrome - Staphylococci
- ***MC*** cause of Streptococcal TSS - Pyrogenic exotoxin A = erythrogenic / Dick / Scarlatinal toxin.
- ***MC*** cause of Staphylococcal TSS - TSST=Pyrogenic exotoxin C = Enterotoxin type F.
- ***DOC*** of TSS (both Streptococcal and staphylococal) is Clindamycin.

23. Ans. is a i.e. Streptococcus pyogenes *Ref. Harrison 17/e, p 885*

Cellulitis :

- Diffuse spreading infection of skin (dermis and subcutaneous tissue) especially of lower leg.
- Caused by Strep pyogenes ***(MC),*** Staph, Cl perfrigens, E.coli.
- Major portal of entry for lower leg cellulitis is toe web *tinea pedis* with fissuring of skin.
- Skin become peud orange in appearance; recurrent attack may sometimes affect lymphatic vessels producing permanent swelling called as *solid edema*.
- Streptococcus cellulitis tends to develop at sites where lymphatic drainage is disrupted.

24. Ans. is b i.e. Enterococcus faecalis *Ref. Ananthnarayan 7/e, p 204*

Growth in 6.5% NaCl is characteristic of Enterococci (E. faecalis, E. faecium, E. durans).

25. Ans. is a i.e. Streptococcus Viridans *Ref. Harrison 17/e, p 789; Jawetz 23/e, p 237*

*It is case of **Subacute bacterial endocarditis (SABE)** as patient has Rheumatic heart disease (so damaged heart valves).*

Remember :	***MC*** cause of SABE	– S. viridans
	MC cause of Acute Bacterial endocarditis	– S. aureus.
	MC cause of Prosthetic valve endocarditis	– S. epidermidis.
	MC cause of Endocarditis in iv drug users	– S. aureus

26. Ans. is a i.e. Post Splenectomy patient *Ref. Harrison 17/e, p 866*

Conditions predispose to pneumococcal infection

- ***Respiratory infection Inflammation***
  - Influenza, other viral respiratory infection
  - Allergies
  - Cigarette smoking
  - Chronic obstructive pulmonary disease
- ***Anatomical disruption of meninges (dural tear)***
- ***HIV infection***
- ***Defective antibody formation***
  - Selective IgG subclass deficiency
  - Multiple myeloma
  - Chronic lymphocytic leukemia
  - Lymphoma
- ***Defective complement function***
- ***Defective clearance of pneumococcal bacterimia***
  - Congenital asplenia, hyposplenia
  - Splenectomy
  - Sickle cell disease
- ***Multifactorial conditions***
  - Alcoholism
  - Malnutrition
  - Glucocorticoid treatment
  - Cirrhosis of the liver
  - Renal insufficiency
  - Diabetes mellitus
  - Anemia
  - Coronary artery disease

27. Ans. is a i.e. Lancefield classification *Ref. Ananthnarayan 7/e, p 203 - 205*

Already explained, Please refer ans. no. 15

28. Ans. is a i.e. Streptococci Viridans *Ref. Harrison 17/e, p 790*

Endocarditis					
	Native Valve		Prosthetic Valve		Injection drug users
	Community associated	*Nosocomial*	*Early (<12Month)*	*late (>12month)*	
Most common organism	Staph.aureus	Staph aureus	Cagulase (–)ve staph	Viridans Streptococci	Staph. aureus

29. Ans. is a i.e. Staphylococcus and b i.e. Streptococci *Ref. CMDT '08, p 416*

"Lymphadenitis and Lymphangitis frequently accompany a Streptococcal or Staphylococcal infection in the distal arm or leg." It usually arises from an area of cellulitis.

In question they have not asked about the commonest cause so both will be answer.

If question about commonest cause will come than go with ***"Streptococci".***

30. Ans. is d i.e. M protein *Ref. Ananthnaryan 7/e, p 206; Jawetz 24/e, p 236*

M Protein

- It is major virulence factor of group A Strep. pyogenes.
- It is hair like projection of cell wall.
- It is of 80 types ***(basis of Griffith classification)*** so immunity is type specific.
- M protein is also found in Group G streptococci.

Remember :

- Carbohydrate is used as the basis of Lancefields classification.
- Streptokinase or fibrolysin and streptodornase or DNAse liquefy pus so used in enzymatic debridement.

31. Ans. is c and e i.e. Group B cause neonatal meningitis and Group D cause UTI

Ref. Ananthnarayan 7/e, p 211 - 212

Streptococcal	Organism	Disease
Lancefield		
Group A	S. pyogenes	RTI, pyoderma, Rheumatic fever, Glomerulonephritis
Group B	S. Agalactiae	Neonatal menintitis
Group C	Strepto. equisimilis	Pharyngitis, endocarditis
Group D	Enterococcal	UTI, endocarditis
	Non Enterococcal	Endocarditis
Group F	Minute streptococci	Rarely cause atypical pneumonia
Group G	Commensal in throat	Tonsillits, endocarditis, UTI
Not typed	Viridans Streptococci	Endocaridits (by S.sanguis)
		Dental caries (by S.mutans)

Remember :

- Strep. commensal in throat : Str. pyogenes, Str. equisimilis.
- Strep. commensal in female genital tract : Str. agalactiae, viridans strep.

32. Ans. is a i.e. Pneumococcal *Ref. Harrison 17/e, p 375*

Splenectomy increase risk of following infections

- **Bacterial :** – Pneumococcal
  – H. influenzae
  – Some Gram (-)ve enteric organism
- **Parasitic** – Babesia
- **Viral** – No ↑ in risk of viral infection

Remember : ***MC*** cause of septicemia in asplenic patient - Pneumococci

33. Ans. is b and c i.e. Anti DNAse; and Anti hyaluronidase *Ref. Ananthnarayan 7/e, p 210*

In streptococcal Glomerulonephritis, ASO titre is often low. So, retrospective diagnosis is made by anti DNAase and antihyaluronidase.

34. Ans. is b i.e. Stereptolysin S *Ref. Ananthnarayan 7/e, p 206*

Streptococci Produce two hemolysin	
Streptolysin O	**Streoptolysin S (Serum soluble)**
• Oxygen labile • Activitiy only on pour plate not on surface • Antigenic protein	• Oxygen stable • Responsible for hemolysis seen around streptococcal colonies on surface • Non Antigenic protein elaborated in presence of serum

So, **ASO** titre used for diagnosis.

35. Ans. is a, b and d i.e. Bile solubility; Inulin fermentation *Ref. Aananthnarayan 7/e, p 221*

Characteristic	Pneumococci	Streptococci
Morphology	Capsulated	Mostly non capsulated
Quellung test	+ ve	– ve
Colonies	Draughtsman colonies	Dome shaped colonies
Bile solubility	++	–
Inulin fermentation	++	–
Optochin sensitivity	++	–
Intraperiotoneal Inoculation of mice	Fatal infection	Not pathogenic
Growth in liquid media	Uniform turbidity	Granular turbidity or powdery deposit.

36. Ans. is b i.e. Strepto. mutans *Ref. Ananthnarayan 7/e, p 204*

Strep. mutans :

- It is member of viridans streptococci (α hemolytic).
- It assumes bacillary form in acid environment.
- Can synthesize acid and large polysaccharide (adhesive dextran or levan) from sucrose.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Which of the following organisms has polysaccharide Capsule : **[JIPMER 90]**

a) Staph saprophytes
b) Strep pneumonia
c) Enterobacter
d) Bacillus anthracis protein

[Ref. Ananthnarayan 7/e, p 217]

2. Quellung reaction is associated with :

a) Capsular degeneration **[Delhi 87, Orissa 91]**
b) Capsular delineation
c) Capsular absence
d) Lecithinase production

[Ref. Ananthnarayan 7/e, p 218]

3. Streptococcus pyogenes with type 12M protein :

a) Fails to adhere to host pharyngeal epithelium
b) Induces immune response but not protective immunity **[Jipmer 89; DNB 91]**
c) Adheres to epithelium but fails to induce an inflammatory response
d) Induces immune responses that may lead to acute glomerulonephritis in 10% to 15 of infections

[Ref. Ananthnarayan 7/e, p 209, 210]

4. C:reactive Protein is : **[AIIMS 91]**

a) Produced by pneumococcus
b) A marker of Septicemia
c) Raised in acute inflammation
d) Low in Rheumatoid arthritis

[Ref. Ananthnarayan 7/e, p 218]

5. Pnemococcus producing mucoid colonies most often is type : **[PGI 92]**

a) I
b) II
c) III
d) IV

[Ref. Ananthnarayan 7/e, p 217]

6. Streptococcus is classified based on :

a) Mprotein **[Kerala 94]**
b) Cultural characteristics
c) Bile solubility
d) Cell wall carbohydrate

[Ref. Ananthnarayan 7/e, p 203]

7. Diplococcus pneumoniae shows the following characters except : **[Karn. 94]**

a) Capsulate
b) Bile solubility test positive
c) Causes meningitis
d) Not pathogenic to mice

[Ref. Ananthnarayan 7/e, p 221]

8. In rheumatic heart disease patient, biopsy is taken from site of lesion and culture it shows : **[UP 98]**

a) Group A beta hemolytic strepococci
b) Streptococci viridans
c) Streptococcus
d) No organism

[Ref. Robbin's 7/e, p 593]

9. True about streptococcus are all except :

a) Group C cause no human infection **[UP 98]**
b) Classification by dancefiled based on carbohydrate Ag
c) Group B cause neonatal meningitis
d) Group B streptococcus lives in female genital tract

[Ref. Ananthnarayan 7/e, p 203 - 204]

10. Which of the following is not true of diplococcus pneumoniae : **[Kar 01]**

a) Bile solubility
b) Optochinin resistance
c) Causes meningitis
d) Possesses capsule

[Ref. Ananthnarayan 7/e, p 216]

Answer

1. b) Strep ...
2. b) Capsular ...
3. d) Induces ...
4. c) Raised ...
5. None
6. c) Bile solubility
7. d) Not ...
8. d) No organism
9. a) Group C ...
10. b) Optochinin ...

11. Which of the following is not true of Diplococcus pneumoniae : [Kerala 01]

a) Bile solubility
b) Optochin resistance
c) Causes Meningitis'
d) Possesses capsule

[Ref. Ananthnarayan 7/e, p 221]

12. Streptococcal toxic shock syndrome is due to liberation of : [Kerala 01]

a) TSST-1
b) Enterotoxin
c) Pyrogenic exotoxin
d) Endotoxin

[Ref. Ananthnarayan 7/e, p 208]

13. Most common cause of community acquired pneumonia: [UP 01]

a) Strep pneumoniae
b) Kleb pneumoniae
c) Vibrio cholera
d) H. influenzae *[Ref. Harrison 16/e, p 871]*

14. True statement about streptococcus faecalis :

a) Growns in 6.5% NaCl solution **[Kolkata 02]**
b) Are lactose fermenter
c) Easily destroyed at 60^0C for 30^0 minutes
d) Classified on the basis of teichoic acid of cell wall

[Ref. Ananthnarayan 7/e, p 212]

15. Neonatal meningitis acquired through birth canal is due to : [TN 02]

a) Streptococcus agalactiae
b) S.equisimilus
c) S.pyogenes
d) Pnemococci during passage

[Ref. Ananthnarayan 7/e, p 204]

16. Dental caries is due to : [JIPMER 02; MP 05]

a) Streptococcus sanguis
b) S.mitis
c) S.mutans
d) S.salivarius

[Ref. Ananthnarayan 7/e, p 204, 215]

17. Quelling phenomenon is seen in: [Kolkata 03]

a) Pneumococcus
b) Streptococcous
c) Staphylococcus
d) Hemophilus *[Ref. Ananthnarayan 7/e, p 210]*

18. Classification of pathogenic streptococci into group A, B, C, D and G is based on : [Kar 03]

a) Color of colonies on blood agr
b) Antigenicity of cell wall carbohydrate
c) Presence or absence of capsule
d) Presence or absence of M protein

[Ref. Ananthnarayan 7/e, p 203]

19. Impetigo contagiosa is caused by :

a) Group A beta hemolytic streptococci
b) Staphylococcus **[Jharkhand 03]**
c) H. Influenzae
d) Psudomonas

[Ref. Harrison 17/e, p 799]

20. Toxic shock syndrome is caused by :

a) Staphylococcus **[Jharkhand 03]**
b) Psudomonas
c) Streptococci
d) bacteroids

[Ref. Ananthnarayan 7/e, p 196]

21. Group-A streptococcus causes causes all, except

a) Scarlet fever **[Bihar 04]**
b) Erysipelas
c) Impetigo
d) Epidermolysis bullae

[Ref. Ananthnarayan 7/e, p 208]

22. Quellung reaction is due to : [Bihar 04]

a) Capsular swelling
b) Mitrochondrial swelling
c) RBC swelling
d) Ribosomal swelling

[Ref. Ananthnarayan 7/e, p 218]

23. Virulence or pathogenicity of pneumococcus depends on : [Kolkata 04]

a) Capsular polysaccharides
b) Cell wall antigen
c) Flagellar antigen
d) Fimbrial antigen

[Ref. Ananthnaryana 7/e, p 219]

24. Griffith denonstrated biotransformation with :

a) H. influenzae **[UP 03; 04]**
b) E. coli
c) Proteus
d) Pneumococcus

[Ref. Ananthnarayan 7/e, p 55]

Answer

11. b) Optochin ... 12. c) Pyrogenic ... 13. a) Strep ... 14. a. Growns ... 15. a) Streptococc ...
16. c) S.mutans 17. a) Pneumococcus 18. b) Antigenicity ... 19. a) Group ... 20. a) Staphyloco...
21. d) Epidermolysis ... 22. a) Capsular ... 23. a) Capsular ... 24. d) Pneumo...

25. Causative agent of SABE should be cultured in :
a) Nutrient agar **[UP 03]**
b) Blood agar
c) L. J medium
d) Tellurite broth
[Ref. Ananthnarayan 7/e, p 204]

26. An infant with neonatal meningitis has a positive CAMP test, the causative agent is : [UP 03]
a) Staphylococcus
b) E.coli
c) Strept agalactiae
d) Hemophiluis
[Ref. Ananthnarayan 7/e, p 204]

27. Streptococcus pneumoniae true is : [SGPGI 05]
a) Vaccine is made from capsular polysaccharide
b) Vaccine is routinely given to Indian children
c) Catalase and oxidase positive
d) Bile insoluble and optochin sensitive
[Ref. Ananthnarayan 7/e, p 221]

28. Draughtsman colonies are seen in : [UP 05]
a) Staphylococcus
b) Salmonella
c) Pneumococcus
d) Corynebacterium
[Ref. Ananthnarayan 7/e, p 217]

29. Streptococcus causing Rheumatic heart is :
a) Streptococcus milleri **[MP 05]**
b) Streptococcus mutans
c) Streptococcus pyogens
d Streptococcus equimilis
[Ref. Ananthnarayan 7/e, p 210]

30. Which of the following microorganism is the most common cause of lobar pneumonia : [MP 06]
a) Klebsiella pneumoniae
b) Streptococci
c) Pneumococci
d) Staphylococci
[Ref. Ananthnarayan 7/e, p 216]

31. Glanders disease is due to : [Bihar 06]
a) Burkholderia mallae
b) Diphtheria
c) Mumps
d) Burkholderia psudomallae
[Ref. Ananthnarayan 7/e, p 321]

Answer
25. b) Blood ... 26. c) Strept ... 27. d) Bile insoluble ...
28. c) Pneumococcus 29. c) Strep ... 30. c) Pneumococci
31. a) Burkholderia ...

3 Neisseria

- Genus consist of Gram (–)ve, aerobic, nonmotile, oxidase + ve diplococci [i.e grow in pairs].
- Oxidase test is key test for identifying Neisseria.
- Can grow both intracellularly and extracellularly.
- It includes :
  - **a. N. meningitidis :** causative agent of :
    - **1. Meningococcal meningitis**
    - **2. Purpura fulminans** (Fulminant meningococcemia)
  - **b. N. Gonorrhoeae :** Causative agent of gonnorhaea

N. meningitidis [meningococci]	N. gonorrhoeae [gonococci]
• Lens shaped	• Kidney shaped
• Capsulated	• Noncapsulated
• Ferment both glucose and maltose	• Ferment glucose only
• Rarely have plasmid	• Plasmid usually present

N. MENINGITIDIS [MENINGOCOCCI]

- Categorize as β *proteobacterium* on basis of genome sequencing. *.....Harrison 17/e, p 908*

Classification :

– On *basis* of *capsular polysccacharide* classified into 13 serogroups.
– 5 serogroups A,B,C, W,Y are responsible for most meningococcal disease.

Group A	– Epidemic
Group B	– Both epidemic and outbreak
Group C	– Localized outbreaks

Virulence factors

Important virulence factors are :

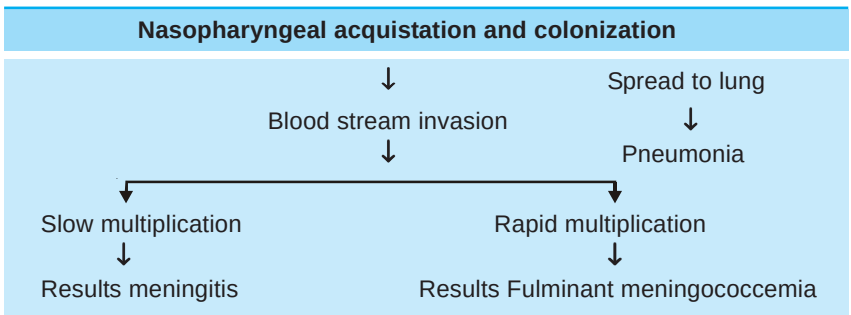
1. *Capsular polysaccharide :* Major virulence factor. Has antiphagocytic and antibacteriocidal properties.
2. *Outer membrane proteins* - Pilli are complex OMP based organelles that facilitates adhesion.
3. *Lipoligosaccharide LOS [endotoxin]* – Morbidity and mortality of meningococcal bacteremia and meningitis is directly proportional to amount of circulating meningococcal endotoxin.

Remember :

- Meningococcal endotoxin is LOS *(Harrison 17/e, p 909)* not lipopolysaccharide as given in *.....Ananthnarayan 7/e, p 224*
- Vascular endothelium is particularly sensitive to endotoxin.

Pathogenesis

- Deficiency of terminal or alternate complement pathway C_5-C_9 increase risk of meningococcal infection.



Thus, *meningitis* is result of blood borne dissemination and not direct invasion. *.....Harrison 17/e, p 909*

Clinical features

a. *Fulminant meningococcemia [Purpura fulminans]*

- Most rapid lethal form of septic shock.
- Differs from other septic shock by *prominence of hemorrhagic skin lesions* (petechiae, purpura) and development of DIC. *Rash* is most distinctive feature.
- LOS (endotoxin) is responsible for most cases.
- CSF may be normal and CSF culture may be (–)ve which is poor prognostic sign.
- Due to rapidity there may be no rise in acute phase reactant.
- May progress to *Water house - Freiderichsen* syndrome - DIC induced microthrombi, hemorrhage, tissue injury and circulatory collapse.

b. *Meningitis -* Common in Age between 3 month to 5 years.

c. *Other manifestation -* Arthritis, Conjuctivitis, urethritis, rarely endocarditis.

Lab diagnosis

- Diagnosis is established by recovering Meningococci from sterile body fluids such as Blood, CSF etc.
- PCR amplification of DNA in buffy coat or CSF samples is the most sensitive method. *... Harrison 17/e, p 912*
- They grow best on *Muller - Hinton* or chocolate agar at 35^0 C in 5 to 10% CO_2.
- ***Thayer Martin media*** is selective media used for culturing throat or nasopharyngeal specimen, as it suppress the competing oral flora.

Treatment

- 3rd generation cephalosporin such as cefataxime or ceftriaxone is ***DOC*** for initial therapy.
- Prophylaxis - Rifampin is ***DOC*** for meningococcal prophylaxis.

Prevention

- ***Vaccine -*** Quadrivalent Meningococcal polysaccharide vaccine [serogroup *A, C, W, Y*].
- ***There is no vaccine against serogroup B*** as its capsule is nonimmunogenic.
- Vaccine is ineffective in Age < 2 years so, given after 2 years.

Indication	*Contra indication*
– Late complement or properdin deficiency – Asplenia or splenectomy patient – Military Persons – Epidemic areas – Pilgrims on Haj – Individual travelling to subsaharan Africa	– Pregnancy

N. GONNORHOEAE [GONOCOCCI]

- ***MC*** cause of PID worldwide [***MC*** cause of PID in India is TB].
- ***MC*** cause of septic arthritis in adult [***MC*** joint knee].
- Cause *most severe* type of ophthalmia neonatorum.

Culture :

- More difficult to grow than meningococci
- Four types of colonies recognised - T_1 to T_4
- Type 3 and 4 = P^- and are avirulent
- Essential to provide 5-10 % CO_2
- Type 1 and 2 = P^+ and P^{++} respectively. They are piliated and virulent.

Pathogenic factors

a. Outer-membrane protein :

- Pilli – Piliated strains adhere better to cells and are more virulent.
- Opacity associated protein (Protein II) – Important for adhesion.
- Porin (Protein I, III) – *Most abundant* gonococcal surface protein.
- H.8 Lipoprotein – Excellent target for antibody based diagnostic testing.
- Transferrin and lactoferrin binding protein.
- IgA1 protease (also produced by meningococci).

Remember : IgA - 1 protease is also produced by S. pneumoniae, H. influenza; some streptococci.

....Jawetz 24/e, p 157

b. Lipooligosaccharide = Endotoxin

- Resemble human glycosphingolipid, contributes to the local cytotoxic effects.

c. Host factors, defeciency of terminal compliment components.

Clinical features

- Mode of infection is almost exclusively veneral except ophthalmia neonatorum.
- Terminal complement component [C_5 - C_9] deficiency predispose to gonococcal infection.
- Higher incidence of gonorrhea occur in blood group B.
- Gonococcal infection in *males* – ***Acute urethritis*** is ***MC*** clinical manifestation of gonorrhoea ***in males*.**
- Gonococcal infection in *females* – *Cervicitis* is ***MC*** *manifestation*. Adult Vagina is resistant to gonococcal infection.
- Gonorrhoea in *pregnant woman* – Salpingitis and PID can occur during 1st trim and can cause abortion. In 2nd and 3rd trim, relative impermeability of cervical mucous prevent ascending infection.
- Gonococcal infection in *neonates* – ***MC*** is opthalmia-neonatorum while *septic arthritis* is ***MC*** manifestation of systemic infection.
- In *children Vulvovaginitis* is ***MC*** gonococcal infection.

Diagnosis

- Rapid diagnosis by Gram's staining of urethral exudates.
- Part of sample should be inoculated on ***Thayer Martin*** Media. Detection of Gram –ve diplococci or monococci is usually specific.
- It is important to process all samples immediately because gonoccoi do not tolerate drying.
- If processing is to occur within 6h, transport of specimens may be facilitated by the use of nonnutritive swab transport systems such as *Stuart* or *Amies medium.*
- For longer holding periods culture media with self contained CO_2 generating systems (such as the JEM BEC or Gono-Pak system may be used).

Treatment :

- 3rd generation cephalosporins cefixime and ceftriaxone are ***DOC.*** [Penicillin is ***DOC]***

..... Park 18/e, p 138; 19/e, p 141

Prevention and Control

- Gonorrhea is transmitted from males to females more frequently than in opposite direction.
- Condoms provide effective protection against transmission.

QUESTIONS

1. The following bacteria are most often associated with acute neonatal meningitis except : [AI 05]

a) Escherichia coli
b) Streptococcus agalactiae
c) Neisseria meningitidis
d) Listeria monocytogenes

2. The following statements about meningococcal meningitis are true except : [AI 03]

a) The source of infection is mainly clinical cases
b) The disease is more common in dry and cold months of the year
c) Chemoprophylaxis of close contacts of cases is recommended
d) The vaccines is not affective in children below 2 years of age

3. Xavier and Yogender stay in the same hostel of same university Xavier develops infection due to group B meningococcus. After few days Yogender develops infection due to Group - C meningococcus. All the following are true statement except : [AI 02]

a) Educate students about meningococcal transmission and take preventive measures
b) Chemoprophylaxis to all against both group B and group C
c) Vaccine prophylaxis of contacts of Xavier
d) Vaccine prophylaxis of contacts of Yogendra

4. Differentiation of N. gonorrhea and N. meningitidis can be done by : [AI 96]

a) Glucose fermentation
b) VP Reaction
c) Maltose fermentation
d) Indole test

5. The best site to obtain a swab in asymptomatic gonorrhea is : [AI 95]

a) Endocervix
b) Urethra
c) Lateral vaginal wall
d) Posterior fornix

6. Conjugate vaccine are available for the prevention of invasive disease caused by all of the following bacteria except : [AIIMS 04]

a) H influenzae
b) Strep pneumoniae
c) Neisseria meningitidis (Group - C)
d) Neisseria meningitidis (Group - B)

7. The virulence factor of Neisseria gonorrhoeae includes all of the following except : [AIIMS 03]

a) Outer membrane proteins
b) IgA Protease
c) M Protein
d) Pilli

8. All are true about Neisseria gonorrhea except :

a) Gram positive cocci **[AIIMS 01]**
b) Causes stricture urethra
c) Involves seminal vesicles and spreads to epididymis
d) Drug of choice is ceftriaxone

9. Which of the following is true regarding Neisseria meningitidis infection : [AIIMS 00]

a) It is the most common cause of meningitis in children
b) All strains are uniformly sensitive to sulfonamides
c) In children less than 2 years the vaccine is not effective
d) In India sero type B is most common cause

10. Least susceptible to gonococcal infection is :

a) Anterior urethra **[AIIMS 95]**
b) Testis
c) Prostate
d) Epididymis

11. Which is the true statement regarding gonococcal urethritis : [PGI 06, 00]

a) Symptoms are more severe in females than in males
b) Rectum and prostate are resistant to gonococci
c) Most patients present with symptoms of dysuria
d) Single dose of ciprofloxacin is effective in treatment
e) Commonly leads to arthritis

12. CSF in meningococcal meningitis shows :

a) Gram (+) Diplococci, in pus cells **[PGI 98]**
b) Gram (-) Diplococci in pus cells
c) Gram (-) bacilli
d) Gram (+) bacilli

Answer

1. c) Neisseria ...
2. a) The source ...
3. c) Vaccine ...
4. c) Maltose...
5. a) Endocervix
6. d) Neisseria ...
7. c) M Protein
8. a) Gram ...
9. a and c
10. b) Testis
11. c and d
12. b) Gram (-) ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is c i.e. N. meningitidis *Ref. Forfar & Arneils - Text book of Paedia, p 319, 1338*

Causes of Meningitis :

- **Neonatal (< 1 month)**
  1. **Bacterial causes :**

Organism	**:**	E. coli >	Gp B streptococci >	other Gram - ve bacilli > L. monocytogenes
Frequency	**:**	34%	30%	8% 6%

  Other bacterias are : Staph, Other Streptococci, Pneumococcus, Pseudomonas, Haemophilus, Meningococcus.

  2. **Viral and protozoal infections :** TORCH, Varicella zoster and HIV.

  3. **Spirochetal and fungal infections**

- **1 month - 11 month** : N-meningitidis > Strep pneumoniae > H. influenza
- **1 year - 20 years** : N. meningitidis > Strep pneumoniae > H. influenza
- **More than 20 years** : Strep pneumoniae ***(MC)*** *..... Harrison 17/e, p 2621*

2. Ans. is a i.e. The source of infection is mainly clinical cases *Ref. Park 18/e, p 138; 19/e, p 141*

"Source of infection are carriers not cases."

Meningococcal meningitis or Cerebrospinal fever.

- It is caused by N. meningitides, a *gram negative diplococci.*
- Fatality of typical untreated cases is about 80%.

Agent : Group A and C and to lesser extent Group B cause major epidemics.

Source : Carriers are the most important source of infection.

Clinical cases present only a negligible source of infection.

Environmental Factors : Seasonal variation is well established. Outbreaks occur more frequently in the dry and cold months.

Mode of Transmission : Mainly by droplet infection.

Incubation Period : Usually 3 - 4 days

Diagnosis : Recovering Gram (–)ve diplococci from sterile body fluids such as CSF, blood

Treatment : Antibiotics save the lives of 95% of patients provided that it is started during the first 2 days of illness.

Cases : Penicillin is drug of choice. [3rd generation cephalosporins are DOC. *..... Harrison 17/e, p 912-913*

Carriers : Rifampicin

Prophylaxis

Chemoprophylaxis **:** Rifampicin (the ***DOC*** unless the organism is known to be sensitive to sulfadiazine).

It is suggested for close contacts. Mass chemoprophylaxis is restricted to closed and medically supervised communities.

Immunization **:**
- Polysaccharide vaccines from Group A, C, Y and W 135
- *No vaccine is available for group B*
- Immunity last for 3 years
- Not recommended for infants and children under 2 years
- Contraindicated in pregnant women.

3. Ans. is c i.e. Vaccine prophylaxis of contacts of Xavier *Ref. Park 19/e, p 142*

For group B meningococcal infection no vaccine is available.

4. Ans. is c i.e. Maltose fermentation *Ref. Ananthnarayan 7/e, p 226*

N. meningitidis [meningoccci]	N. gonorrhoeae [gonococci]
• Lens shaped • Capsulated • Ferment both glucose and maltose	• Kidney shaped • Noncapsulated • Ferment glucose only

Remember : Indole and VP reaction is done to differentiate genera of Enterobacteriaceae.

5. Ans. is a i.e. Endocervix *Ref. Harrison 17/e, p 919; Ananthnarayan 7/e, p 228*

DIAGNOSIS OF GONOCOCCAL INFECTION

SPECIMEN	
In Acute Gonorrhea	**In chronic gonorrhea**
• Endocervical culture - 80 - 90% sensitivity • Urethral discharge - 50% sensitivity • High vaginal swab are not satisfactory • Rectal wall swab - if there is history of rectal sex	• Morning drop secretion • Exudate after prostatic massage • Centrifuged deposits of urine when no urethral discharge

Microscopy : Fluorescent antibody technique

Transport Media : Stuart's or Amies media processing is to occur within.

For longer holding period culture media with self CO_2 generating system (such as JEMBEC or Gono- pak systems) may be used.

Culture Media : *Acute* → Chocolate agar or Muller - Hinton agar.
Chronic → Selective media like Thayer Martin medium.

Serology : Done in chronic case or with metastatic lesion Eg CFT, Precipitation, passive agglutination, Immunofluorescence, RIA.

Chemiluminescent DNA Probe : in high risk patient undergoing screening for STD's.

Blood Culture (Eg. of synovial fluid) : in suspected cases of disseminated infection.

- Preferred method for diagnosis of gonococcal infection in children is a standardized culture, from urethera and cervix. However cervical specimen are not recommended in prepubertial girls unless necessary.

6. Ans. is d i.e. Group B *Ref. Ghai 6/e, p 197 - 198*

"No vaccine is available for protection against group B meningococci."

- ***Conjugate vaccines*** are prepared by conjugating protein carrier with polysaccharide capsule.
- ***Conjugate vaccine*** are available for :
  a. Hemophilus influenza B.
  b. Menigococcal serotypes A, C, Y and W - 135.
  c. Streptococcal pneumoniae (pneumococcus).

7. Ans. is c i.e. M protein *Ref. Harrison 17/e, p 915; Ananthnarayan 7/e, p 226*

M protein is the virulence factor of strept. pyogenes not of gonococci.

Virulence factors of neisseria gonorrhoea	
1. Outer Membrane Proteins	
• Pilli • Porin (Protein I and III) • IgA1 protease	• Opacity associated protein (Protein II) • Lipoprotein H. 8 • Transferrin and lactoferrin binding protein
2. Lipooligosaccharide (endotoxin)	

8. Ans. is a i.e. Gram positive cocci *Ref. Harrison 17/e, p 916*

Gonococcal Infection In Males	
• ***MC*** Clinical manifestation	– Acute urethritis.
• Major symptoms	– Urethral discharge and dysuria usually without urinary frequency or urgency.
• Other features	– Epididymitis (uncommon) – Prostatitis (rare) – Edema of penis and Balanitis. – Urethral stricture and Periurethral abscess or fistulae (=Watercan perineum) – Inflammation or abscess of Cowper's gland. – Seminal vesiculitis
• **DOC**	– 3rd generation cephalosporin - cefixime and ceftriaxone

Remember :
- All cocci are gram positive except **GMC** i.e N. **go**norrhoea, N. **me**ningococci, N. **ca**tarrhalis.
- All important bacilli are gram negative except **ABC, CML** i.e. **Ac**tinomycetes, **Ba**cillus, **Cl**ostridia, **Co**rynebacteria, **My**cobacteria, **Li**steria.

9. Ans. is a and c i.e. It is the most common cause of meningitis in children; and In children less than 2 years the vaccine is not effective

Ref. Park 18/e, p 138; 19/e, p 140; Forfar & Arneil's, p 1338

- ***MC*** cause of neonatal meningitis : E. coli
- ***MC*** cause of meningitis in age group 1 month to 20 year is N. meningitidis.
- ***MC*** cause of meningitis > 20 years : Strep pneumoniae. *... Harrison 17/e, p 2621*
- Sulphonamides once the mainstay, are not used now due to widespread resistance. *... AA 7/e, p 225*
- ***MC*** serotype is not given in Park or any other book so as the rule first written is the *most common* so group A is ***MC*** not group B.
- Vaccine (not available for group B) is contraindicated in pregnancy and ineffective in children < 2years.

10. Ans. is b i.e. Testis *Ref. Ananthnarayan 7/e, p 227*

Spread of infection in males	
Acute urethritis ↓ Prostate, seminal vesicles epididymis	Chronic urethritis ↓ Urethral stricture + periurethral infection ↓ Abscess + multiple sinuses (= Water can perineum)

11. Ans. is c and d i.e. Most patients present with symptoms of dysuria; and Single dose of ciprofloxacin is effective in treatment *Ref. Harrison 17/e, p 916; Ananthnarayan 7/e, p 227*

Gonococcal infection in Females

- Initial infection involves urethra and cervix uteri.
- Cervicitis is ***MC*** manifestation.
- Vaginal mucosa is resistant due to stratified squamous epithelium but can involve in anestrogenic women (prepubertal, post menopausal).
- Infection spreads to endometrium, fallopian tube, bartholin gland, peritoneum with perihepatic inflammation (Fitz-Hugh-Curtis syndrome).
- Clinical disease (as a rule) is less severe in women.
- Proctitis occur in both sexes.

Gonococcal infection in males - *Already described*

Disseminated Gonococcal infection (DGI) or Arthritis. Occur in very few patient. DGI also cause skin lesion, meningitis, endocarditis etc.

Treatment : – 3rd generation cephalosporin cefixime and ceftriaxone.
– Single dose ciprofloxacin, ofloxacin, Levofloxacin etc. also affective.

Remember : Incubation period of Gonococcal infection is 2-8 days.

12. Ans. is b i.e. Gram negative Diplococci in pus cells *Ref. Ananthnarayan 7/e, p 223*

Gram negative diplococci – Neisseria
Gram positive diplococci – Pneumococcus

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Differentiation of neisseria gonorrhoea and neisseria meningitidis is by : [AI 90]

a) Glucose fermentation
b) Maltose Fermentation
c) V.-P. reaction
d) Indol test

[Ref. Ananthnarayan 7/e, p 226]

2. Which is not a metastatic complication of gonococci : [JIPMER 91]

a) Endocarditis
b) Meningitis
c) Nephritis
d) Arthritis

[Ref. Ananthnarayan 7/e, p 227]

3. Incubation period of gonorrhoea is :

a) Less than 24 hrs **[JIPMER 92]**
b) 1 to 2 days
c) 2 to 15 days
d) 12 to 25 days

[Ref. Ananthnarayan 7/e, p 226]

4. Gonococci in gram stained smears are seen inside the : [Kerala 94]

a) Lymphocytes
b) Neutrophils
c) Mast cells
d) Macrophages

[Ref. Ananthnarayan 7/e, p 225]

5. Skin lesion in meningococcal meningitis is due to:

a) Exotoxin **[Kerala 94]**
b) Endotoxin
c) Allergic reaction
d) Direct vascular Damage

[Ref. Ananthnarayan 7/e, p 224]

6. Which f the following is most resistance to gonococcal infection : [Kerala 94]

a) Prostate
b) Epididymis
c) Testis
d) Urethra

[Ref. Robbins 7/e, p 1039]

7. Neisseria infection are associated with :

a) Deficiency of early complements **[CUPGEE 95]**
b) Deficiency of late complements
c) There is not such association
d) Any deficiency can be associated

[Ref. Ananthnarayan 7/e, p 224]

8. Gonococcus ferments : [AP 97]

a) Glucose
b) Maltose
c) Sucrose
d) Fructose

[Ref. Ananthnarayan 7/e, p 226]

9. The diagnosis of gonorrohea is established by :

a) Comliment fixation tests **[Orissa 98]**
b) Pili agglutination tests
c) Haem agglutination tests
d) All of the above tests

[Ref. Ananthnarayan 7/e, p 228]

10. Meningococci differ from gonococci in that they :

a) Are intra-cellular **[ICS 98]**
b) Possess a capsule
c) Causes fermentation of glucose
d) Are oxidase positive

[Ref. Ananthnarayan 7/e, p 222]

Answer

1. b) Maltose ...
2. b) Meningitis
3. None
4. None
5. b) Endotoxin
6. c) Testis
7. b) Deficiency ...
8. a) Glucose
9. d) All of the ...
10. b) Possess ...

11. The following are gram-negative cocci except :
a) Pneumococci **[Kar 01]**
b) Meningococci
c) Gonococci
d) Veillonella

[Ref. Ananthnarayan 7/e, p 216]

12. The vaccine against N:meningitides contains :
a) Whole bacteria **[ICS 00]**
b) Capsular polysaccharide
c) Somatic '0' antigen
d) Lipo polysaccharide protein complex

[Ref. Ananthnarayan 7/e, p 225]

13. A pus culture on chocolate agar shows gram negative cocci most likely organism is : **[UP 04]**
a) Haemophilis ducreyi
b) Neisseria gonorrhoea
c) Streptococcus pyogenes
d) Streptococcus pneumoniae

[Ref. Ananthnarayan 7/e, p 225]

14. Water can perineum" is caused by : **[UP 06]**
a) E. coli
b) Enterococcus faecalis
c) Neiserria-gonorrhoea
d) Treponemia palladium

[Ref. Ananthnarayan 7/e, p 227]

Answer
11. a) Pneumococci
12. b) Capsular ...
13. b) Neisseria ...
14. c) Neiserria ...

4 Clostridium

COMMON GRAM-POSITIVE BACILLI	
Aerobic Gram-Positive Bacilli with high G +C content and Irregular shape	**Aerobic Gram-Positive Bacilli with lower G + C content and more regular shape**
Genera	**Genera**
• Common – Corynebacterium – Mycobacterium • Aerotolerant anaerobes – Actinomyces – Propionibacterium G + C = Guanine plus cytosine	• Common – Listeria – Erysipelothrix – Gardnerella • Aerotolerant anaerobes/strict anaerobes – Lactobacillus – Clostridium (spore-forming) • Aerobes – Bacillus (spore-forming)

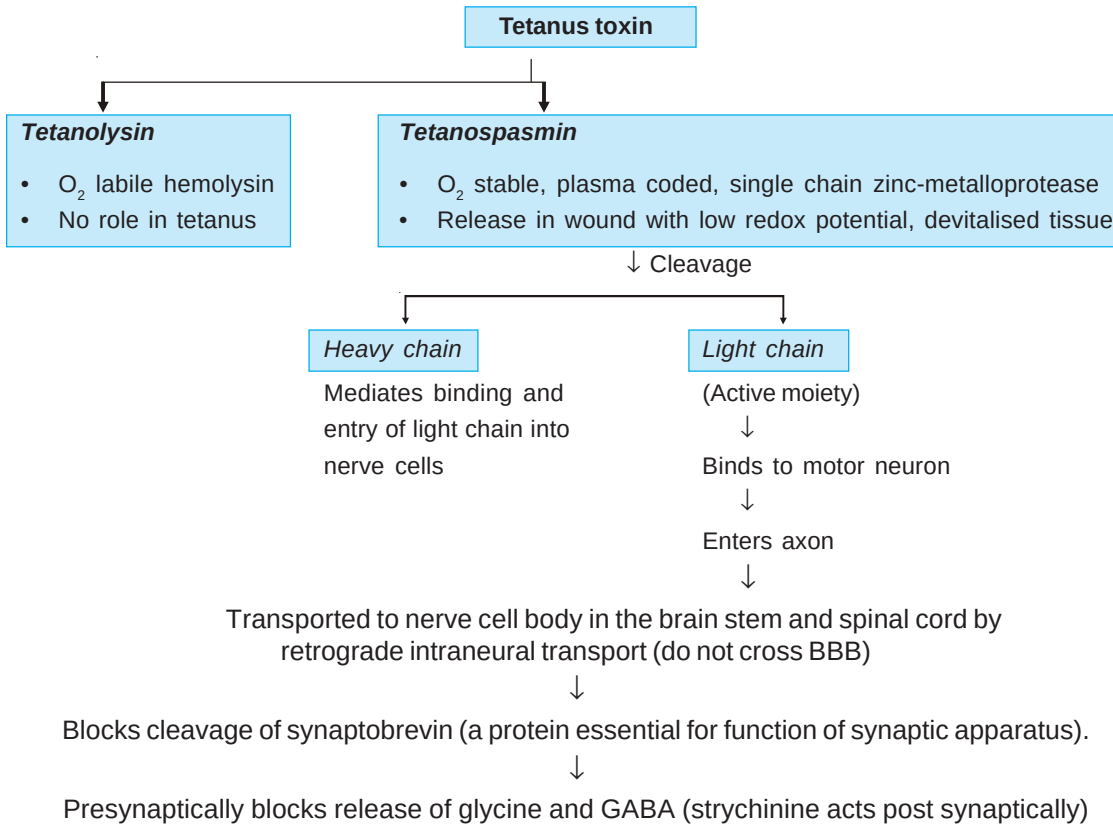
- ***Anaerobic*** obligatory ***Gram positive spore*** bearing bacilli.
- ***Motile*** except ***Cl perferinges*** and ***Cl tetani type VI.***
- Cl. perferingens and Cl. tetani are found normally in intestine.
- Spores may be : – Spherical and terminal *(=Drumstick)* in Cl. tetani, Cl. tetanomorphum, Cl. sphenoides.
  – Oval and terminal *(= Tennis racket)* Cl. difficle, Cl. tertium, Cl. cochleurum.
  – Others have either central *(spindle shape)* or sub terminal (club shaped) spores.
- Useful ***medium*** for ***Clostridia –*** *Robertson's cooked meat broth.*
- *Important members* – Cl. difficle, Cl. perferinges, Cl. tetani, Cl. botulinum.
- Non capsulted except C.perfringens and C.butyricum which are capsulated.

I. CLOSTRIDIUM TETANI

Causative agent of Tetanus.

Culture :

- Marked tendency to ***swarm***. Extremely fine translucent film of growth enables its separation from mixed cultures.
- α hemolysis is produced which later develops into β hemolysis.
- It is strict anaerobe and form surface growth only when O_2 tension is less than 2 mm Hg.
- Spores are resistant to various disinfectants and to boiling for 20 min. Vegitative cells, however are easily inactivated.



Clinical Manifestations :

- Contraindicated tetani has little invasive property.
- ***MC*** from of tetanus is *Generalized tetanus in which toxins enters the lymphatics and blood stream.*
- Median time of onset after injury is 7 days.
- ***First symptom –*** increase tone in masseter muscles called as *trismus or lock jaw*, followed by sequential involvement of nerves of head, trunk and extremities (*Descending tetanus*) since *short nerves are affected earlier. Hands and feet are relatively spared. Sustained contraction contraction of facial muscles results in sinus sardonius.*
- Mentation is unimpaired.
- ***Deep tendon reflex increase.***
- Autonomic dysfunction (sympathetic increase), sudden cardiac death may occur.
- *Short Incubation period = Grave prognosis.*
- Neonatal tetanus usually occurs as generalized form.
- In local tetanus, only the nerves supplying the affected muscles are involved.

Remember : Tetanus patients are not infectious and there is *no person to person transmission.*

Diagnosis : *Always clinical* since microscopy is unreliable because it can be isolated from wounds without tetanus and can't be isolated from wounds with tetanus.

Treatment :

1. Antitoxin

- *Best* to give before wound manipulation.
- *Human tetanus immune globulin (TIG)* is *preparation of choice* . T½ = 30 days. It decrease mortality.
- Alternative is IV Ig
- *Management of wound is as follows :*

All wound receive surgical toilet

Wound <6 hr, clean non penetrating and with negligible tissue damage			*Other wounds*		
Immunity category		***Treatment***	***Immunity category***		***Treatment***
A		Nothing more required	A		Nothing more required
B		Toxoid one dose	B		Toxoid 1 dose
C		Toxoid one dose	C		Toxoid 1 dose + Human Tetanus Ig
D		Toxoid complete course	D		Toxoid complete course + Human Tetanus Ig

A = Has had a complete course of toxoid or booster dose with in past 5 years.
B = Has had a complete course of toxoid or booster dose with in past > 5 years and <10 years.
C = Has had a complete course of toxoid or booster dose with in past >10 years.
D = Has not had complete course of toxoid or immunity status is unknown.

2. Antibiotic : – Penicillin or metronidazole eradicate source of toxin i.e. vegetative cells.
– Alternative clindamycin or erythromycin.
– It is of no role if given > 6 hours.

Prevention :

- Best prevented by ***active immunisation.*** Protective level of antitoxin > 0.01 IU/ml serum
- Active immunisation – Monovalent Vaccine :
  - 2 dose of Purified tetanus toxoid (TT) should be given at interval of 1-2 month
  - Ist booster after 1 year of 2nd dose.
  - 2nd booster after 5 year of 3rd dose.
  - Combined Vaccine - DPT
- Passive immunisation – Human tetanus hyperimmunoglobulin (TIG) is *best* prophylactic to use. Toxin already bound to neural tissue is not affected.
- Combined active and passive immunisation – Patient is given TIG in one arm and TT in other arm followed by another dose of TT 6 weeks later and third dose 1 year later.

II. CL. BOTULINUM

- Causative agent of botulism
- It is agent of bioterrorism
- Classified in to type A to G based on immunological difference in the toxins.

Toxin :

- Botulinum toxin is *most potent bacterial toxin known.*
- Produce 8 distinct toxin (A, B, C_1, C_2, D, E, F, G).
- All toxins except C_2 are neurotoxin. C2 is the cytotoxin of unknown clinical significance.
- Acts on *peripheral cholinergic nerve endings* including Neuromuscular junctions, postganglionic parasympathetic nerve endings and peripheral ganglion, *CNS is not involved. It blocks release of Acetylcholine.*
- A, B, E and rarely F cause human disease. Type G (from C argentinense) has been associated with sudden death. *..... Harrison 17/e, p 901*
- Type A toxin used for treatment of strabismus, blepharospasm, cervical dystonia.

Clinical Features :

- Cause noninvasive botulism of three types :
  1. *Food borne botulism* : Due to *preformed toxin* of canned food. With incubation period of 18-36 hr. Nausea vomiting, abdominal pain and *characteristic symmetric descending paralysis occurs.*
     - Symptoms begins with Cranial Nerve involvement producing diplopia, dysphagia, ptosis, diminished pupillary reflex.
     - DTR decrease or normal, *severe constipation* no fever, no sensory finding, mentally intact.
     - Death is due to respiratory failure.
  2. *Wound botulism :* Toxin is produced in wound. It resemble food borne illness except I.P is longer (~ 10days) and gastrointestinal symptoms are lacking.
  3. *Infant or intestinal botulism :* – Due to ingestion of subterminal spores – Toxin is produced inside.
     – Source of infection is usually honey – Occur in infant < 6 months.

Remember :

– Botulism is a food poisoning that do not cause diarrhea.

– Infant botulism is most common form of botulism

Diagnosis :

- Demonstration of organism in serum by bio assay in mice is definitive.
- Diagnosis must be considered in patient with symmetric descending paralyis who are mentally intact.

Treatment :

• *Food borne botulism*	– No role of antibiotics
	– Guanidine hydrochloride and Bivalent antitoxin given
• *Wound botulism*	– Antitoxin
• *Infant botulism*	– Supportive care and human botulism immunoglobulin

III. CL. DIFFICLE ASSOCIATED DISEASE [CDAD]

- ***MC*** diagnosed diarrheal illness *acquired* in the hospital, which results from ingestion of spores.
- This colon infection is acquired almost **exclusively** in association with **Antimicrobial use** (***MC clindamycin***).
- **Risk factors** for CDAD : old age, severe illness, use of electronic rectal thermometer, enteral tube feeding, antacid treatment and gastrointestinal surgery.
- Acquired exogenously and carried in stool of symptomatic and asymptomatic patients.
- Asymptomatic fecal carriage is very common in healthy neonates.
- It release toxin A (enterotoxin) and toxin B (cytotoxin), both **glucosylate the GTP binding proteins** and disrupt cell cytoskeleton, so fliud is leaked leading to whitish yellow plaque formation over, colon, known as *Pseudomembranous colitis.*
- ***MC*** symptom caused by Cl difficle - **Diarrhoea**
- *Complication* - Toxic megacolon and sepsis.

Diagnosis :

- Demonstrating toxin in feces by its characteristic effect on Hepatitis 2 and human diploid cell culture (Tissue culture) is ***gold standard***.
- ELISA – Rapid and easy but has less sensitivity.

Treatment :

- ***DOC*** – Metronidazole
- ***DOC even*** for relapse is Metronidazole
- If not respond for >48 hrs, give vancomycin
- Rifampin, Bacitracin, Saccharomyces boulardii or lactobacillus GG, colonization with nontoxigenic strain of Cl difficle, anion exchange binding resin cholestyramine, IV Ig can also given.

IV. CL. PERFRINGES = CL. WELCHII

- Causative agent of gas gangrene, enteritis necroticans *(type C)*
- Toxigenic as well as invasive.
- Capsulated, non-motile, shows ***Stormy fermentation***
- Absence of its central or subterminal spore in artificial media or pathological tissue is the characteristic feature.
- Classified on the basis of toxin, they produced.
- It is the ***MC*** clostridial species isolated from tissue infection and bacteremia.
- Clostridia are present in the normal colonic flora, Clostridia ramosum is the most abundant and is followed by C.perfringens.

Toxins :

- Produce twelve distinct toxin. Four major entero toxins are : α, β, ε and ι.
- *α Toxin* = Phospholipase C= lecithinase : Associated with Gas gangrene.
  - Hemolytic, Hot-cold variety toxin produced by all Cl perfringes but most abundantly by Type A.
  - Shows Nagler reaction in which zone of opacity is formed where there is no antitoxin.
  - Lecithinase also produced by Cl novyi, Cl. bifermentans, some vibrios.
  - It initiates muscle infection that may progress to gas gangrene.
- β and iota (i) toxin also have lethal and necrotizing properties. Increase capillary permeability.
- θ *(theta) toxin* - Hemolysin, antigenically related to streptolysin O. Also known as ***Perfringolysin O.***
- Also produce neuraminidase, histamine - bursting factor etc.

Clinical features :

It cause following diseases :

1. **Skin and soft tissue infection :** It includes Gas gangrene = *Clostridial myonecrosis.*
   - Most commonly cause by Cl. perfringes Type A. Also caused by Cl septicum, Cl novyi, Cl histolyticum etc.
   - Characteristic pathology – *Near absence of PMNs despite extensive tissue destruction.*
   - Essential factor - Trauma particularly deep muscle laceration.
   - Incubation period usually short : *10-48 hr* with Cl perfringes, *2-3 days* with Cl septicum, *5-6 days* with Cl novyi.
   - Pain and *crepitus* present and death is due to circulatory failure.

- ***Diagnosis :*** – Frozen section biopsy of muscle.
  - – Gram's staining :
    - Showing gram positive bacilli *without spores* - Cl perfringes
    - Showing *citron* bodies & *boat or leaf shaped* pleomorphic bacilli - Cl septicum
    - Showing large bacilli with oval or subterminal spores - Cl novyi.
- ***Treatment :*** – Surgery - mainstay of therapy
  - – ***DOC*** Clindamycin + penicillin *..... Harrison 17/e, p 907*
  - – Hyperbaric O_2 may also used.

2. Intestinal disorders :

a. Food poisoning : Cl. perfringens (type A) is 2nd or 3rd ***MC*** cause of food poisoning mediated by Cytotoxin which act on small bowel brush border and induces Ca^{2+} dependent alteration in permeability.

- Usually caused by cold or warmed up meat dish after 8-24 hrs. It is self limited.

b. Enteritis necroticans (Pigbel) Caused by β toxin of type C strain.

- Following ingestion of high protein meal with trypsin inhibitors (sweat potato) by host having limited proteolytic activity of small intestine. Patient present with acute abdominal pain, bloody diarrhea, vomiting, signs of peritonitis.

c. Neurotropenic enterocolitis

QUESTIONS

1. The following statements are true regarding Clostridium perfringes except : [AI 05]

a) It is the commonest cause of gas gangrene
b) It is normally present in human faeces
c) The principal toxin of C. perfringens is the alpha toxin
d) Gas gangrene producing strains of C. perfringes produces heat resistant spores

2. Regarding gas gangrene one of the following is correct : [AI 04]

a) It is due to Clostridium Botulinum infection
b) Clostridial species are gram-negative anaerobes forming spores
c) The clinical features are due to the release of protein endotoxin
d) Gas is invariably present in the muscle compartments

3. A person has received complete immunization against tetanus 10 years ago. Now he presents with a clean wound without any lacerations from an injury sustained 2.5 hours ago. He should now be given : [AI 01]

a) Full course of tetanus toxoid
b) Single dose of tetanus toxoid
c) Human tet. globulin
d) Human tet. globulin and single dose of toxoid

4. True regarding pseudomembranous colitis are all except : [AI 00]

a) It is caused by Clostridium difficle
b) The organism is a normal commensal of gut
c) It is due to production of phospholipase A
d) It is treated by vancomycin

5. Most common organism responsible for gas, gangrene is : [AI 99]

a) Clostridium-perfringens
b) Clostridium-difficile
c) Clostridium tetani
d) Clostridium botulism

6. Most common organism, responsible for pseudo membranous colitis is : [AI 99]

a) Clostridium difficle
b) Clostridium botulism
c) Clostridium bifermentans
d) Clostridium histolyticum

7. All of the following statements about Botulism are true except : [AI 97]

a) Boutlism is caused by endotoxin
b) Honey ingestion causes infant botulism
c) Constipation is seen
d) Detection of antitoxin in the serum can aid in diagnosis

8. Swarming growth on culture is characteristic of which Gram-negative organism : [AI 95]

a) Clostridium welchi
b) Clostridium tetani
c) Bacillus cereus
d) Proteus mirabilis

9. An 18 year old male presented with acute onset descending paralysis of 3 days duration. There is also a history of blurring of vision for the same duration. On examination, the patient has quadriparesis with areflexia. Both the pupils are non-reactive. The most probable diagnosis is :

a) Poliomyelitis **[AIIMS 06]**
b) Botulism
c) Diptheria
d) Porphyria

10. A patient of Acute lymphocytic leukemia with fever and neutropenia devlops diarrhoea after administration of amoxicillin therapy, which of the following organism is most likely to be the causative agent ? [AIIMS 05]

a) Salmonella typhi
b) Clostridium difficle
c) Clostridium perfringens
d) Shigella flexneri

11. The following statement are true regarding botulism except : [AIIMS 03]

a) Infant boutlism is caused by ingestion of performed toxin
b) Cl botulinum A, B, E and F cause human disease
c) The gene for botulinum toxin is coded by bacteriophage
d) Cl. Bratii may cause botulism

Answer

1. d) Gas ... 2. d) Gas ... 3. b) Single ... 4. c) It is ... 5. a) Clostridium ...
6. a) Clostridium ... 7. a) Boutlism ... 8. d) Proteus ... 9. b) Botulism 10. b) Clostridium ...
11. a) Infant ...

12. A 10 year old boy following a road traffic accident presents to the casualty with contaminated wound over the left leg. He has received his complete primary immunization before preschool age and received a booster of DT at school entry age. All of following can be done except :

a) Injection of TT **[AIIMS 01]**
b) Injection of human antiserum
c) Broad spectrum antibiotics
d) Wound debridement and cleaning

13. The most effective way of preventing tetanus is :

a) Surgical debridement and toilet **[AIIMS 01]**
b) Hyperbaric oxygen
c) Antibiotics
d) Tetanus toxoid

14. All occurs in botulism except : [AIIMS 97]

a) Diplopia
b) Diarrhoea
c) Dysphagia
d) Dysarthria

15. Not true about Botulinum toxin : [PGI 07]

a. Short life span
b. Increased acetyl-choline release
c. Used for treatment in Blepharospasm, static and dyanmic wrinkles
d. Effective for 3-4 months
e. Irreversibly decreases Ach in NM junction

16. Gastro-intestinal enteritis necroticans caused by:

a. Cl difficile **[PGI 07]**
b. Cl. perfringens
c. Botulinum
d. C jejuni
e. Pseudomonas

17. True about clostridium tetani : [PGI 03]

a) It is gram +ve
b) Drum stick appearance
c) Grows in aerobic environment
d) It is gram –ve
e) Produces endotoxin

18. Naeglers reaction is shown by : [PGI 00]

a) Cl. Tetani
b) Cl. Botulinum
c) Cl. Perfringenes
d) Cl. Septicum

Answer 12. b) Injection ... 13. d) Tetanus ... 14. b) Diarrhoea 15. a and b 16. b) Cl. perfringens 17. a and b 18. c) Cl. Perfrin ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is d i.e. Gas gangrene producing strains of C. perfringes produces heat resistant spores

Ref. Ananthnarayan 7/e, p 249 - 255

- Gas gangrene is caused by Cl perfringens (***MC*** by type A), Cl novyi, Cl septicum, Cl. histolyticum.
  Others - Cl. sporogenes, Cl. fullax, Cl. bifermantans, Cl. Sordelli Cl. aerofoetidium and C. tertium.
- *Most important* toxin for gas gangrene is Alpha toxin = lecithinase which is responsible ***Naegler's Reaction***.
- Cl. perfringes is found in feces and contaminates the skin of perineum, buttocks, thigh.
- Its spores is used as remote indicator of fecal contamination of water.
- *Spores are usually destroyed within 5 minutes by boiling but those of food poisoning strains of Type A and certain type C strain resist boiling for several hours.*
- Spores are destroyed by autoclaving at 121^0C for 20 minutes.
- Spores are resistant to antiseptics and disinfectants in common use.

2. Ans. is d i.e. Gas is invariably present in the muscle compartments

Ref. Ananthnarayan 7/e, p 249; Harrison 17/e, p 906

- Clostridia are Gram positive (so produce exotoxin as endotoxin are usually produced by gram negative bacteria) spore forming anaerobic bacilli.
- Gas gangrene clostridia are already mentioned (Cl. botulinum doesn't cause gas gangrene).
- Gas gangrene is characterized by rapid and extensive necrosis of muscle, accompanied by gas formation (clinically as crepitations) and systemic toxicity.

3. Ans. is b i.e. Single dose of tetanus toxoid *Ref. Park 18/e, p 252; 19/e, p 263*

- Management of wound depend on nature of wound and immune status of person.
- All wounds should receive surgical toilet.

Category	*Immunization status*	*Clean wound of < 6 hrs. and with negligible tissue damage*	*Other wounds eg. (contaminated wound)*
A.	Complete immunization with in past 5yrs	Nothing	Nothing
B.	Complete immunization within 5 - 10 years	1 dose of toxoid	Toxoid 1 dose
C.	Complete immunization more than 10 years	Toxoid 1 dose	Toxoid 1 dose + Human Tet. Ig
D.	Has not had complete immunization or immunity status is unknown	Toxoid complete course	Toxoid complete course + Human Tet Ig

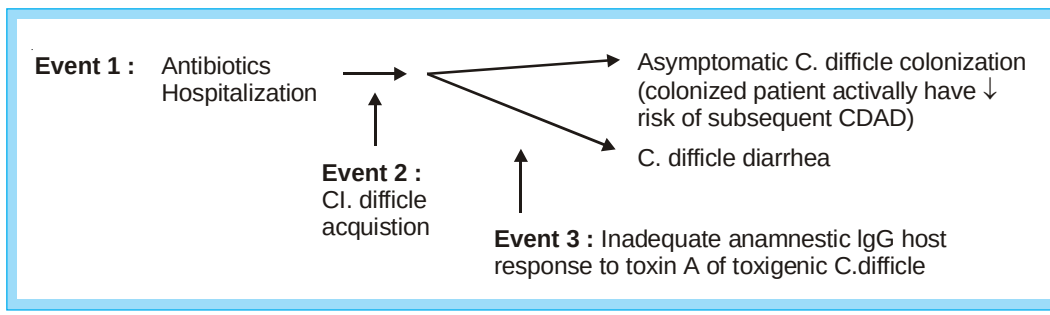
Patient in question falls in category B.

4. Ans. is c i.e. It is due to production of phospholipase A

Ref. Harrison 17/e, p 819; Ananthnarayan 7/e, p 265

"Cl difficle cause pseudomembranous colitis (PMC) due to the production of toxin A (enterotoxin) and toxin B (cytotoxin) not phospholipase A."

- Toxin A is potent neutrophil chemoattractant and both toxin A and B glucosylate the GTP binding protein of Rho subfamily resulting in disruption of cytoskeleton causing loss of cell shape adherance with consiquent fluid leakage.
- Asymptomatic fecal carriage of Cl difficle in healthy neonates is very common. It also colonizes the colon of 3% of healthy adults. *..... CMDT' 08, p 543*
- For Cl difficle associated diarrhea (CDAD) three events are essential :



Diagnosis

- Diagnosis of CAD is based a combination of clinical criteria :
  - Diarrhea (≥ 3 unformed stools per 24 hours for > 2 days)
  - Toxin A or B detected by stool culture or pseudomembrane seen in colon.
- Endoscopy is a rapid diagnostic tool in seriously ill patient with suspected PMC but a negative result does not rule out CDAD.
- **Treatment :** Discontinue offending antibiotic
  - ***DOC*** – Metronidazole
  - ***DOC*** – For relapse Metronidazole
  - If not respond > 48 hrs, give Vancomycin.

5. Ans. is a i.e. Cl. Perfringens *Ref. Ananthnarayan 7/e, p 225*

MC cause of gas gangrene is Cl. perfringes type A.

6. Ans. is a i.e. Cl difficle *Ref. Ananthnarayan 7/e, p 265*

Already explained, please see answer no. 4

7. Ans. is a i.e. Botulism is caused by Endotoxin *Ref. Ananthnarayan 7/e, p 263*

- Cl. botulinum produce exotoxin (since endotoxin is usually produced by gram negative bacteria) which differs from other exotoxin in that it is produced intracellularly and appears in the medium only on death/ autolysis of cell.
- Toxin production is determined by bacteriophage at least in types C and D toxin.

- All toxin are neurotoxin except C_2 which is cytotoxin.
- Toxin acts by blocking production or release of Ach. at synapse and Neuromuscular junction (= parasympatholytic = effect of atropine) so cause constipation, paralysis etc.
- Human disease is caused by type A, B, E and rarely F.
- ***MC*** Type of botulism is 'Infant botulism' which is produced by eating of honey containing spores so toxin is produced inside.
- *Food borne botulism and wound botulism are produced by preformed toxin.*
- Diagnosis may be confirmed by demonstration of bacillus or toxin in food or feces.
- A retrospective diagnosis may be made by detection of antitoxin in the patient serum but it may not be seen in all cases.

8. Ans. is d i.e. Proteus mirabilis *Ref. Ananthnarayan 7/e, p 257, 283; Jawetz 24/e, p 207*

Swarming growth is shown by :

a. Cl. tetani, Bacillus cereus – Gram positive bacilli
b. Proteus mirabilis and Proteus vulgaris – Gram negative bacilli.

9. Ans. is b i.e. Botulism *Ref. Harrison 17/e, p 902; Madell's infectious disease 6/e, p 2824*

Diagnosis of boutulism should be considered in patient with symmetric descending paralysis with bilateral cranial neuropathies in addition of following features :

- Absent fever
- Patient remain responsive
- Heart rate normal or slow
- Sensory deficit don't occur except for blurred vision.

Remember : Neurologic signs and symptom of botulism :

- Dysphagia
- Dysarthria
- Blurred vision
- Dry mouth
- Upper limb weakness
- Dyspnea
- Diplopia
- Lower limb weakness

Also know : Polio present with asymmetric descending paralysis.

10. Ans. is b i.e. Clostridium difficle *Ref. Harrison 17/e, p 818 - 820, 761; KDT 6/e, p 672 - 673*

- It is a typical presentation of CDAD (Cl. difficle associated diarrhoea).
- ***MC*** antibiotics causing CDAD - clindamycin, ampicillin and cephalosporins.
- Antibiotics altered the normal intestinal flora which allows overgrowth of non-pathogenic organism. This called as superinfection.
- Superinfection also occur by candida albicans, resistant staphylococci, Proteus and Pseudomonas.
- Superinfections are common when host defence is compromised as in steroid therapy, Leukemia and other malignancies treated with anticancer drugs, AIDS, agranulocytosis, Diabetes.

11. Ans. is a i.e. Infant boutlism is caused by ingestion of preformed toxin

Ref. Ananthnarayan 7/e, p 263; Harrison 17/e, p 901

- Infant botulism is caused by ingestion of spores which produce toxin in gut.
- Most of these infants recover with supportive therapy alone.
- Spores of botulinum is highly resistant to heat, withstand 100^{0}C for several hours.

12. Ans. is b i.e. Infection of human antiserum *Ref. Park 18/e, p 252; 19/e, p 263*

"According to table given in** Answer 3, **this child belongs to category B of other wounds since wound is contaminated and child received booster at school entry (so booster > 5 year but < 10 year)."

So, Human antiserum is not needed.

13. Ans. is d i.e. Tetanus toxoid *Ref. Park 18/e, p 252; 19/e, p 263*

Remember :

Best way of prevention	=	Active immunization	=	TT
Best passive immunization	=	Antitoxin	=	Human tetanus immunoglobulin.

14. Ans. is b i.e. Diarrhoea *Ref. Ananthnarayan 7/e, p 264*

"Botulism toxin act as parasympatholytic so it cause severe constipation not diarrhoea."

- Also produce vomiting, thirst, ocular paresis, difficulty in swallowing/ speaking/ breathing.

15. Ans. is a and b *Ref. CMDT '08, p 893; Jawetz 24/e, p 207*

Botulinum toxin decrease the release of acetylcholine by proteolysis of SNARE proteins. The SNARE proteins are synaptobrevin SNAP-25 and syntaxin. The toxin of C.botulinum types A and E cleaves SNAP-25 while type B toxin cleaves synaptobrevin.

- Though botulinum toxin is the most lethal toxin known (lethal dose 1-2 μg) it is used therapeutically for many conditions.

Therapeutic uses of Botulinum toxin

Muscular disorders	Ophthalmic disorders
Myoclonus	Strabismus
Palatal myoclonus	Lower lid entropion
Focal dystonias	Aquired Nystagmus
Tics, tremor	Thyroid ophthalmopathy
Hemi-facial spasm	Dwayne's syndrome
Tourette's syndrome	Oscillopsia
Synkinesia	Apaxia of eye lid opening
Tardive disroders	Hyper-lacrimation
Rigid akinetic syndromes	
Parkinson's Progressive supranuclear palsy	
Hallovorden Spatz	
Stiff person syndrome	

Plastic surgery	Otolaryngology
Wrinkles Masseter hypertrophy Facial asymmetry (post Bells) Muscle flap paralysis druing healing	Vocal cord polyps Stutterin Hypersalivation
Genitourinary	**Gastroenterology**
Detrusor - sphincter dyssynergia Vaginismus	Achalasia Cricopharyngeal spasms Rectal fissures
Rehabilitation Medicine	
Disorders of Painful Muscular Spasm Spasticity : Focal myofascial pain TMJ associated muscle spasm.	

Note : Botulinum toxin once bound leads to permanent dysfunction of that neuron. Recovery (or duration of action) takes 10-20 weeks (usually 3 months) when dysfunctioned nerve terminals are replaced as a result of sprouting.

16. Ans. is b i.e. Cl. perfringens *Ref. Harrison 17/e, p 904*

"Necrotizing enteritis (enteritis necroticians, or pig bel) is caused by β toxin produced by type C strains of C.perfringens following ingestion of a high protein meal in conjunction with trypsin inhibitors by a susceptible host who has limited intestinal proteolytic activity". Source of organism is patient own intestinal flora.

Clinical features

- Acute abdominal pain, diarrhea, vomiting, shock and peritonitis, 40% of patient die.
- Pathological studies shows an acute ulcerative process of the bowel restricted to small intestine.

17. Ans. is a and b i.e. It is gram +ve; and Drum stick appearance *Ref. Ananthnarayan 7/e, p 250*

- Clostridium is obligatory anaerobic gram positive spore bearing bacilli.
- **Spores of Clostridia :**

Spherical and terminal spore *(=Drum stick appearance)*	***Oval and terminal*** *(= Tennis racket)*
– Cl. tetani – Cl. tetanomorphum – C. sphenoides	– Cl difficle – Cl tertium – Cl. cochleurum
Others **:** Have either central (spindle shape) or sub terminal (club shaped) spores.	

18. Ans. is c i.e Cl. perfringes *Ref. Ananthnarayan 7/e, p 251*

Naeglers reaction is due to α toxin = lecithinase C = Phospholipidase
So, given by Cl. perfiringes.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Pseudomembranous colitis is caused by :
a) Cl. welchii **[AI 91]**
b) Cl. difficle
c) Yersinia enterocolitis
d) Pseudomonas
[Ref. Ananthnarayan 7/e, p 251]

2. Botulinum toxin acts on : [AI 92]
a) Sympathetic system
b) Parasympathetic system
c) Amygdala
d) Motor cortex
[Ref. Ananthnarayan 7/e, p 263]

3. Swarming growth is seen in which gram positive bacilll : [AI 95]
a) Cl. welchii
b) Cl. tetani
c) Proteus
d) Bacillus cereus

4. Opacity around colonies of clostridium perfringes is due to : [JIPMER 95]
a) Theta toxin
b) Lecithinase
c) Desmolase
d) Cytokinin
[Ref. Ananthnarayan 7/e, p 251]

5. Crepitus in a wound is produced by : [AMU 97]
a) Staph aureus
b) Clostridium tetani
c) Clostridiulm-welchii
d) Pseudomonas
[Ref. Ananthnarayan 7/e, p 255]

6. Among the toxin produced by botulinum, the non neurotoxic one is: [Kerala 00; AIIMS 92]
a) A
b) B
c) Cl.
d) C2
e) D *[Ref. Ananthnarayan 7/e, p 263]*

7. Drumstick appearence is seen in :
a) Cl. tetani **[Keral 00, Orissa 00]**
b) Cl. tetanomorphum
c) Cl. sphenoids
d) All of the above
[Ref. Ananthnarayan 7/e, 250]

8. Foomy liver is caused by : [UP 00]
a) Clostridium tetani
b) Clostridium welchii
c) Pseudomonas
d) Staph aureus
[Ref. Ananthnarayan 7/e, p 255]

9. Gas gangrene is caused by : [Kar 01]
a) Clostridium tetani
b) Clostridium difficle
c) Clostridium perfringens
d) Peptostreptococci
[Ref. Harrison 17/e, p 903]

10. Oval bulging terminal spores seen in :
a) Cl. tertium **[UP 04; M.P. 03]**
b) Cl. welchii
c) Cl. perfringes
d) Cl. histolyticeen
[Ref. Ananthnarayan 7/e, p 250]

11. Each of the following statements concerning Clostridium perfringes is correct except :
a) It causes gas gangrene **[SGPGI 04]**
b) It causes food poisoning
c) It produces an exotoxin
d) It is a gran negative rod that does'not ferment lactose
[Ref. Ananthnarayan 7/e, p 250 - 252]

Answer
1. b) Cl. difficle
2. b) Parasympathetic
3. b) Cl. tetani
4. b) Lecithinase
5. c) Clostridiulm ...
6. e) D
7. d) All of the ...
8. b) Clostridium ...
9. c) Clostridium ...
10. a) Cl. tertium
11. d) It is a gran ...

12. Diagonsis of tetanus is made by : **[MP 05]**

a) Culture of bacteria from wound
b) Clinically
c) Four fold raise in antibody against tetanus toxin
d) Gram staining of biopsy from wound

[Ref. Ananthnarayan 7/e, p 260]

13. The organism causing pseudomembranous colitis : **[DNB 05]**

a) Clostridium difficile
b) Clostridium perfringens
c) Clostridium tetani
d) Clostridium botulium

[Ref. Ananthnarayan 7/e, p 265]

14. Non motile clostridia is : **[UP 06]**

a) Cl. perferingens
b) Cl. novyi
c) Cl. botulism
d) Cl. difficle

[Ref. Ananthnarayan 7/e, p 249]

15. Site of action of tetanus toxin : **[UP 07]**

a) Presynaptic terminal of spinal cord
b) Postsynaptic terminal of spinal cord
c) Neuromuscular junction
d) Muscle fibres

[Ref. Ananthnarayan 7/e, p 259]

Answer 12. b) Clinically 13. a) Clostridium ...
14. a) Cl. perferingens 15. a) Presynaptic ...

5 Corynebacterium

Gram positive non-motile rods with *high G+C (guanine + cytosine)* content.

It includes : C. diphtheria, C. ulcerans and other coryneform bacteria like Arcanobacterium, Rhodococcus.

CORYNEBACTERIUM DIPHTHERIAE (KLEBS- LOFFLER BACILLUS)

Morphology

- Characteristically ***club shaped*** pleomorphic, non capsulated, nonsporing bacilli.
- Arranged in pairs, palisades, clusters *(chinese letter or cuneiform arrangement).*
- Contain Granules known as *Babes Ernst or volutin granules* which are composed of polymetaphosphate and are ***more strongly Gram positive.***
- On staining with *Loeffer's methylene blue,* granules show *metachromatism.*
- Special stain to see granules clearly – Albert's, Neisser's and Ponder's. Granules are also called as *polar bodies* since arranged on poles.

Culture

- Enrichment is necessary.
- *Selective medium* : ***Cysteine - Tellurite blood agar (grow in 2 days) or Tinsdale*** medium.
- For rapid growth (6 - 8 hours) - ***Loeffler's serum slope*** used (also used for Mycobacteria TB).
- Mcleod classified it into 3 types :

Feature	*C. gravis*	*C. intermidius*	*C. mitis*
• *Colony on tellurite*	Daisy head	Frog's Egg colony	Poached egg colony
• *Hemolysis*	Variable	Non hemolytic	Usually hemolytic
• Glycogen and starch fermentation	Positive	Negative	Negative
• *Most common Complication*	Paralytic and Hemorrhagic	Hemorrhagic	Obstructive lesion in air passage

Diptheria Toxin

- *Polypeptide exotoxin,* production depends on iron concentration.
- Composed of 2 fragments : Fragment. B for binding and fragment A (enzymatic activity) for inactivating EF-2 in presence of NAD. Hence, *inhibits protein synthesis.*
- Toxin is inactive when it is released by bacteria.

- Toxin acts both locally and systemically (mainly) while bacilli remain localized. Hence Diphtheria is *toxemia not bacteremia.*
- Corynephage controls production of toxin, Hence it shows *lysogenic or phage conversion.*
- The strain almost universally used for toxin production is the *'Park William 8' Strain.*
- Exotoxin is also produced by C. ulcerans, C. pseudotuberculosis.
- Both tox + and Tox - strains are infectious.

Clinical features

- Cause diphtheria which is localized infection of mucous membrane or skin. It primarily involves respiratory tract.
- Diphtherias are of following types :
  1. ***Respiratory Diphtheria***
     - ***MC*** type Tonsillo pharyngeal (Faucial)
     - ***MC*** symptoms - Fever, sore throat and weakness.
     - Also cause malignant or hypertoxic or bull neck appearance
     - ***Complications of Respiratory Diphtheria***
       - Mechanical complication (Asphyxia) due to membrane.
       - Systemic effects due to toxin eg myocarditis, peripheral polyneruopathy of descending type.
       - Risk is greater when involves larynx or tracheobroncial tree and in children (because of small airway size).
       - Neurologic complication appear during first or second week of illness and begins with dysphagia.
       - Cardiac damage is permanent while recovery of nerve damage is the rule.
       - 1st muscle involve in paralysis - palatopharynges.
       - Cilliary paralysis occur but not pupillary paralysis i.e. blurred vision with preserved light reflex.
     - Cause of death is circulatory failure.
  2. ***Cutaneous Diptheria*** – Punched out ulcers commonly caused by non-toxigenic strains (tox-).
  3. ***Invasive infection*** – (Rare) Risk factors are prexisting cardiac abnormality, IV drug abusers, alcoholic cirrhosis.

Diagnosis

- Diagnosis of respiratory diphtheria is usually clinical while cutaneous diptheria requires lab confirmation.
- Lab diagnosis can be either by demonstration of organism or demonstration of toxignicity by in vivo or in vitro test.

a. Demonstration of organism

- By Gram staing of throat swab.
- Culture in specified media

b. Test for toxicigenicity

In vivo	In vitro
• Done on guinea pigs can be intra-cutaneous or subcutaneous	• Elek's gel ppt. test • PCR for detection of toxgene • ELISA • Immunochromatographic strip assay (fastest,with in hours)

... Jawetz 24/e, p 216

Treatment

- Most important element in treatment of respiratory diphtheria.
  - Antitoxin but it does not prevents colonization nor eradicates carrier state.

- Antibiotics ***DOC*** Erythromycin or procaine pencillin G. Alternative is Rifampicin or clindamycin.
- Sedatives or hypnotics are contraindicated.
- Glucocorticoids do not reduce the risk of myocarditis or polyneuropathy.

Prevention

- Active immunisation by Toxoid is best method to prevent diphtheria. Though active immunisation can prevent manifestion of Diphtheria, it can not prevent carrier stage.
- Active immunisation - Combined DPT is used most commonly.
- Pertusis component in DPT increase potency of Diphtheria toxoid.
- Toxoid of Diptheria shows Danysz phenomenon and Ehrlich phenomenon.

SCHICK TEST

Intradermal test which provide information regarding :

a. Immune status
b. Hyper senstivity to diptheria toxin.

In one arm toxin is injected, in other arm heat inactivated toxin is injected and following reaction may be seen.

a. ***(–)ve reaction –*** No reaction in both arm Shows patient is immune to diphtheria.
b. ***+ ve reaction –*** Red flush of 10 - 50 mm with in 24 - 36 hours, reaching its maximum by 4^{th} to 7^{th} day. Control arm shows no change. Patient is susceptible to diphtheria.
c. ***Pseudo-positive reaction –*** Red flush equally on both arm, reaction fades very quickly. This is an allergic type of reaction interpeted as Schik's negative.
d. ***Combined reaction –*** Test arm shows (+)ve, and control arm shows pseudo (+)ve. Dose of vaccine should be reduced.

C.ULCERANS

- Transmitted by cow's milk, usually present as pharyngitis and can mimic respiratory diphtheria.

C. PSEUDOTUBERCULOSIS *(=Preisz Nocard bacillus)*

- Typically present as suppurative granulamatous lymphadenitis.

C. MINUTISSIMUM

- Cause *Erythrasma* and exhibits coral-red fluorescene under wood's light.

C. PARVUM

- Used as immunomodulator.

DIPHTHEROIDS

- Normal commensals, stain more uniformly with few or no metachromatic granules eg. C.pseudodiphtheriticum.

QUESTIONS

1. The following statements are true about DPT vaccine except : [AI 04]
a) Aluminium salt has an adjuvant effect
b) Whole killed bacteria of Bordetella pertussis has an adjuvant effect
c) Presence of acellular pertusis component increases its immunogenecity
d) Presence of H.influenza type B component increases its immunogenecity

2. Positive shick's test indicates that person is :
a) Immune to diphtheria [AI 02]
b) Hypersensitive to diptheria
c) Susceptible to diptheria
d) Carrier of diptheria

3. A child presents with a white patch over the tonsils; diagnosis is made by culture in : [AI 01]
a) Loeffler medium
b) LJ medium
c) Blood agar
d) Tellurite medium

4. True about corynebacterium diptheria are all except : [AI 98]
a) Iron is required for toxin production
b) Toxin production is responsible for local reaction
c) Nonsporing, noncapsular and non motile
d) Toxin production is by lysogenic conversion

5. True statement regarding diptheria is : [AI 97]
a) It can be diagnosed by demonstration of antibodies by ELISA
b) Immunization prevents carriers state
c) Treatment of contacts is not indicated
d) Iron has critical value in the production of toxin

6. True about corynebacterium diptheria includes all of the following except : [AIIMS 07]
a) Deep invasion is not seen
b) Elek's test is done for toxigenicity
c) Metachromatic granules are seen
d) Toxigenicity is mediated by chromosomal change

7. Positive Shick's test indicates that the person is:
a) Immune to diptheria [AIIMS 07]
b) Hypersensitive to diptheria
c) Susceptible to diptheria
d) Susceptible and hypersensitive to diphtheria

8. In a completely and adequately immunized child against Diptheria, the throat swab was collected. It showed the presence of C.diptheriae organisms on Albert staining. These organisms can have one of the following properties on further processing : [AIIMS 04]
a) It can grow on potassium tellurite media
b) It would show a + ve Elek's gel precipitation test
c) It can be pathogenic to experimental guinea pig
d) It can produce cytotoxicity in tissue culture

9. A 12 year old child presents with fever and cervical lymphadenopathy. Oral examination shows a grey membrane on the right tonsil extending to the anterior pillar. Which of the following medium will be ideal for the culture of the throat swab for a rapid identification of the pathogen :
a) Nutrient agar [AIIMS 02, 99]
b) Blood agar
c) Loeffler's Serum slope
d) LJ Medium

10. Regarding Schik's test which of the following is false : [AIIMS 00]
a) Erythematous reaction in both arms indicate hypersenstivity
b) Positive test means that person is immune to diptheria
c) Diptheria antitoxin is given intradermally
d) Test done to find out immune status against diptheria

11. A child with fever and pharyngitis which of the following investigation should not to be done:
a) Widal test [AIIMS 00]
b) ASO
c) Throat swab and culture
d) Chest x-ray

12. Investigation of choice of diptheria carrier is :
a) Throat swab culture [AIIMS 97]
b) Gram's stain
c) Albert's stain
d) Zeil Nelson's stain

13. All are true regarding diptheria toxin except :
a) Toxin blocks elongation of protein [AIIMS 97]
b) Beta lysogenic strain produces toxin
c) Iron is critical for toxin production
d) Toxin is necessary for local wound production

14. Which of the following is true about Diptheria except : [PGI 05]
a. Faucial diptheria is more dangerous than laryngeal diptheria
b. Laryngeal diptheria mandates tracheostomy
c. Child is infectious with faucial diptheria
d. Myocarditis may be a complication
e. Palatal paralysis is irreversible

Answer

1. d) Presence ...	2. c) Susceptible ...	3. a) Loeffler ...	4. b) Toxin ...	5. d) Iron ...
6. d) Toxigenicity ...	7. c) Susceptible ...	8. a) It can ...	9. c) Loeffler's ...	10. b) Positive ...
11. a) Widal ...	12. a) Throat ...	13. d) Toxin ...	14. a and e	

15. Metachromatic granules are found in : [PGI 00]

a) Diptheria
b) Mycoplasma
c) Gardenerella vaginalis
d) Chlamydia
e) Staphylococcus

16. Corynebacterium diptheriae can be grown within 6-8 hours on : [PGI 98]

a) Potassium tellurite media with iron
b) McConkey's agar
c) Dorset egg medium
d) Loeffler's serum slope

Answer 15. a) Diptheria 16. d) Loeffler's ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is d i.e. Presence of H.influenza type B component increases its immunogenecity

Lets consider each choice one by one.

Option 'a' : Two types of Diphtheria toxoid are in use now. *... Ananthnarayan 7/e, p 238*

1. Fluid toxoid
2. Adsorbed toxoid

Adsorbed toxoid is purified toxoid adsorbed into insoluble aluminium compounds *usually aluminium phosphate* less often the hydroxide.

Adsorbed toxoid is much more immunogenic than fluid toxoid.

Option 'b' : Pertussis component in DPT (whole killed bacteria of bordetella pertusis) vaccine enhances the potency of the diptheria toxoid. *... Park 18/e, p 135*

Most serous complication of DPT is neurological which is primarily due to pertusis component.

Duration of immunity after whole cell pertusis vaccination is short lived, with little protection remaining after 10-12 years.

Option 'c' : To reduce complications of whole killed bacteria of pertusis in DPT, acellular vaccine developed.

- Protection against pertussis by vaccines correlated best with the production of antibody to pertactin, fimbriae and pertussis toxin.
- All acellular pertussis vaccines currently available contain pertussis toxoid.

Acellular vaccine is more immunogenic has less adverse effects. It is given as DTaP.

.... CMDT '06, p 1304

Option 'd' : Quadriple vaccine of DPT with H.influenza B is available in India but conjugate vaccine (eg. HIb vaccine) do not interfere with immunogenicity of simultaneously given other vaccines.

.... Ghai 6/e, p 197

2. Ans. is c i.e. Susceptible to diptheria *Ref. Ananthnarayan 7/e, p 237; Park 19/e, p 137*

Shick's test

- Intradermal test which provide information regarding :

  a. Immune status, b. Hypersensitivity & susceptibility to diptheria toxin before giving active immunization.
- In one arm toxin is injected (test arm) and in other arm heat inactivated toxin is injected (control arm).

Type of Reaction	Observation	Inference
i. *Negative reaction*	No reaction in both arm (toxin is neutralized by circulating antitoxin)	No susceptibility. No hypersensitivity Patient is immune to diptheria
ii. *Positive reaction*	No change in control arm. Red flush in test arm that persist	No hypersensitivity Susceptibility present
iii. *Pseudo positive reaction* (Schick's negative)	Red flush equally on both arm that fades very quickly	Hypersensitivity present No susceptibility
iv. *Combined reaction*	Test arm shows positive and control arm shows pseudo-positive reaction	Hypersensitivity present Susceptibility present Dose of vaccine should be reduced

Remember :
- Antitoxin level of 0.01 unit or more per ml of blood is considered as index of immunity.
- Shick's test is no longer in use. The level of antitoxin, is assesed by passive hemagglutination or by neutralization in cell culture.

3. Ans. is a i.e. Loeffler medium *Ref. Ananthnarayan 7/e, p 231 - 232*

In a child white patch over tonsils, probable diagnosis is of Diphtheria.

Culture media for corynebacterium are :

i. *Loefflers serum slope :* Growth is very rapid and colonies *seen in 6-8 hrs*, before other bacteria grows. It is also used for M. tuberculosis. Diptheria is emergency condition, so Loeffler's slope is prefered media in this child.

ii. *Tellurite blood agar media :* Selective media but growth is delayed and may take about 2 days to appear.

Remember :
- LJ media, is for Mycobacteria TB.
- Mcleods and Hoyle's are modified Tellurite media.
- Blood agar is used to differentiate Staph. and Sterpt. pharyngitis.

4. Ans. is b i.e. Toxin production is responsible for local reaction

Ref. Ananthnarayan 7/e, p 233 - 235; Jawetz 24/e, p 215

"Mechanical complications of diptheria are due to the membrane while the systemic effects are due to the toxin."

- Toxin acts *mainly systemically though there are partial local effects.*
- It has affinity for myocardium, adrenals and nerve endings.
- Toxin acts by inactivating EF-2 *thus inhibiting protein synthesis.*
- Toxin production is influenced by ***iron*** concentration in the medium. Toxin production is optimal at 0.14 μg/ml and is suppressed at 0.5 μg/ml.
- Toxigencity of diptheria bacullus depends on symbiotic bacteriophages so it shows *lysogenic or phage conversion* i.e. nontoxigenic strain → toxigenic strain by infecting with beta phage.

Remember :
- Corynebacteria are gram positive, non acid fast, non sporing, non capsulated, non motile bacteria.
- It contains polar bodies or volutin or babes-ernst or metachromatic granules of polymetaphosphate which are more gram positive.
- Granules are also stained by loeffler's methylene blue, Albert's, Neisser's and ponder's stain.

5. Ans. is d i.e. Iron has critical value in the production of toxin

Ref. Ananthnarayan 7/e, p 234 - 236; Jawetz 24/e, p 216

Diagnosis of Diptheria

i. *Isolation by culture :*

Swabs are inoculated on :

– Loeffler's serum slope (growth is rapid) : for rapid diagnosis.

– Tellurite blood agar (growth is delayed but it is particularly important in isolation of bacilli from

convalescent, contacts, carriers) : Selective media.

– Blood agar (for differentiating staphylococcal and streptococcal pharyngitis).

ii. ***Demonstration of toxicity of isolated strain :***

In vivo test **–** done by infected broth emulsion of culture subacutaneously and intracutaneously into guinea pigs.

In vitro test **–** Elek's gel precipitation test and tissue culture test on agar overlay of cell culture monolayer.

Control of Diptheria

i. ***Cases*** – Antitoxin + penicillin or erythromycin *... Park 19/e, p 137*

ii. ***Carriers*** – Erythromycin

iii. ***Contacts*** – a. When primary immunization or booster dose was received within the previous 2 years.
- No further treatment.

b. When primary immunization or booster dose was received more than 2 years ago.
- Only a booster dose of diphtheria toxoid.

c. Non immunized close contacts :
- Prophylatic penicillin or erythromycin
- 1000 - 2000 units of diphtheria antitoxin
- Active immunization against diphtheria.

iv. ***Community*** – Only effective control is by active immunization with diphtheria toxoid of all infants with subsequent booster doses every 10 years thereafter.

Remember : Vaccine 'being a toxoid' is not directed against organism and hence ***immunization does not prevent carrier state which is due to organism not due to toxin.***

6. Ans. is d i.e. Toxigenicity is mediated by chromosomal change *Ref. Harrison 17/e, p 890*

"Corynebacteriophage beta carries the structural gene (tox^+) encoding diptheria toxin and a family of closely related corynebacteriophage are responsible for toxigenic conversion of tox^- C.diptheria to tox^+ phenotype."

- Elek's gel precipitation test is in vitro test for toxin detection.

7. Ans. is c i.e. Susceptible and hypersensitive to diphtheria *Ref. Ananthnarayan 7/e, p 237*

Already explained, refer answer no. 2

8. Ans. is a i.e. It can grow on potassium tellurite media *Ref. Ananthnarayan 7/e, p 235*

This child is carrier of diptheria.

- Postassium tellurite is selective media for isolation of diptheria bacillus from convulescent contact, carriers.
- Other three test are done for testing virulence only when isolated strain is C.diptheria.

9. Ans. is c i.e. Loeffler's Serum slope *Ref. Ananthnarayan 7/e, p 235*

Already explained, refer see answer no. 3

10. Ans. is b i.e. Positive test means that person is immune to diptheria

Ref. Park 19/e, p 137; Ananthnarayan 7/e, p 236

Already explained, refer asnwer no. 2

11. Ans. is a i.e. Widal test *Ref. Ananthnarayan 7/e, p 235*

Widal is test for diagnosing Typhoid which is not a cause of pharyngitis so there is no need to perform widal in this child.

12. Ans. is a i.e. Throat swab culture *Ref. Park 19/e, p 136*

- Carriers can be detected only by cultural method.
- Swab should be taken from both the nose and throat.

13. Ans. is d i.e. Toxin is necessary for local wound production *Ref. Ananthnarayan 7/e, p 235 - 236*

Already explained, refer answer no. 4

14. Ans. is a and e i.e. Faucial diptheria is more dangerous than laryngeal diptheria; and Palatal paralysis is irreversible *Ref. Dhingra 3/e, p 348*

Diptheria

- ***Causative agent*** – Corynebacterium diptheriae (Gr+ve bacillus)
- ***Incubation period*** – 2 - 6 days
- ***Depending on site present as :***
  - Nasal diptheria - Mildest, Toxemia is minimal.
  - Faucial diptheria (most common) = Nasopharyngeal diptheria - More severe than nasal diptheria.
  - Laryngotracheal diptheria - Most severe, maximum obstructive symptom, tracheostomy may be essential.
- ***Complications :***
  - Myocarditis - Occurs towards the end of 1st or begining of 2nd week.
  - Peripheral neuropathy of descending type.
  - Renal failure.

Remember : Cardiac damage is permanent while recovery of nerve damage is rule.

15. Ans. is a i.e. Diptheria *Ref. Ananthanrayan 7/e, p 231*

Metachromatic granules

- It is type of ***intracytoplasmic*** inclusions characteristically seen in diptheria bacilli.
- Also known as *volutin* or *metachromatic* or *Babes Ernst granules.*
- Strongly ***basophilic*** bodies consist of polymetaphosphate.
- They are reservoir of energy and phosphate.

- They are most frequent in cells growing under nutritional deficient condition.

Remember :
- Dorset egg media is for M. tuberculosis.
- MacConkey is for differentiating between lactose and Non-lactose fermenters of Enterobacteriacea.
- Metachromatic granules also seen in B.pertusis.

16. Ans. is d i.e. Loeffler's serum slope *Ref. Ananthnarayan 7/e, p 231*

Already explained, refer answer no. 3

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. One of the following about corynebacterium diptherias is wrong : [Kerala 91]

a) Gram negative
b) Ernest babes granules seen
c) Chinese letter pattern
d) Prevented by immunisation

[Ref. Ananthnarayan 7/e, p 231]

2. Tellurite stimulates growth of : [Kerala 91]

a) E. coil
b) Cl. tetani
c) Corynebacterium diptheriae
d) Salmonella

[Ref. Ananthnarayan 7/e, p 232]

3. Growth on a cell-free artifical solid medium is possible for following except : [TN 92]

a) Ureaplasma urealyticum
b) Mycoplasma Pneumoniae
c) C and L form of proteus vulgaris
d) Chalmydia

[Ref. Ananthnarayan 7/e, p 423]

4. Effective vaccine is available against :

a) Staphylococcus aureus **[Kerla 94]**
b) Streptococcus
c) Pneumococcus
d) Gonococcus

[Ref. Ananthnarayan 7/e, p 221]

5. Elecks gel precipitation test is for : [Delhi 96]

a) Gonococcus
b) Diptheria
c) H. influenza
d) Anthrax

[Ref. Ananthnarayan 7/e, p 236]

6. True about diptheria is : [MP 98]

a) Loffler's serum is highly selective medium for C. diphtheria
b) Elecks's Gel is a precipitation test
c) Metachromatic granules is produced on stain only by one strain of C. deptheria
d) Gm -ve bacilli, non motile, non capsuhlated

[Ref. Ananthnarayan 7/e, p 236]

7. Culture medium for corynebacterium diphtheria:

a) Loefflers serum slope **[JIPMER 01]**
b) McConkey
c) Sabarauds agar
d) Lowenstein Jensen medium

[Ref. Ananthnarayan 7/e, p 235]

8. The type of Diphtheria with highest mortality is :

a) Pharyngeal **[JIPMER 00]**
b) Nasal
c) Laryngeal
d) Conjuctival

[Ref. Harrison, 17/e, p 893]

9. Erythrasma is caused by: [SRMC 02]

a) S.pyogenes
b) Corynebacterium miniutisonium
c) S aureus
d) Ricketessiae

[Ref. Ananthnarayan 7/e, p 240]

10. Literally leather term is used for : [UP 03]

a) Anthrax
b) Proteius
c) Diptheria
d) Neiserria

[Ref. Ananthnarayan 7/e, p 234]

Answer

1. a) Gram negative	2. c) Corynebac ...	3. d) Chalmydia	4. c) Pneumococcus	5. b) Diptheria
6. b) Elecks's ...	7. a) Loefflers ...	8. c) Laryngeal	9. c) S aureus	10. a) Anthrax
11. b) Treatment ...	12. a) Ponder's ...	13. a) 100 MLD ...	14. a and c	15. a) Corynebac ...

11. True about diphtheria is : **[SGPGI 03]**

a) Cause cranial nerve palsies in 2nd and 3rd week
b) Treatment with erythromycin
c) It is Gram negative organism
d) Passive immunization is harmful and should not be tried

[Ref. Harrison 17/e, p 890-893]

12. Metachromatic granules are stained by :

a) Ponder's stain **[JIPMER 03]**
b) Negative stain
c) Gram's stain
d) Leishmans stain

[Ref. Ananthnarayan 7/e, p 231]

13. One unit of diptheria antitoxin was defined as the smallest amount of antitoxin required to neutrilise:

a) 100 MLD of toxin **[SGPGI 04]**
b) 200 MLD of toxin
c) 300 MLD of toxin
d) 400 MLD of toxin

[Ref. Ananthnarayan 7/e, p 238]

14. Toxigenicity of C. diphtheria is determined by :

a) Elek's gel ppt test **[Bihar 04]**
b) Aselole's reaction
c) Nagler's reaction
d) All

[Ref. Ananthnarayan 7/e, p 236]

15. KLB another name is : **[Jharkhand 04]**

a) Corynebacterium diphtheria
b) Corynebacterium psudodiptheriae
c) Clostridia tetanae
d) Anthrax

[Ref. Ananthnarayan 7/e, p 231]

Answer 11. b) Treatment ... 12. a) Ponder's ... 13. a) 100 MLD ...
14. a and c 15. a) Corynebac ...

6 Actinomycetes & Bacillus

ACTINOMYCETES

- Transitional forms between bacteria and fungi.
- Gram positive, non motile, non sporing, non capsulated filaments.
- It includes : a. Actinomyces
  b. Nocardia.

Actinomyces

- Anaerobic bacillus cause : Lumpy jaw (in cattle) and Actinomycosis in human.

Actinomycosis

- **It is endogenous** infection since actinomyces normally present in mouth, intestine, vagina.
- ***MC*** causative agent A. israelii.
- Usually a cooperative disease.
- Characterized by indurated swelling (mainly in connective tissue), suppuration, multiple sinsuses towards skin with discharge of sulphur granules.

Types of Actinomycosis :

- ***MC type* cervico facial**
  - ***MC* site** of cervicofacial is lower jaw often adjacent to carious tooth. No lymph node involvement.
- **Abdominal** – Usually around caecum.
- Thoracic
- **Pelvic** – In association with **IUCD's.**
- **Mycetoma –** Painless localized woody induration without systemic symptoms. Granulomatus involvement of subcutaneous and deeper tissue induced by traumatic inoculation of saprophytic fungi or bacteria.
  - ***MC* site foot,** present as tumour with multiple discharging sinus called as ***Madura foot.***
  - ***MC* cause** is fungi called as eumycotic mycetoma / Maduramycosis / Madura foot. Black granules, stout filament seen on microscopy.
  - Fungal agents of mycetoma :
    - Pseudallescheria boydii
    - Madurella mycetomatis
    - Madurella grisea
    - Exophiala jeanselmei
    - Acremonium falciforme

– Bacterial mycetoma are usually caused by Actinomyces, Nocardia, Streptomyces, Nocardiopsis.
– Even S. aureus and other pyogenic bacteria may cause mycetoma like lesion called **Botryomycosis.**
– In actinomycotic mycetoma - granules are white to yellow and thin filaments seen on microscopy.
– **Treatment :**
  - *Actinomycetoma :* Streptomycin + Dapsone or cotrimoxa-zole
  - *Eumycetoma of Madurella mycetoma :* Keto / Itra-conazole
  - *Other Eumycetoma :* rarely responds to chemotherapy.

Diagnosis of Actinomycosis

- Specimen – Sputum
  – Shake it in test tube with saline - Sulphur granules seen.
- Microscopy – Granules are infact, bacterial colonies
  – Gram positive filaments in the form of radiating ***club shaped = sun ray appearance*** seen.
  – Club is formed due to antigen - antibody reaction
  – Culture on solid media - shows spidery colonies which later develop into "molar tooth" colonies.

Treatment

- **Penicillin is *DOC.***

NOCARDIA

- **Aerobic, partially urease positive, catalase positive, partially acid fast**, causing exogenous infection, Nocardiosis (which refers to invasive disease).
- ***MC*** species associated with invasive disease **N. asterodes.**
- ***MC*** **risk factor** - Contact with soil or vegetable matter.
- Cell mediated immunity is important as neutrophil limit its growth but not kill them efficiently.
- Nocardiosis is usually initiated by inhalation and their is no person to person transmission. *... Jawetz 24/e, p 219*

Clinical Manifestation

- ***MC*** manifestation is **pneumonia** and disseminated disease which follows inhalation of bacteria.
- ***So, manifestation can be divided into :***
  a. *Respiratory tract disease* – ***MC*** **is pneumonia.** Prominent cough, small amount of thick purulent sputum that is not malodorous.
  b. *Extrapulmonary Dissemination* – ***MC*** site **brain**. Typical manifestation is subacute abscess usually **supratentorial.** *... Harrison 17/e, p 994*
  c. *Disease Following Transcutaneous inoculation* – Cellulitis, Lymphocutaneous syndrome (most cases associated with N. brasiliensis), actinomycetoma (old Fistula disappear with appearance of new fistula).

Diagnosis

- **First step :** examine sputum or pus for crooked, branching, beaded, gram positive, acid fast filaments. It also takes silver stains.
- Transtracheal aspiration should be avoided as it frequently leads to cellulitis in tissue around puncture wound.
- ***Culture :*** It use paraffin as carbon source *so paraffin baiting is used for isolation.*

Treatment

- ***DOC*** **Trimethoprim - Sulfamethoxazole** *... Harrison 17/e, p 995*
- **Best** alternative oral drug Minocycline
- **Best** parenteral drug Amikacin.

BACILLUS

- Genus consist of ***sporogenous aerobic*** gram positive bacilli.
- They are generally ***motile*** with peritrichous flagella ***except*** anthrax bacilli.
- Spores are heat resistant and constitute the commonest contaminants of bacteriological culture media.
- Its important species are : 1. Bacillus anthracis
  2. B. cereus.

1. BACILLUS ANTHRAX

– ***First*** pathogenic bacteria to be observed under microscope.
– ***First*** bacterium used for preparation of attenuated vaccine.
– ***First*** communicable disease shown to be transmitted by inoculation of infected blood.
– ***First*** bacillus to be isolated in pure culture and shown to possess spores.

Morphology :

- Non motile, capsulated bacilli.
- Capsule is polypeptide in nature ***(exception since usually capsule is of lipo polysaccharide in nature).***
- Bacilli arranged in BAMBOO STICK / BOX CAR LIKE APPEARANCE.
- Colonies of B.anthracis are round and have a *"cut glass"* appearance in transmitted light.
- On staining with polychrome methylene blue, it shows M'FADYEANS reaction; which represents capsular material.
- *Spores* – Used in biological warfare or **bioterrorism.** Formed in culture or soil but never in animal body. Not stained by ordinary methods. Not cause bulging of vegetative cells (in comparison of clostridia spores).

Culture :

- **Selective** medium : **PLET** medium.
- On ***Agar plates –*** frosted glass appearance seen.
- On microscopy it has Medusa Head Appearance.
- On ***Gelatin stab –*** characteristic Inverted Fir Tree Appearance.
- ***Solid Media*** with penicillin – String of pearl reaction.
- **Cut glass appearance –** In transmitted light.

Resistance :

- Bacilli remain viable in bone marrow for a week and in skin for 2 weeks.
- Spores are destructed by oxidising agents H_2O_2, 4% $KMnO_4$, formaldehyde (called as *Duckering*)

Virulence gactor :

i. ***Capsular poly - D-glutamic acid :*** plasmid mediated, inhibit phagocytosis. Loss of plasmid cause loss of virulence (basis of live attenuated anthrax spore vaccine).
ii. ***Toxin*** **:** Plasmid coded, complex of ***three fractions :***
  – Factor I or Edema factor - activated only intracellularly leading increased CAMP.
  – *Factor II or Protective antigen factor (PA)* – *Antibody* to PA is protective because it blocks first step in toxin activity i.e. binding to target cells.
  – Lethal factor or Factor III - cause cell death.

Disease :

- Cause Anthrax which occurs primarily in herbivores ***(zoonosis).***
- ***Humans*** are ***more resistant*** to anthrax than herbivores.

- Transmitted by spores, by contact with infected animals or contaminated animal products, insects bites, ingestion or inhalation.
- Human anthrax is of 3 types :
  a. ***Cutaneous Anthrax* (Hide Porter's disease) : *MC*** (95%); characterized by ***malignant pustule*** i.e. central eschar surrounded by nonpitting edema.
     – Toxemia always present.
     – Smear of vesicle fluid is used to confirm diagnosis by culture and animal inoculation.
  b. ***Pulmonary/Inhalational Anthrax / Wool Sorter's Disease :*** Typically cause hemorrhagic mediastinitis. Characteristic X-ray finding is *symmetric mediastinal widening.*
  c. ***Gastrointestinal anthrax :*** *rare* form

Laboratory diagnosis :

- ***Microscopy* :** – Gram postive bacilli with M.Fadyean's reaction - presumptive diagnosis made.
  – Immunofluorescent microscopy can confirm identification.
- If sample is putrid, ***Ascoli's thermoprecipitin (ring precipitin)*** test is done which demonstrate anthrax antigen in tissue extract.
- Test for ***antibody by immunoassays*** are useful in *confirming* diagnosis.

Treatment :

- ***DOC*** Penicillin
- ***In Penicillin allergy –*** Ciprofloxacin, erythromycin, tetracycline or chloramphenicol.

2. BACILLUS CEREUS

- Resembles B. anthrax *except* that it is *motile (Swarming), non-capsulated*, *not susceptible to gamma bacteriophage, not show 'string of pearls' reaction.*
- Isolated from feces and other sources on **MYPA** (mannitol egg yolk phenol red polymyxin agar).
- It cause two type of food poisoning manifest by nausea, vomiting and abdominal cramps.

Features	*Diarrheal type*	*Emetic Type*
Incubation period	8-16 hrs	1-5 hrs
Food	Cooked meat and vegetables	Exclusively by rice
Enterotoxin	Resemble heat labile toxin of **E.coli** Either preformed or produced in intestine	Resemble heat stable toxin of **S.aureus** Already preformed in rice
Clinical Features	Fever, Vomitting rare	Diarrhea is not common
Serotype	2, 6, 8, 9, 10, 12	1, 3, 5

Remember :

- Presence of B. cereus in patient stool is not sufficient for diagnosis since it may be present in normal stool specimen; concentration of 10^5 or more bacteria per gram of stool is considered diagnostic. *... Jawetz 24/e, p 206*
- It also cause eye infections; localized and systemic infections (occur in patient with medical device or IV drug users).

QUESTIONS

1. An abattoir worker developed pustule which later progress to necrotic ulcer. Which of the following stain is useful demonstration of organism from smear made from pustule ?
a) Polychromic methylene blue **[AI 07; AIIMS 06]**
b) Chalkofluor white
c) Geimsa
d) Modified kinyon stain

2. A man, after skinning a dead animal, developed a pustule on his hand. A smear prepared from the lesion showed the presence of Gram positive bacilli in long chains which were positive for McFadyean's reaction. The most likely aetiological agent is : [AI 04]
a) Clostridium tetani
b) Listeria monocytogenes
c) Bacillus anthracis
d) Actinomyces sp

3. All of the following are true about anthrax except : [AI 98]
a) Plasmid is responsible for toxin prodcution
b) Cutaneous anthrax generally resolve spontaneously
c) Capsular polypeptide aids virulence by inhibiting phagocytosis
d) Toxin is a complex of two fractions

4. The causative organism of Mycetoma is : [AI 96]
a) Nocardia
b) Dimorphic fungus
c) Aspergillus
d) Dermatophytes

5. Which of the following is False about mycetoma : [AI 96]
a) Can affect lower and upper extremities
b) Caused by actinomycetes and filamentous fungi
c) Diagnosis is by examination of pus
d) Uncommon in India

6. A discharging sinuses seen in : [AI 95]
a) Sporotrichosis
b) Cryptococcosis
c) Histoplasmosis
d) Myceotma

7. Which of the following is not true of Actinomycosis : [AI 95]
a) Demonstration of filaments
b) Caused by actinomyces israelii
c) Organism cannot be cultured
d) Sulphur granules in pus

8. Nocardia is stained by : [AIIMS 08]
a) Acid fast stain
b) Kiram's stain
c) Alcian blue
d) Mucin stain

9. Which of the following is the most predominant constituent of sulfur granules of Actinomycosis is : [AIIMS 04, 02]
a) Organisms
b) Neutrophils and monocytes
c) Monocytes and lymphocytes
d) Eosinophils

10. A clinical specimen was obtained from the wound of a patient diagnosed as Nocardiosis. For the selective isolation of Nocardia sp. which one of the following would be the best method :
a) Paraffin bait technique **[AIIMS 04]**
b) Castaneda's culture method
c) Craige's culture method
d) Hair bait technique

11. A malignant Pustule is a term used for :
a) An infected malignant melanoma **[AIIMS 03]**
b) A carbuncle
c) A rapidly spreading rodent ulcer
d) Anthrax of skin

12. A farmer present with multiple discharging sinuses in the leg not responding to antibiotics. Most likely diagnosis is : [AIIMS 02]
a) Madurella
b) Actino-mycetoma
c) Nocardia
d) Sporothrix

13. True regarding anthrax is all except : [AIIMS 97]
a) Caused by insect bite
b) Caused by rubbing of skin
c) Cutaneous type is rare nowdays
d) Pulmonary infection occurs by inhalation

Answer

1. a) Polychromic	2. c) Bacillus ...	3. d) Toxin is a ...	4. a) Nocardia	5. d) Uncommon ...
6. d) Myceotma	7. c) Organism ...	8. None	9. a) Organisms	10. a) Paraffin ...
11. d) Anthrax ...	12. a) Madurella	13. c) Cutaneous ...		

14. A patient present with vomiting he had eaten rice 6 hour before. The most probable cause is :

a) Bacillus cereus **[PGI 07]**
b) Staph. aureus
c) Cl. difficle
d) All

15. Actinomycotic mycetoma is caused by :

a. Actinomyces **[PGI 05]**
b. Nocardiasis
c. Streptomyces
d. Madura mycosis
e. Staphylococcus

16. Nocardia is differentiated from Actinomyces by :

a) Gram stain **[PGI 02]**
b) ZN Stain
c) Nocardia causes mycetoma, Actinomyces do not
d) Nocardia is faculative anaerobe

17. Which of the following is true regarding anthrax:

a) M'Fadyean reaction shows capsule **[PGI 01]**
b) Humans are usually resistant to infection
c) Less than 100 spores can cause pulmonary infection
d) Gram stain shows organism with bulging spores
e) Sputum microscopy helps in diagnosis

18. The most common cause of mycetoma in India :

a) Nocardia braziliensis **[PGI 97]**
b) Actinomadura madure
c) Piedra
d) Tinea cruris

Answer 14. a) Bacillus cereus 15. a, b and c 16. b) ZN Stain
17. a, b and e 18. a) Nocardia ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is a i.e. Polychromic methylene blue *Ref. Ananthnarayan 7/e, p 242 - 244*

It is case of cutaneous anthrax in abattoir worker (slaughterhorse worker).

- Cutaneous anthrax is also common in *dock workers* (who carry loads of hides and skin on their bare backs), *butchers, farmers, veterinarians, workers* involved in meat packing.
- Pulmonary anthrax is common in *workers of wool facotries.*
- Intestinal anthrax occur in communities who eat carcasses of animals dying of anthrax.
- **Stains used in case of Anthrax :**
  - Gram's stain
  - Sudan black B
  - Polychrome methylene blue (stains capsule = **M'Fadyean reaction**).

2. Ans. is c i.e. Bacillus anthrax *Ref. Ananthnarayan 7/e, p 242 - 244; Harrison 17/e, p 1344*

This is typical presentation of Cutaneous Anthrax.

Bacillus Anthrax is

- Gram positive, Aerobic, Non-motile, Capsulated (polypeptide in nature), Spore forming bacilli.
- Spore are formed in culture or in the soil but never in the animal body during life and do not cause bulging of vegetative cell (In comparison of clostridium spores).
- Chain of bacilli present *bamboo stick* or *Box car like appearance.*
- When blood film containing anthrax bacilli is stained with polychrome methylene blue and then examined under microscope, amorphous purplish material representing capsular material is noticed around bacilli This is called ***M. 'Fadyean's reaction*** ***(characteristic of anthrax bacilli)*** and is used for presumptive diagnosis of anthrax in animals.

Cultural characteristic

- Agar : ***frosted glass*** appearances
- Microscopy : ***Medusa head*** appearance
- Gelatin stab : ***Inverted fir tree*** appearance
- **String of perals** reaction – ***For differentating B. anthrax from B. cereus*** and other aerobic spore bearers.

Clinical features

- Anthrax is zoonotic disease primarily of herbivores. Humans are *more resistant* than animals.
- Human become infected when spores are introduced into body by contact with infected animal or contaminated animal products, insect bites, ingestion, inhalation.

Types of Human Anthrax

Cutaneous anthrax (Hide porter's disease) (= Malignant pustule)	Pulmonary anthrax (Wool sorter's disease) (= Inhalation anthrax)	Gastrointestinal anthrax
• ***MC* type** of anthrax • Usual sites arms, hand, face, neck • Characterized by presence of malignant pustule – Central necrotic painless lesion covered by black eschar surrounded by satellite lesions • Generally resolved spontaneously but 10-20% patients develop fatal septicemia • Also caused by shaving brushes of animal hair or occasionally by insect bite	• *Earliest symptom are* are typically viral like prodrome with fever, malaise, abdominal or chest symptoms • 100% fatal though with prompt treatment, survival is possible • *Characteristic X-ray* mediastinal widenning, hemorrhagic pleural effusion	• Rare form • High mortality rate • Primary lesion is most often located on tonsil

Remember :
- 10,000 spores are required to produce lethal disease in 50% of animals exposed to this dose, (LD_{50}) though few as one to three spore may be adequate sometime.
- Incubation period of cutaneous anthrax is 1 to 7 days while that of pulmonary anthrax may be as long as 6 weeks. *..... Jawetz 23/e, p 204*

3. Ans. is d i.e. Toxin is a complex of two fractions *Ref. Ananthnarayan 7/e, p 243; Jawetz 24/e, p 204*

Toxin of B. anthrax is complex of three factors not two.

Virulence factors of B. anthrax are :

a. Capsular polypeptide :
- Plasmid mediated
- Inhibit phagocytosis.

b. Toxin :
- Plasmid coded
- Complex of three fractions :
  - i. Factors I or Edema factor/ EF (= Adenylate cyclase)
  - ii. Factor II or protective antigen factor (PA)
  - iii. Factor III or lethal factor / LF

EF + PA = Edema toxin

LF + PA = Lethal toxin = Major virulence factor and kill animals.

4. Ans. is a i.e. Nocardia *Ref. Ananthnarayan 7/e, p 402; Jawetz 24/e, p 633*

Mycetoma

- Chronic granulomatous disease.
- Involve subcutaneous and deeper tissues destructing the contagious bone and fascia.

- Commonly affecting foot, lower extremities, hands and exposed areas.
- It was first described from Madurai (South India).
- Presents as abscess, tumors with multiple sinuses discharging pus with sulphur granules.
- Granules are tightly clumped colonies of causative agent.
- ***Caused by :***
  - Fungi ***(MC)*** called as *Eumycotic mycetoma* : Exophiala Jeanselmei, Madurella grisea, Acremonium falciforme by Madurella mycetomatis, Pseudoallesheria boydii.
  - Bacteria : Actinomycetes (Actinomyces, Nocardia, Actinomadura, Streptomyces, Nocardiopsis); Staph aureus and other pyogenic bacteria **(Botryomycosis).**
- ***Diagnosed by :***

A.

EXAMINING THE PUS			
↓		↓	
Colour of discharged granules		***Crushed smear of granules***	
↓	↓	↓	↓
White to yellow	Black	Thin filaments	Stout filament
↓	↓	↓	↓
Actinomycotic myetoma	*Eumycotic myetoma*	*Actinomycotic mycetoma*	*Eumycotic mycetoma*

B. Isolation of agent **by culture.**

5. Ans. is d i.e. Uncommon in India *Ref. Ananthnarayan 7/e, p 402*

It was first decribed from Madurai (in South India) so it is quite common in India.

6. Ans. is d i.e. Mycetoma *Ref. Ananthnarayan 7/e, p 402*

Already explained, refer answer no. 4

7. Ans. is c i.e. Organism cannot be cultured *Ref. Ananthnarayan 7/e, p 400, 402*

Actinomycetes are true bacteria (possess cell wall, prokaryotic nuclei, etc) bearing superficial resemblance to fungi (form mycelium or branching filaments).

Actinomyces cause actinomycosis in human.

MC cause is ***A. israelii***

MC type of actinomycosis - Cervicofacial (lower jaw).

Diagnosis of actinomycosis is made by :

1. Demonstrating organism in the lesion by microscopy :
   Specimen - Pus/ sputum containing sulphur granules.
   - Granules are crushed, gram positive filaments seen as **'sun ray appearance'.**
   - These granules are infact bacterial colonies.
2. Isolation in culture :
   In thioglycollate liquid media – A. israelli as **fluffy ball** at bottom of tube.
   Solid media – **Spidery colonies** of A. israelii

8. Ans. is a i.e. Acid fast *Ref. Jawetz 24/e, p220*

- No cardiac is urease positive, catalase positive partially acid fast organism.

Stains for nocardia :

Acid fast staining - Nocardia cell wall contains mycolic acid that are shorter chain than mycobacteria. If they are stained with routine acid fast reagant (carbol-fuchsin) but decolorized with 1-4% sulfuric acid instead of the stronger acid decolorent, most isolate will stain acid fast.

Silver stains.

9. Ans. is a i.e. Organism *Ref. Ananthnarayan 7/e, p 401*

Already explained, refer answer no. 7

10. Ans. is a i.e. Paraffin bait technique *Ref. Harrison 17/e, p 994 - 995*

Diagnosis of Nocardiosis

Specimen – Sputum or pus or spinal fluid or urine or biopsy material.

i. *Microscopy* – Crooked, branching, beaded, gram positive filament seen.
ii. *Stain* – They are **Acid fast** and also take silver stains.
iii. *Isolation* – Paraffin baiting mixed culture's done as it use paraffin as carbon source.
iv. In case of pneumonia, sampling done by *bronchoscopy or lung aspiration* but transtracheal aspiration should be avoided as it frequently leads to nocardial cellulitis around the puncture wound.
v. If brain involved – *CT or MRI*
vi. In actinomycetoma – *granules* are examined.

Remember : – Castaneda culture is method of blood culture (eg. S. typhi, Brucella).
– Craigie's tube is used for the separation of motile from non-motile bacteria and also used to obtain phase variants in salmonella species.

11. Ans. is d i.e. Anthrax of skin *Ref. Ananthnarayan 7/e, p 244*

Cutaneous anthrax is also known as Hide porter's disease or malignant pustule.

Remember : Carbuncle is infection of 2 - 3 hair follicles.

12. Ans. is a i.e. Madurella *Ref. Harrison 17/e, p 1266*

Actinomycetoma, usually responds to antibiotics.

Treatment of Mycetoma	
Actinomycetoma	**Eumycetoma**
Prolonged combination chemotherapy eg. with streptomycin and either dapsone or cotrimoxazole	Rarely responds to chemotherapy, some cases caused by Madurella mycetomatic respond to Ketoconazole or itraconazole

13. Ans. is c i.e. Cutaneous type is rare nowdays *Ref. Ananthnarayan 7/e, p 244*

Cutaneous anthrax is ***MC*** type of **anthrax.**

For more details, refer answer no. 2

14. Ans. is a i.e. Bacillus cereus *Ref. Ananthnarayan 7/e, p 246*

This is a characteristic presentation of B.cereus food poisoning (emetic type).

Features	*Diarrheal type*	*Emetic Type*
Incubation period	8-16 hrs	1-5 hrs
Food	Cooked meat and vegetables	Exclusively by rice
Enterotoxin	Resemble heat labile toxin of **E.coli** Either preformed or produced in intestine	Resemble heat stable toxin of **S.aureus** Already preformed in rice
Clinical Features	Fever, Vomitting rare	Diarrhea is not common
Serotype	2, 6, 8, 9, 10, 12	1, 3, 5

15. Ans. is a, b and c i.e. Actinomyces; Nocardiasis; and Streptomyces *Ref. Jawetz 23/e, p 633*

Mycetoma

Localised chronic granulomatous involvment of the subcutaneous and deeper tissue.

Eumycotic mycetoma **= Fungal** *(More common)*	**Actinomycotic mycetoma** **= Bacterial**
– Madurella mycetomatis	– Actinomyces
– Pseudollescheria boydii	– Nocardia
– Madurella grisea	– Streptomyces
– Acremonium falciforme	– Nocardiposis
– Exophiala jeanselmei	

Remember :
- *Most common* site of mycetoma - foot - *(Called as Madura foot).*
- Staphylococcus is causative agent of botryomycosis.

16. Ans. is b i.e. ZN stain *Ref. Ananthnarayan 7/e, p 401, 402; Harrison 17/e, p 994*

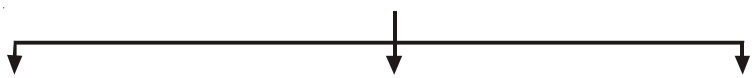
Both are gram positive filaments causing mycetoma.

Features	**Actinomyces**	**Nocardia**
Morphology	Non acid fast	Acid fast (Ziehl and Neelsen stain); Fite Faraco Method
Growth in media	Anaerobes	Aerobic
Mode of infection	Endogenous	Exogenous
Diseases	***MC*** is cervicofacial	***MC*** is pneumonia and disseminated disease
Treatment	Penicilin G	Sulfonamides
Paraffin	Can't use	Can use

17. Ans. is a, b and e i.e. M' Fadyean reaction shows capsule; Humans are usually resistant to infection; and Sputum microscopy helps in diagnosis *Ref. Harrison 15/e, p 914; Ananthnarayan 7/e, p 245*

Diagnosis of Anthrax

1. **Microscopy :**
   - Examination of cut piece of ear or swab soaked in blood of animals, if reveals gram positive bacilli and positive M'Fadyeans reaction; presumptive diagnosis is made.
   - ***Immunofluoroscent*** microscopy ***confirm*** the diagnosis.
2. Any large Gram positive bacillus with morphology and cultural features of anthrax i.e. non motile, non hemolytic on blood agar, catalase positive - presumptive report of anthrax can given.



Initial confirmation	Further confirmation	For Epidemiological studies and strain characterization
Lysis by gamma phage and direct fluorescent antibody test (DFA) for capsule specific staining and for polysaccharide cell wall antigen	By PCR for bacillus specific chromosomal markers	MLVA (multiple locus variable number tandem repeat analysis) and AFLP (amplified fragment length polymorphism) can be done

18. Ans. is a i.e. Nocardia braziliensis *Ref. Jawetz 24/e, p 220*

Remember :
- ***MC*** cause of mycetoma is **fungi.**
- ***MC*** cause of Actinomycetoma are :
  - Nocardia brasiliensis
  - Streptomyces somaelinsis and
  - Actinomadura madurae.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Medussa head colony is found in : [UP 00]

a) Clostridium
b) Bacillus
c) Pneumococcus
d) Staph. aureus

[Ref. Ananthnarayan 7/e, p 242]

2. All are causes of madura mycosis except :

a) Streptomyces **[UP 02]**
b) Nocardia
c) Actino boydii
d) Circumvento-geniculta

[Ref. Ananthnarayan 7/e, p 402]

3. All are true about cutaneous anthrax except :

a) Extremely painful lesions **[UP 02]**
b) The whole area is congested and edematous
c) Central crustation with black eschar
d) Satellite nodule around inguinal region

[Ref. Ananthnarayan 7/e, p 244, Harrison 16/e, p 115]

4. A wool cutter is suffering from fever with a cervical lymphnode enlargement for last 15 days, most likely he is suffereing from : [UP 04]

a) Anthrax
b) Mycetoma
c) Sporotrichosis
d) Coccidimycosis

[Ref. Ananthnarayan 7/e, p 244]

5. Actinomycosis caused by : [Bihar 05]

a) Gram+ve organism
b) Gram–ve bacteria
c) Anaerobic bacteria
d) Fungus

[Ref. Ananthnarayan 7/e, p 400]

6. Medusa head appearance : [Jharkhand 05]

a) Bacillus anthrax
b) Bacillus subtulis
c) Bacillus cereus
d) Bacillus licheniformis

[Ref. Ananthnarayan 7/e, p 241]

7. Sulphure granules are seen in :

a) Rhinoscleroma **[UP 06]**
b) Actinomycetes
c) Candida fungi
d) Listeria-mono

[Ref. Ananthnarayan 7/e, p 400-401]

8. Anthrax bacilli differes from anthracoid bacilli by being : [Kar 06]

a) Non-capsulated
b) Strict aerobe
c) Non-motile
d) Hameolytic colonies on blood

[Ref. Ananthnarayan 7/e, p 246]

9. Malignant pustule is seen in infection :

a) Yersinia pestis **[Kar 06]**
b) Bacillus cereus
c) Clostridium welchii
d) Bacillus anthracic

[Ref. Ananthnarayan 7/e, p 244]

Answer

1. b) Bacillus
2. d) Circumvento ...
3. a) Extremely ...
4. a) Anthrax
5. a) Gram+ve ...
6. a) Bacillus ...
7. c) Candida ...
8. c) Non-motile
9. d) Bacillus ...

7 Listeria Monocytogenes

- Short coccoid, Catalase positive, Gram positive non-spore forming rod with tendency to occur in chains.
- Shows slow *tumbling motility at 20^0-25^0 C* and is non motile at 37^0C.

Culture

- Grows on ordinary media. (Muller - hinton agar).
- Growth is improved if material is stored in tryptose phosphate or thioglycollate broth at 4^0C called *cold enrichment.*

Listeria monocytogenes can be differentiated from other Listeria by :

- β hemolysis on sheep blood agar.
- Production of acid from glucose, mannose but not from D.xylose.

Listeria monocytogenes is divided into serotypes on the basis of somatic [O] or flagellar [H] antigen.

- Most human infections are caused by 1/2a, 1/2b, 4b.
- Human disease due to L.monocytogenes generally occurs in pregnancy or Immunosuppression.

Mode of Transmission

Food borne [Ready to eat food are most likely].

Pathogenesis

- Intracellular pathogen [so, no role of humoral immunity] hence immunity is primarily cell - mediated.
- Lack of gastric acidity increase risk.
- Most important determinant of pathogenesis is Listerolysin O. *... Harrison 17/e, p 896*
- **Life cycle of Listeria monocytogenes in host macrophages includes following steps :**

1. Listeria has cell surface protein called internalin that interacts with E.cadherin receptor on epithelial cells promoting phagocytosis.
2. Listeria is phagocytosed by a epithelial cell and incorporated into a phagolysosome.
3. The bacterial product listeriolysin O lyses the phagolysosome, allowing the escape of the listeria.
4. Listeria multiplies and assembles an actin filament tail that pushes the bacterium to the surface of the macrophage.
5. A filopods extension forms, facilitating transfer of the listeria into another phagocyte.

Clinical presentation

1. ***Pregnancy Associated Listeriosis :***
   - Most infections detected in 3rd trimester.
   - Woman experience mild illness characterized by fever, myalgia, backache.
   - Transplacental spread results in chorioamnionitis, premature labor, intrauterine fetal death, stillbirth, early onset disease of newborn, recurrent spontaneous abortion.
2. ***Neonatal Listeriosis :***
   - Early onset - Before 7 days
   - Late onset - 7 - 21 days

   A. *Early onset disease :* Most infants are symptomatic by 2nd day.
      - Transmitted by aspiration of infected amniotic fluid.
      - Present as : a. Intrauterine sepsis
        b. Respiratory distress
        c. Skin lesions
        d. Granulomatosis infantisepticum – Characterized by abscesses involving liver, spleen, adrenal gland and other sites.
      - Mostly follow complicated labor.

   B. *Late onset disease :*
      - Mostly present as meningitis
      - Born at term by uncomplicated labor
      - Transmitted during passage through birth canal.

3. ***Listeriosis not associated with pregnancy :***
   - ***MC*** underlying condition are *chronic glucocorticoid therapy,* diabetes, solid and hematologic *malignancy (particularly fludarabine treated), liver disease, AIDS*
   - Bacteremic infection without evident focus is ***MC*** clinical manifestation while infection in CNS ranks **2nd** in which meningitis is ***MC*****.** It can directly invade brain parenchyna producing ***carebritis or focal abscess.***
   - L.monocytogenes is ***MC*** cause of *meningitis* in kidney ***transplant*** patient after ***1 month.***
   - Listeria meningitis must be considered in chronically ill patient with aseptic meningitis particularly when presentation is subacute.

Diagnosis

- Invasive listeriosis is diagnosed when organism is cultured from Blood, CSF or amniotic fluid.
- Antibody to listeriolysin O :
  - For epidemiological purpose.
  - For diagnosis of culture negative CNS infection.
- **Antons test –** Instillation into rabbit eye cause conjuctivitis.

Treatment

- IV administration of ***Ampicillin*** ***(DOC)*** or penicillin often in combination with aminoglycoside.
- ***Cotrimoxazole*** in case of pencillin allergy.
- Cephalosporins are not effective.

QUESTIONS

1. A 30 year old woman with a bad obstetric history presents with fever. The blood culture from the patient grows gram-positive small to medium coccobacilli that are pleomorphic, occurring in short chains. Direct wet mount from the culture shows tumbling motility. The most likely organism is : **[AI 04]**

a) Listeria monocytogenes
b) Corynebacteriumsp.
c) Enterococcus sp
d) Erysepelothrix rusiopathiae

2. All the following are true about Listeria except :

a) Transmitted by contaminated milk **[AI 02]**
b) Gram (-)ve bacteria
c) Causes abortion in pregnancy
d) Causes meningitis in neonates

3. A 3 week old child presented to the pediatrician with meningitis A presumptive diagnosis of late onset of perinatal infection was made . The CSF culture was positive for gram positive bacilli which of the following characteristic of this bacteria would be helpful in differentiating it from other bacterial agents : **[AIIMS 05]**

a) Ability to grow on blood agar
b) Ability to produce catalase
c) Fermentative attack on sugars
d) Motility at 25^0C

4. A major step in the pathogenesis of listeriosis is:

a) The formation of antigen-antibody complex with resultant complement activation and tissue damage **[AIIMS 05]**
b) The release of hyaluronidase by L. monocytogenes, which contributes to its dissemination from local sites
c) The antiphagocytic activity of the L. monocytogenes capsule
d) The survival and multiplication of L. monocytogenes within mononuclear phagocytes and host epithelial cells

5. In patient with Listeria meningitidis who is allergic penicillin the treatment of choice is :

a) Vancomycin **[AIIMS 04]**
b) Gentamycin
c) Trimethoprim - sulphome-thoxazole
d) Ceftriaxone

Answer 1. a) Listeria ... 2. b) Gram (-)ve ... 3. d) Motility at ... 4. d) The survival ... 5. c) Trimethoprim ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is a i.e. Listeria monocytogenes *Ref. Ananthnarayan 7/e, p 403*

Tumbling motility is characteristic of Listeria monocytogenes - *(other three are non motile).*

Listeria monocytogenes is :

- Catalase positive, non-sporing gram positive, Cocco bacilli.
- Tendency to occur in chains.
- Characterisitics ***slow tumbling motility at 25^{0}C*** and at 37^{0}C is non-motile because peritrichous flagella are produced optimally at 20 to 30^{0}C but only scantily or not at all at 37^{0}C.
- Grows *best* between 30^{0}C and 37^{0}C (temperature range is 1 to 45^{0}C).
- Aerobic or microaerophilic.
- Intacellular as well as able for direct cell to cell spread so not eliminate by antibodies and cause infection in deficient cell mediated immunity.

Mode of transmission of Listeriosis

- Food borne by ready to eat foots ***(eg. pasteruized milk, cheese, pate, undercooked chicken).***
- Nosocomial transmission.

Forms of Human Listerosis

Pregnancy associated listeriosis	Neonatal listeriosis	Listeriosis not associated with pregnancy
• Most infections in 3rd trimester • Transplacental spread result in recurrent sponta neous abortion, premature labour, IUD, chorioamnionitis	a) ***Early onset*** **-** transmitted by aspration of infected amniotic fluid b) ***Late onset*** **-** transmitted during passage through birth canal Mostly present as meningitis	• ***MC*** underlying condition in non pregnant adults is chronic glucocorticoid therapy

Remember :

- E. rhusiopahtial is a-hemolytic non-motile Gram positive bacillus with tendency to form long filaments.
- Its ***MC*** infection in humans is called erysipeloid = Seal finger = whole finger.

2. Ans. is b i.e. Gram –ve bacteria *Ref. Harrison 17/e, p 895 - 897*

Already explained, please see answer no. 1

3. Ans. is d i.e. Motility at 25^0 C *Ref. Ananthnarayan 7/e, p 403*

- This is a case of **'Late onset neolnatal meningitis'** of Listeria monocytogenes as culture reveals gram positive bacillus.

- Bacterial cause of neonatal meningitis are :
  - E. coli > Group b streptococci (Strep. agalactiae) > other gram negative bacilli > L. monocytogenes.

  ..... Forfar & Anelus text book of pedia 319, 1338

  Other – Staph, other strept, Pneumococcus, Pseudomonas Hemophilus, meningococcus.
- E. coli is gram negative bacilli while group b streptococci is gram positive cocci.

Important bacterias causing meningitis

	Listeria	E.coli	Streptococci	Staphylococci	H. influenzae
Ability to grow on blood agar	+	+	+	+	+
Production of catalase	+	+	–	+	+
Fermentation of Sugars	+	Both acid and gas is produced	+	+	+
Motility at 25^{0}C	+	–	–	–	–

Remember :
- Catalase production and β hemolysis is used to differentiate listeria monocytogenes from other listeria not from other bacterias.
- Only Listeria and E.coli is motile in above mentioned bacterias.

4. Ans. is d i.e. The survival and multiplication of L. monocytogenes within mononuclear phagocytes and host epithelial cells

Ref. Jawetz 24/e, p 218

Pathogenesis of Listeria monocytogenes

Listeria
↓
Enters body through GIT after eating contaminated foods
↓
Interlin interacts with E Cadherin (recepter on epithelial cells)
↓
Phagocytosis of listeria in epithelial cells forming phagolysosome
↓
In phagolysosome bacteria produce lysteriolysin which lyse the membrane of phagolysosome
↓
Listeria escapes into cytoplasm
↓
Induce host cell actin polymerization
↓
Listeria is propelled to cell membrane
↓
In membrane Listeria forms protrusion called filopods
↓
Filopods is ingested by nearby epithelial cells or macrophages
↓
Listeria is released and cycle begins again

So, in this way Listeria can move from cell to cell without being exposed to antibodies, complement or polymorphs.

Remember :

- Iron is important virulence factor of Listeria
- Shigella flexneri and rickettsia also use the host cell actin and contractile system to spread infection.

5. Ans. is c i.e. Trimethoprim - sulphomethoxazole *Ref. Harrison 17/e, p 897*

- ***DOC*** for listeriosis (non pregnant, neonate, pregnant) is ampicillin or penicillin often in combination with aminoglycosides.
- During last month of pregnancy (in case of penicillin allergy), may be treated with erythromycin.
- Other wise in all cases of penicillin allergy ***DOC*** is trimethoprim-sulfamethoxazole.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.

1. Tumbling motility is shown by : **[DNB 04]**

a) Proteus vulgaris
b) Proteus mirabilis
c) Virbio
d) Listeria

[Ref. Ananthnarayan 7/e, p 403]

Answer 3. d) Listeria

8 Mycobacteria

Gram positive, ***Aerobic,*** acid fast, non motile, non capsulated and non sporing fungus like bacteria.

Classification of mycobacteria is as follows :

1. Tubercle bacilli - M.tuberculosis, M.bovis, M. africanum
2. Lepra bacilli - M.leprae
3. Mycobacteria causing skin ulcers - M.ulcerans, M.haemophilum, M.marinum or balnei
4. Atypical mycobacteria = Nontuberculous = Paratubercle = MOTT

Group I	*Photochromogenes* Eg. M.kansasii, M.marinum, M.simiae, M.asiaticum.
Group II	*Scotochromogens* Eg. M.scrofulaceum, M.gordonae, M.szulgai, M. flavescens.
Group III	*Nonphotochromogens* Eg. M.avium, M.intracellulare, M.xenopi, M.ulcerans, M.malmoense, M celatum, M. Hemophilum, M. gastri, M. genavense, M. shimoidei, M. trivale, M. terrae, M. nonchromogenicum.
Group IV	*Rapid growers* – M.fortuitum, M.chelonae Chromogenic rapid growers are saprophytes Eg. M.smegmatic, M.phlei.

5. Johne's bacillus - M.paratuberculosis

MYCOBACTERIA LEPRAE

Morphology

- Obligate intracellular bacilli with polar bodies and intracellular elements, resist decolourization of 5% H_2SO_4 (acid fast).
- Live bacilli in tissue (solid and uniformly stained) - *Morphological index (MI).*
- Dead bacilli – fragmented and granular appearance.
- *Bacteriological index (BI)* – number of *bacilli* in tissue.
- BI and MI suggests relapse/drug resistance if increase.
- Bacilli arranged intracellularly in the form of globi, having 'cigar bundle' appearance.
- Virchow's lepra cells or foamy cells are large undifferentiated histiocytes in origin.
- Strain variability is demonstrated recently.
- *(PGL-I) phenolic glycolipid act as virulence factor.*

Culture

- Unique in exhibiting dopa oxidase activity and acid fastness that is pyridine extractable.

- *Not grow in artificial media* but multiply in foot pad of mice at low temperature of 20^0C.
- Nine banded *armadillo* (Dasypus novemcinctus) is highly *susceptible to* it.
- Grows ***best in*** cooler tissues (skin, peripheal nerves, anterior chamber of eye, upper respiratory tract, testis) ***sparing*** warmer areas (axilla, groin, scalp, midline of back, ovary).
- ***Generation time -*** 12-13 days [14 hrs - tubercle bacillus ; 20 min - coliform bacillus].

Transmission

- Nasal droplet, contact with infected soil, insect vectors. Skin to skin contact is not an important route. Physicians and nurses caring for leprosy patient are not at risk.

Clinical Features

- It causes Leprosy (Hansen's Disease) having spectrum of manifestations.
- Incubation period generally 5-7 years.
- There is no increased risk of leprosy in AIDS patient.

Tuberculoid Leprosy :

– Symptoms confined to skin and peripheral nerves.
– ***MC*** **nerve involved -** Ulnar, posterior auricular, peroneal and posterior tibial nerve.
– Invasion and destruction of nerves in dermis by T_1 cells (by bacilli in LL) are ***pathognomic for*** leprosy.
– Medial popliteal nerve ***never*** involved.

Lepromatous Leprosy :

– Bacilli are present in blood and in all organ system ***except lungs and CNS.*** Even than patient are afebrile and not susceptible to opportunistic infection.

Other important Clinical features are as follows :

Clinical & Histologic features	Tuberculoid (TT) Leprosy	Borderline Tuberculoid (BT) Leprosy	Mild-Borderline (BB) Leprosy	Borderline Lepromataus (BL)	Lepromatous (LL) Leprosy
	MC type in India		**Most unstable** leprosy		
1. Skin lesions	Up to 3 in number; sharpy defined, hypopigmented asymmetric macules or plaques with tendency toward central clearing, elevated borders	Smaller or larger than in TT; potentially more numerous than in TT; usually annular lesions with sharp margination on exterior & interior borders; borders not as elevated as in TT	Dimorphic lesions intermediate between BT & BL	LL-type lesions; illdefined palques with an occasional sharp margin; few or many in number, shiny appearance	Symmetric, poorly marginated, multiple infiltrated nodules & plaques or diffuse infiltration; xanthoma-like or dermatofibroma papules; leonin facies & eyebrow alopecia Granzee zone seen
2. Nerve lesions	Skin lesions anesthetic early; nerve near lesions sometimes enlarged	Skin lesion anesthetic early; nerve trunk palsies asymmetric; nerve abscesses most common in BT	Anesthetic skin lesions; nerve trunk palsies	Skin lesions usually hypoesthetic, may be anesthetic; nerve trunk palsies common & frequently symmetric	Hypesthesia a late sign; nerve palsies variable; acral, distal, symmetric anesthesia common
3. Acid fast bacilli (BI)	3	0 – 1+	3 – 4+	4 – 5+	4 – 6+
4. Lymphocytes	3+	2+	1+	1+	0 – 1+

Continue .....

5. Macrophage differentiation	Epithelioid	Epithelioid	Epithelioid	Usually undifferentiated; epithelioid foci sometimes present; may show foamy change	Foamy change the rule; may be undifferentiated in early lesions
6. Langhan's ginat Cells	1 – 3+	2+	–	–	–
7. Lepromin test	+++	+++	–	–	–
8. Lymphocyte transformation test	95%	40%	10%	1 – 2%	1 – 2%
9. CD.4 +/CD 8+T cell ratio in lesions	1.35	1.11	NT	0.48	0.50 [CD-8/CD-4 =
10. M. leprae	1 + (60%)	2+	2+	3+	3+ (95%)

Reactional states

I. Type I Lepra reaction / Jopling Type I :

- *Type IV hypersensitivity* seen in *Borderline* leprosy not in polar form.
- *If precede* therapy than termed *down grading* reaction i.e. towards LL.
- If *after* therapy than termed *Reversal reaction* i.e. towards more tuberculoid.
- Most characteristic microscopic feature of type I reaction is *Edema.*
- It is associated with increased T cells bearing γ/δ receptors a unique feature of leprosy.
- ***MC*** nerve trunk involved - *Ulnar at elbow*
- ***Treatment :*** ***DOC*** glucocorticoids
  Clofazimine also given
  Thalidomide - ineffective.

II. Type 2 lepra reaction – Erythema Nodosum Leproticum / Jopling Type II :

- *Type III hypersensitivity* occurs exclusively in BL, LL
- Usually follows therapy (sulfone syndrome) but may precede therapy.
- ***MC*** feature - crops of painful erythematous papules that resolve spontaneously in a few day to weeks but may recur.
- Central role in pathobiology : TNF
- ***Treatment :***
  - Mild - antipyretics alone
  - Moderate to severe – Ist drug to be used glucocorticords
    DOC thalidomide
    Clofazimine - More active than in Type I.

III. Lucio's Phenomenon :

- ***Type III Hypersentivity*** exclusively in diffuse lepromatosis form of LL, usually in untreated patient.
- ***Treatment :***
  - Neither glucocortiord nor thalidomide is effective.
  - Wound care and therapy for bacteremia.

Complications

- ***MC*** complication of leprous neuropathy is *plantar ulceration* particularly at metatarsal heads.
- *Nerve abscess :*
  - ***MC*** site is ulnar nerve.
  - Treatment is rapid surgical decompression.

Diagnosis

- Biopsy of advancing edge of lesion in TT but in LL, biopsy of normal skin is also taken.
- Hyperglobulinemia in LL.
- *Lepromin test –* Type IV delayed hypersentivity which is biphasic.
  Early reaction of Fernandez – read in ***24 - 48 hours*** (***analogous to tuberculin reaction***).
  Late reaction of Mitsuda – peak ***in 4 weeks.*** More meaningful.
  It is of little diagnostic value but has more prognostic importance.

Treatment

Form of leprosy	More Intensive regimen	WHO recommended regime
i. Tuberculoid (paucibacillary)	Dapsone 100 mg/d X 5 years	Dapsone 100 mg/d + Rifampin 600 mg/month for 6 months
ii. Lepromatous (Multibacillary) or > 6 skin lesions	Rifampin 600 mg/d for 3 years + dapsone 100 mg/d indefinitely	Dapsone 100 mg/d + Clofazimine 50 mg/d and Rifampin 600 mg + clofazimine 300 mg monthly for 1year

- Single lesion paucibacillary leprosy - Single dose of ROM - rifampin, ofloxacin, minocycline.

MYCOBACTERIA TUBERCULOSIS

Morphology

- Mammalian tubercle, isolated by Koch is stained by Ziehl - Neelsen method or by ***fluorescent dyes (auramine O, rhodamine).***
- Resist decolourization by 20% H_2SO_4 and absolute alcohol for 10 minutes. Hence acid and alcohol fast.
- Acid fastness is due to unsaponifiable wax (mycolic acid) or to a semipermeable membrane.
- It has thick cell wall; shows spheroplast and L forms.

Culture

- Generation time 14 – 15 hours.
- Colonies appear in about ***2 weeks (may take upto 8 weeks).***
- Grows ***luxuriantly in culture (Eugonic)*** and addition of 0.5% glycerol improves its growth but has no effect on ***M.bovis*** (causative agent of bovine tuberculosis) ***which is dysgonic (grows sparsely).***
- Solid medium most widely employed for routine culture is Lowenstein - Jensen (LJ) medium without starch.
- Liquid media are not generally used routinely, but used for senstivity testing, chemical analyses and preparation of antigens and vaccines.
- *Virulent strain form long serpentine rods in liquid media while avirulent strain grow in dispersed manner. Though cord factor itself is not a virulence factor but cord formation is coorelated with virulence. ... Jawets 24/e, p 322*

BIOCHEMICAL REACTION			POSITIVE IN	NEGATIVE IN
Niacin Test	:	**N**	Human tubercle	Bovine tubercle
Aryl Sulphatase	:	**A**	Only with Atypical mycobacteria	
Neutral red test	:	**N**	Virulent strain of tubercle	Avirulent strain
Peroxidase test	:	**P**	Tubercle bacilli	Atypical mycobacteria
Catalase test	:	**C**	Most atypical mycobacteria	Weakly positive in tubercle
Nitrate reduction text	:	**N**	M.tuberculosis	M. bovis

- Catalase and peroxidase activities are lost when tubercle bacilli become INH resistant.
- Ureas test is positive in M. tuberculosis, M. bovis and most of the atypical mycobacteria except MAIC complex.

	M.tuberculosis	M.bovis
Morphology	Curved long rod	Straighter, shorter, stouter
Stain	Less uniform	more uniform
O_2 requirement	Obligate aerobe	Microaerophilic
Culture	Dry, rough, raised, irregular	Flat, smooth, moist, break up easily
Growth	Eugonic	Dysgonic

Virulence factors :

- **Kat-G gene :** encodes for oxidase, catalase enzyme.
- **rpoV :** main sigma factor initiating transcription of several genes.
- **Erp gene :** encodes for protein required for multiplication.
- **Strains of Beijing / w genotype family.**

Antigenic Property

- Group specificity is due to polysaccharide while type specificity is due to protein antigen.
- Antibodies are not useful for diagnosis and immunity.

Pathogenicity

- It is due to escape killing by macrophages and inducion of type IV hypersensitivity.
- *Following factors contribute in pathogenesis :*
  - Cord factor
  - Lipoarabinomannan
  - Complement system
  - M.TB heat shock protein.
- Risk of ***acquiring*** infection is determined mainly by *exogenous* factors while risk of developing ***disease*** depends largely on *endogenous* factors.
- Most potent risk factors - HIV coinfection.

Clinical features

- Divided into two categories : Pulmonary and extrapulmonary TB.

1. **Pulmonary TB :** Divided into two :

   a. Primary Disease : usually localized in middle and lower zones.

   Primary focus is usually peripheral in subpleural region and is accompained by draining lymphatics, inflamed regional lymph nodes which are collectively called *Primary complex/Ghon's facus.*

   Depending on the host immune response development of complex can follow healing by fibrosis/ calcification; cavitation or progressive primary TB in form of consolidation; obstructive emphysema or atelactasis; TB bronchitis; miliary TB; occult hematogenous dissemination to apex of lung **(Simons Focus).**

b. Post primary disease (adult type or reactivation or secondary tuberculosis or chronic pulmonary TB).
   - Usually localized to apical and posterior segments of upper lobe due to high O_2 concentration **(Puhl's Lesion)**.
   - ***MC hematologic*** finding - mild anemia and leucocytosis
   - Infraclavicular lesion is called *Assman's Focus.*

2. Extrapulmonary TB
- ***MC*** site **lymph node** (***MC*** *cervical and supraclavicular*).
- Also involved-Pleura in the form of pleural effusion and empyema.
  - Genitourinary tract (culture negative pyuria in acidic urine).
  - Skeletal TB (***MC*** site spine, hip, knee).
  - TB meningitis (paresis of cranial nerves especially ocular, is frequent finding).
  - ***GI TB*** (***MC*** site terminal ileum and caecum).
  - Tuberculous pericarditis (***MC*** cause of chronic constrictive pericarditis).

Diagnosis

Specimen – sputum is best collected in the ***morning*** before any meal *(3 sample).*

i. AFB microscopy : smear should be prepared from thick purulent part of sputum.
- Atleast ***10000 AFB*** should be present per ml of sputum for demonstrating in direct smears. Positive report can be given only if >2 typical bacilli have seen.
- ***Fluorescent microscopy*** (stained with auramine phenol or auramine rhodamine fluorescent dye and examined under UV illumination) screened smear *rapidly* in comparison of Ziehl–Neelsen method.
- Concentration method for microscopy can also used eg. Petroff's method using NaOH solution is widely used.

ii. Culture :
- Very ***sensitive diagnostic*** technique detecting 10 to 100 bacilli per ml.
- LJ is standard solid media.
- Negative report is given, if no growth occur after 8-12 weeks.
- Slow growing, nonpigmented niacin positive AFB is taken as M.tuberculosis.
- Liquid media with radiometric growth detection (eg. BACTEC 460) and nucleic acid probes, enables results to be given in 2-3 weeks.

iii. Nucleic acid technology :
- PCR and Ligase chain reaction are used as diagnostic technique.
- RFLP and 15 fingerprinting used for epidemiological typing of strain.

iv. Immunodiagnosis :
- Demonstation of hypersensitivity to tuberculo protein (tuberculin test / Montoux intradermal test) is a standard procedure.
- 1 purified protein derivative (PPD) = 50000 tuberculin units per milligram.
- WHO advocates PPD tuberculin known as - RT 23 with Tween 80.
- ***Routinely*** 1TU used.
- ***Clinically*** 5 TU used.
- Read after 72 hrs in which induration is measured in horizontal transverse diameter.
- > 10 mm positive, < 5 mm negative.
- < 6 and > 15 mm have more risk of developing TB.

- Positive tuberculin test indicates exposure to bacilli *(infection, immunization)* with or without clinical disease. so persons who have never had contact with bacilli are tuberculin negative.
- Used as aid in diagnosing active infection in infants and young children; measure prevalence of infection; to select susceptibles ; as an indicator of successful vaccination.
- Tine Multiple puncture test and heaf test is used for screening and surveys.

Treatment

ATT is given : First line drug are :

Drugs	*Daily dose*	*Dose in DOTS*	*Thrice weekly dose*
H Isoniazid	5 mg/kg	600 mg	10 mg/kg
R Rifampin	10 mg/kg	450 mg	10 mg/kg
Z Pyrazinamide	25 mg/kg	1500 mg	35 mg/kg
E Ethambutol	15 mg/kg	1200 mg	30 mg/kg
S Streptomycin	15 mg/kg	750 mg	15 mg/kg

Prevention

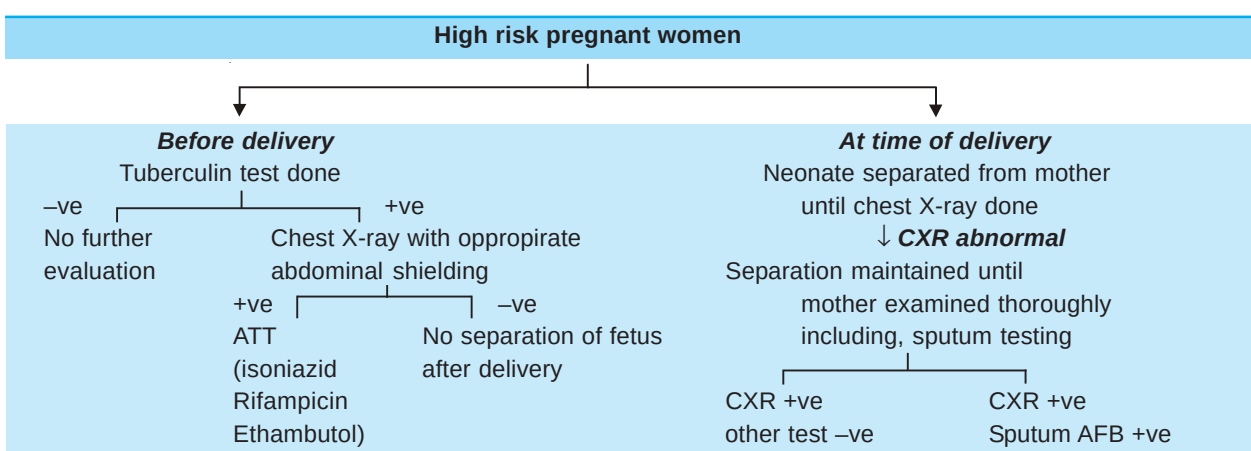
- *BCG vaccine* : Live attenuated vaccine derived from attenuated bovine strain of tubercle bacilli.
  - Normal saline is diluent
  - Dose of 0.05 ml for age < 4 week and 0.1 ml for > 4 wk should be given intradermal (subcutaneous administration may lead to abscess).
- Neonate of infected mother : Give INH resistant BCG + INH prophylaxis for 6 wks.
- Chemoprophylaxis (preventive treatment)

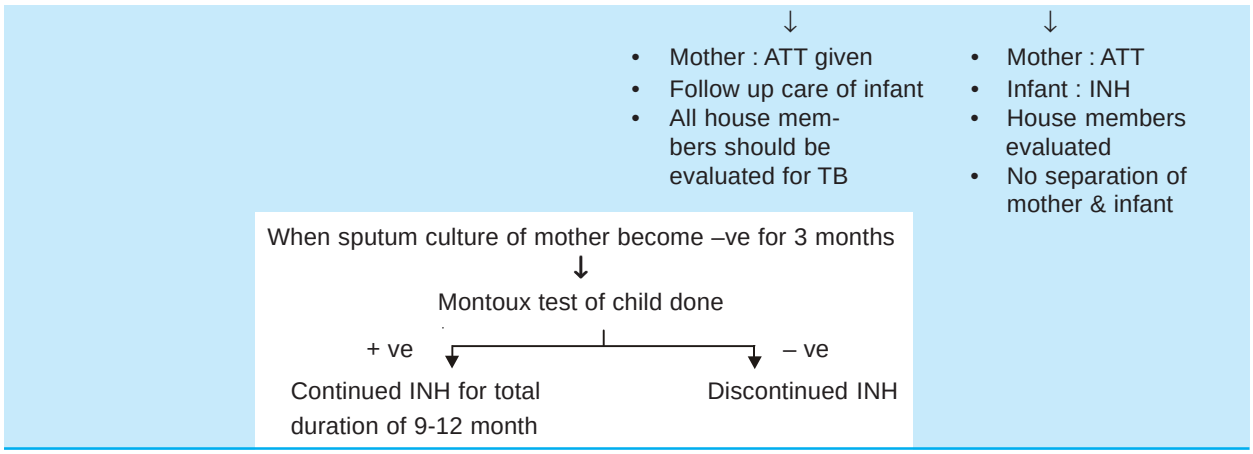
  INH for 1 year or INH plus ethambutol for 9 months.

PERINATAL TB

..... Nelson 17/e, 967, 971

- ***MC*** sign and symptoms of congenital TB are respiratory distress, fever, hepatic or splenic enlargement, poor feeding, lethargy, irritability, lymphadenopathy, abdominal distension, failure to thrive, ear drainage and skin lesions.
- Symptoms most commonly begin by 2nd or 3rd week of life.
- A positive acid fast stain of an early morning gastric aspirate from newborn usually indicate TB.
- Most important clue for rapid diagnosis is maternal or family history of TB.
- Most effective way of preventing congenital TB is appropriate testing and treatment of mother and other family members.





ATYPICAL MYCOBACTERIA

- Also known as Unclassified or Environmental or Oppurtunistic mycobacteria.
- It includes mycobacterial species other than Mycobacterium tuberculosis complex and M.leprae, hence, called as Paratubercle or tuberculoid or MOTT (mycobacteria other than tubercle) bacilli.
- It is divided into 4 group based on colony pigmentation (Runyon's classification).

Group I – Photochromogens - Produce pigment only in light.

- Slow growing though growth is faster than that of tubercle bacilli. It includes :
  a. ***M.kansasii*** **–** cause chronic pulmonary disease in old persons with pre-existing lung disease.
  b. ***M.marinum*** **–** cause warty skin lesion *(swimming pool granuloma).*

Group II – Scotochromogens - Form pigment even in dark.

a. ***M.scrofulaceum*** **–** cause scrofula (cervical adenitis) in children.
b. ***M.gordonae*** **–** called as *Tap water scotochromogen.*
c. ***M.szulgai*** **–** scotochromogen and photochromogen.

Group III – non photochromogens - Not form pigment even in light.

- Colonies may resemble those of tubercle bacilli.
  a. ***M.intracellulare*** **–** also known as *Battey bacillus.*
  b. ***M.avium*** **–** MAIS complex (i.e. avium, intracellulare, scrofulaceum) cause lymphadenopathy, pulmonary lesion and disseminated disease particularly in **AIDS** patient.

Group IV – rapid growers - Colonies appear within seven days. They can be photochromogenic, scotochromogenic non chromogenic.

a. All chromogenic rapid growers are saprophytes eg. M.smegmatis, M.phlei
b. ***M. fortuitum and M.chelonae*** **–** Not form pigment.
   – Cause chronic abscesses (may follow injection of vaccines).
   – Pulmonary lesion of M.fortuitum can't be distinguished radiologically from typical TB.
c. ***M.vaccae*** **–** Immunomodulator.

Skin Pathogen

- Regional lymph nodes are not involved as they multiply optimally at skin temperature.
- ***M. ulcerans :*** Exclusive skin pathogen which cause *Buruli ulcer* usually seen on legs or arms.
  – Infection occur through minor injuries.
  – Grows on LJ medium slowly in 4 - 8 weeks at critical temperature (30 - 33^{0}C).
  – It is the *only mycobacteria* which produce *toxin.*
- ***M. marinum (M.balnei) :*** Its infection (but not of M.ulcerans) may cause low grade *tuberculin reaction.*

QUESTIONS

1. Leprosy affects all the following except :
a) Testes **[AI 07]**
b) Ovaries
c) Eyes
d) Nerves

2. Which one of the following statement is true regarding pathogenicity of Mycobacteria species:
a) M. tuberculosis is more pathogenic than M.bovis to humans **[AI 06]**
b) M. Kansasii can cause disease indistinguishable from tuberculosis
c) M. africanum infection is acquired from environmental source
d) M. marinum is responsible for tubercular lymphadenopathy

3. In the management of leprosy, Lepromin test is most useful for : [AI 03]
a) Herd immunity
b) Prognosis
c) Treatment
d) Epidemological investigations

4. Which of the following is true regarding globi in a patient with lepromatous leprosy : [AI 02]
a) Consists of lipid laden macrophages
b) Consist of macrophages filled with AFB
c) Consists of neutrophils filled with bacteria
d) Consists of activated lymphocytes

5. Basanti, 29 year aged female from Bihar present with active TB. She delivers baby. All of the following are indicated except : [AI 01]
a) Administer INH to the baby
b) Withhold breast feeding
c) Give ATT to mother for 2 years
d) Ask mother to ensure proper disposal of sputum

6. Tuberculin test denotes : [AI 00]
a) Previous or present sensitivity to tubercule proteins
b) Patient is resistant to TB
c) Person is susceptible to TB
d) Protective immune status of individual against TB

7. The medium used for Mycobacterium tuberculosis is : [AI 96]
a) Sabouraud's meidum
b) L J meidum
c) Pick's medium
d) NIH medium

8. Rapid examination of Tubercle bacilli is possible with : [AI 96]
a) Ziel-nelson stain
b) Kinyoun stain
c) Auramine-Rhodamine stain
d) Giemsa stain

9. The commonsest focus of Scrofuloderma is :
a) Lung **[AI 96]**
b) Lymph node
c) Larynx
d) Skin

10. For experimental work, Lepra bacilli are best cultured in : [AI 96]
a) Armadillos
b) Mouse foot pad
c) Guinea pigs
d) Rabbit testes

11. True about mycobacterium other than tuberculosis : [AIIMS 08]
a. Causes disseminated infection
b. Occurs in persons with normal immunity
c. Causes decreased efficacy of BCG due to corss immunity
d. Person to person transmission is seen

12. The main cytokine, involved in erythema nodosum leprosum (ENL) reaction, is :
a) Interleukin-2 **[AIIMS 06]**
b) Interferon - gamma
c) Tumor necrosis factor - alpha
d) Macrophage colony stimulating factor

13. The following drug is not used for the treatment of type II lepra reaction : [AIIMS 06]
a) Chloroquin
b) Thalidomide
c) Cyclosporine
d) Corticosteroids

Answer

1. b) Ovaries
2. b) M. Kansasii ...
3. b) Prognosis
4. b) Consist ...
5. b) Withhold ...
6. a) Previous ...
7. b) L J meidum
8. c) Auramine ...
9. b) Lymph ...
10. b) Mouse ...
11. c) Causes ...
12. c) Tumor ...
13. c) Cyclosporine

14. The following test is not used for diagnosis of leprosy : [AIIMS 06]

a) Lepromin test
b) Slit skin smear
c) Fine needle aspiration cytology
d) Skin biopsy

15. Which of the following statement about lepromin test is not true : [AIIMS 07, 06]

a) It is negative in most children in first 6 months of life
b) It is a diagnostic test
c) It is an important aid to classify type of leprosy disease
d) BCG vaccination may convert lepra reaction from negative to positive

16. Under leprosy eradication programme the management of single lesion is : [AIIMS 02]

a) Single dose of Rifampicin and Dapsone
b) Rifampicin and Dapsone for 6 months
c) Rifampicin, Ofloxacin and Minocycline single dose
d) Rifampicin and Monocycline for 6 months

17. Collection of urine sample of a patient of TB kidney is done : [AIIMS 00]

a) 24 hrs urine
b) 12 hrs urine
c) In early morning
d) Any time

18. The characteristic finding in a case of leprosy is:

a) Culture test is positive in 2-3 months in LJ media
b) Long contact with tuberculoid leprosy can transmit the disease [AIIMS 98]
c) CMI is seen in Lepromatous leprosy
d) Macule lesion heals spontaneously

19. True about mantoux test : [PGI 03]

a) <5mm always +ve
b) Usually -ve after treatment
c) Positive reaction in children <2 is not improtant like in adult
d) Usually read after 48 - 72 hours
e) False +ve in post measles state

20. True regarding mycobacterium tuberculosis is :

a) Produces visible colonies in 1 week time on Lowenstein Jenson media [PGI 02]
b) Decolorised by 20% sulphuric acid
c) Faculatative aerobe
d) Niacin positive

21. Which of the following are acid fast positive with 20% sulphuric acid : [PGI 02]

a) M. avium
b) M. leprae
c) M. tuberculosis
d) Nocardia
e) Rhizopus

22. Selective media for TB bacilli is : [PGI 01]

a) NNN media
b) Dorset media
c) LJ. media
d) Nutrient agar
e) Mac'Conkey media

23. Exacerbation of lesions in patients of borderline leprosy is seen in : [PGI 01]

a) ENL (erythema nodosum leprosum)
b) Lepra reaction type 1
c) Jarisch-Herxheimer reaction
d) Resolving leprosy

24. Not easily culturable but well viable and used in epidemiology are : [PGI 00]

a) Staph
b) Mycobacterium TB
c) E.Coli
d) Salmonella

25. True about tuberculin test are all except :

a) Recent conversion in adult is an indication for ATT [PGI 98]
b) INH prophylaxis is started if the test is positive
c) No risk in negative
d) May be false negative in immunocompromised patients

26. Mycobacterium leprae can be grown on :

a) Culture media [PGI 98]
b) Foot pad of mouse / Armadillo
c) Liver of guinea pig
d) Kidney of rabbit

27. In TB, immunity is provided by : [PGI 98]

a) CD 4+
b) CD 8+
c) IgG
d) IgM

Answer

14. a) Lepramin ... 15. b) It is a ... 16. c) Rifampicin ... 17. c) In early ... 18. b) Long ...
19. d) Usually ... 20. d) Niacin ... 21. c) M. tuber ... 22. b and c 23. a and b
24. b) Mycobacte ... 25. c) No risk ... 26. b) Foot pad ... 27. a) CD 4+

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b i.e. Ovaries

Ref. Harrison 17/e, p 1022; International Journal of Leprosy, Vol. 71, No. 2, p 101 - 105

Mycobacterium leprae grows best in cooler (the skin, peripheral nerves, anterior chamber of the eye, upper respiratory tract, and testes), sparing warmer areas of the skin (the axilla, groin, scalp, and midline of the back).

Thus, ovary is the answer of exclusion.

Complications of M. leprae

- ***Eye :*** uveitis, cataracts, glaucoma, corneal insensitivity and lagophthalmus.
- ***Testes :*** orchitis followed by impotence.
- ***Nerve abscesses :*** mostly seen in BT form, ulnar nerve is most frequently involved.
- ***Extremities :*** planter ulceration (most frequent complication of leprous neuropathy), footdrop, charcot's joints.
- ***Nose :*** epistaxis, saddle-nose deformity or anosmia.

2. Ans. is b i.e. M. Kansasii can cause disease indistinguishable from tuberculosis

Ref. Jawetz 24/e, p 322

"Some atypical bacteria (eg. Mycobacterium kansasii) produce human disease indistinguishable from tuberculosis." *..... Jawetz*

Other options :

Option 'a' : M. tuberculosis and M. bovis are equally pathogenic for humans. *.....Jawetz*

Features	M.tuberculosis	M.bovis
Shape	Curved long rod	Straighter, shorter, stouter
Staining	Less uniform	more uniform
O_2 requirement	Obligate aerobe	Microaerophilic
Colonies	Dry, rough, raised, irregular	Flat, smooth, moist, break up easily
Growth	Eugonic	Dysgonic

Options 'c' : M.africanum is acquired from human and cattles.

Remember :

- M. tuberculosis, M.bovis; M.africanum belongs to TB complex group of Runyons classification.
- Mycobacterium acquired from environmental source :
  - M. **a**vium complex
  - M. **m**almoense ***(Mneumonic :*** **AMU – A**ligarh **M**uslim **U**niversity)
  - M. **u**lcerans

Option 'd' : M. marinum causes chronic cutaneous infection when open cutaneous lesion is exposed to colonized water source.

Remember : Atypical bacteria causes lymphadenitis are : M.avium, M. intracellulare, M. malmoense, M. scrofulaceum, M. Kansasii.

M. Kansasii : Most pathogenic nontubercular mycobacteria.

- 2nd ***MC*** cause of lung disease due to NTM.
- Risk factors : COPD; Silicosis, Lung carcinoma, Prior tuberculosis.
- Clinical features and treatment is similar to tuberculosis with rifampicin being the most effective drug.

3. Ans. is b i.e. Prognosis *Ref. Ananthnarayan 7/e, p 373 - 374*

Lepromin test :

- It is intradermal test which shows delayed type IV hypersensitivity.
- It is biphasic : a. Early reaction of Fernandez : read in 24-48 hours (analgous to tuberculin reaction)
  b. Late reaction of Mistuda – Peak in 4 weeks
  – It is more meaningful.
- It distinguishes betwen persons who can mount CMI against lepra bacillus antigens and those who cannot.
- So, ***finally lepromin test is of little diagnostic value but has more prognostic value.***
- It is used to : – Classify the lesions of leprosy
  – To assess prognosis and respose to treatment
  – To assess resistance of individual to leprosy
  – To verify the identity of candidate lepra bacilli.
- Antigen used in lepromin test :
  – Modern antigens contain $4x10^7$ lepra bacilli per ml.
  – Standard lepromins derived from armadillo derived lepra bacilli (lepromin A) replacing human derived human lepromin H.

4. Ans. is b i.e. Consists of macrophages filled with AFB *Ref. Ananthnarayan 7/e, p 370*

- Acid fast lepra bacilli may lie extracelularly or intracellularly in large undifferentiated histiocytes (type of macrophage) called as **Virchows *'Lepra cells'* or *'foamy cells'*.**
- Bacilli are bound together by lipid like substance *the glia* forming masses known as ***'Globi'.***

5. Ans. is b i.e. Withhold breast feeding *Ref. Nelson 17/e, p 971*

If the mother is suspected of having active disease or detection of an acid fast bacilli in sputum shows evidence of current tuberculosis disease. Beside giving ATT to mother certain additional steps are necessary to protect the infant. The most important :

a. INH therapy

"INH threapy for newborns is so effective that separation of mother and infant is no longer considered mandatory."

- Separation should done (until mother become non-infectious) only if :
  – Mother is so ill so as to require hospitalization.
  – She is expected to become non-adherent with her treatment.
  – There is strong suspicion that she has drug resistant tuberculosis.

- INH treatment of infant should be continued until the mother has been shown to be sputum culture negative for at least 3 months.

b. Appropriate treatment of mother and other family members.

- Though there is controversy in the question as according to 'Some books' Breast feeding is contraindicated and isolation of infant from the mother having active TB should done.
- *But as all other three options are totally correct and as Indian child must have breast feeding, I have to go with Nelson only.*

6. Ans. is a i.e. Previous or present sensitivity to tubercule proteins

Ref. Park 19/e, p 153; Ananthnarayan 7/e, p 361

- Tuberculin test denotes Type IV hypersensitivity to tuberculoprotein but not cellular immunity.
- Positive tuberculin test indicates exposure to bacilli either in the form of infection or immunization with or without clinical disease.
- It does not indicate that active infection is present *(except in infants and young children).*
- It does not indicate whether person is able to mount immune response against bacilli or not **(as in lepromin test).**
- It does not indicate resistance or susceptibility to TB **(as in Schik's test).**

7. Ans. is b i.e. LJ medium *Ref. Ananthnarayan 7/e, p 352*

Media For M. Tuberculosis	
Solid	**Liquid**
• Lowenstein Jensen media *(most widely used)* • Dorset egg media • Loeffler's media • Pawlowsky media	• Dubos contain Tween 80 • Middle brook's • Proskauer

- Selective agent inhibiting other bacteria in LJ media is Malachite green.
- Human tubercle bacilli do not grow in presence of para-nitrobenzoic acid.
- Traces of fatty acid is toxic for tubercle bacilli in culture media.
- Optimum pH for M. tuberculosis : 6.4 – 7.0.

Remember :
- Sabouraud's is culture media for fungi.
- Pike's media is transport media of S.pyogenes.
- NIH swab is used for taking sample in pinworm infection.

8. Ans. is c i.e. Auramine Rhodamine stain *Ref. Ananthnarayan 7/e, p 357*

- ***Flourescent microscopy*** is preferred when several smears are to be examined daily ***(rapid screening).***
- In this, smears are stained with auramine phenol or auramine rhodamine fluorescent dyes and examined under UV illumination.
- Bacilli will appear as bright rods against dark backgound.

Remember :
- Modified Ziehl-Neelsen stain is used for Actinomycetes and brucella.
- Kinyoun stain also demonstrate AFB.
- Giemsa stain demonstrate Negri bodeis, Tunga sp., spirochetes and protozoans.

9. Ans. is b i.e. Lymphnode *Ref. Dashore Manual of Skin Disease, p 85*

- Scrofuloderma is a type of cutaneous tuberculosis.
- It results from direct extension of infections from underlying tuberculous focus i.e. infected lymph glands, muscles or bones.
- Patient's immunity is poor or moderate.
- Diagnosis of TB mainly depends on clinical examination.
- Lab investigations – demonstration of bacilli in smears of biopsy material, culture.

10. Ans. is b i.e. Mouse foot pad *Ref. Ananthnarayan 7/e, p 370 - 371; Harrison 17/e, p 1021*

- Lepra bacilli ***can't be cultivate*** in artificial culture media like viruses, rickettsia, chlamydia, pathogenic treponemes.
- It can multiply in the foot pads of mice kept at low temperature so this has become the standard procedure for experimental work with the bacillus.
- Though nine banded armadillo is highly susceptible to infection with lepra bacilli, no book has mentioned this is done experimentally or not.

11. Ans. is c i.e. Causes decreased efficacy of BCG due to cross immunity *Ref. Park 19/e, p 161*

Exposure to some non-tuberculous environmental mycobacteria (M.vacae, M.non-chromogenicum) may have conferred partial immunity on the population and thus masked the potential benefit of BCG vaccination. There is also evidence that exposure to other species (M.kansasi, M.scrofuloceus) have an antagonistic action against BCG.

MOTT (Mycobacteria Other Than Tuberculosis)

MOTT are mycobacterial species that may cause human disease but do not cause tuberculosis.

Spread : Unlike tuberculosis, which is spread from person to person, MOTT infections are not considered contagious. There is no evidence that the infection can be transmitted from one person to another. The mode of infection with MOTT is not clear.

Clinical features : Like tuberculosis, a MOTT infection primarily affects the lungs and the symptoms are similar. Usually MOTT infections progress slowly.

Symptoms include : Fever, Weight loss, Cough, Loss of appetite, Night sweats, Blood in the sputum.

Diagnosis : MOTT infections can be more difficult to diagnose than tuberculosis. A diagnosis is generally based on the following :

- Medical history including your symptoms
- Chest X-ray
- *Sputum culture :* Several sputum cultures are often necessary.
- *Other procedures :* More complicated diagnostic procedures (BAL) may be required in certain cases.

Treatment : Many MOTT infections are benign with no need for treatment. MOTT infections are naturally resistant to conventional antibiotics and it is necessary to use several ATT at the same time in order to overcome drug resistance.

12. Ans. is c i.e. Tumor necrosis factor - alpha *Ref. Harrison 17/e, p 1023; KDT 6/e, p 756*

TNF plays a central role in pathobiology of ENL.

Type 1 lepra reaction	Type 2 Lepra reaction
• Down grading or reversal reaction	• Erythema nodosum leproticum
• Type IV hypersensitivity	• Type III hypersensitivity
• TNF play a central role	• IFNγ and IL-2 are main cytokines involved
• Edema is characteristic microscopic feature	• Vasculitis and panniculitis are seen
• **Treatment :** ***DOC*** – Glucorticoid Other drugs : – Clofazimine – Chloroquine – Analgesics Thalidomide – Ineffective.	• ***DOC*** – Thalidomide Other – Clofazimine – Chloroquine – Glucocorticoids – NSAID's & antibiotics.

13. Ans. is c i.e. Cyclosporine *Ref. Harrison 17/e, 1026; KDT 6/e, p 756*

Cyclosporine has no role in lepra reaction.

For more details, refer just above answer.

14. Ans. is a i.e. Lepromin test *Ref. Ananthnarayan 7/e, p 374; Harrison 17/e, p 1023*

Lepromin test is *not* used for diagnosis.

15. Ans. is b i.e. It is a diagnostic test *Ref. Ananthnarayan 7/e, p 373 - 374*

Already explained, refer see answer no. 3

16. Ans. is c i.e. Rifampicin, Ofloxacin and Minocycline single dose *Ref. Harrison 17/e, p 1026*

Form of Leprosy	WHO recommended regime
i. Tuberculoid (paucibacillary)	Dapsone 100 mg/d unsupervised plus Rifampin 600 mg/mth supervised for 6 month
ii. Single skin lesion paucibacillary	Single dose of : ***R*** – 600 mg **R**ifampcin ***O*** – 400 mg **O**floxacin ***M*** – 100 mg **M**inocycline
iii. Lepromatous (multibacillary) >6 skin lesion	Dapsone 100 mg/d plus Clofazimine 50mg/d unsupervised; and rifampcin 600 mg plus clofazimine 300 mg monthly (supervised) for 1 year

17. Ans. is c i.e. Early morning *Ref. Harrison 17/e, p 1011*

GENITO - URINARY TB

– Accounts for 15% of all extrapulmonary cases.
– Urinary frequency ***(MC),*** dysuria, hematuria and flank pain are common presentation.

Diagnosis : i. Urinalysis gives abnormal result in 90% of cases.
ii. Culture of three morning urine specimens yields a definitve diagnosis in nearly 90% cases. Culture negative pyuria in acidic urine raises the suspicion of TB.
iii. IVP – Calcification, ureteral sticture and Hydornephrosis may seen.

GENITAL TB :

Female > male

MC site in **female** – Fallopian tube

MC site in **male** – Epididymis

Genitourinary TB respond well to chemotherapy.

18. Ans. is b i.e. Long contact with tuberculoid leprosy can transmit the disease

Ref. Harrison 17/e, p 1022

Transmission of Leprosy

- Nasal droplet infection.
- Contact with infected soil and Contact with a tuberculaid leprosy case carries a very low risk.
- Insect vectors.
- Direct dermal inoculatiion (during tatooing).
- Household contact with infected lepromatous case.
- Skin to skin contact is ***gernerally not considered an important route of transmission.***
- Physicians and nurses caring for leprosy patients & the coworkers of these patients are not at risk leprosy.
- According to *Park 18/e, p 254* ***"All patients with active leprosy must be considered infectious".***

Remember :

- Cell mediated immunity is present in tuberculoid lieprosy.
- Lepra bacilli can't grow in artificial culture media.
- *Park, Ananthnarayan, Harrison* do not mention that macules of Tuberculoid leprosy heals spontaneously.

19. Ans. is d i.e. Usually read after 48 - 72 hours

Ref. Ananthnarayan 7/e, p 361; Park 19/e, p 153

- Tuberculin test is the only means of estimating prevalence of infection in a population.
- It is of three types :
  - Monotoux intradermal test
  - Heaf test - for testing large goups
  - Tine multiple puncture test - not recommended.
- Standard PPD (Purified protein derivative) contains 50,000 tuberculin units per milligram.
- WHO advocates PPD tuberculin known as PPD RT - 23 with Tween 80.
- For routine testing 1 TU used, while clinically 5TU used.

Montoux Test

- 0.1 ml of 1 TU injected intradermally
- Examined after 72 hours and induration is measured horizontally in mm.
  - >10mm : Positive
  - < 6mm : Negative
  - 6-9 mm : Doubtful that is the reaction may be due to M. tuberculosis or atypical mycobacteria
  - > 20mm : Strong reactors – Greater chance of developing TB
  - < 5 mm : More risk of developing TB than those with 6-9 mm induration
- Positive reaction indicates that person is infected with M. TB but it does not prove that person is suffering from disease.
- Positive reaction is significant in younger age groups (< 2 year).

- ***Negative test can't taken as exclusion of TB*** since dermal Hypersensitivity to tuberculin can also be lost in immunosuppressive states which gives ***false -ve result*** eg. Malignancy, Hodgkin's disease, post measles state, corticosteroid therapy.
- Repeat test may appear to be negative or exerts a booster effect.
- Positive tubercullin test may occasionally revert to negative upon INH treatment.
- ***After infection patient becomes tuberculin positve in 3-6 weeks (=I.P of TB).***
- ***After 8 weeks of BCG vaccination it becomes positive.***

20. Ans. is d i.e. Niacin positive *Ref. Ananthnarayan 7/e, p 351 - 353, 366*

Mycobacteria tuberculosis is :

– Gram positive, non motile, non capsulated, non sporing.
– Obligate Aerobic.
– Acid (resist decolorization by 20% H2SO4) and alcohol fast.
– Generation time 14 - 15 hours.
– Colonies appear slowly in about 2 weeks and may some time take upto 8 weeks.
– Niacin, Neutral red, Nitrate reduction test positive (3N is positive).
– Peroxidase and urease test is also positive.

21. Ans. is c i.e. M. tuberculosis *Ref. Ananthnarayan 7/e, p 351, 370*

Features	M. tuberculosis	M. leprae
Acid fastness	Resist desoulourization by 20% H2SO4	Resist decolourization by 5% H2SO4
Alcohol fastness	Present	Absent
Culture	Possible	Not possible
Niacin	Positive (also some strain of M. microti)	Negative
Generation time	14 - 15 hours	12 - 13 days

Remember : Nocardia resist 1-4% of sulphuric acid (weakly acid fast).

22. Ans. is b and c i.e. Dorset media; LJ media *Ref. Ananthnarayan 7/e, p 352*

NNN media – for Leishmania donovani
Nutrient agar – simple media
Mac Conkey media – differential as well as indicator media for lactose and non lactose fermenters.

23. Ans. is a and b i.e. ENL; Lepra reaction 1 *Ref. Harrison 17/e, p 1023*

Reactional state	Type of Leprosy
i. Type I lepra reaction	Borderline leprosy
ii. Type II lepra reaction (ENL)	Exclusively in Borderline Lepromatous (BL) & lepromatoous leprosy
iii. Lucio's phenomenon	Diffuse lepromatous form of LL

- Jarisch Hexhimer reaction is seen in syphilis patient taking penicillin.

24. Ans. is b i.e. Mycobacterium TB *Ref. Ananthnarayan 7/e, p 352*

- ***S. aureus :*** grow *rapidly on* ordinary media within a temperature range of 10-42^{0}C.
- ***E. Coli :*** *good growth* occurs on ordinary media.
- ***Salmonella :*** grow *readily* on simple media over range pH 6-8 and temperature 15-41^{0}C.
- ***M. TB :*** grow slowly, colonies appear in 2 - 8 weeks. Culture remain viable at room temperature for 6-8 months and may be stored upto 2 year at -20^{0}C.

25. Ans. is c i.e. No risk in negative *Ref. Park 18/e, p 150 - 151; KDT 6/e, p 749*

Risk of developing TB is more in patient with montoux result < 6 mm i.e. negative.

INDICATION OF CHEMOPROPHYLAXIS

i. Contacts of open cases who show recent monotoux conversion.
ii. Children with positive Montoux and a TB patient in the family.
iii. Neonate of tubercular mother.
iv. Patient of leukemias, diabetes, silicosis or those who are HIV positive but are not anergic or are on corticosteriod therapy who show a positive montoux.
v. Patient with old inactive disease who are assessed to have received inadequate therapy.

Now drug used for chemoprophylaxis :

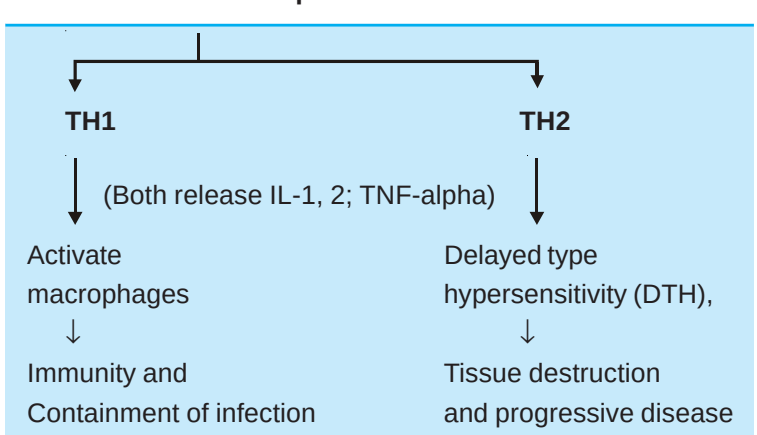
– Combination of Isoniazid (5 mg/kg).
– Rifampicin (10mg/kg) for 6 month.

26. Ans. is b i.e. Foot pad of mouse and armadillo *Ref. Ananthnarayan 7/e, p 370 - 371*

Already explained, please see answer no. 10

27. Ans. is a i.e. CD-4 *Ref. Ananthnarayan 7/e, p 355*

- Only specific immune mechanism effecitve in TB is the *'cell mediated type'* ***(since it is intracellular).***
- Humoral immunity appears to be irrevalent.
- ***Key cell*** is the activated **CD4 + Helper** T cell.



Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Battey bacillus or mycobacterium intracellulary is
a) Photochromogen **[JIPMER 90]**
b) Scotochromogen
c) Non–photochromogen
d) Rapid grower
[Ref. Ananthnarayan 7/e, p 366]

2. Reactivation tuberculosis is almost excusively a disease of the : [JIPMER 90]
a) Lungs
b) Bones
c) Joints
d) Brain
[Ref. Ananthnarayan 7/e, p 355]

3. Which of the following is not a pathogenic mycobacteria : [AI 91]
a) M. Kansasii
b) M. scrofulaceum
c) M. cheoleni
d) M. smegmatis
[Ref. Ananthnarayan 7/e, p 351]

4. Which of the following is scotochromogen :
a) M. scrofulaceum **[JIPMER 91]**
b) M. ulcerans
c) M. Kansasii
d) M. fortuitum
[Ref. Ananthnarayan 7/e, p 365]

5. Cutaneous lesions may be produced by the following mycobacteria except : [Delhi 91]
a) M. intracellulare
b) M. Leprae
c) M. marinum
d) M. tuberculosis
e) M. ulcerans
[Ref. Ananthnarayan 7/e, p 367]

6. Acid fastness of tubercle bacilli is attributed to :
a) Presence of mycolic acid
b) Integrity of cellwall **[AIIMS 91, 85; PGI 85]**
c) Both of the above
d) None of the above
[Ref. Ananthnarayan 7/e, p 352]

7. In which type of Cutaneous Tuberculosis, caseation is most commonly seen : [PGI 93]
a) Papulonecrotic
b) Scrofuloderma
c) Lupus Vulgaris
d) Erythema nodosum

8. True about M. tuberculosis is : [Delhi 93]
a) Strict aerobes
b) Gram negative
c) Thin cell wall
d) Curved rod
[Ref. Ananthnarayan 7/e, p 351]

10. Single skin lesion is seen in which type of Leprosy: [AI 93]
a) LL
b) TT
c) BL
d) BT
[Ref. Harrison 17/e, p 1022]

11. Lepra bacilli are best cultivated in : [AI 93]
a) Guinea pig
b) Armadillos
c) Mouse toot pad
d) Nutrient agar
[Ref. Ananthnarayan 7/e, p 370]

Answer

1. c) Non–photoc ...
2. a) Lungs
3. d) M. smegmatis
4. a) M. scrofulaceum
5. None
6. c) Both of the ...
7. b) Scrofuloderma
8. a) Strict aerobes
10. b) TT
11. b) Armadillos

12. Lepra cells found in lepromatous leprosy are :
a) Neutophils **[Kam 94]**
b) Lymphocytes
c) Macrophages
d) Plasma cells
[Ref. Ananthnarayan 7/e, p 370]

13. The animal model frequently used tor M. Leperae is : **[Karn 94]**
a) Mice
b) Gninea pig
c) Rabbits
d) Golden hamsters
[Ref. Ananthnarayan 7/e, p 370]

14. Leprosy spreads by : **[Kerala 95]**
a) Skin to skin contact
b) Blood transfussion
c) Droplet spread
d) Ingestion
[Ref. Harrison, 17/e, p 267]

15. Mycobacterium tuberculosis is differentiated from other atypical mycobacteria by :
a) Niacin test **[SGPGI 95; AIIMS 91]**
b) AFB staining
c) PAS staining
d) None
[Ref. Ananthnarayan 7/e, p 353]

16. Leprosy bacilli are cultured in : **[AP 97]**
a) LJ. medium
b) Foot pad of mice
c) Agar plate
d) None
[Ref. Ananthnarayan 7/e, p 370]

17. The local lession in BCG is maximum in :
a) 2 days **[Kerala 98]**
b) 7 days
c) 28 days
d) 1 year
[Ref. Park, 19/e, p 161]

18. Mitsuda reaction is read after : **[MP 98]**
a) 3 days
b) 3 hours
c) 3 weeks
d) 3 months
[Ref. Ananthnarayan 7/e, p 374]

19. The factor which promotes, virulence of M. tuberculosis : **[TN 98]**
a) Wax D
b) Cord factor
c) Muramyl dipeptide
d) Mycolic acid
[Ref. Jawetz, 23/e, p 321]

20. BCG differs from mantouxe test by : **[UP 98]**
a) Less sensitive and more specific
b) More sensitive and more specific
c) More sensitive and more specific
d) Less sensitive and more specific
[Ref. Ghai 6/e, p 235, 192]

21. Not a pathogenic mycobacterium to human :
a) M. paratuberculosis **[TN 99]**
b) M. kansasii
c) M. ulcerans
d) M. intracellular
[Ref. Ananthnarayan 6/e, p 324]

22. Rapid diagnosis of tuberculosis is possible with:
a) Auramine rhodamine ~ stain **[ICS 2K]**
b) Zeil - Neelsen stain
c) Geimsa stain
d) Leishman stain
[Ref. Ananthnarayan 7/e, p 357]

23. Mycobacterium scrofulaceum which cause scrofula, belongs to which groups of Atypical mycobacteria: **[Kerala 2K]**
a) Photochromogens
b) Scotochromogens
c) Non-photochromogens
d) Rapid growers
e) None of the above
[Ref. Ananthnarayan 7/e, p 365]

24. Mycobacterium leprae can be grown in :
a) Teepol agar **[Kar 2000]**
b) Tomato juice agar
c) Foot pad of mouse
d) LJ media
[Ref. Park 19/e, p 270]

25. Photochromogenic strain of mycobacterium species is : **[Kar 2001]**
a) M. kansasii
b) M. scrofulaceum
c) M. avium intracellular/lare
d) M. smegmatis
[Ref. Ananthnarayan 7/e, p 365]

Answer

12. c) Macrophages	13. a) Mice	14. c) Droplet spread	15. a) Niacin test	16. b) Foot pad ...
17. c) 28 days	18. c) 3 weeks	19. b) Cord factor	20. b) More sensitive	21. a) M. paratuber ...
22. a) Auramine	23. b) Scotoch ...	24. c) Foot pad ...	25. a) M. kansasii	

26. Mycobactium TB can be differentiated from other mycobacterium by : **[Kerala 01]**

a) Production of niacin
b) Arylsulphate test
c) Coagulase test
d) Bile solubility test

[Ref. Ananthnarayan 7/e, p 353]

27. Mantoux test is an indicator of : **[Kolkata 02]**

a) Immediate of hypersensitivity
b) Delayed hypersensitivity
c) Cell-mediated cytotoxicity
d) Of no interest

[Ref. Ananthnarayan 7/e, p 166]

28. The best diagnostic procedure of M. tuberculosis

a) PCR **[SGPGI 02]**
b) Auramine rhodamine stain
c) Sputum culture
d) Sputum examination

[Ref. Harrison, 17/e, p 1014]

29. Drug resistance in tuberculosis is due to :

a) Transformation **[Kar 2002]**
b) Transduction
c) Conjugation
d) Mutation

[Ref. Ananthnarayan 7/e, p 59; Jawetz 24/e, p 326]

30. Subtype of leprosy has maximum number of TH:1 cells: **[UP 03]**

a) TT
b) BB
c) LL
d) Borderline leprosy

[Ref. Harrison, 17/e, p 1023]

31. All are rapid growers except : **[SGPGI 03]**

a) M. fotuitum
b) M. chelonei
c) M. auiuim intracellulare
d) M. smeqmatis

[Ref. Ananthnarayan 7/e, p 367]

32. All of the following are acid fast bacteria except :

a) Cryptosporidia **[SGPGI 03]**
b) Mycoplasma
c) Mycobacteria
d) Nocardia

[Learn the list from our book]

33. In a patient the lymphnodes show necrosis with poor granuloma formation with plentiy of acid fast bacilli sugessts : **[SGPGI 04]**

a) Tuberculosis in an immunocompromised patient
b) HIV with tuberculsis
c) Sarcoidosis
d) Mycobacterium bovis infection

[Ref. Harrison, 17/e, p 1011]

34. Culture of lepra bacilli done in : **[Kolkata 05]**

a) Nine banded armadillo
b) Tail of mouse
c) Foot pads of mice
d) nutrient agar

[Ref. Ananthnarayan 7/e, p 370-371]

35. Mycobacterium non-pathogenic to man :

a. M.bovis **[Kolkata 05]**
b. M.kansai
c. M.aviun intracellular
d. M.phlei

[Ref. Chakarborty 2/e, p 414]

36. Swimming pool granuloma is caused by :

a) Myco kansasi **[UP 05]**
b) Myco. avium intracellulare
c) Myco. scrofulaceum
d) M. marinum

[Ref. Ananthnarayan 7/e, p 365]

37. Most common organism in AIDS in TB, India :

a) M. tuberculosis **[MP 06]**
b) M. avium intracellular
c) M. bovis
d) M. ulcerans

[Ref. Ananthnarayan 7/e, p 589; Park 19/e, p 291; Harrison 17/e, p 1013]

38. Stain for the diagnosis of tuberculosis : **[MP 07]**

a) Auramine-rhodamine
b) India ink
c) Geimsa stain
d) Zeil - Neelsen stain

[Ref. Ananthnarayan 7/e, p 357]

39. Globi is : **[Jharkhand 05]**

a) Histocyte containing acid-fast bacillus
b) Lymphocyte containing acid-fast bacillus
c) Nutrophill containing acid-fast bacillus
d) Large lymphocyte containing acid-fast bacillus

[Ref. Ananthnaraya 7/e, p 370]

Answer

26. a) Production ...	27. b) Delayed ...	28. b) Auramine ...	29. None	30. a) TT
31. c) M. auiuim ...	32. b) Mycoplasma	33. a and b	34. c) Foot pads ...	35. d) M.phlei
36. d) M. marinum	37. a) M. tuberculosis	38. a) Auramine ...	39. a) Histocyte ...	

9 Enterobacteriaceae

- **Enterobacteriaceae** includes large group of Gram negative rods whose natural habitat is large intestine.
- They are predominantly aerobic or facultative anaerobes, nonsporing and non acid fast.
- They have following **common characteristics :**
  - Grow well on ***Mac* conkey media.**
  - Catalase (+)ve; except Shigella dysentriae type 1.
  - Oxidase (-)ve; reduces nitrates to nitrite.
  - Urease (-)ve; except Proteus, Klebsiella, Morganella.
  - Motile by peritrichate flagella except shigella, klebsiella and salmonella gallinarum - pullorum.
  - Ferment glucose except shigella.

Classification :

MC and oldest method to classify these bacteria is on ***basis*** of ***fermentation of lactose.***

Lactose fermented rapidly = Coliforms	Lactose fermented slowly = Late lactose fermenter = Paracolons	Lactose not fermented = Mostly pathogenic
• *Escherichia* • *Klebsiella* • *Enterobacter aerogenes* They forms pink colony on Mac conkey's medium and are usually part of normal flora.	• *Edwardsiellla* • *Serratia* • *Citrobacter* • *Arizona* • *Providencia* • *Erwinia* • *Shigella sonnei*	• *Shigella except S.sonnei* • *Salmonella* • *Proteus*

Remember : Differential media which distinguishes lactose fermenting (coloured) from non-lactose fermenting colonies (non pigmented) includes Eosin methylene blue (EMB), MacConkey or deoxycholate medium.

ESCHERICHIA COLI

Morphology

Motile by peritrichate flagella, non sporing. Many pathogenic isolates are *capsulated.*

Culture and Biochemical characterstics

- Grows well on ordinary media.
- *On blood agar shows hemolysis.*
- Indole and Methyl red (+)ve while VP and citrate (-)ve [IMVC ++--].

Antigenic structure

- *Somatic antigen O* – Lipopolysaccharide in nature, heat stable. Antibodies to O antigen are predominantly IgM.
- *Capsular antigen K* – Heat labile responsible for attachments of bacteria to epithelial cells.
  – Associated with virulence.
- *Flagellar antigen*
- Serotyping based on these three antigens is :
  – **Normal colon strains = commensal strains belong to early 'O' group (1, 2, 3, 4, etc).** These strains generally lack specialized virulent traits. However they may be involved in extraintestinal infection.
  – **Enteropathogenic strains : Belong to later 'O' group (25, 55, 86 etc).**
  – **Extraintestinal pathogenic E. coli [EXPEC] :** ***MC*** cause of extraintestinal E.coli infection. Like commensal E.coli they can be found in normal intestinal flora without causing gastroenteritis, but they have acquired diverse virulence factor that enable them to live extraintestinally.

Virulence factors

Surface antigen :

- O antigen – It has endotoxic activities and also protects bacteria from phagocytosis.
- K-antigen– Protect against phagocytosis.
- Fimbriae – *Plasmid coated fimbrae increase virulence*, while chromosomally determined fimbriae has no effect on virulence.

Toxin : E.coli produce two kind of exotoxin :

- Hemolysins – No role in pathogenesis of dirrhoea.
- Enterotoxins – Important in pathogenesis of diarrhoea.

- **E.coli enterotoxins**

Heat stable toxin [ST_A]	Heat labile toxin [LT]	Verocytotoxin [VT] = Shiga like toxin [SLT]
• Plasmid mediated	• Plasmid mediated	• Phage coded
	• Consist of 2 subunit	• Belong to ribosome inactivating protein [RIP] toxins
• Activates cGMP	A ↓ — B ↓	
• Acts very rapidly	Activates CAMP ↓ Diarrhoea; Binds GM_1 gangliosides	• A subunit of SLT inhibit ribosme and ↓ protein synthesis and shows cytotoxicity

Clinical findings

A. Diarrhoea – 5 types of diarrhoeagenic E.coli are recognised :

- **Enteropathogenic = enteroadherant E.coli**
  – Cause diarrhoea in infant and children.
  – Non toxigenic and non invasive.
  – Produce diarrhoea by disruption of brush border.

– They are unable to ferment sorbitol.

- **Enterotoxigenic E.coli (eg. 06, 08, 015, 025, 027, 0167)**
  – Affect *all age group.*
  – ***MC*** cause of traveller's diarrhoea (indistinguishable from cholera).
  – Produce either or both LT and STa.
  – Produce diarrhoea, only when it adheres to intestinal mucosa by fimbrial or colonization factor antigen and produce toxin.
- **Enteroinvasive E. coli**
  – Called *atypical E. coli* as many strains don't ferment lactose or ferment it late.
  – Resemble Shigella flexneri except in fermenting dulcitol and forming alkali in litmus milk.
  – Cause illness resembling shigellosis.
  – Ability to *penetrate cells is due to* presence of plasmid which codes for outer membrane antigen called virulence marker antigen *[VMA].*
  – For *diagnosis* of EIEC - Sereny test is used. Cell penetration of Hela or HEP-2 in culture is also *diagnostic test.*
- **Enterohemorrhagic E.coli [EHEC] = Verotoxingenic E.coli (VTEC)**
  – Source of infection appears to be salad as washing only doesn't remove bacteria.
  – Produce *Verocytotoxin VT* whose major target is vascular endothelial cells.
  – Cause disease ranging from mild diarrhoea to fatal hemmorhagic colitis and hemolytic uremic syndrome [HUS].
  – **HUS :** – Mainly caused by O157 H7 type which does not ferment sorbitol (Some 0157 and non 0157 strain ferment sorbitol).
  – Antibiotics increase the incidence of HUS.
- **Enteroaggregative E. coli - (EAEC)**
  – Cause *persistent diarrhoea.*
  – Stacked brick' formation on Hep -2 cells.
  – Produce ***EAST*** – Enteroaggregative heat stable enterotoxin.

B. UTI

- ***MC cause of both uncomplicated and nosocomial UTI.***
- UTI causing serotypes are those normally found in faeces.
- Only one serotype is generally isolated from infected urine at a time while in diarrhea many serotypes are present in a single culture.
- Nephropathogenic E. coli typically produce Haemolysin.
- Pyelonephritis is associated with specific type of pilus, P. pilus.
- **Diagnosis** - UTI is said when there is :
  – Bacteriuria $\geq 10^5$/ml in *asymptomatic*
  – Bacteriuria of $> 10^4$/ml in *symptomatic*
  – Bacteriuria of $\geq 10^2$/ml in *catheterized* sample
  – Bacteriuria of *any degree* in *suprapubic* aspirate.
- **Presumptive diagnosis of bacteriuria is made by :**
  – *Griess Nitrite test*
  – *Catalase Nitrite test*
  – *Triphenyl tetrazolium chloride test.*

C. Pyogenic Infection – E.coli is ***MC*** Cause of intrabdominal abscess, peritonitis and cholangitis.

D. Meningitis – E.coli is ***MC*** cause of neonatal meningitis.

E. Pneumonia – E. coli is **2nd *MC*** cause of nosocomial pnenumonia [*1st being* **Staph aureus**]

F. Bacteremia – UTI is ***MC*** source of E.coli bacteremia leading to septic shock

Treatment

- **UTI** – ***Fluroquinolone*** are ***DOC.***
- **Diarrhoea** – Fluids and electrolyte correction with **no antibiotics.**
- **Drug resistance is plasmid mediated.**

KLEBSIELLA

- Non motile, capsulated rods (capsule seen as haloes around bacilli).
- **Classified** into **3 species** on the *basis* of **biochemical characteristics** and into ***serotypes*** on *basis* of ***K-antigen*** *(capsular antigen).*

Klebsiella pneumoniae = Friedlander's bacillus

- Rarely cause disease in normal person.

Clinical manifestation

– Cause community acquired pneumonia in alcoholics, chronic bronchopulmonary disease or diabetes.

– ***MC*** clinical syndromes it causes are pneumonia, UTI, abdominal infections, surgical site infection, soft tissue infection and bacteremia.

– **Pneumonia** : - Mainly Hospital acquired. Abscess are *more common* than in pneumococcal pneumonia.
- Cause classic lobar infiltrate with bulging fissure.
- Sputum is red current jelly in character.

– **UTI** : Mainly in settings of prolonged catheterization.

– **Diarrhoea** : By toxin similar to ST_A of E. coli.

***Klebsiella Ozaenae* :** Causative agent of ozoena characterised by foul smelling nasal discharge.

Klebsiella rhinoscleromatis : Causative agent of rhinoscleroma.

Treatment

- **Carbipenim** (Imipenam) – Most active antibiotic against klebsiella.

SHIGELLA

- Non motile, non capsulated, non lactose fermentar (except S. sonnei which ferments it late).
- **Classified** on the *basis* of *somatic O Antigen (LPS) and carbohydrate fermentation (mannitol) pattern.*
- Catalase is produced by *all except* Sh. dysnteriae I.
- Mannitol is fermented by *all except* Sh. dysnteriae I.
- ***MC*** Shigellosis worldwide – Sh. sonnei.
- ***MC*** Shigellosis in India – Sh. flexneri.
- Most clinically severe form of Shigellosis is caused by Sh. Dysenteriae type I while mildest form of bacillary dysentery is by Sh. sonnei (may occur as food poisoning).
- Only species that exist as single serotype – Sh. sonnei.

- Pathogenic species of shigella are :

Present Designation	Group & Type	Mannitol	Ornithine Decarboxylase
S dysenteriae	A	–	–
S flexneri	B	+	–
S boydii	C	+	–
S sonni	D	+	+

Culture

- **Selective media :** – Deoxycholate citrate agar (DCA).
  – Hektoen enteric agar or Salmonella - Shigella agar. *..... Jawetz 24/e, p 257*
- Triple sugar iron (TSI) agar is used to differentiate salmonella and Shigella from other gram-negative rods in stool cultures.

Pathogenesis

a. Invasiveness (main) :

- Bacteria invade basolateral surface of colon epithelium → intracellular replication and cell to cell spread with the help of microbial protein Ics A (ATP-ase) and host protein cadherin L - CAM.
- This process present in all virulent shigellae as well as in EIEC. It is responsible for late dysentery. Hence *nontoxic mutants can cause dysentery but non-invasive can't produce dysentery.*

b. Toxins :

i. Endotoxin – LPS present in all shigella causing irritation of bowel.

ii. Shigella Dysenteriae – I or Shiga bacillus exotoxin :

– It has *neurotoxicity* on blood vessel of CNS.
  - *Enterotoxicity* causing fluid accumulation in ligated rabbit ileal loop.
  - *Cytotoxicity* same as Verotoxin I or Shiga like toxin produced by some strain of EHEC including 0157:H7.

– *Toxin has two peptide subunit. A unit (N-glycosidase) of cytotoxin* hydrolyzes adenine form specific sites of 60s RNA and thus *inhibits protein synthesis*. It contributes to fatal nature of S. dysenteriae infection.

– Toxins produce early, *non bloody* voluminous diarrhoea.

Clinical Features

- Most cases of bacillary dysentery occur in < 10 year children.
- Infective dose is in the order of 10^2 organisms (while in vibrio and Salmonella 10^5-10^8). *..... Jawetz 24/e, p 256*
- Transmitted faecorally generally direct person to person contact; *anal-oral sex (esp. in Sh. sonnei).*
- Majority of lesion are in *distal colon.*
- **Complications** – Toxic dilatation , Colonic perforation.
  – *Extraintestinal* (esp. with *S. dysenteriae* and *S. flexneri*) like HUS, Thrombotic thrombocytopenic purpura reactive arthritis, Reiter's syndrome.

Diagnosis

- **Specimen** – Best to use mucus flakes of stool.
- **Transport media** – Sach's buffered glycerol saline.
- **Specific diagnosis** – Culture of shigella from stool.

Treatment

- **Mild to moderate dehydration** – Oral rehydration therapy (No antibiotics).
- **Severe cases with bloody diarrhea** – ***DOC*** Ampicilin or cotrimoxazole (Amoxicillin is not effective).
- ***DOC*** **for Multiresistant :** Nalidixic acid.

SALMONELLA

- Genus consist of bacilli that parasitise small intestine leading to enteric fever, gastroenteritis, septicemia.
- They are motile with peritrichate flagella except *S.gallinarum pullorum.*
- They are non-capsulated and non-sporing.

Culture and Biochemical characterstics

- Grows readily on simple media.
- On Wilson – Blair bismuth sulphite media S. typhi produce jet black colonies due to production of H_2S.
- ***Enrichment media*** – Selenite F and Tetrathionate broth.
- ***Selective media*** – Salmonella-shigella agar, Deoxycholate citrate agar which promotes growth of salmonella over other enterobacteria.
- Salmonella ferment sugar producing acid and gas *except S. typhi which is anaerogenic.*
- S. typhi need *tryptphan as growth factor.*
- Boiling or chlorination of water and pasteurisation of milk destroy the bacilli.

Classification

- Originally Salmonella was classified on the *basis* of *O, H* and *Vi antigenic* structure and biochemical reactions. But now on the *basis* of *DNA hybridization* studies only *7 groups have been identified.*
- ***Nearly all the salmonella serotypes that infect human are in DNA hybridization group 1.***

..... Jawetz 24/e, p 258

Antigenic structure

1. **Flagellar antigen (H)**
   - Heat labile protein which is strongly immunogenic. When mixed with antisera, it rapidly produce-*flufty clumps.*
2. **Somatic antigen (O)** (Biovin antigen)

   Phospholipid polysaccharide complex identical with endotoxin. It remains unaffected by boiling. When mixed with antisera, forms chalky, granular clumps.
3. **Vi antigen** – Heat labile surface polysaccharide antigen enveloping O antigen. Found only in S.typhi and S.paratyphi. Poorly analogous to K antigen of coliforms. Heat-labile and inmmunogenic. *Associated with Virulence.*

   Remember : Order of immunogenic nature of antigen : H > O > Vi

Pathogenicity

- On reaching gut, bacilli are phagocytosed.
- Salmonella typhi *resist intracellular killing* by macrophages and polymorphs and enter mesentric lymph node and from there via thoracic duct enter blood stream to produce bacteremia (Enteric fever).

Clinical Manifestation

I. **Enteric fever** – Systemic disease characterized by fever and abdominal pain caused by S.typhi (called as typhoid) and S.paratyphi. A, B and C.
   - ***I.P*** – 14 days.
   - ***Typical features*** – *Step ladder pyrexia with relative bradycardia*
     – *Rose spots* (located primarily on chest) usually appear at the end of 1st week and resolve after 2 - 5 days.

- Paratyphoid fever of S. paratyphi is generally milder.
- ***Transmission*** **-** Transmitted through close contact with cases and carriers.

Carriers **:**

- Those who excrete bacilli for more than a year are called as *Chronic carrier.*
- Carrier rate is 3% (i.e. 3% of cases become chronic carrier).
- Though cases occur more in males, carriers are common in females.
- Faecal carrier are ***MC.***
- Urinary carrier signify abnormality in urinary tract.

Diagnosis (BASU)

A. Cases

- **Blood culture (B)**
  - Positive in 1st week *(Diagnostic gold standard).*
  - Clot culture has *higher rate of isolation*, than blood culture.
- **Agglutination (A)** = Widal reaction
  - Becomes (+)ve by end of 1st week, *peaks at 3rd week*, decline afterwards.
- **Stool culture *(S)*** – 3rd week, particular valuable in *patient on antibiotics* in which blood culture is (-)ve Sample are plated directly on *MacConkey, DCA,* and *Wilson - Blair media (highly selective).*
- **Urine culture *(U)*** – (+)ve only in 2nd and 3rd weeks.

B. ***Carriers***

- **Widal** – No value in detection of carrier.
- *Demonstration of Vi agglutinin has been claimed to indicate carrier state and used as screening of carrier.*

Treatment

Cases*:*

- First line – Ciprofloxacin, Ceftriaxone
- Alternative – Azithromycin
- Multidrug resistant [MDR] *S. typhi* - Ciprofloxacin is ***DOC***. Multidrug resistant is due to R factor.

Carriers : Amoxicillin, Cotrimoxazole, Ciprofloxacin are effective.

Prevention

Following vaccines are available :

Vaccine	Nature	Dose	Minimum age
Type 21a	Live attenuated	4 oral dose	6 years
ViCPS	Purified Vi polysacchride	1 Parenteral dose	2 years
VirEPA	Vi bound to recombinent protein	2 parenteral dose	6 month

Vir EPA is most effective.

II. Gastroenteritis = (Food poisoning)

- ***MC*** caustive agent is ***S.typhimurium.***
- Most frequent sources are poultry, meat, milk and milk products.
- Never caused by S. typhi.
- ***IP***-6-48 hours.
- ***Clinical features*** – Nausea, vomiting, diarrhoea, Abdominal cramps and fever.

- Blood culture is negative.
- ***Treatment*** – No antibiotics are given but for serious invasive cases, antibiotics is given.

III. Bacteremia and Endovascular infection

Salmonella serotypes S. cholerae-suis and S. dublin are frequently associated with sustained bacteremia.

PROTEUS BACILLI

- Non lactose fermenter.
- ***P. Mirablis*** which is responsible for 90% of proteus infection is a normal commensal.
- Proteus differs from other enterobacteria by presece of enzyme phenyalanine deaminase *(responsible for PPA reaction).*
- Culture of proteus bacilli have characteristic fishy or seminal smell.
- P mirablis and P. vulgaris swarms on solid culture media.
- **Antigenic structure** – Proteus posses Flagelar (H) and somatic O antigen.
- **Infectious syndromes** – UTI (20-30% of complicated UTI); Pneumonia (primarily in hospitalized patient); Intraabdominal infections; soft tissue abscess.

Remember : Some strains of ***P. vulgaris*** called ***X strains*** are agglutinated by sera from typhus fever patient. This is due to sharing of carbohydrate hapten between ***Rickettsiae*** and proteus and forms basis of *Weil Felix reaction.*

QUESTIONS

1. With reference to infection with Escherichia coli the following are true except : [AI 05]

a) Enteroaggregative E. coli is associated with persistent diarrhoea

b) Enterohemorrhagic E. coli cause hemolytic uremic syndrome

c) Entero-invasive E. coli produces a disease similar to salmonellosis

d) Entero toxigenic E. coli is a common cause of traveller's diarrhoea

2. A 20 year old man presented with hemorrhagic colitis. The stool sample grow Escherichia coli in pure culture. The following serotype of E. coli is likely to be the causative agent : [AI 04]

a) 0 157:H7

b) 0 159:H7

c) 0 107:H7

d) 0 55:H7

3. A microbiologist wants to develop a vaccine for prevention of attachment of diarrhoeagenic E. coli to the specific receptors in the gastro-intestinal tract. All of the following fimbrial adhesions would be appropriate vaccine candidates except:

a) CFA-1 **[AI 04]**

b) Pi-Pili

c) CS-2

d) K88

4. In patient with typhoid, diagnosis after 15 days of onset of fever is best done by : [AI 02]

a) Blood culture

b) Widal

c) Stool cuture

d) Urine culture

5. All are true about EHEC except : [AI 01]

a) Sereny test is positive

b) Ferments sorbitol

c) Causes HUS

d) Elaborates Shiga like exotoxin

6. All of the following are true except : [AI 01]

a) E.coli is an aerobe and facultative anaerobe

b) Proteus forms uric acid stones

c) E.coli is motile by peritrichate flagella

d) Proteus caused deamination of phenylalanine to phenylpyrivic acid

7. E. coli attached to a surface with the help of :

a) Fucose **[AI 00]**

b) Concanavalin

c) Phytohaemagglutinin

d) Lactin

8. True statement about Widal test in typhoid is :

a) O-antigen titre remians positive for several months and reaction to it is rapid **[AI 99]**

b) H-antigen titre remains positive for several months and reaction to it is rapid

c) Both remains positive for several months and reaction to both is rapid

d) None

9. True statement about widal test in typhoid is:

a) Widal test is confirmative in endemic areas

b) Antibiotic treatment does not alter widal test results

c) Previous infection alters widal test **[AI 99]**

d) Widal test does not alter with prior vaccination

10. Shigella can be differentiated from E. coli by all of the following features except : [AI 99]

a) Shigella does not produce gas from glucose

b) Shigella does not ferment lactose

c) Shigella does not ferment mannitol

d) Shigela has no flagella and is non motile

11. Which of the following statement regarding Shigella dysenteriae type I is true : [AI 99]

a) It can lead to hemolytic uremic syndrome

b) It produces an invasive enterotoxin

c) It is an facultative aerobes

d) It is MR negative

12. Shigella are be divided into sub group on the basis of ability to ferment : [AI 97]

a) Lactose

b) Maltose

c) Fructose

d) Mannitol

13. Which of the following is a true statement regarding Enterobacteriaceae : [AI 96]

a) Motility is by polar flagellum

b) Glucose is not fermented by all members of the family

c) All members are oxidase positive

d) Nitrate reduction negative

Answer

1. c) Entero-... 2. a) 0 157:H7 3. b) Pi-Pili 4. b) Widal 5. a) Sereny ...
6. b) Proteus ... 7. a) Fucose 8. b) H-antigen ... 9. c) Previous ... 10. c) Shigella ...
11. a) It can ... 12. d) Mannitol 13. b) Glucose ...

14. Most common organism causing UTI : **[AI 96]**

a) E. coli
b) Proteus
c) Klebsiella
d) Staphylococci

15. Which of the following is true about Enteropathogenic E. coli : **[AI 96]**

a) Causes diarrhea in infants
b) Acts by invasion of intestinal epithelial cells
c) Adults are mostly affected
d) Affects immunocompromised host

16. Which of the following is true regarding Salmonella infection : **[AI 96]**

a) Urine culture is +ve in 1st week
b) Stool culture is +ve in 1st week
c) Blood culture is +ve in 3-7 days
d) Widal test is +ve in 1st week

17. Which of the following produces enterotoxin:

a) Sh. dysenteriae **[AI 95]**
b) Sh. sonnei
c) Sh. flexneri
d) Sh. boydi

18. Which antigen blocks the agglutination of salmonella by 0 antiserum : **[AI 95]**

a) H.
b) Fimbirae
c) Vi
d) 0

19. Salmonella typhi is the causative agent of typhoid fever. The infective dose of S. typhi is :

a) One bacillus **[AIIMS 06]**
b) 10^8 - 10^{10} bacilli
c) 10^2 - 10^5 bacilli
d) 1 - 10 bacilli

20. A 20 year old male had pain in abdomen and mild fever followed by gastroenteritis. The stool examination showed presence of pus cells and RBC's on microscopy. The most likely etiological agent is : **[AIIMS 03]**

a) Enteroinvasive E. coli
b) Enteropathogenic E. coli
c) Etnerotoxigenic E. coli
d) Enteroaggregative E. coli

21. There has been an outbreak of food borne salmonella gastroenteritis in the community and the stool sample is received in the laboratory. Which is the enrichment medium of choice :

a) Cary-Blair medium **[AIIMS 03]**
b) V - R medium
c) Selenite F medium
d) Thioglycholate medium

22. A 24 year cook in a hostel is suffering from enteric fever 2 years back. The chronic carrier state in patient is diagnosed by : **[AIIMS 02]**

a) Vi aglutination test
b) Blood Culture in Brain Heart infusion broth
c) Widal test
d) C reactive protein

23. For typhoid endemic country like India, immunization of choice is : **[AIIMS 01]**

a) TAB vaccine
b) Typhoral 21A oral vaccine
c) Monovalent vaccine
d) Any of these

24. Kallu, a 22 year old male had an outing with his friends and developed fever of 38.5°C, diarrhoea, and vomiting following eating chicken salad, 24 hours back. Two of his friends developed the same symptoms. The diagnosis is : **[AIIMS 01]**

a) Salmonela enteritis poisoning
b) Bacillus cereus
c) S. aureus
d) Vibrio cholera

25. All are true about Shigella except : **[AIIMS 99]**

a) Large dose is required for infection
b) Associated with hemolytic uremic syndrome
c) Causes bloody diarrhoea with mucus
d) Gut pathology is due to toxin

26. A person returns to Delhi from Bangladesh after 2 days and has diarrhoea. Stool examination shows RBCs in stool. The likely organism causing is : **[AIIMS 99]**

a) Enteropathogenic E. coli
b) Enterotoxigenic E. coli
c) Salmonella typhi
d) Shigella dysenteriae

27. All are true about enterohemorrhagic E. coli except : **[AIIMS 99]**

a) Sereny test positive
b) May cause diarrhoea
c) Can cause hemolytic uremic syndome
d) Verocytotoxin is produced

Answer

14. a) E. coli ... 15. a) Causes ... 16. c) Blood ... 17. a) Sh. dysente ... 18. c) Vi
19. c) 10^2 - 10^5 ... 20. a) Enteroinva ... 21. c) Selenite F ... 22. a) Vi aglutinat ... 23. c) Monovalent ...
24. a) Salmonela ... 25. a) Large ... 26. d) Shigella ... 27. a) Sereny ...

28. All of the following are true regarding typhoid except : [AIIMS 99]
a) Urinary carriers are more dangerous
b) Vi ab is used for detecting carrier
c) Vi is seen in normal population
d) Urine carrier is associated with anomalies

29. Which toxin is mediated by C-AMP except :
a) V. cholera 01 **[AIIMS 98]**
b) Heat stable E. coli toxin
c) Heat labile E. coli toxin
d) V. cholera 0137

30. Traveller's diarrhoea, is caused by : [AIIMS 97]
a) Shigella
b) E. coli
c) E. histolytica
d) Giardiasis

31. HUS is caused by : [PGI 07]
a. EIEC
b. Shigella
c. Salmonella
d. Cholera
e. Klebsiella

32. Enterobacteriaecae all except : [PGI 06]
a) Pseudomonas
b) Klebsiella
c) V. cholera
d) Proteus
e) E. Coli

33. True about salmonella gastroentritis is/are :
a) Mainly diagnosed by serological tests **[PGI 06]**
b) Blood & mucous are present in stool
c) Caused by animal products
d) Symptoms appear between 4 - 48 hours
e) Features are mainly due to exotoxin

34. True about typhoid : [PGI 03]
a) It is caused by S.typhi
b) Water can transmit the disease
c) Type 21 a is an oral vaccine
d) Chronic carrier is called when transmitted up to 6 month
e) Widal test +ve in 1st week

35. Which of these are true about E.coli : [PGI 02]
a) The L.T., (labile toxin), in ETEC acts via CAMP
b) UTI causing E.coli attaches through pilli
c) The ST (Stable toxin) of ETEC is responsible for causing hemolytic-uremic syndrome
d) EIEC invasiveness is under plasmid control
e) In EPEC, the toxin helps in invasion

36. Salmonella gastroenteritis is : [PGI 02]
a) Mainly diagnosed by serology
b) Blood and mucous present in blood
c) Caused by animal products
d) Symptoms appear by 4-48 hrs
d) Features are due to exotoxin released

37. True about Salmonella typhi infection in intestine are : [PGI 01]
a) Affects peyer's patches
b) Common in mesenteric border
c) Erythrophagocytosis is characteristic
d) Strictures are common
e) Typhoid ulcer always bleed very much

38. M.C cause of liver abscess : [PGI 00]
a) Streptococcus
b) Staph'aureus
c) E. coli
d) Staph pyogenes

39. Maximum urease is produced by : [PGI 00]
a) H. pylori
b) P. Mirabilis
c) K. rhinomatis
d) Ureaplasma

40. E. coli gives pink colour with : [PGI 99]
a) Chocolate agar
b) L J medium
c) MacConkey's medium
d) Saline broth

Answer
28. c) Vi is seen ... 29. b) Heat ... 30. b) E. coli 31. b) Shigella 32. a and c
33. c and d 34. a, b and c 35. a, b and d 36. c and d 37. a) Affects ...
38. c) E. coli 39. b) P. Mirabilis 40. c) MacConkey's ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is c i.e. Enteroinvasive E. coli produce a disease similar to Salmonellosis

Ref. Ananthnarayan 7/e, p 278

"Enteroinvasive E. coli produce disease similar to Shigellosis not salmonellosis."

Enteroinvasive E. coli (EIEC) :

- Also called ***atypical E. coli*** as many strains don't ferment lactose or ferment it late.
- Cause illness *similar to Shigellosis.*
- Ability to penetrate cells is due to presence of *plasmid* which *codes for virulence marker antigen (VMA).*
- **Diagnosis :**
  - Sereny test
  - Cell penetration of Hela or HEP. 2 in culture is diagnostic.

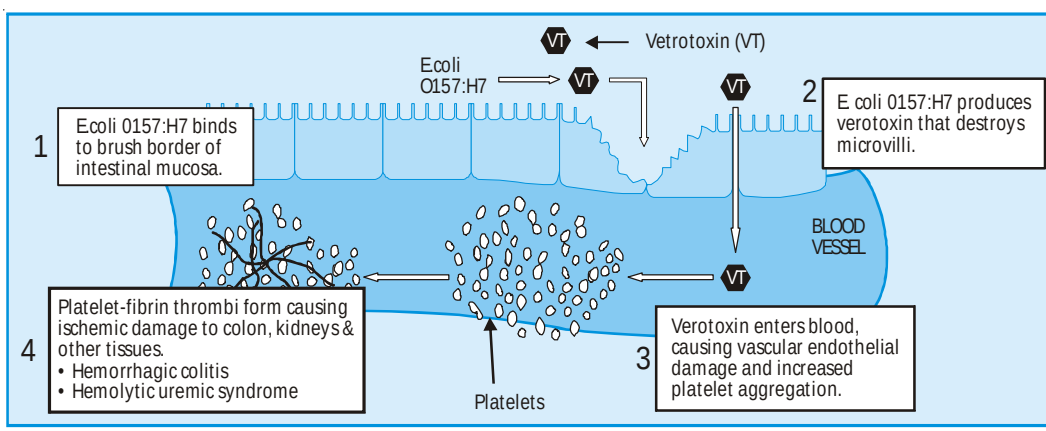
Remember :

• *Enteropathogenic E. coli* (EPEC)	– ***Diarrhoea in infants and children***
• *Enterotoxigenic E. coli* (ETEC)	– ***Traveller's diarrhea***
• *Enteroinvasive E. coli* (EIEC)	– Diarrhoea to dysentery ***similar to Shigellosis***
• *Enterohemorrhagic E. Coli* (EHEC)	– ***Hemolytic uremic syndrome***
• *Entero aggregative E. coli*	– ***Persistent diarrhea***

2. Ans. is a i.e. 0 157:H7 *Ref. Aananthnarayan 7/e, p 279; Harrison 17/e, p 940*

"Typically O 157:H7 and few other such as O 26:H1 E.coli are associated with hemorrhagic colitis."

Pathogenesis of O157:H7



Enterohemorrhagic E. coli (EHEC) = Shigatoxigenic E. coli (STEC) = Verotoxigenic E.coli (VTEC) :

- These strains produce verocytotoxin (VT) = Shiga like toxin (SLT).
- Cause diarrhoeal disease ranging in severity from mild diarhoea to ***fatal hemmorhagic colitis*** and ***haemolytic uremic syndrome.***
- Primary ***target of VT is vascular endothelial cells.***
- *'A' subunit of Shiga toxin irreversibly inhibit ribosomal function.* *... Harrison 17/e, p 940*

- Typical EHEC is serotype 0 157:H7 and few others such as 0 26:H1.
- Diagnosis of EHEC diarrhoea can be made by demonstration of bacilli or VT in feces.
- *Usually O 157:H7* serotype does *not ferment sorbitol* So, use of sorbitol Mac-Conkey medium helps in screening of O:157 VTEC.

3. Ans. is b i.e. Pi Pilli *Ref. Jawertz 24/e, p 252; Harrison 17/e, p 937*

Correctly speaking guys we are unable to find all choices but **Pi Pilli is related in pathogenesis of pyelonephritis not GIT pathology.**

So, most probably that would be the answer.

4. Ans. is b i.e. Widal test *Ref. Ananthnarayan 7/e, p 297 - 299*

" In 3rd week Widal test is investigation of choice."

Diagnosis of Typhoid

I. Cases (BASU)

Blood culture (B) :

– Test of choice in first week (Diagnostic gold standard).
– Becomes negative on treatment with antibiotics.
– *Clot culture :* Yields higher rate of isolation than blood culture as bactericidal action of serum is obviated.

Widal test :

– **A**gglutinins usually appear by end of first week, Titre increase steadily till the 3rd or 4th week after which it declines gradually.
– Maximum titre is found in 3rd week.

Stool culture (S) :

– Salmonella are shed in faeces throughout the course of disease, even in convalescence. A positive faecal culture occur in carriers also, so can't differentiate between case and carrier.

Urine culture :

– Culture is positive in 25% of cases during 2nd or 3rd week.
– Less useful than blood culture.

II. Carriers

– Widal reaction – No value in detection of carriers.
– Demonstration of Vi agglutinins indicate carrier state.
  This is usefull screening test which is confirmed by culture.
– Isolation of bacillus from faeces or bile. Cholagogue purgatives increase chance of isolation.
– Tracing of carriers in cities is done by 'Sewer Swab Technique' or by filtration of sewage through millipore membrane and *culturing the membrane* on *Wilson* and *Blair media.*

5. Ans. is a i.e. Sereny test is positive *Ref. Ananthanrayan 7/e, p 279; Harrison 17/e, p 942*

"Sereny test is positive in cases of EIEC not EHEC."

Mostly 0 157:H7 serotype of EHEC don't ferment sorbitol but some 0157:H7 and non 0157 strain ferment sorbitol *so, option B (Ferments sorbitol) is partly correct.* *..... Harrison 17/e, p 942*

Sereny test – Installation of suspension of freshly isolated *EIEC* or *Shigella* in to the eyes of guinea pigs leads to mucopurulent conjuctivitis.

6. Ans. is b i.e. Porteus forms uric acids stone *Ref. Harrison 17/e, p 942-943*

"Proteus results in formation of struvite stone not uric acid stone."

- Uric acid stone forms in acidic urine in presence of hyperuricemia.
- All members of enterobacteriacea are aerobes or facultative anaerobes.
- **Features of proteus bacilli :**
  - Non lactose fermenter
  - *Differs from other enterobacteria by presence of enzyme* phenylalanine deaminase which is responsible for deamination of phenylalanine to phenyl pyruvic acid (PPA test).
  - By producing urease it degrades urea to NH_3 and CO_2, NH_3 raises urinary pH. NH_4^+ (formed from NH_3) precipitate PO_4^{3-} Mg^{2+} to form MgNH4PO4 (Struvite).
    The result is stone of struvite admixed with $CaCO_3$
  - Some strains *(X-strains)* are agglutinated by sera from *typhus fever patient* (weil felix reaction).

Remember :
- Peritrichate flagella (flagella all around the cell) seen in :
  - Proteus – E.coli – Listeria
  - Clostridia – Typhoid bacilli – Bacillus
- PPA test is also seen in Morganella, Providencia.

7. Ans. is a i.e. Fucose *Ref. Still searching*

I am unable to find the Answer from any book. I am just mentioning the Answer which is taken as correct by my seniors.

Remember : Concanavalin A and phytohemagglutinin is mitogen that cause blast transformation of T cells not of B cell.

8. Ans. is b i.e. H-antigen titre remains positive for several months and reaction to it is rapid
Ref. Ananthnarayan 7/e, p 299

Widal reaction :
- *Test for measurment of H and O agglutinins for typhoid and paratyphoid bacilli in patient serum.*
- Agglutinins usually appear by the end of 1st week. Titre ↑ steadily till the 3rd or 4th week.
- **O Agglutinins** – O antigen is *common between S. typhii and S. paratyphii*, so doesn't specify whether infection is due to S. typhii or S. paratyphii.
  - It has better diagnostic value than H.
  - O antibodies disappear after infection.
  - O agglutination is seen as disc like pattern at bottom of tube.
- **H agglutinins** – H antigen are different for S. typhii or S. paratyphii so indicates type of infection
  - May be present due to prior disease, inapparent infection, thus it does not have good diagnostic value.
  - Persist longer than O agglutinins.
  - Reaction to it, is rapid and leads to formation of cotton wooly clumps.

Remember : Order of disappearance of antibody in typhoid $V_1 \rightarrow O \rightarrow H$.

9. Ans. is c i.e. Previous infection alters widal test *Ref. Ananthnarayan 7/e, p 297 - 299*

"Widal test is false positive in case of prior infection and immunization."

- Agglutinins may be present on account of prior disease, innaparent infection or immunisation, so widal test may be false positive and only +ve widal test should not be taken as proof of typhoid fever.
- In cases where antibiotics are given early, agglutinins response is poor and Widal may be false –ve.
- **Widal test is never confirmatory. *Only culture of blood is confirmatory for typhoid.***

Remember : Typhoid investigation which are not affected by antibiotics : Stool culture and Bone marrow culture.

10. Ans. is c i.e. Shigella does not ferments mannitol *Ref. Ananthanrayan 7/e, p 285*

- Differentiating features between Shigella and E.coli :

Features	Shigella	E.coli
Motility	—	+
Lactose fermentation	—	+
Glucose fermentation	—	+
Lysine decarboxylase	—	+

- Shigella ferment mannitol and this property is used for its classification.

Classification :

Mannitol fermenters	Non fermenters
S. flexnerii S. boydii S. sonnei	S. dysenteriae

So, guys mannitol fermentation can't diferentiate E. coli and Shigella as ***E.coli also ferments mannitol.***

Remember :
- S. sonnei is late lactose fermenter.
- All members of Enterobacteriacea are motile except shigella, Klebsiella and salmonella gallinarum-pallorum.
- E.coli also ferments maltose.

11. Ans. is a i.e. It can lead to HUS *Ref. Ananthnarayan 7/e, p 287; Harrison 17/e, p 963*

"HUS occurs with S. dysenteriae type 1 infection." *..... Harrison 17/e, p 963*

Unique feature of S. dysenteriae :

- ***Mannitol*** non fermenter (All other Shigella are mannitol fermenter).
- ***Catalase*** –ve (All other Shigella are catalase +ve).
- It produce ***exotoxin*** **(*Remember :* it is a Gram (-)ve bacteria producing exotoxin)** which has less role in dysentery, but has major role in pathogensis of :
  1. Microangiopathic complications
  2. Hemolytic uremic syndrome
  3. Thrombotic thrombocytopenic purpura.

- **Infective dose - 10 to 100 bacilli**
- It has invasive property which is responsible for dysentery.
- Complications occur mostly after S. dysenteriae in comparison to other Shigella.

Similarities to other members of Shigella :

- It is MR (+)ve *(all members of enterobactereciae except Klebsiella are MR (+)ve and VP (–)ve).*
- It is an aerobe and facultative anaerobe.

Remember : *"Seizures and reactive arthritis are extraintestinal complication which occur usually due to infection with S. flexneri strain."* *.....Harrison 17/e, p 964*

12. Ans. is d i.e. Mannitol *Ref. Ananthnarayan 7/e, p 285*

Remember : All Shigella are mannitol fermenter except Sh. dystenteriae.

13. Ans. is b i.e. Glucose is not fermented by all members of the family

Ref. Ananthnarayan 7/e, p 274

"Members of enterobacteriaceae reduce nitrates to nitrites, form catalase but not oxidase."

..... Ananthnarayan 7/e, p 271

Enterobacteriaceae : Important distinguishing features

Features	Escherichia	Salmonella	Shigella	Proteus
Motility by peritrichous flagella	+	+	–	+
Gas from glucose	+	+	–	d
Acid from glucose	+	–	–	–
Acid from sucrose	d	–	–	d
Growth in KCN	–	d	–	+
Indole	+	–	d	d
MR	+	+	+	+
VP	–	–	–	–
Citrate	–	+	–	d
H2S	–	+	–	+
Urease	–	–	–	+
Phenylalanine deaminase (PPA)	–	–	–	+
Arginine dehydrolase	d	+	–	–
Lysine decarboxylase	+	+	–	–
Ornithine decarboxylase	d	+	d	d

* **(d= result different in different species or strains)**

Remember :

– *Polar flagella* : Vibrio, pseudomonas, legionella, spirilla, campylobacter, H. pylori, spirochetes.

– V. parahemolytic produce both polar and peritrichous flagella.

14. Ans. is a i.e. E. coli *Ref. Harrison 17/e, p 1820*

"***E. coli cause 80% of acute UTI in patients with out catheterization."*** *.....Harrison 17/e, p 1820*

Strains of E. coli causing UTI are called extraintestinal pathogenic strains of E.coli.

Remember :

- E.coli is ***MC*** cause of catheter associate UTI too. *.....Harrison 17/e, p 1823*
- UTI is ***MC*** nosocomial infection.
- E. coli is ***MC*** cause of neonatal meningitis.
- E.coli is ***MC*** cause of intraabdominal abscess.
- Other gram negative rods causingUTI are : Proteus, klebsiella, serratia, pseudomonas, enterobacter.

15. Ans. is a i.e. Cause diarrhoea in infants *Ref. Ananthnarayan 7/e, p 277*

"Enteropathogenic E.coli have been associated with diarrhoea in infants and children usually occuring as institutional out breaks."

5 types of diarrhoeagenic E. coli are recognised :

1. **Enteropathogenic E. coli; (EPEC) = Entero adherant E. coli (EAEC)**
   - Cause diarrhea mainly in infants and children
   - Neither invasive, nor produce enterotoxin
   - Bacilli adheres to upper small intestine
   - Usually cause epidemic, but sporadic cases can also occur.
2. **Enterotoxigenic E. coli (ETEC)**
   - It is the MC cause of traveller's diarrhoea
   - Produce either labile toxin (LT) or stable toxin (ST)
   - Affect all age groups
   - Most case occur as endemic.
3. **Enteroinvasive E. coli (ETEC)**
   - ***Similar to Shigellosis***
   - Detected by Sereny's test or by demonstration of penetration of Hep or Hela cells.
4. **Enterohemmorhagic E.coli**
   - These strains produce verocytotoxin (VT) = Shigalike toxin (ST)
   - Cause diarrhoeal disease ranging in severity from mild diarhoea to ***fatal hemmorhagic colitis*** and ***hemolytic uremic syndrome.***
5. **Enteroaggregative E. coli**
   - Appear aggregated as stacked brick formation on Hep - 2 cells or glass.
   - Produc low molecular weight ***heat stable enterotoxin*** (EAST1)
   - Cause ***persistent diarrhoea.***

16. Ans. is c i.e. Blood culture is positive in 3 - 7days *Ref. Ananthnarayan 7/e, p 297 - 299*

Investigation for enteric fever :

Test	Timing
– Blood culture	1st week
– Widal test	3rd week
– Urine culture	2nd week

17. Ans. is a i.e. Shigella dysentriae *Ref. Ananthnarayan 7/e, p 287; Jawetz 24/e, p 155*

Exotoxins associated with diarrheal diseases are called as enterotoxins. They are produced by :

– Shigella dysenteriae I	– Staph. aureus	– B. cereus
– Cl. perfringes	– Y. enterocolitica	– V. parahemolyticus
– V. cholera	– Kleibsella pneumonia	– ETEC
– Aeromonas		

18. Ans. is c i.e. Vi *Ref. Ananthnarayan 7/e, p 291*

Vi antigen – ***Polysaccharide antigen enveloping the O antigen because of which many strains of S. typhi fails to agglutinate with the 'O' antiserum.***

Antigens of Salmonella :

H antigen	O antigen	Vi. antigen
– Present on flagella	– Integral part of cell wall	– Envelops the 'O' antigen
– Heat labile protein	– Phospholipid - protein - polysaccharide complex	– Surface polysaccharide
– Strongly immunogenic	– Identical with endotoxin so, is less immunogenic	– Acts as virulence factor and is poorly immunogenic
– Antibody formation is rapid and in high titre	– Antibody formation is slow and titre is low	– Antibody production is slow and titres is low

- Salmonella are *classified* into groups on *basis of O antigen* on the bacterial surface.
- Vi antigen is used for epidemiological typing.

19. Ans. is c i.e. 10^2 - 10^5 bacilli *Ref. Harrison 17/e, p 957; Jawetz 24/e, p 258*

Infective dose of salmonella varies from 10^3 to 10^6 colony forming units.

Organism	Infective dose
Shigella	10 - 1000
Vibrio	$>10^{10}$ (if source of infection is water) 10^2 - 10^4 (if source of infection is food)
Campylobacter jejuni	10^4
Yersinia enterocolitica	10^8 - 10^9
EHEC	10 - 100

20. Ans. is a i.e. Enteroinvasive E. coli *Ref. Ananthnarayan 7/e, p 278; Harrison 17/e, p 941*

EIEC cause illness resembling Shigellosis i.e. ranging from mild diarrhoea to frank dysentery.

21. Ans. is c i.e. Selenite 'F' medium *Ref. Ananthnarayan 7/e, p 290, 303*

"Selenite F and Tetrathionate broth are commonly employed enrichment media of salmonella."

Salmonella Gastroenteritis = Food poisoning

- May be caused by **any Salmonella except S. typhi**
- ***MC*** caused by **S. typhimurium**
- Human infection occurs due to ingestion of contaminated foods.
- **Most frequent source** – Poultry, meat, milk and milk products
- **IP** – 16 - 48 hours
- ***Clinical feature*** : Diarrhoea, vomiting, fever
- ***Diagnosis*** : Isolation of salmonella from faeces
- ***Treatment*** : No antibiotics

Remember :

Differential media for salmonella :

- *Mac Conkey and Deoxycholate media :* Form *colourless* colonies due to absence of lactose fermentation.
- *Wilson and Blair bismuth sulphite medium : Jet black* colonies are formed due to production of H_2S.
- *Selective media for salmonella :* SS agar, Deoxycholate citrate agar.

22. Ans. is a i.e. Vi. agglutination test *Ref. Ananthnarayan 7/e, p 300*

Already explained, refer answer no. 4

23. Ans. is c i.e. Monovalent vaccine *Ref. Park 18/e 189 - 190; 19/e, p 197*

Since S. typhi is the major cause of typhoid fever in India, the vaccine of choice is the monovalent typhoid vaccine.

Antityphoid vaccine in India are :

a. Monovalent antityphoid vaccine – Heat killed and phenol preserved.
b. Bivalent antityphoid vaccine – Contains S. typhi and paratyphi A.
c. TAB vaccine (WHO recommended that TAB vaccine should be discontinued).
d. ***Live oral typhoid 21a vaccine (Typhoral)***
   - Enteric coated capsule of lyophilized vaccine containing not less than 10 viable organism of attenuated S. typhi strain Ty 21a.
   - It is indicated for immunization of adults and children aged more than 6 years.
   - ***Protection commences 2 weeks after taking last capsule and last for at least 3 years***
   - **Dose -** 1 capsule on days 1, 3 and 5 one hour before meal with cold or luke warm milk or water.

24. Ans. is a i.e. Salmonella enteritis poisoning

Ref. Ananthnarayan 7/e, p 303; 6/e, p 279; Harrison 17/e, p 960

- I.P of S. aureus food poisoning – 1-6 hours
- I.P of B. cereus food poisoning – Diarrhoea- 8 to 16 hours.
  Vomiting - 1 to 6 hours.
- I.P of V.cholera food poisoning – > 16 hours.

For more details, refer answer no. 21

25. Ans. is a i.e. Large dose is required for infection

Ref. Ananthnarayan 7/e, p 287; Harrison 17/e, p 962

Correctly speaking 2 choices are wrong i.e. ***option "a"*** and ***option "d".***

- ***Infective dose for bacillary dysentery is just 10 to 100 bacilli as Shigella survive gastric acidity better than other enterobacteria.***

So, ***option "a"*** is clearly wrong.

- ***Sh. dysenteraie forms enterotoxin (acts by inhibiting protein synthesis) which appears to be less important in pathogenesis than invasive property.***

So, ***option "d"*** is also wrong but not completely.

So, Answer would be clearly wrong ***option*** i.e. ***"a"***

Remember : Small infective dose (10 - 100 bacilli) required in EHEC, entamoeba, giardia.

26. Ans. is d i.e. S. dysentriae *Ref. See below*

Causes of bloody diarrhoea :

Organism	Incubation period
• Shigella	>16h
• EHEC	> 16h
• EIEC	>16h
• Campylobacter jejuni	2 - 6 days

Salmonella cause inflammatory diarrhoea with only WBC in stool not RBC and ETEC, EPEC causes watery diarrhea.

Cause of Traveller's diarrhea

Bacterial	*Viral*	*Parasitic*
ETEC (***MC***)	Rotavirus (***MC***)	Giardia (***MC***)
V. cholera	Norwalk virus	Entamoeba histolytica
Shigella		Cryptosporodium
Salmonella		Cyclospora
C. jejuni		

27. Ans. is a i.e. Sereny test positive *Ref. Ananthnarayan 7/e, p 279*

Sereny test is positive in EIEC not in EHEC.

28. Ans. is c i.e. Vi is seen in normal population *Ref. Ananthnarayan 7/e, p 291; Park 18/e, p 189*

"Vi antigen is seen in person harbouring the S.typhi (i.e. cases & carrier) not in normal individual."

Chronic carriers of S. typhi :

- Persons who excrete bacilli for more than a year after clinical attack.
- Average carrier rate is 3% (i.e. 3% cases become chronic carriers).
- Carrier state is more common in females (cases are more common in males).

- Faecal carriers are more frequent than urinary carriers but urinary carriers are more dangerous.
- Urinary carrier state is often associated with some abnormality of the urinary tract.
- Faecal carrier stage is *more common* in patients with biliary abnormality and GI malignancy.
- ***Diagnosis of carriers :*** – Demonstration of Vi antigen
  – Isolation of S. typhi by sewer swab technique.
- ***Treatment :*** – Ampicilin (4 - 6 g a day) together with probenecid for 6 week.
  – Cholecystectomy with concomitant ampilcillin therapy has been regarded as the sucessfull approach to treatment of carriers. *... Park 19/e, p 197*

29. Ans. is b i.e. Heat stable E. coli toxin *Ref. Ananthnarayan 7/e, p 274*

Enterotoxins of E.coli

Stable Heat toxin	Heat labile toxin	Verocytotoxin = Shiga like toxin
• Acts through activation of CGMP	• Acts through activation of CAMP	• Inhibits protein synthesis

Remember : Toxin of V. cholera also acts through activation of cAMP.

30. Ans. is b i.e. E.coli *Ref. Ananthnarayan 7/e, p 278*

All of them can cause travellers diarrhoea but ***MC*** cause is **E.coli.**

For more detail, refer answer no. 26

31. Ans. is b i.e. Shigella *Ref. Harrison 17/e, p 963*

Already explained, refer answer no. 11

32. Ans. is a and c i.e. Pseudomonas; and V. cholera *Ref. Ananthnarayan 7/e, p 272*

Enterobacteriaceae			
Tribe I	**Tribe II**	**Tribe III**	**Tribe IV**
Escherichiae	***Klebsielleae***	***Proteeae***	***Erwinieae***
Genus • Escherichia • Edwardsiella • Citrobacter • Salmonella • Shigella	Genus • Klebsiella • Enterobacter • Hafnia • Serratia	Genus • Proteus • Morganella • Providencia	Genus • Erwinia

33. Ans. is c and d i.e. Caused by animal products; and Symptoms appear between 4 - 48 hours
Ref. Aananthnarayan 7/e, p 303

Already explained, refer answer no. 21

34. Ans. is a, b and c i.e. It is caused by S.typhi; Water can transmit the disease; and Type 21 a is an oral vaccine *Ref. Ananthnarayan 7/e, p 295 - 300*

- Typhoid is caused by S.typhi.
- Water is mode of transmission.

- Ty 21a is a live oral vaccine.
- Chronic carriers are those who excrete bacilli for more than a year (not 6 months).
- Widal test gives negative results in 1st week.

35. Ans. is a, b and d i.e. The L.T., (labile toxin), in ETEC acts via CAMP; In types causing UTI the organism attaches through pilli; and EIEC invasiveness is under plasmid control

Ref. Ananthnarayan 7/e, p 274 - 279

- LT acts via cAMP and ST via cGMP. ***Mnemonic –*** **L**abile Toxin c**A**MP
- Fimbriae (P fimbriae) or pilli binds to epthelium of urinary tract and helps in causing UTI.
- HUS is caused by verocytotoxin = Shiga like toxin of EHEC not by ST of ETEC.
- Invasiveness of EIEC is due to plasmid coated outer surface antigen called virulence marker antigen.
- EPEC or Enteroadherent E.coli causes diarrhea by disruption of brush border not by toxin or invasion.

36. Ans. is c and d i.e. Caused by animal products; and Symptoms appear by 4 - 48 hrs

Ref. Ananthnarayan 7/e, p 303

Already explained, refer answer no. 21

37. Ans. is a i.e. Affects peyer's patches *Ref. Harrison 17/e, p 958*

Enteric manifestations of S.typhi :

- *S. typhi* ***invades peyer's*** patches and form ***oval ulcer*** with their long axis along the length of bowel (Tuberculosis result in transverse ulcer).
- Peyer's patches lie along antimesentric border so ulcer are common in antimesentric border.
- Stricture is rare but ***perforation can occur (Stricture common in TB ulcer).***

Remember : Erythrophagocytosis is feature of E. histolytica.

Neurologic manifestations of enteric fever :

- Meningitis
- GB syndrome
- Neuropsychiatric symptoms (described as muttering delirium or coma vigil)

38. Ans. is c i.e. E. coli *Ref. Harrison 17/e, p 938*

Remember : E.coli is ***MC*** cause of : – Intraabdominal abscess – Neonatal meningitis – UTI.

39. Ans. is b i.e. P. mirabilis *Ref. Ananthnarayan 7/e, p 282*

Urease production (in order of decreasing) : ***– Proteus – Klebsiella – Citrobacter***

40. Ans. is c i.e. MacConkey's medium *Ref. Ananthnarayan 7/e, p 271*

Being Lactose fermenter E.coli give pink colour with MacConkey's medium.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Enteropathogenic E. coli : **[AIIMS 90]**

a) Causes acute gastroenteritis in infants
b) Invades intestinal epithilium
c) Produces cholera like toxin
d) It is Non-motile

[Ref. Ananthnarayan 7/e, p 277]

2. Following are true of Widal test except : **[AI 92]**

a) High titre in first sample is diagnostic
b) 'H' antigen is specific for serotyping
c) Highly + ve H titre not diagnostic
d) Maximum titre in third week

[Ref. Ananthnarayan 7/e, p 299]

3. The following are gas producing salmonella except : **[AI 92]**

a) S. typhi
b) S. Enteritidis
c) S. Cholera
d) S. typhimurium

[Ref. Ananthnarayan 7/e, p 290]

4. Agglutination with 'O' antigen of S. typhi is inhibited by : **[AIIMS 92]**

a) Vi antigen
b) Pili antigen
c) Flagellar antigen
d) All of the above

[Ref. Ananthnarayan 7/e, p 291]

5. Which is true about Widal reaction :

a) Antibody to H Ag appears first and persists
b) Antibody to 0 Ag appears first and persists
c) Anitbodyes to H and 0 Ag appears simultaneously and persists **[PGI 92; AIIMS 90]**
d) None of the above

[Ref. Ananthnarayan 7/e, p 299]

6. Prolonged salmoella septicemia is caused by:

a) S. enteritidis **[PGI 93, 94]**
b) S. cholerae - suis
c) S. typhimurium
d) S. typhi

[Ref. Ananthnarayan 7/e, p 303]

7. Which is true of Entero bacteriacae : **[AI 93]**

a) All are Oxidase negative
b) Nitrate reduction negative
c) Glucose not fermented by all
d) Motility bipolar flagellum

[Ref. Ananthnarayan 7/e, p 271]

8. Agent which on addition to a colony inhibits its growth and on removal the colony regrows is :

a) Bacteriostatic **[AI 93]**
b) Bactericidal
c) Antibiotic
d) Antiseptic

[Ref. Jawartz 24/e, p 57]

9. Buruli Ulcer is caused by : **[JIPMER 93]**

a) Streptococcus
b) Spirillium minus
c) M. Ulcerans
d) Brucella

[Ref. Ananthnarayan 7/e, p 367]

10. Traveller's diarrhoea is caused by: **[PGI 94;**

a) Enteropathogenic E. coli **AIIMS 93; UP 01]**
b) Enterohaemorrhagic E. coli
c) Enterotoxigenic E. coli
d) Enteroinvasive E. coli

[Ref. Ananthnarayan 7/e, p 278]

Answer

1. a) Causes ... 2. a) High titre ... 3. a) S. typhi 4. a) Vi antigen 5. a) Antibody ...
6. b) S. cholerae ... 7. a) All are ... 8. a) Bacteriostatic 9. c) M. Ulcerans 10. c) Enterotoxi ...

11. Hemolytic-uremic syndrome is due to :
a) Enterotoxigenic E. coli **[JIPMER 95]**
b) Enterohemorrhiagic E. coli
c) Shigella
d) Salmonella
[Ref. Ananthnarayan 7/e, p 287]

12. The machanism of action of Enteropathogenic E. coli is : [Kerala 97]
a) Adherance to enterocytes
b) Stimulates adenyl cyclase
c) Produces secretory diarrohea
d) None of the above
[Ref. Ananthnarayan 7/e, p 278]

13. Growth factor needed for salmonella :
a) Tryptophan **[Kerala 98]**
b) Niacin
c) B-12
d) Citrate
[Ref. Ananthnarayan 7/e, p 290]

14. True about salmonella are all except : [UP 98]
a) Non lactose fermenter
b) Only 'O' (somatic antigen) is used for classification of salmonella
c) Aerobic and facultatively anaerobic
d) Selenite F and tetrathionate broth are used
[Ref. Ananthnarayan 7/e, p 293 - 294]

15. Swarming growth is found in : [UP 98]
a) Proteus
b) Bacillus
c) Pneumococcus
d) Snigella
[Ref. Ananthnarayan 7/e, p 283]

16. Shigellosis is best diagnosis by :
a) Stool examination **[AIIMS 89, UPSC 99]**
b) Stool culture
c) Sigmoidoscopy
d) Enzyme
[Ref. Ananthnarayan 7/e, p 288]

17. Test showinng invasiveness of shigella is :
a) DICK' stest **[Orissa 00]**
b) Sereny's test
c) Shick's test C
d) Rabbit ileal loop
[Ref. Ananthnarayan 7/e, p 278]

18. Labile toxin of E. coli can be detected by the following methods of incubation except :
a) Into infant rabbit bowel **[Kerla 2K]**
b) Into adult rabbit' skin
c) Intra gastrically into infant Mouse
d) Into Tissue culture of chinese hamster ovary cells
e) Into YI Mouse adrenal cells
[Ref. Ananthnarayan 7/e, p 276]

19. True about widal test is : [UP 00]
a) Widal test confirmative in endemic area
b) Antibiotic treatment does'nt alter widal test
c) Previous infection affects widal test
d) Does not alter with prior vaccination
[Ref. Ananthnarayan 7/e, p 299 point 5]

20. Traveller's diarrhoea is caused by:
a) Enterotoxigenic E. coli **[UP 00, 98]**
b) Enteropathogenic E. coli
c) Enteroin vasive E. coli
d) Eenterohemorrhagic E. coli
[Ref. Ananthnarayan 7/e, p 278]

21. True about typhoid is : [UP 00]
a) Incubation period 3-6 weeks
b) Chronic carrier is 10-15%
c) Widal test is specific
d) Vibolyaccharide of bacterial cell used for vaccination
[Ref. Ananthnarayan 7/e, p 302]

22. Correct statement about Widal test is :
a) Only O antigen is used **[Kolkata 02]**
b) Is a tube agglutination
c) Any antibody titre is diagnositic
d) Antibody appears after 1 - 10 days of fever
[Ref. Ananthnarayan 7/e, p 99]

23. True about shigella dysentriae except: [UP 03]
a) It invades the colonic mucose
b) It can cause hemolytic coremic syndrome
[Ref. Ananthnarayan 7/e, p 287]

24. Widal test is done for : [Jharkhand 03]
a) Typhoid fever
b) Salmonella
c) Brucellosis
d) All
[Ref. Ananthnarayan 7/e, p 299]

Answer

11. b and c	12. a) Adherance ...	13. a) Tryptophan	14. b) Only 'O' ...	15. a) Proteus
16. b) Stool culture	17. b) Sereny's ...	18. c) Intra gastrically ...	19. c) Previous ...	20. a) Enterotox
21. d) Vibolyaccharide	22. None	23. b) It can cause ...	24. a) Typhoid ...	

25. Microorganisms that enter freshly laid eggs are :
a) Salmonella **[Kar 03]**
b) Brucella
c) Shigella
d) Vibrio cholerae
[Ref. Ananthnarayan 7/e, p 303]

26. Microorganism that enter feshly laid eggs are :
a) Salmonella **[Karn 03]**
b) Brucella
c) Shigela
d) Vibriocholara
[Ref. Ananthnarayan 7/e, p 303]

27. All of the following Salmonella are motile except :
a) S. typhi **[SGPGI 04]**
b) S. enteridis
c) S. gallinarum pullorum
d) S. Chester
[Ref. Ananthnarayan 7/e, p 290]

28. Widal test is an example of : **[DNB 05]**
a) Flocculation
b) Agglutination
c) Both
d) None
[Ref. Ananthnarayan 7/e, p 297]

29. Non lactose fermenter includes all the following except : **[MP 07]**
a) Shiglla soneei
b) Shigella dysenteriae
c) Shigella flexneri
d) Shigella boydii
[Ref. Ananthnarayan 7/e, p 271]

30. Persistant diarrhea is caused by : **[UP 07]**
a) EAEC
b) EIEC
c) ETEC
d) EPEC
[Ref. Ananthnarayan 7/e, p 279]

31. Verocytotoxin of E. coli acts by : **[BHU 07]**
a) Increasing CAMP
b) Decreasing cAMP
c) Decreasing protein synthesis
d) Decreasing cGMP
[Ref. Harrison 17/e, p 940]

32. Typhoid carries are detected by following except :
a) Isolation of bacteria from urine **[UP 06]**
b) Isolation of the bacteria from bile
c) Vi antigen
d) Widal test
[Ref. Park 19/e, p 197]

33. Which strain associated with persistent diarrhea?
a) ETEC **[Jharkhand 06]**
b) EPEC
c) EIEC
d) EAEC
[Ref. Anantharayan 7/e, p 279]

34. "Pea-soup stool" is characteristically seen in :
a) Cholera **[DNB 04]**
b) Typhoid
c) Botulism diarrhoea
d) Traveller's diarrhoea
e) Salmonellosis
[Ref. Ananthnarayan 7/e, p 332]

Answer
25. a) Salmonella
26. a) Salmonella
27. c) S. gallinarum...
28. b) Agglutination
29. a) Shiglla soneei
30. a) EAEC
31. c) Decreasing ...
32. d) Widal test
33. d) EAEC
34. b) Typhoid

10 Vibrio

- Gram negative, rigid, motile curved rods. **All are halophilic except V. chloera and V. mimicus.**
- They are oxidase positive, which differentiates it from Gram negative enteric bacteria.
- They are susceptible to compound 0/129 which differentiate them from aeromonas species.

..... Jawetz 24/e, p 270

VIBRIO CHOLERA

- Comma shaped, isolated by Koch.
- Arranged as ***'fish in stream appearance'.***
- Posses single polar flagella and shows *darting type motility (=swarm of gnats).*

Culture Characteristics

- Grows well on ordinary media.
- Strongly aerobic, better growth in alkaline medium.
- Required NaCl (0.5-1%) for optimal growth; however 6% and above are inhibitory.
- MacConkey's Agar : Late lactose fermenters.
- Gelatin Stab : Infundibuliform (funnel shaped) or napiform (turnip shaped) liquification occurs.

Special media		
Holding or transport media	**Enrichment media**	**Plating media**
• VR medium • Cary-blair medium also for shigella and salmonella • Autoclaved sea water	• Alkaline peptone water • Monsour's taurocholate tellurite peptone water * Both used as transport media when specimen reach labortories within few hours.	• Alkaline bile salt agar • Monsour's gelatin taurocholate trypticose tellurite agar (GTTA) • TCBS : *Best selective media*

- Colonies are identified by *string test.*

Biochemical characterstics

C : Catalase +ve
O : Oxidase +ve
I : Indole +ve
N : Nitrates reduced to nitrites
S : Sucrose fermenter

} Responsible for ***cholera red*** reaction

Enzymes : – Neuraminidase [receptor destroying enzyme] – Elastase
– Lipase – Mucinase – Chitinase

Vibrios are suceptible to heat drying but resist high alkalinity

Classification : *Gardner and Venkat raman's Serological Classification of vibrio :*

Common flagellar H antigen

+	–
Gp. A	***Gp. B***
V. cholera and biochemically similar vibrios	Heterogenous vibrios

↓

Based on ***(LPS)***
somatic 'O' Antigen

01	Non 01 (upto O - 139)

- Only 01 serogroup cause cholera till 1992, so Non 01 serogroup were known as Non Cholera Vibro (NCV) or Non Agglutinable Vibrios (NAG vibrios).
- The latest serogroup O -139 identified in 1992 causes epidemic of cholera emphasising that they can not longer be considered as non-cholera vibrios.

01 Serogroups

	Classical cholera	E1 Tor
• Polymyxin B sensitivity	+	–
• Group IV phage susceptibility	+	–
• E1 tor phage susceptibility	–	+
• Chick erythrocyte agglutination	–	+
Serotypes	Ogawa	Inaba / Hikojima

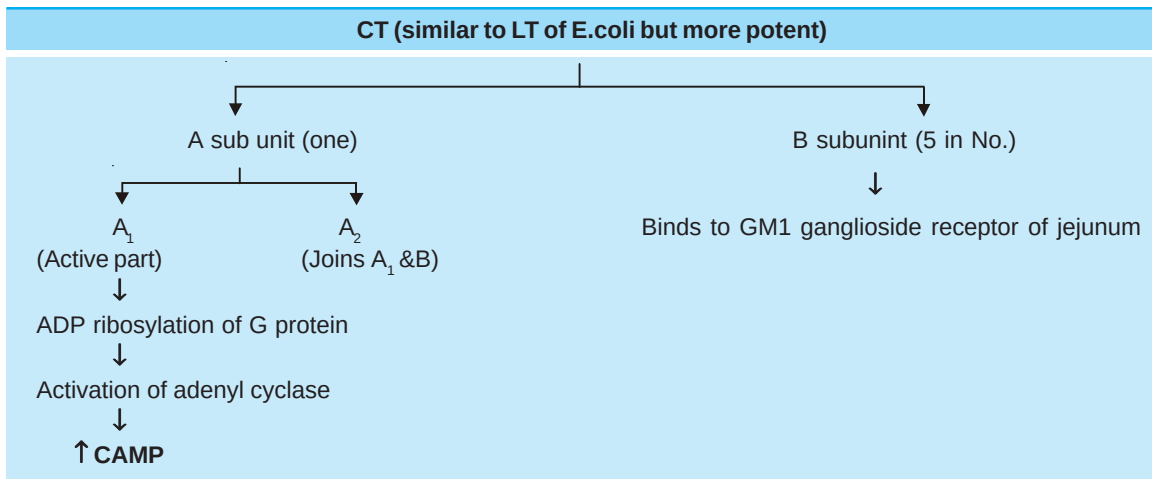
- ***Ogawa serotype of E 1 tor is MC*** strain causing cholera [7th Pandemic].
- Ogawa and Inaba strain are agglutinated by their own antisera while hikojima is agglutinated by both Ogawa and Inaba antisera.
- ***0-139 strain is called Bengal V.cholera*** (arise from E1 tor by *horizontal gene transfer*) signaled begininig of 8th pandemic. If differs from E1 tor in production of 0-139 LPS and an immunologically related O antigen polysaccharide *capsule.* *..... Harrison 17/e, p 970*

Remember : V.cholera belong to group I of ***"Heiberg grouping of vibrios".***

Cholera

- ***Incubation period –*** 1 - 2 days
- ***Infective dose –*** 10^6 bacilli
- ***Source of infection –*** Water contaminated with infective faeces.
- ***Symptoms –*** Painless rice water diarrhoea.

- ***Pathogenesis –*** Individuals with *O group most susceptible* and with blood group *AB- least susceptible. Achlorhydria predispose to cholera* [also Salmonella typhi].
  - Cause *non invasive toxin mediated diarrhoea.*
  - Adheres to jejunal epithelial cell by special fimbria and toxin coregulated pilus [TCP].
  - Then vibrio produces exo-toxin called CTX = CT (Cholera toxin)= cholera enterotoxin = Choleragen = Permeability factor.
  - CT production is determined by flamentous phage.
  - CT can be demonstrated by 'Skin blueing test'.
  - *CT Inhibits absorption of Na^+ and Cl^-* as well as, ↑ secretion of K^+ and HCO_3; resulting in isotonic diarrhea, acidosis with elevated anion gap. *..... Harrison 17/e, p 970*
  - CT also ↑ intestinal secretion via prostaglandins and neural histamine receptors
  - It has no effect on any other tissue except intestinal cells.



- Vibrio cholera also possess LPS O Antigen ***(endotoxin)*** which has ***no role*** in pathogenesis, but *0-139 strain produce novel 0-139 LPS which is responsible for its increased virulence.*
- Changes in intestine are biochemical rather than histological.

Virulence Factor of 01 V. Cholera are :

- CTx
- TCP
- Gene encoding CTx which are part of genome of bacteriophage CTX ϕ.

Clinical difference

Features	*Classical*	*E1 Tor.*
Severity	High	Low
Mortality	High	Low
Carriers	Low	High
Survival in Adverse conditiion	Less capable	Capable

Lab diagnosis

Specimen :

- Rectal swabs for convalescent phase.
- ***Stool collected*** by introducing a lubricating catheter into rectum is best specimen.
- Rapid diagnosis by characteristic **darting motility** and its inhibition by antiserum under the dark field or phase contrast microscope.

- ***Serological examination :*** Helpful in assessing prevlalance of cholera in an area. Complement dependent vibriocidal antibody test is most useful.

For examination of water sample for vibrios, enrichment or filtration method used.

Treatment

Treatment of choice : Rehydratiion therapy

- For **mild to moderate** dehydration : **ORS**

Composition of WHO ORS :

	Na^+	Cl^-	K^+	Citrate	Glucose
m mol/l	75	65	20	10	75

..... Harrison 17/e, p 970

  - If available rice based ORS is considered superior to standard ORS.

- For **severe** dehydration : IV fluid ***(Ringer Lactate is best).***
- ***Drug of choice for adults*** *: single dose tetracycline or doxycycline.*
  Alternative erythromycin. In areas where tetracycline resistance in prevelant, ciprofloxacin is recommended.
- ***For children < 8 years*** – Furazolidone *..... Harrison 17/e, p 971*
  But in India cotrimoxazole is ***DOC***
- ***For pregnant mother – DOC*** Furazolidone

VIBRIO MIMICUS

Non halophilic, non sucrose fermenter causing *gastroenteritis* by eating *seafood* especially oyster.

HALOPHILIC VIBRIOS

Vibrio Parahaemolyticus

- Capsulated vibrio showing *bipolar staining* with peritrichous flagella.
- Grows only in media containing NaCl. It tolerates 8% NaCl but not > 10%.
- String test is positive.
- ***Exhibits Kanagawa Phenomenon*** (ablility to show hemolysis on Wagatsuma agar).
- Cause ***gastroenteritis (= food poisoning)*** after eating sea fish (shell fish).
  - Cause of entertis is ***invasion*** not enterotoxin.

Vibrio Alginolyticus

- ***Most salt tolerant*** species of cholera. Can tolerate > 10% NaCl.
- Cause infection of eye, ear and wounds exposed to sea water.

Vibrio Vulnificus

Cause : a. Primary sepsis in patient with underlying liver disease.
b. Primary wound infection without underlying disease.

QUESTIONS

1. All of the folowing are true about V. cholera O139 except : [AI 08]
a) Clinical manifestations are similar to O1 E1 tor
b) First discovered in chennai
c) Produces O139 lipopolysaccharide
d) Epidemiologically indistinguishable from O1E1tor

2. Which of the following bacteria acts by increasing cAMP : [AI 07; AIIMS 06]
a) Vibrio cholera
b) Staphylococcus aureus
c) E. coli heat stable toxin
d) Salmonella

3. About V. cholera all statements are true except :
a) Non halophilic **[AI 07]**
b) Can not grow in ordinary media
c) Can survive outside the intestine
d) Man is the only reservoir of cholera

4. Not true about vibrio O139 : [AI 07]
a) Can cause disease indistinguishable from $E\text{-}_1$ or clinically
b) First isolated in chennai
c) Has O polysaccharide capsule
d) Antibody to V. cholera is not protective against O139

5. All of the following vibrio species are halophilic except : [AI 05]
a) V. cholerae
b) V. parahemolyticus
c) V. alginolyticus
d) V. flovialis

6. In the small intestine, cholera toxin acts by :
a) ADP ribosylation of G regulatory protein **[AI 05]**
b) Inhibition of adenyl cyclase
c) Activation of GTPase
d) Active absorption of NaCl

7. Antibiotic treatment of choice for treating cholera in an adult is a single dose of : [AI 05]
a) Tetracycline
b) Cotrimoxazole
c) Doxycycline
d) Furazolidone

8. Which of the following statement is true about : Vibrio cholera : [AI 99]
a) There is no natural reservoir
b) Transported in alkaline peptone water medium
c) Halophilic
d) Oxidase negative

9. All of the following statements about cholera are true except : [AI 97]
a) O and H antigens measure carrier state
b) Culture medium is TCBS agar
c) Produces indole and reduces nitrate
d) Synthesize neuraminidase

10. All of the following statements are true for El- tor cholera except : [AI 97]
a) Infection is mild and asymptomatic
b) They are resistant to polymyxin-B unit disc
c) Chronic carriers are common
d) Secondary attacks rate is high in families

11. Selective media for vibrio : [AIIMS 08]
a) TCBS
b) Stuart
c) Skirrows
d) MYPA

12. The best sutied medium for Vibrio cholerae is :
a) Thayer martin **[AIIMS 07]**
b) TCBS medium
c) Scirrow medium
d) Loeffler's medium

13. The endotoxin of the following gram-negative bacteria does not play any part in the pathogenesis of the natural disease : [AIIMS 06]
a) Escherichia coli
b) Klebsiella sp.
c) Vibrio cholerae
d) Pseudomonas aeruginosa

14. Cholera toxin : [AIIMS 06]
a) Increases the levels of intracellular cyclic GMP
b) Acts through the receptor for opiates
c) Causes continued activation of adenylate cyclase
d) Inhibits the enzyme phosphodiesterase

Answer

1. b) First... 2. a) Vibrio ... 3. b) Can not ... 4. b) First isolated ... 5. a) V. cholerae
6. a) ADP ... 7. c) Doxycycline 8. b) Transported ... 9. a) O and H ... 10. d) Secondary ...
11. a) TCBC 12. b) TCBS 13. c) Vibrio cholerae 14. c) Causes ...

15. The drug of choice for treating cholera in pregnant women is : [AIIMS 05]

a) Tetracycline
b) Doxycycline
c) Furazolidone
d) Cotrimoxazole

16. Which of the following is the drug of choice for chemoprophylaxis of cholera ? [AIIMS 05]

a) Tetracycline
b) Doxycycline
c) Furazolidone
d) Cotrimoxazole

17. True about V. cholerae is : [AIIMS 02]

a) One attack of V. cholerae gives life-long immunity
b) Affects adults and children with equal propensity in non epidemic regions
c) In between epidemics, carrier states maintain the organism
d) Pathogenicity of 0-139 vibrio is due to 0 antigen

18. A 32 year old male, kallu who recently visited a sea coast presented with ulcer over the left leg. The probable cause is : [AIIMS 01]

a) Pasturella multocida
b) Micrococcus halophillus
c) Vibrio vulnificus
d) Neisseria gonorrhea

19. True regarding cholera is : [AIIMS 95]

a) Toxin acts on GM1 receptor
b) Toxin action is CAMP mediated
c) Peritrichate flagella
d) Utilises arginine, lysine

20. Which toxin acts by ADP ribosylation :

a. Botulinum toxin **[PGI 07]**
b. Shiga toxin
c. V.cholerae
d. Diphtheria toxin
d. Pertusis

21. V. cholera able to stay in GIT because of :

a) Acid resistance **[PGI 06]**
b) Bile resistance
c) Motility
d) Binds to specific receptors
e) Anaerobic potential

22. Cholera transmission by : [PGI 06]

a) Food transmits
b) Vaccination gives 90% efficiency
c) Healthy carrier
d) Chlorination is not effective

23. In patient presenting with diarrhoea due to vibrio cholera, which of the following will be present :

a) Abdominal pain **[PGI 05, 01]**
b) Presence of leukocytes in stool
c) Fever
d) Neutrophilia
e) Occurence of many cases in the same locality

24. True about epidemiology of cholera : [PGI 03]

a) Chemoprophylaxis is not effective
b) Boiling of water cannot destroy the organism
c) Food can transmit the disease
d) Vaccination give 90% protection

25. Strain of V. cholerae in Bengal : [PGI 04]

a) 0:037
b) 0:139
c) 0:17
d) 0:40
e) 0:149

26. In a patient presenting with diarrhea and pus cells in stool, the causative organism can be all except:

a) Non vibrio cholera 01 **[PGI 01]**
b) Enterotoxigenic E. Coli
c) Enteroinvasive E. coli
d) Shigella dysenteriae 1
e) Vibrio cholera

27. True about cholera vibrios is : [PGI 97]

a) Can tolerate wide range of alkaline pH
b) Non motile bacilli
c) Can't be grown in media
d) NaCl stimulates growth

Answer

15. c) Furazolidone
16. a) Tetracycline
17. d) Pathogenicity ...
18. c) Vibrio vulnificus
19. b) Toxin ...
20. c) V.cholerae ...
21. c and d
22. a and c
23. d and e
24. c) Food can ...
25. b) 0:139
26. a, b and e
27. a) Can tolerate ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b i.e. First discoverd in Chennai *Ref. Harrison 17/e, p 969*

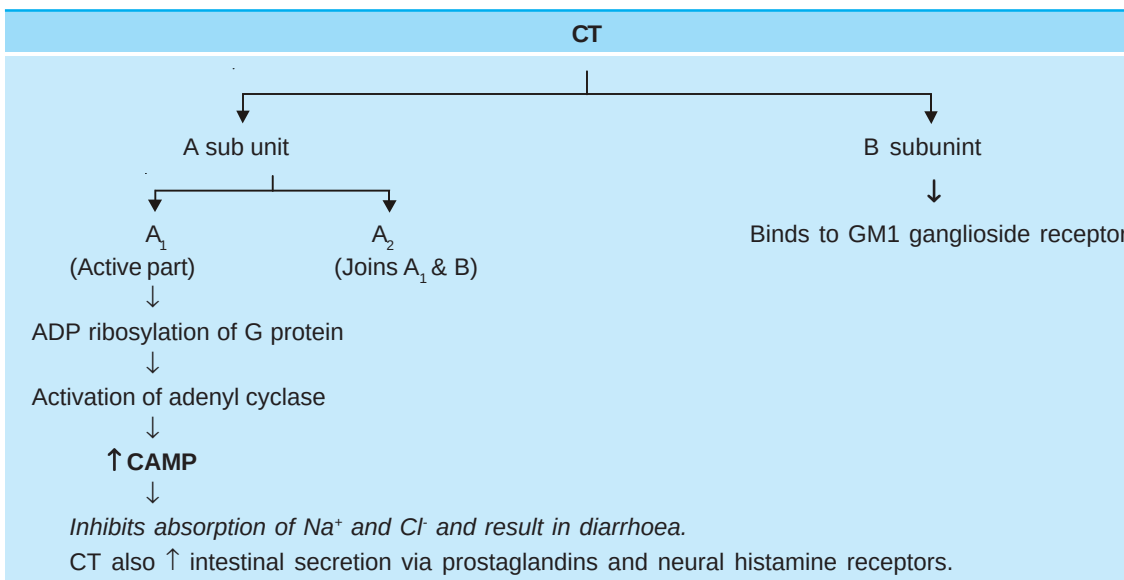
- O139 Vibrio was isolated in Bengal in 1992.
- The clinical manifestation and epidemiological features of the disease caused by V. cholera O139 are indistinguishable from those of 01 cholera.
- V. cholera is identical to E1 tor except for two important difference :
  - Production of novel O - 139 Lipopolysaccharide.
  - Immunologically related O antigen polysaccharide capsule.

Remember : E1 tor biotype was first isolated at the E_1 tor quarantine station in Egypt in 1905.

2. Ans. is a i.e. Vibrio cholera *Ref. Harrison 17/e, p 970*

Cholera toxin (CT)

- Protein ***enterotoxin***
- Composed of 2 subunit : **A** – (Active monomeric moiety)
  B – (Pentameric binding moiety)
- **Mechanism of action :**



Remember : *Mechansim of action* of some important bacterial toxin.

- Heat labile toxin of E. coli - ↑ cAMP
- Heat stable toxin of E. coli - Increase cGMP
- Botulism toxin - Inhibit release of acetylcholine from peripheral nerves.
- Tetanus toxin - Inhibit release of glycine and GABA at presynaptic terminals.
- Diptheria toxin - Inhibit protein synthesis by inactiviting EF-2.

3. Ans. is b i.e. Can not grow in ordinary media

Ref. Ananthnarayan 7/e, p 305; Park 18/e, p 177; 19/e, p 189

- Cholera grows well on ordinary media.
- Growth is better on alkaline medium. NaCl is required for optimal growth though high concentrations are inhibitory.
- ***Option "c"*** – Natural habital of V. cholera is coastal salt water and brackish estuaries, where the organism live in close relation to plankton.
  - Human become infected incidentally, but once infected can acts as vehicle for spread.
  - Man is the only reservoir of cholera infection. He may be the case or carrier.

Carriers in Cholera			
Preclinical or incubatory	***Convalescent carrier*** – Last for 2 - 3 weeks after attack	***Contact or healthy carrier*** – Result from subclincial infection – Duration less than 10 days – Gall bladder is not infected	***Chronic carrier*** – Can excreate up to 10 yrs. – Gall bladder is infected

4. Ans. is b i.e. First isolated in chennai *Ref. Harrison 17/e, p 969*

Already explained, refer answer no. 1

5. Ans. is a i.e. V. cholerae *Ref. Ananthnarayan 7/e, p 316*

Halophilic vibrios :

- Vibrios that have high requirement of NaCl.
- All vibrios are halophilic except *V. cholerae* and *V. mimicus.* .....*Harrison 16/e, p 909*
- Natural habitat of halophilic vibrios is sea water.
- ***Disease caused are :***

V. parahaemolyticus	Gastroentritis; wound infection
V. vulnificus	Sepsis (in immunocompromised); secondary cellulitis
V. alginolyticus (Most halophilic)	Wound infections, cellulitis

6. Ans. is a i.e. ADP ribosylation of G regulatory protein *Ref. Harrison 17/e, p 970*

Already explained, refer see answer no. 1

7. Ans. is c i.e. Doxy cycline *Ref. Park 18/e, p 181; 19/e, p 193; Harrison 17/e, p 970 - 971*

"Doxycycline in single dose is the antibiotic of choice for adults (excepting pregnant women)."

Antibiotic treatment of Cholera

- Doxycycline is the antibiotic of choice for adults (excepting pregnant women).
- TMP-SMX is the antibiotic of choice for children < 8 years. Tetracycline is equally effective.
- Furazolidone is the antibiotic of choice for pregnant women.
- Ciprofloxacin is the recomended agent in area where doxycycline resistance is prevelant.

Chemoprophylaxis – Tetracycline is ***DOC*** for chemoprophylaxis

According to *Harrison 17/e, p 971* ***"Furazolidone has been the recommended agent and TMP-SMX as second choice for treatment in children".***

Note : In ***India it is TMP-SMX*** so if questions comes, go with TMP-SMX as ***DOC*** in children.

8. Ans. is b i.e. Transported in Alkaline peptone water medium *Ref. Ananthnarayan 7/e, p 306*

In holding or transport media, Vibrios don't multiply but remain viable.

Holding or Transport media	Plating media
1. VR medium	1. Alkaline bile salt agar
2. Caryblair medium	2. GTTA
3. Alkaline peptone water	3. TCBS (best selective media)
4. Monsur's taurocholate tellurite water	
• ***3 and 4 are also enrichment media***	

Mnemonic **of Transport media** - *Venkatraman carry alkaline peptone water to Maysoore* (Monsour).

Biochemical charateristics – ***[COINS]***

C – **C**atalase +ve

O – **O**xidase +ve

I – **I**ndole +ve

N – **N**itrate reducer

S – **S**ucrose fermenter

} Responsible for cholera red reaction.

9. Ans. is a i.e. O. and H. antigen measures carrier stage *Ref. Park 18/e, p 177; 19/e, p 190*

In carriers antibody titre (not antigen) against V. choleare 01 rises and **remains positive** as long as person harbours the organism.

Remember :

- Enzymes produced by vibrio cholera :
  - **N**euraminidase
  - **E**lastase
  - **L**ipase
  - **M**ucinase
  - **C**hintinase.

Mnemonic **- Cute NELaM**

10. Ans. is d i.e. secondary attack rate is high in family *Ref. Anathnarayan 7/e, p 309*

Classification of Vibrio cholera

Common flagellar antigen

+ : Group A (V. cholerae and biochemically similar vibrios)

Based on LPS somatic 'O' antigen

- 01
- Non 01 (Upto 0-139) = ***NAG virbios***

– : Group B (Heterogenous vibrios)

	01 Serogroup	
	↓	↓
	Classical cholera	***E1 Tor***
• Group IV phage susceptibility	+	–
• Polymyxin sensitivity	+	–
• Chick erythrocyte agglutination	–	+
• E1 Tor phage 5 susceptibility	–	+
Clinical		
• Severity	High	Low
• Secondary attack rate	High	Low
• Carriers	Low	High
• Survival in adverse condition	Less capable	Capable

"Previously it was thinked that non 01 (NAG vibrios) don't cause cholera but in 1992 0-139 serogroup has caused cholera epidemic in Bengal. so, they are no longer be considerd as non cholera vibrios."

11. Ans. is a i.e. TCBS *Ref. Ananthnarayan 7/e, p 314*

TCBS *(media containing thiosulphate, citrate, bilesalts, sucrose)* is the best selective media for vibrio.
Vibrio produces yellow convex colonies.
For more details, refer answer no. 8

12. Ans. is b i.e. TCBS *Ref. Ananthnarayan 7/e, p 314*

Already explained, refer answer no. 8

13. Ans. is c i.e. Vibrio cholera *Ref. Ananthnarayan 7/e, p 310*

Beside Cholera toxin, V.cholera also posses the lipopolysaccharide O antigen (LPS endotoxin) which apparently plays no role in pathogenesis of cholera but is responsible for the immunity induced by killed vaccine.

Other options :

E.coli – pathogenesis is mediated by endotoxin, adhesins, capsule present in some strain, enterotoxin.

Pseudomonas – Exotoxin produce tissue necrosis by blocking protein synthesis.
– Endotoxin plays a role in causing fever, shock, oligouria, leukocytosis, DIC, ARDS.

Klebsiella – Pathogenesis is mediated by endotoxin and fimbriae or other adhesin.

Remember : – Endotoxin levels can be assayed by 'Limulus test'.
– Plague toxin also has no role in natural disease.

14. Ans. is c i.e. Causes continued activation of adenylate cyclase *Ref. Harrison 17/e, p 970*
Already explained, refer answer no. 5

15. Ans. is c i.e. Furazolidine *Ref. Park 18/e, p 181; 19/e, p 193*

Antibiotics used in the **treatment of cholera.**

Condition	Antibiotic
Adult except pregnancy	Doxycycline once
Chemoprophylaxis	Tetracycline 4 times a day for 3 days
Children	Trimethroprim (TMP) sulfamethoxazole (SMX) twice a day for 3 days
Pregnancy	Furazolidone 4 times day for 3 days

16. Ans. is a i.e. Tetracycline *Ref. Park 18/e, p 182; 19/e, p 193*

Already explained, refer answer no. 6

17. Ans. is d i.e. Pathogenicity of 0-139 vibrio is due to O antigen *Ref. Harrision 17/e, p 969-970*

Vibriocholerae 0:139 Bengal is identical to E1 Tor ***except for :***

– Production of the novel ***0-139 LPS***

– Presence of immunologically related O antigen polysaccharide ***capsule.***

Both of these ***acts as virulence factor*** and explain resistance of 0 - 139 strain.

– In between epidemics the organism is maintained in their natural habitate i.e. water.

18. Ans. is c i.e. Vibrio vulnificus *Ref. Ananthnarayan 7/e, p 317*

V. vulnificus :

- Halophillic vibro
- Natural habitat is sea water
- Cause two **types of illness :**
  - In ***normal host*** - Wound infection following contact of open wound with sea water.
  - In ***immunocompromised host*** *(particularly with liver disease)* - Sepsis.

19. Ans. is b i.e. Toxin actions is CAMP mediated *Ref. Harrison 17/e, p 969-970*

V. cholera is motile by single polar flagellum not pertrichate flagella.

For more details, refer answer no. 5

20. Ans. is c i.e. V. cholera toxin *Ref. Ananthnarayana 7/e, p 310*

Already explained, refer answer no. 2

21. Ans. is c and d i.e. Motility; and Binds to specific receptors *Ref. See below*

- To cause cholera, Vibrio cholera must reach in small intestine where it produces cholera toxin.
- Vibrio encounters following barriers :

Barrier	Mechanism to invade
• Gastric acidity	– Large inoculum size (>10^6 organism)
• Mucosal lining of small bowel	– Chemotaxis, motility & variety of protease
• Adhesion to epithelial cells	– Toxin corregulated pilus

22. Ans. is a and c i.e. Food transmit; and Healthy carrier

Ref. Ananthnarayan 7/e, p 313; Park 18/e, p 177, 182; 19/e, p 191]

Mode of transmission of cholera :

- Faecally contaminated water ***(MC)***
- Contaminated food and drinks
- Direct contact.

Cholera Vaccine	
Parenteral vaccine	***Oral vaccines***
Killed Protective value 50%	Killed ***(wc/rbs)*** or live ***(CVD 103 HgR)*** Protective value 80% for live vaccine

So, no vaccine of cholera provide 90% protection.

Remember :

- **V. cholerae are killed with in 30 minutes by heating at 56^{0}C or within a few seconds by boiling.** Also killed by ***chlorination.***
- ***DOC*** for chemoprophylaxis is tetracycline. Alternative is doxycycline.
- Carriers in cholera includes preclinical or incubatory (1 - 5 days), convalescent (2 - 3 weeks), contact or healthy (> 10 days) and chronic carrier.

23. Ans. is d and e i.e. Neutrophilia; and Occurence of many cases in the same locality

Ref. Park 18/e, p 177; 19/e, p 191; Harrison 17/e, p 970

- V. cholera cause ***non inflamatory (no WBC in stool)*** painless watery diarrhoea.
- Neutrophilic leucocytosis occurs.
- As secondary attack is high, many case occurs in same locality.

24. Ans. is c i.e. Food can transmit the disease *Ref. Ananthnarayan 7/e, p 313*

Already explained, refer answer no. 21

25. Ans. is b i.e. 0:139 *Ref. Park 18/e, p 175; 19/e, p 189*

0 - 139 posses novel 0 - 139 LPS which is responsible for its virulence. 0 : 139 has replaced E1 tor and is predominant cause of cholera in areas where it had appeared.

26. Ans. is a, b and e i.e. Non vibrio cholera 01; Enterotoxigenic E. Coli; Vibrio cholera

Ref. Harrison 17/e, p 814

Causes of diarrhoea with pus cells / RBC's in stool (inflammatary diarrhoea or dysentery). :

- Shigella
- Campylobacter
- Yersinia
- Vibrio parahemolyticus
- EIEC, EHEC
- Salmonella
- Cl. difficle

27. Ans. is a i.e. Can tolerate wide range of alkaline pH *Ref. Ananthnarayan 7/e, p 305*

- Vibrio cholera can grow in **pH range 6.4-9.6** (Optimum - 8.2).
- NaCl (0.5-1%) is required for optimal growth though high concentration (6% and above) is inhibitory.
- Can be grown on media.
- Motile by single polar flagellum.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Which of the following about cholera is true :
a) Invasive **[AI 90]**
b) Endotoxin is released
c) Recent infections in India are of classical type
d) Vibriocidal antibody titre measures prevalence
[Ref. Ananthnarayan 7/e, p 314]

2. Vibrio cholera was discovered by : [Kerala 94]
a) Koch
b) Mekintoff
c) John snow
d) Virchow
[Ref. Ananthnarayan 7/e, p 305]

3. Vibrio parahemolyticus food poisoning is caused by ingestion of : [MP 96]
a) Eggs and Paultry products
b) Raw vegetable
c) Catfish, shellfish, seafood
d) Milk products
[Ref. Ananthnarayan 7/e, p 316-317]

4. Vibrio cholera was discovered by : [Delhi 96]
a) Louis pastuer
b) Robertkoch
c) Eberth and Gaffky
d) Bordet
[Ref. Ananthnarayan 7/e, p 305]

5. The transport medium for stools sample in cholera is : [ICS 98]
a) Thioglycolate
b) Cary Blair medium
c) Dubos medium
d) Selenite 'F' broth
[Ref. Ananthnarayan 7/e, p 306]

6. The growth factor required for the growth of vibrio parahemolyticus is : [Kerala 98]
a) Saline
b) Tryptophan
c) Bile
d) Citrate
[Ref. Ananthnarayan 7/e, p 316]

7. In cholera the highest case fatality is observed in case of : [Orissa 98]
a) Classical cholera vibrio
b) Vibrio EL tor
c) Vibrio parahemolyticus
d) NAG -vibrios
[Ref. Ananthnarayan 7/e, p 311]

8 Cholera toxin acts by : [Kolkata 03]
a) Na+K+ATPase inhibition
b) Adenylate cyclase stimulation
c) Opening of chloride channel
d) Stimulation of Ca++channel
[Ref. Ananthnarayana 7/e, p 310]

9. True about vibriocholera is : [SGPGI 03]
a) Disease more commonin woman
b) Classical vibrio protect against development of 0.139 strain disease
c) E1-tor is more milder than classical
d) Erythronycin is used in treatment
[Ref. Ananthnarayan 7/e, p 311]

10. Transport media for cholera : [Jharkhand 04]
a) VR medium
b) LZ mdeium
c) Bile salt agar
d) TCBS
[Ref. Ananthnarayan 6/e, p 306]

Answer

1. d) Vibriocidal	2. a) Koch	3. c) Catfish ...	4. b) Robertkoch	5. b) Cary Blair
6. a) Saline	7. a) Classical ...	8. b) Adenylate	9. c) E1-tor is more ...	10. a) VR medium

11. Transport medium for cholera bacteria :

a) V R medium **[Jharkhand 05]**
b) L Z medium
c) Carry blair medium
d) Staruert medium

[Ref. Anantharayan 7/e, p 306]

12. Non-Halophillic vibrios indudes all of the following except : [SGPGI 07]

a) V. vulnificus
b) V. cholera
c) V. parahaemolyticus
d) V. alginolyticus

[Ref. Ananthnarayan 7/e, p 316]

13. The function of B subunit of cholera toxin is :

a) ADP ribosylation of G protein **[BHU 07]**
b) To bind GM1 ganglioside recepter
c) To stablize cholera toxin
d) To increase cGMP

[Ref. Harrison 17/e, p 969]

14. 7th pandemic of cholera is caused by : [UP 07]

a) E_1tor
b) 0139 V. cholera
c) Classical V. cholera
d) V. mimicus

[Ref. Ananthnarayan 7/e, p 311]

Answer 11. a) V R medium 12. b) V. cholera
13. b) To bind GM1 ... 14. a) E_1tor

11 Pseudomonas & Yersinia

PSEUDOMONAS

Gram (–)ve aerobic motile bacilli with polar flagella.

Pseudomonas aeruginosa the *MC* human pathogen in this group.

P. AERUGINOSA = P. PYOCYANEA

- *Obligate aerobic bacilli* which is differentiated from enteric Gram (–)ve bacilli by its ability to oxidise indophenol and inability to ferment lactose.
- Non capsulated but many strains have mucoid slime layer of alginate particularly from patient of cystic fibrosis.

Culture and Growth characteristic

- Grows well at 37-42^{0}C on ordinary media.
- Growth at 42^{0}C helps differentiate it from other pseudomonas species.
- ***Selective media*** – Cetrimide agar
- **Pigment :**
  - **a. *Pyocyanin*** – Bluish green pigment produce *only by P. aeruginsoa*. It inhibits growth of many other bacteria.
  - **b. *Fluorescin*** – Greenish yellow. Produce by all species of pseudomonas.

Classification

- *On the basis of difference of lipopolysaccharide*.
- Restriction endonuclease typing with pulsed gel electrophoresis is most reliable method.
- Used for epidemiological purpose.

Pathogenicity and Resistance

- ***MC*** and ***most serious*** cause of infection in burns.
- ***MC infection*** outside hospital is suppurative otitis.
- Causative agent of Shanghai fever.
- ***Blue pus*** with characteristic fruity odour.
- ***Pathognomic*** skin lesion termed ecthyma gangreosum which occur singly or in small number on the perineum, buttocks and extremities
- Resistant to common antiseptic and disinfectant such as dettol. Even may grow profusely in bottle of these antiseptic.

Virulence factors :

- Pilli or fimbriae
- Mucoid exopolysaccharide/alginate
- Elastase
- Exotoxin (A, S, T, U, Y)
- Lipopolysaccharide or endotoxin
- Alkaline protease
- Phospholipased hemolysin

Exotoxin A – Acts as NADase, ↓ protein synthesis.

Exotoxin S – Ribosylation of GTP binding protein, disruption of cellular actin cytoskeleton.

Remember : Extracellular virulence factos *exhibits Quorum Sensing* (= cell to cell signaling system).

Treatment

Antimicrobials effecive against pseudomonas are :

Penicillin	*Cephalosporins*	*Aminoglycoside*	*Quinolones*
Piperacillin/Tazobactam	Ceftazidime	Tobramycin	Ciprofloxacin
Tazobactem	Cefoperazone	Gentamycin	Levofloxacin
Ticarcillin/Clavulanate	Cefepime	Amikacin	Trovafloxin
Meizlocllin			

Other Agent : Polymyxin B. Colistin, *Monobactams* - Aztreonam

- ***DOC*** – **Aminoglycoside + Penicillin except :**
  - **In UTI – Ciprofloxacin**
  - **In CNS infection –** Ceftozidime ± Aminoglycoside.
  - **In Malignant external otitis** – Cephalosporin or carbapenem or ciprofloxacin.

BURKHOLDERIA PSEUDOMALLEI [PSEUDOMONAS PSEUDOMALLEI]

- ***Causative agent of*** 'Meliodosis'.
- Resembles Ps. Mallei but differs in being motile.
- ***MC*** manifestation of meliodosis : Acute pulmonary infection.
- May cause hemoptysis resembling TB.
- Another common manifestation is acutely localized skin infection with ulceration or abscess that is associated with nodular lymphangitis and regional lymphadenits.
- Latency and reactivation may occur as bacillus can survive intracellulary in reticuloendothelial system.
- Human infection occurs commonly through skin abrasion or by inhalation.
- **Diagnosis :** – ***Typical bipolar safety pin appearnce*** of bacillus in exudates on microscopy.
  – Confirmed by culture or ≥ 4 fold rise in antibody.
- **Treatment :** – ***Ceftazidime or carbpenems*** is ***DOC.***

BURKHOLDERIA MALLEI (PSEUDOMONAS MALLEI)

- ***Causative agent of*** 'Glanders', a disease of equine.
- Non-motile with bipolar stained organism.
- ***On potato :*** characteristic amber, honey like growth appears, becoming greenish yellow resembling Ps. aeruginosa
- It is agent of biological Warfare and terrorism, classified as 'category B biological agent'.

- In human it cause acute localized suppurative infection, acute pulmonary infection; acute septicemic infection and chronic suppurative infection.
- *It induce **'straus reaction'.***
- Human infection is usually ***occupational.***
- **Diagnosis :** – *Mallein test* which is analogous to tuberculin test.
  – *Molecular methods for rapid identificatiion – 16s rRNA gene sequencing. Also distinguish it from B.pseudomallei.*
- **Treatment :** – Same as **meliodosis.**

PASTEURELLAE

- Group consist of gram negative, short, Pleomorphic bacilli that are primary pathogen of rodents.
- It is divided into 3 genus :
  - **a Yersinia :** • includes plague bacillus (y.pestis); Y. pseudotuberculosis (primary pathogen of rodents); Y. enterocolitica.
    • it is assigned in the family enterobacteriaceae.
  - **b. Pasteurella :** • includes P. multiocida (non-motile, oxidase positive).
  - **c. Francisella :** • includes F. Tularensis.

Remember : – Pasteurellae which Grow on MacConkey and are urease positive : Y.pseudotuberculosis, Y. enterocolitica.
– ***'a'*** and ***'b'*** are short pleomorphic, gram negative rods with bipolar staining. They are catalase positive, oxidase negative except P. multiocida and are microaerophilic or facultative anaerobic.

..... Jawetz 24/e, p 294

YERSINIA. PESTIS = PLAGUE BACILLUS

Morphology

- Non motile, Non sporing, microaerophilic, biochemically unreactive, pleomorphic bacilli/coccobacillus.
- Characteristic bipolar (safety pin) appearance, with Wayson's stain/Giemsa/Methylene.
- It is noncapsulated but at $\geq 30^0$C it produce envelop (= F1 antigen) – a virulence factor that serves as the principal immunodiagnostic marker of infection.
- *Serotypes do not exist.*

Remember : Growth occur *fastest* at 30^0C and envelop develop *best* at 37^0C.

Cultural Characteristics

- Optimum growth occurs at 27^0C and pH 7.2 (unlike most pathogen which usually usually grow at 37^0C).
- Shows 'Stalactite growth' in ghee broth.

Biochemical reactions :

- Based on fermentation of glycerol and reduction of nitrate, it is divided into 3 varieties.
- Catalase and Aesculin positive; urease and oxidase negative.

Pathogenesis

- From the site of flea bite (xenopsylla cheopis) it is carried to regional lymph nodes (=bubo) via lymphatic channel.
- Monouclear phagocytes play role in dissemination of infection to distant sites (secondary pneumonia and septicemia).
- **Primary pneumonia** results by droplet infection of plague patient.
- **Primary septicemic plague** consist of sepsis in absence of bubo while secondary septicemic plague is complication of bubonic or pneumonic plague.
- **Toxin** has **no role.**

Remember : It produce coagulase at 28^{0}C but not at 35^{0}C. *..... Jawetz 24/e, p 291*

Clinical Features

- Characterized by rapid onset of fever and other systemic manifestations of Gram –ve bacterial infections.
- It is of 3 types :

a. Bubonic Plague :
- I.P 2 - 7 days
- ***MC*** type of plague and is almost always caused by ***bite of infected flea.***
- ***MC*** site of bubo femoral, inguinal region >axillary, cervical. *... Harrison 17/e, p 982*
- Distinguished from lymphadentis by its rapid onset, its extreme tenderness, accompanying signs of toxemia and absence of cellulitis or obvious ascending lymphadenitis.
- DIC is common and may lead to gangrene.
- Y. pestis can also be cultured from blood of most bubonic plague patient.

b. Septicemic plague :
- Often present with GI symptoms, DIC, multiorgan failure.
- I.P 2 - 7 days

c. Pneumonic Plague :
- ***Most infectious, most fatal*** type of plague with I.P of 1 - 3 days.
  - Primary pneumonia : Cyanosis is very prominent, with bloody mucoid sputum.
  - Secondary pneumonia : Diffuse ***interstitial*** pneumonia, less infectious.

Treatment : Streptomycin ***(DOC)***

Prevention :
- ***Prophylaxis of choice*** – Tetracycline.
- Recombinant vaccine that use F_1 and V antigen is available.

FRANCISELLA OR PASTEURELLA OR BRUCELLA TULARENSIS

- Capsulated, non-motile, intracellular parasite which grows in special media such as Francis blood dextrose cystine agar.
- It resembles mycoplasma.
- It cause ***tularemia***, a disease of rabbits and other rodents which is transmitted by ticks.
- In human it present as local ulceration with lymphadenitis, typhoid like fever with glandular enlargement or influenza like respiratory infection.
- **Treatment :** Streptomycin is ***DOC*** for adults and children.

YERSINOSIS

- It denotes infection with yersinae other than Y.pestis (i.e. by enterocolitica and pseudotuberculosis).
- They are motile at 25^{0}C but non-motile at 37^{0}C.
- They show antigenic cross reaction with Y.pestis, Vibrio, Salmonella, Brucella.
- For culture *'cold enrichment'* is done.

Y.pseudotuberculosis :
- Most human infection occur by serotype 01.

Y. Enterocolitca :
- Most human infection occur by serotypes 03, 08, 09.
- It causes gastroenteritis or enterocolitis; Mesentric adenitis or terminal ileitis; system disease with bacteremia; erythema nodosum, reactive arthritis (in HLA - B 27).

QUESTIONS

1. A young boy had a flea bite while working in a wheat grain godown. After 5 days he developed fever and had axillary lymphadenopathy. A smear was sent to the laboratory to perform a specific staining. Which one of the following staining method would help in the identification of the suspected pathogen : [AI 06]

a) Albert staining
b) Zeihl-Nelson staining
c) McFadyean's staining
d) Wayson staining

2. Which one of the following drugs is an antipseudomonal penicillin ? [AI 06]

a) Cephalexin
b) Cloxacillin
c) Piperacillin
d) Dicloxacillin

3. The following statements are true regarding meliodosis except : [AI 05]

a) It is caused by Burkholderia mallei
b) The agent is a gram negative aerobic bacteria
c) Bipolar staining of aetiological agent is seen with methylene blue
d) The most common form of meliodosis is pulmonary infection

4. An organism grown on agar shows green colored colonies; likely organism is : [AI 01]

a) Staphylococcus
b) E. Coli
c) Pseudomonas
d) Peptostreptococcus

5. All of the following statement about plague are wrong except : [AIIMS 04]

a) Domestic rat is main reservoir
b) Bubonic is the most common variety
c) The causative bacillus can survive upto 10 years in the soil of rodent burrows
d) Incubation period for pneumonic plague is one to two weeks

6. A 50 year old chronic alcoholic male agriculture worker presented with high grade fever of one week with spells of chills and rigor. Examination of the respiratory system reveals bilateral crepitation with scattered ronchi. Multiple subcutaneous nodules were found on extensor surface of left forearm and left leg. Direct microscopy of the pus aspirate from the nodules reveals plenty of Grams (–)ve bacilli with bipolar staining. Culture reveals distinct rough corrugated grey white colonies on blood agar. The organism were motile and oxidase positive. The most likely diagnosis is : [AIIMS 03]

a) Plague
b) Meliodosis
c) Bartonellosis
d) Actinomycosis

7. The drug of choice for chemoprophylaxis in contacts of a patient of pneumonic plague is : [AIIMS 02]

a) Penicillin
b) Rifampicin
c) Erythromycin
d) Tetracycline

8. True about Y. pestis : [PGI 06, 03]

a) Gram +ve
b) Gram -ve
c) Motile
d) Non-motile
e) It is coccobacilli

9. True statement(s) about Y. pestis is/are : [PGI 04]

a) Gram positive
b) Non-motile
c) Benzyl penicillin is given in prophylaxis
d) Patients are kept isolated till 48 hrs. of treatment
e) Repeated blood culture is diagnostic

Answer

1. d) Wayson ... 2. c) Piperacillin 3. a) It is caused by ... 4. c) Pseudomonas 5. b) Bubonic is ...
6. b) Meliodosis 7. d) Tetracycline 8. b, d and e 9. b and e

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is d i.e. Wayson staining

Ref. Park 19/e, p 244 - 246; Jawetz 24/e, p 292; Ananthnarayan 7/e, p 329

"It is typical clinical presentation of bubonic plague."

PLAGUE :
- It is a zoonosis.
- Causative agent is Yersinia pestis which is :
  - Gram negative, Non motile, Coccobacilli
  - Exhibits bipolar staining with ***Wayson's stain / Giemsa stain / Methylene blue.***
  - Plague bacilli can survive and indeed multiply in the soil of rodent burrows where microclimate and other conditions are favourable.

Reservoir :
- ***Wild rodents*** (eg. field mice) ***are natural reservoirs*** of plague.
- *In India wild rodent*, ***Tatera indica*** *has been incriminated as main reservoir,* not the domestic rat.

Source of infection :
- ***Infected rodents*** and ***fleas*** and ***case of pneumonic plague (not bubonic plague).***

Immunity : After recovery is relative.

Vector : – Commonest vector is rat flea, (X-cheopis). Infected flea may live upto 4 year.
- Human **infection** is ***most frequently*** contracted from bite of infected flea.
- ***Basic cycle*** in epidemic bubonic plague is : Commensal rats → rat fleas → man
- **Incubation period :**
  - Bubonic plague - *2 to 7 days*
  - Septicaemic Plague - *2 to 7 days*
  - Pneumonic plague - *1 to 3 days*
- ***MC type*** of human ***plague*** is **Bubonic plague** characterized by enlarged tender lymph nodes (Bubos).
- MC site of bubo is femoral, inguinal, axillary and cervical nodes.
- **Pneumonic plague** – Rare variety but most infectious variety of plague.
- **Septicaemic plague** – Rare variety.

Diagnosis :
- ***Specimens*** - Blood for culture.
  - Aspirates of enlarged lymph nodes for smear and culture.
- ***Smears*** - Stain with giemsa and specific immunofluorescent stains.
  - Prime face diagnosis is by examination of smears which show characteristic bipolar appearance with Wayson's stain.
- ***Culture*** - Blood culture are often positive in 24 hours.
  - Definite identification of culture is best done by immunofluorescence.
- ***Serology*** - Antibodies to F. 1 antigen may be detected by passive hemagglutination.

Treatment :
- ***DOC*** – Streptomycin (Alternative tetracycline)

Chemoprophylaxis :
- ***DOC*** – Tetracycline (Alternative sulfonamide)

Remember :

- Flea bone disease
  - Endemic typhus
  - Hymenoplepis diminata
  - Chiggerosis

Stain	Organism
Albert's	C. diptheria
Zeihl Nelson	Acid fast organism
Mc Fadyean's	B. anthrax

2. Ans. is c i.e. Piperacillin *Ref. Harrison 16/e, p 894*

Antimicrobial agents active against pseudomonas aeruginosa			
Antipseudomonal penicillins	**Antipseudomonal cephalosporins**		**Carbapenems**
• Piperacillin • *Mezlocillin* • Ticarcillin • Ticarcillin / clavulanate	• Ceftazidime • Cefoperazone • Cefepime		• Imipenem/cilastatin • Meropenem
Monobactams	**Aminoglycosides**	**Fluoroquinolones**	**Other agents**
• Aztreonam	• Tobramycin • Gentamicin • Amikacin	• Ciprofloxacin • Levofloxacin	• Polymyxin B • Colistin

3. Ans. is a i.e. It is caused by Burkholderia mallei

Ref. Harrison 17/e, p 955; Jawetz 24/e, p 265

Meliodosis

- Caused by Burkhoderia Pseudomallei *(Pseudomonas Pseudomallei).*
- It is free living small, motile (differentiating feature from pseudo. mallei) *aerobic gram negative* bacillary saprophyte normally found in soily ponds and rice paddies.
- It grows at 42^0C and oxidise glucose, lactose and is *oxidase positive.*
- ***MC*** form of meliodosis is *Acute pulmonary* infection.
- Acute pulmonary infection vary from mild bronchitis to extensive necrotizing pneumonia.
- Chronic pulmonary infection mimics TB.
- It also cause acute, localized skin infection with ulceration or abscess that is associated with nodular lymphangitis and regional lymphadenitis.
- Also cause suppurative parotitis particularly in children.
- Progression of disease is more common in chronic debilitated patient (D.M, chronic renal disease, alcoholics).

Diagnosis :

- Considered in patient present with acute lower respiratory tract illness, parotitis, lymphadenitis or unusual skin or subcutaneous lesion or chest ray suggest TB (upper lobe infiltrate) in absence of tubercle bacilli in sputum.
- Gram's stain of appropriate specimen will show small gram negative bacilli; **bipolar regularly staining** (safety pin appearance) is seen by Wright's stain or methylene blue stain.

– **Positive culture is diagnostic.**
– Positive serologic test is evidence of past infection.
– **X-ray** - upper lobe infiltrate occasionally with thin walled cavities.

Treatment : Ceftazidime or Carbepenems are ***DOC.***

4. Ans. is c i.e. Pseudomonas *Ref. Ananthnarayan 7/e, p 319*

Pseudomonas

Aerobic, nonsporing gram negative, motile bacilli, forms many pigments :

a. ***Pyocyanin :*** – Bluish green pigment, produced ***only by*** Ps. aeruginosa
b. ***Fluorescin (Pyoverdin) :***
– Greenish yellow pigment which oxidise in old culture to yellowish brown pigment
c. ***Pyrubin :*** – Red
d. ***Pyomelanin :*** – Brown

Other pigment forming bacteria are :

• **S. aureus**	– Golden yellow pigment
• **B. melanogenicus**	– Black pigment
• **Rhodococcus**	– Red pigment
• **Nocardia**	– Yellow to red pigment
• **Pepto and peptostreptococcus**	
• **Photo and Scoto chromogen**	– Yellow orange pigment

5. Ans. is b i.e. Bubonic is the most common variety
Ref. Jawetz 24/e, p 292; Ananthnarayan 7/e, p 329
Already explained, refer answer no. 1

6. Ans. is b i.e. Melioidosis *Ref. Harrison 17/e, p 955; Jawetz 24/e, p 265*

- Actinomycosis is ruled out as it is gram positive bacilli.
- Plague is ruled out as it is gram negative non motile coccobacilli.
- Bartonellosis is ruled out as it does not exhibits bipolar staining.
- Bacteria showing bipolar staining = safety pin appearance are :
  – Calymmatobacterium granulomatis – Yersinia and Pasteurella – H. ducreyi
  – V. parahemolyticus – Ps. pseudomallei

7. Ans. is d i.e. Tetracycline *Ref. Park 18/e, p 237; Jawetz 24/e, p 292; Ananthnarayan 7/e, p 329*
Already Explained, refer answer no. 1

8. Ans. is b, d and e i.e. Gram -ve; Non-motile; and It is coccobacilli
Ref. Jawetz 24/e, p 292; Ananthnarayan 7/e, p 329
Yersinia is Gram –ve, non motile cocobacilli.

9. Ans. is b and e i.e Non - motile; and Repeated blood culture is diagnostic
Ref. Park 18/e, p 233, 237; Jawetz 24/e, p 292; Ananthnarayan 7/e, p 329
Already Explained, refer answer no. 1

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.

1. Granuloma with stellate abscess : **[JIPMER 99]**

a) T.B.
b) Tuleremia
c) Sarcoidosis
d) Staphylococcus

[Ref. Jawetz 24/e, p 288]

Answer 1. d) Staphylococcus

12 Hemophilus, Bordetella & Brucella

HEMOPHILUS

- Genus comprised of non motile, N. sporing, oxidase positive Gram negative bacilli, characterized by requirement of one or both of two accessory growth factors (X and V) in blood. Important species are H. influenza, H. aegypticus and H. ducreyi. These requirement are used to identify the bacteria.
- Both H.influenzae and H. haemolyticus have identical growth (factor X & V) requirement. So H. hemolyticus is distinguished from H. influenzae by hemolysis on horse blood agar.

H. INFLUENZAE = PFEIFFER'S BACILLUS

Morphology

- Capsulated Coccobacilli shows pleomorphism.
- Stained by ***Loeffler's methylene blue*** or Dilute carbol fuchsin.
- On the basis of indole production, urease and ornithine decarboxylase activity, it is divided into eight biotypes.

Culture

- ***Flides agar*** is ***best for*** primary isolation.
- On ***Levinthal's medium*** – capsulated strain shows distinctive iridescence.
- Require ***both X factor*** (heat stable haemin) and V factor (heat labile coenzyme present in RBC) so heated or boiled blood agar (Chocolate agar) is superior to plain agar. X factor is not required for anaerobic growth.
- Shows *'Satellitism'* (dependnce on V factor) when S.aureus is streaked across blood agar.

Antigenic Properties

- There are three major surface antigen - the capsular polysaccharide; the outer membrane protein (OMP) and Lipo-oligosacharide.
- Major antigenic determinant is capsular polysaccharide based on which, it is typed into six capsular types a to while non-capsulated strains are non typable.
- Most isolates from acute invasive infections belong to 'b'.
- Type b capsule has unique structure containing pentose sugar (ribose and ribitol) in the form of Polyribosyl ribitol phosphate (PRP) instead of hexoses and hexosamines as in other 5 serotypes. Hib PRP is used in vaccine.
- H. influenza is first free living organism whose complete genome is sequenced.

Feature	Type b Strains	Nontypable Strains
Capsule	Ribosyl-ribitol phosphate	Unencapsulated
Pathogenesis	Invasive infections due to hematogenous spread	Mucosal infections due to contiguous spread

Age	2 months – 3 years	Adults
Clinical manifestations	Meningitis and invasive infections in incompletely immunized infants and children	Otitis media in infants and children; lower respiratory tract infections in adults with chronic bronchitis and pneumonia
Vaccine	Highly effective conjugate vaccines	None available; under development

Clinical features

Meningitis : **Most** frequently by **biotype - I**

- Occur in children (<2 years of age) due to absence of PRP antibodies.
- ***MC*** **Complication** of its meningitis - *Subdural effusion*

Epiglotitis :
- Particularly affects 2-7 year age group.

Cellulitis :
- Seen in young children. The most common location is on the head or neck.

Pneumonia :
- Particularly in infants.

Diagnosis

Meningitis :
- CSF gram's stain and culture
- If culture negative - Detection of PRP.

Respiratory tract infection :
- Suggested by predominance of gram negative coccobacilli among abundant polymorphonucelar leukocytes in sputum.

Treatment : ***DOC*** ceftriaxone or cefotaxime (also in other invasive infection).

Vaccination : Hib conjugate vaccine :
- 1st dose 2 months
- Rest of primary series 2 - 6 months
- Booster dose 12 - 15 months.

Remember : No vaccine is available for non typable H influenza.

HAEMOPHILUS AEGYPTIUS

Cause highly contagious form of conjunctivitis ***(PINK EYE)*** and Brazilian purpuric fever ***(BPF).***

HAEMOPHILUS DUCREYI

- Bipolar stained *(safety pin)* bacilli arranged in group or whorls or parallel chains [school of fish or rail road track appearace].
- Cause *Chancroid or soft sore* – STD characterized by tender, non indurated irregular genital ulceration and inguinal adenitis.

Treatment :
- Single oral dose of azithromycin.
- Alternative ciprofloxacin or erythromycin.

BRUCELLA

- Gram negative, non-motile, non capsulated, non sporing, strict aerobic, intracellular coccobacilli.
- Major virulence factor : LPS which possess endotoxin activity.
- Brucella is agent of biological warfare.
- Form both caseating and non caseating granuloma.

- Resist intracellular killing by suppression of myeloperoxide - hydrogen peroxide-halide system and production of superoxide dismutase.

Clinical features

- It cause Brucellosis, a zoonotic diseases, also know as mediterranean fever or Malta or undulant fever.
- ***Source :*** Sheep, goats, camels.
- ***Route of transmissiion :*** Occupational exposure, ingestion of untreated milk or milk products, raw meat (blood); inhalation; transplacental; during breast feeding and during sexual activity.
- ***MC*** and ***most virulent*** cause of brucellosis : B. melitensis.
- ***MC*** **symptoms** are fever, chills, diaphoresis, headaches.

  Pancarditis, Sleep disturbances, lymphadenopathy, Hepato splenomegaly, GBS syndrome, abortion or IUD during pregnancy. are other important findings.
- ***MC*** focal feature is musculoskeletal pain and physical findings in the peripheral and axial skeleton.
- **Death is** usually a consequence of *cardiac involvement.*
- Immunity is mainly cell - mediated.

Diagnosis

1. Most defenitive method -blood culture
   - – Castaneda method of blood culture is employed.
   - – Preferred media are serum dextrose agar; trypticose soy agar.
2. PCR : More sensitive and more quicker than blood culture.
3. Serological test :
   - a. *Acute infection* – Standard agglutination (SAT) test done
     - – Shows prozone phenomenon
     - – SAT also +ve in cholera, tularemia, yersinia, and immunization.
   - b. Chronic infection – Complement fixation test.
   - c. For diagnosing animal infection – Rapid ***plate agglutination, rose bengal card*** and ***milk ring test done.***

Treatment :

- TB must always be excluded.
- ***Gold standard*** treatment in adults : ***streptomycin + doxycycline.*** *... Harrison 17/e, p 976*
- Alternative rifampin + doxycycline.
- In children, pregnant women or who can't tolerate tetracycline – Cotrimoxazole given.

BORDETELLA

- Genus consist of Gram negative, strict aerobic coccobacilli which grows only on complex media.
- Its two important members :
  - a. ***B. pertussis*** – Causative agent of pertussis (whooping cough = 100 day fever).
  - b. ***B. parapertussis*** – Silent copy of pertussis toxin gene causing milder form of pertussis.

Morphology

- B.Pertussis is pleomorphic, non motile, non sporing, ***capsulated, fimbriated*** coccobacilli, which show Bipolar metachromatic granules on staining with toulidine blue.

Culture

- Grows on enriched media like *Regan towe or Bordet Gengou glycerine potato blood agar,* forming colonies resembles bisected pearls or Mercury drops or Aluminium paint appearance.
- Culture films has **'Thumb print'** appearance.
- Charcoal containing media (as for legionella) is preferred.
- Blood is required to neutralise the inhibitory materials formed during bacterial growth.

Virulent Factors

a. Most important is pertussis toxin ***(PT) – exotoxin*** protein consist of B - binding unit and A active unit having ADP ribosylating activity of G protein ***(like of cholera toxin)*** B-parapertusis don't express the gene coding for pertusis toxin. Also serves as adhesin, lymphocytosis producting factor, histamine sensitizer and islet activating protein.

b. ***Filamentous hemagglutinin (FHA) secreted protein.***
   - Both PT and FHA hemagglutinin promotes secondary infection by coating H. influenza and pneumococci so that they bind. This is known as *'PIRACY OF ADHESINS'.*

c. Surface adhesins (pertactin, Fimbriae), Adenylate cyclase, Hemolysin, tracheal cytotoxin, heat labile toxin LPS endotoxin, pertactin agglutinogens are other virulence factor.

   Infection is initiated by attachment of the organism to the ciliated epithelial cells of the nasopharynx, attachment is mediated by surface adhesions.

Pathogenesis

- Local cellular invasion with intracelluar persistence (systemic dissemination not occur). Systemic manifestation is due to toxin.
- Both cellular and humoral immunity are important.
- First defence is by antibody which prevents attacments of bacteria.
- Neurological manifestation are due to hypoxia.

Clinical features

- Incubation period - 7 - 14 days.
- It has 3 stages :

a. Catarrhal stage :
   - Maximum infectivity

b. Paroxysmal stage :
   - Posttussive vomiting is frequent with mucus plug occassionally at end of episode.
   - Vomiting with cough is the best predictor of diagnosis of pertussis.
   - Episodes are often worsen at night and interfere with sleep.
   - Most complication occur during paroxymal stage.
   - Paroxysm is precipitated by noise, eating and physical contact

c. Convalescent stage

Complication

Subconjunctival hemorrhages, abdominal and inguinal hernia, pneumothorax, petechiae, weight loss, apnea, pneumonia, seizures, encephalopathy.

Diagnosis

i. ***Best specimen*** is obtained by ***nasopharyngeal aspiration*** *..... Harrison 17/e, p 935*

ii. ***Gold standard – Culture of nasopharyngeal secretion***

iii. Absolute lymphocytosis without ↑ in ESR

iv. Most sensitive is PCR

v. Serology – If symptoms > 4 weeks.

Treatment

DOC – Macrolide (Erythromycin, Clarithromycin Azithromycin)

Alternative – Cotrimoxazole

β agonist, Glucocorticoids and cough suppressants are not effective.

Prevention

- ***Chemoprophylaxis*** – For house hold contact of cases.
  – Erythromycin is ***DOC.***

- ***Immunization*** – ***main stay*** of preventions is active immunization.

  Two types of vaccine are available :

  a. ***Whole cell vaccine :***
     – Associated with many adverse effects and may also cause - encephalopathy, sudden infant death syndrome, and autism.
     – It is contraindicated in individual ≥ 7 year age.

  b. ***Acellular vaccine :***
     – Less reactogenic and is recommended for routine immunization.
     – It contains pertussis toxoid.
     – Two component vaccine are more effective than monocomponent, since addition of pertactin increase efficacy.
     – Protection against pertussis by vaccine correlated best with the production of antibody to pertactin, fimbriae, and pertussis toxin.

QUESTIONS

1. A veterinary doctor had pyrexia of unknown origin. His blood culture in special laboratory media was positive for gram negative short bacilli which was oxidase positive. Which one of the following is the likely organism grown in culture? **[AI 06]**
a) Pasturella spp.
b) Francisella spp.
c) Bartonella spp.
d) Brucella spp.

2. A farmer presenting with fever off-and on for the past 4 years was diagnosed to be suffering from chronic Brucellosis. All of the following serolocical tests would be helpful in the diagnosis at this state except : **[AI 04]**
a) Standard Agglutination test
b) 2 Mercapto-ethanol test
c) Complement fixation test
d) Coomb's test

3. The following are true for Bordetella pertussis except : **[AI 03]**
a) It is a strict human pathogen
b) It can be cultured from the patient during catarrahal stage
c) It leads to invasion of the respiratory mucosa
d) Infection can be prevented by a acellular vaccine

4. Malta fever is caused by : **[AIIMS 08]**
a. Legionella
b. Borrelia burgdorferi
c. Brucella melitensis
d. Pseudomonas

5. Brucellosis can be transmitted by all of the following modes, except : **[AIIMS 07, 06]**
a) Contact with infected placenta
b) Ingestion of raw vegetables from infected farms
c) Person to person transmission
d) Inhalation of infected dust or aerosol

6. Brucella is transmitted by all the following means except : **[AIIMS 06]**
a) Through placenta of animals
b) Person to person transmission
c) Aerosol
d) Eating uncooked food

7. The usual incubation period of pertusis is :
a) 7 - 14 days **[AIIMS 05]**
b) 3 - 5 days
c) 21 - 25 days
d) Less then 3 days

8. All the following are true about H. influenzae except : **[AIIMS 03]**
a) It can be part of normal flora of some persons
b) The serotyping is based on bacterial outer membrane protein
c) It requires Haemin and NAD for growth in culture medium
d) Type b is responsible for invasive disease

9. A 2 years old child is brought to the emergency with history of fever and vomiting. On examination he has neck rigidity. CSF examination shows polymorhphs more that 200/µl; protein 100mg/dl and glucose 10mg/dl. the Grams stain shows the presence of Gram negative coccobacilli. The culture shows of bacteria only on chocolate. agar and not on blood agar. The causative agent is :
a) Neisseria meningitides **[AIIMS 02]**
b) Haemophilus influenzae
c) Branhamella catarrhalis
d) Legionella pneumophila

10. A farmer rearing sheep, presented with complaints of fever and weakness for the last one month. There is generalised lymphadenopathy. There was also associated hepatomegaly Biopsy of liver showed non-caseating granuloma. There are most likely due to infection with : **[AIIMS 00]**
a) Yersinia pesitis
b) Brucella canis
c) Francisella tularensis
d) Brucella melitenesis

11. True regarding pertussis vaccine is :
a) 95% of vacinated are protected **[AIIMS 00]**
b) Erythromycin should be given to contacts
c) Neuroparalytic complication is seen in 1 in 15000
d) Leucocytosis is diagnotic

12. Regarding Brucellosis, all of these are true except: **[PGI 02]**
a) Man to man transmission
b) A zoonosis
c) Blood cultures used in diagnosis
d) Transmitted via animal products

Answer

1. d) Brucella	2. a) Standard ...	3. d) Infection ...	4. c) Brucella	5. c) Person ...
6. b) Person to ...	7. a) 7 - 14 ...	8. b) Serotyp ...	9. b) H. Influen ..	10. d) Brucella ...
11. b) Erythromy ...	12. a) Man to ...			

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is d i.e. Brucella *Ref. Ananthnarayan 7/e, p 346*

Oxidase positive gram negative organism producing pyrexia of unknown origin in veterinary doctor is pointing towards Brucella (coccobacilli or short rods).

- **Brucella is the causative agent of Brucellosis** *(Malta fever, undulent fever).*
- **Other options :** Pasturella spp. (P. multocida)
  - It is also short bacilli and oxidase positive, but it can grow over normal media and does not present with pyrexia of unknown origin. It is non-motile and produce indole.
  - Manifestation of pasturella : Local suppuration, Meningitis, Respiratory tract infection.
  - Francisella (Casuative agent of Tularemia) : It is also short bacilli with fastidious growth requirement. But it is oxidase negative.

Remember :

- Brucella is oxidase and catalase positive except B.neotomae and B.ovis.
- Risk factors for Brucellosis (Zoonotic disease).
  - Occupational - Farmers, shepherds, Veterinanrians, Goats herds, Slaughter house workers.
  - Domestic - family members of individual in animal husbandry.
  - Laboratory workers - involved in handing cultures.
  - Travellars and Urban dwellers.
- Brucella can grow over normal media but growth is improved by addition of serum or liver extract.

2. Ans. is a i.e. Standard agglutination test

Ref. Ananthnarayan 7/e, p 349; Harrison 17/e, p 975; Jawetz 24/e, p 286

Diagnosis of Brucellosis

1. ***Culture :***
   - Blood culture is the most definitive method.
   - ***Castaneda method*** of blood culture is recommended.
2. ***Serology***
   a. ***Standard agglutination (tube agglutination) test (SAT)*** *is performed most often. It identifies mainly the IgM antibody.*
      - *Titre tends to decline after acute phase of the illness* so not helpful in chronic brucellosis.
      - *Positive agglutination test may be produced by cholera, tularemia or yersinia infection or immunisation.*
      - *Cholera induced agglutinins may be differentiated by agglutination absorption test and also as they are removed by treatment with* 2-mercapto ethanol.

   b. ***Blocking or non agglutinating antibodies –*** *Most reliable method for obviating the blocking effect and detecting the incomplete antibodies is antiglobulin (coombs) test.*

   c. ***Complement fixation test –*** *Detects both IgG and IgM so it is more useful in chronic cases.*

   d. ***ELISA –*** *Sesitive, specific and can detect IgM and IgG antibody separately so useful for differentiating acute and chronic infections.*

   e. ***PCR –*** *To detect bacteremia, to predict relapse and to exclude chronic brucellosis. More sensitive and quicker than blood culture.*
3. ***Hypersensitivity test –*** **Not** useful in diagnosing acute infections.

3. Ans. is d i.e. Infection can be prevented by an acellular vaccine

Ref. Ananthnarayan 6/e, p 342; Harrison 17/e, p 936

"All acellular vaccine curently available contain pertussis toxoid hence they only prevent disease not infection." *..... Harrison 17/e, p 936*

- Bordetella pertusis is an obligate human parasite.
- **Source** of infection is case of pertussis.
- **Carriers** and **Subclinical** infection are not found.
- Infection is limited to respiratory tract; in advance conditions leads to desquamation of alveolar epithelium (invasion of respiratory mucosa).
- Bacilli do not invade blood stream.
- **Diagnosis :**
  - *Culture* of *nasopharyngeal secretions* remains the gold standard of diagnosis.
  - *Best specimen* is collected by *nasopharyngeal aspiration.*
  - Culture is positive in catarrhal and early proxysmal stage.
  - Media used is Bordet-Gengou or Regan-Lowe.

Remember : Regan-Lower charcoal medium – Transport media.

4. Ans. is c i.e. Brucella melitensis *Ref. Ananthnarayana 7/e, p 346*

Already explained, refer answer no. 1

5. Ans. is c i.e. Person to person transmission *Ref. Park 19/e, p 242*

Brucellosis is transmitted from infected animal to man and there is evidence of transmission from man to man.

Modes of Transmission of Brucella

Contact infection (MC)	Food borne infection	Airborne infection
– Direct contact with infected tissue, blood, urine etc. – Mostly occupational	– Ingestion of raw milk or dairy products – Water contaminated with excreta of infected animal	– From aerosols in cowshed and slaughter house

6. Ans. is b i.e. Person to person transmission *Ref. Park 19/e, p 242*

Already explained, refer just above answer.

7. Ans. is a i.e. 7 - 14 days *Ref. Park 19/e, p 139*

Incubation period of pertusis is usually 7 to 14 days, but never exceed 3 weeks.

Important points about pertussis :

- Caused by B.pertusis
- Source of infection is case, there is no evidence of subclinical infection

- Pertusis is most infectious in catarrhal stage
- Infective period extends from a week after exposure to about 3 weeks after the onset of paraoxymal stage
- Secondary attack rate is about 90%.

8. Ans. is b i.e. Serotyping is based on bacterial outer membrane protein

Ref. Ananthnarayan 7/e, p 335

"H. influenzae strains have been classified on the basis of capsular polysaccharide not on the basis of outer membrane protein."

Important features of H. influenzae

- Gram (–)ve coccobacilli
- Require ***Factor V*** (nicotinamide nucleotide) and ***Factor X*** (haemin) for growth. So grow well on choclate agar as factor V is free in choclate agar. (Growth is poor in blood agar).

Antigenic structure :

a. Capsular antigen : – Basis of classification
– Most isolates of acute invasive infection belongs to type b.

b. Bacterial outermembrane protein

c. Lipooligosaccharide

– Non capsulated strains of H. Influenzae can colonize the upper respiratory tract of childrens and adults.

9. Ans. is b i.e. H. Influenzae *Ref. Ananthnarayan 7/e, p 332 - 337*

See the morphology of asked bacteria, you will know the answer.

H.influenzae	–	Gram negative coccobacilli
N. meningitides	–	Gram negative cocci
Legionella	–	Gram negative coccobacilli
B. catarrhalis	–	Gram negative cocci

10. Ans. is d i.e. Brucella melitensis *Ref. Harrison 17/e, p 974*

"History of contact with sheep and clinical feaures of fever, weakness, lymphadenopathy with non caseating granuloma signifies Brucellosis."

- Brucella melitensis is most pathogenic and most common cause of brucellosis and usually infect sheep, goats and camels.
- Brucella canis usually infect dogs
- Brucella abortus – Cattle or buffalo
- Brucella suis – swine
- *No* man to man transmission occurs.

Clinical features of Brucellosis :

- Fever with profuse sweats, especially at night. If untreated fever follows undulating pattern i.e., fever → afebrile period → fever.
- Fever is associated with musculoskeletal symptoms i.e. pain.
- Osteomyelitis commonly in lumbar and low thoracic vertebrae.

- Septic arthritis ***(MC knee)***
- Neurologic involvement with depression and lethargy
- Endocarditis (MC in aortic valve)

11. Ans. is b i.e. Erythromycin should be given to contact *Ref. Park 19/e, p 139 - 141*

"Those known to have in contact with whooping cough should be given prophylactic erythromycin for 10 days."

Pertussis vaccine

1. Killed whole cell vaccine :
- Given in the form of DPT
- Protection 70 - 90%

Adverse reaction :– Neurologic complication 1:170000
– Convulsions
– Prolonged screaming
– Hyporesponsible state.

Contraindication : – Epilepsy, convulsion or other CNS disorder.

2. Acellular vaccine :
– Contain pertussis toxoid and filamentous hemagglutinin.
– Same efficacy but less reactogenic
– Two component (which contain pertacin and pertussis toxoid) are more effective than monocomponent acellular vaccine. *..... Harrison 17/e, p 936*

In pertusis lymphocytosis (not leucocytosis) is diagnostic.

12. Ans is a i.e. Man to man transmission *Ref. Harrison 17/e, p 973*

Already explained, refer answer no. 5

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Satellitism is seen in cultures of :
a) Hemophilus **[Nimhans 86, PGI 86,TN 95]**
b) Streptococcus
c) Proteus
d) Salmonella
[Ref. Ananthnarayan 7/e, p 333]

2. Hemophilus needs : **[TN 99]**
a) X factor
b) V factor
c) X and V factor
d) VII fector
[Ref. Ananthnarayan 7/e, p 333]

3. Milk ring test : **[JIPMER 99]**
a) Brucellosis
b) Bacteroides
c) Tuberculosis
d) Salmonellosis
[Ref. Ananthnarayan 7/e, p 350]

4. Thumb print appearence in culture film smear is seen : **[Karnat 99]**
a) Bacillus antracis
b) Brucella species
c) Bordetella pertussis
d) Clostridum Welchii
[Ref. Ananthnarayan 7/e, p 339]

5. Hemophilus ducreyi is the causative agent is :
a) Soft sore **[Kar 01]**
b) Hard chancre
c) Urethritis
d) Granuloma inguinale
[Ref. Ananthnarayan 7/e, p 337]

6. Haemophilus ducreyi causes : **[Kolkata 04]**
a) Lymphogranuoma venereum
b) Chancroid
c) Syphilis
d) Psittacosis
[Ref. Ananthnarayan 7/e, p 337]

7. Satellitism is seen in culture of : **[DNB 05]**
a) Hemophilus
b) Streptococcus
c) Klebsiella
d) Proteus
e) Salmonella
[Ref. Ananthnarayan 7/e, p 332]

Answer 1. a) Hemophilus 2. c) X and V factor 3. a) Brucellosis 4. c) Bordetella ... 5. a) Soft sore 6. b) Chancroid 7. a) Hemophilus

13 Campylobacter & Helicobacter

CAMPYLOBACTER

- Motile, curved rods; non sporing (comma shaped on S shaped) shows *darting motility.*
- Important pathogenic organisms are C.jejuni and C.fetus.

CAMPYLOBACTER JEJUNI

Comma's or gull wing shaped bacteria motile with single polar flagellum.

Very common cause of diarrhoea.

Culture

- Growth occurs under microaerophillic condition 5% O_2 optimal with added CO_2 [10%]. Although C.jejuni grows well at 36-37^{0}C, but incubation at 42^{0}C prevents most of other fecal bacteria thus helps in selective growth.
- ***Selective media –*** Skirrow's medium; Butzler's media

Pathogensis and clinical feature

- Infection is acquired by oral route. Source of infection is raw or under cooked food products from poultry, cattle sheep, swine.
- Organism multiply in small intestine, invade the epithelium and cause inflammation.
- Usually present : with in 2-4 dayus
- ***Clinically*** present as acute onset of crampy abdominal pain, profuse bloody diarrhoea.

Diagnosis

- Faeces shows polymorphonuclear leucocytes.
- Gram stained smear may show ***typical 'S' shaped*** bacteria.
- Dark field or phase contrast microscopy may show *darting motility.*
- *Culture on selective media at 42^{0}C* is **definitive diagnostic test.**

Treatment :

- ***Erythromycin is DOC.***

CAMPYLOBACTER FETUS

- Oppurtunistic pathogen that cause systemic infection in immunocompromised.
- Cause diarrhoeal illness in normal host.

HELICOBACTER PYLORI

Spiral shaped gram (–)ve rod associated with gastritis and peptic ulcer.

Motile with lopotrichous flagella.

The sole source is human gastric mucosa.

Culture :
- Grows well when incubated at 37^0C in micro aerophillic condition.
- Media used include skirrow's medium, chocolate medium.

Biochemical reaction : Catalase (+) ve, Oxidase + ve, Urease + ve

Pathogenesis

1. Grows optimally at pH 6.0-7.0 and would be killed at pH with in the gastric lumen.
2. But it survives as it is found deep in mucus layer near epithelial surface, without invading mucosa where physiologic pH is present. It produce potent urease which provide ammonia to buffer acid.
3. Major disease associated H.pylori ***virulence factor*** are vacuolating cytotoxin ***(Vac A)*** and group of genes termed CagPaI.
   - H pylori colonization decrease somatostatin producing cells → ↑ Gastrin → ↑ Acid → Gastricmetaplasia in duodenum → Inflammation → Ulceration.
   - ***Best characterized host determinent*** of disease is enhanced H. pylori stimulated secretion of IL - 1 β in some peoples due to genetic polymorphism. *..... Harrison 17/e, p 946*
4. Colonization induce chronic superficial gastritis which includes both mononuclear and polymorphonuclear cell infiltration. ***Gastric antrum is MC site of*** colonization.

Clinical Manifestation

- ***80% of duodenal*** ulcer and ***60% of gastric*** ulcer are related to H.pylori.
- ***Increase risk of gastric adenocarcinoma, Gastric MALT lymphoma.***
- Extragastrointestinal pathologies that are linked include ischemic heart disease and cerebrovascular disease.

Diagnosis

Invasive test :	***Non invasive tests :***
• Requires upper GI endoscopic biopsy • *Most convenient biopsy based test is biopsy urease test.* • Microbiologic culture is ***most specific*** but insensitive.	• Most consistently accurate test is urea breath test. • Stool antigen test is less expensive and more convenient but slightly less accurate • Simplest test are serologic assays measuring IgG levels in serum by ELISA or immunoblot. – Unlike serologic test urea breath tests can be used to asses outcome of treatment 1 month after its completion. *.... Harrison 17/p 947*

Treatment

Symptomatic cases - *First line :*

Regimen 1 -	O C A	7 days	(**O**meprazole , **C**larithromycin, **A**moxicilline)
Regimen 2 -	O C M	7 days	(**O**meprazole**, C**larithromycin, **M**etronidazole)
Second line :	OBTM	14 days	(**O**meprazole, **B**ismuth, **T**etracycline, **M**etronidazole)

No treatment is given for asymptomatic cases.

Remember : H. pylori and H. influenzae are bacteria whose complete genome has been mapped.

QUESTIONS

1. A child was diagnosed to be suffering from diarrhoea due to Campylobacter Jejuni. Which of the following will be the correct environmental conditions of incubation of culture plates of the stool sample : **[AI 05]**

a) Temperature of 42°C and microaerophilic
b) Temperature of 42°C and 10% CO_2
c) Temperature of 37°C and microaerophilic
d) Temperature of 37°C and 10% CO_2

2. All of the following are true about helicobactorpylori except : **[AI 98]**

a) About 50% of world population affected
b) 85% of population is affected, in some developing countires
c) All children in developing countries have immunity by five years of age
d) Infection is common in low socio-economic status

3. True about helicobacter pylori is : **[AI 98]**

a) Culture and gram staining of biopsy is the gold standard investigation
b) Controlled urea breath is negative with massive infection
c) Anti urease antibody are produced only by invasive strains
d) Ureas activity provides protective environment to the bacilli

4. True about Helicobacter, pylori are all except :

a) Urea, breath test is diagnostic **[AI 98]**
b) Gram negative, flagellated bacilli
c) Risk factor for development of adenocarcinoma of stomach
d) It provides life ling immunity

5. A 35 year old patient complaint of abdominal cramps along with profuse diarrhoea. Treating physician wants to process the stool specimen for isolation of Campylobacter jejuni. Which of the following is method of choice for culture of stool : **[AIIMS 04]**

a) Culture on TCBS media incubated at 37°C on aerobic condition
b) Culture on Skirrow's medium incubated at 42°C under microaerophillic condition
c) Culture on Mac conkeys medium incubated at 42°C under anaerobic condition
d) Culture on Wilson and Blairs medium at 37°C under microaerophillic condition

6. Helicobacter pylori is not associated with :

a) Gastrointestinal lymphoma **[AIIMS 03]**
b) Gastric cancer
c) Gastric leiomyoma
d) Peptic ulcer

7. Which of following is false regarding H. pylori :

a) With chronic infection urease breath test become negative **[AIIMS 00]**
b) H. Pylori infection remains life long if untreated
c) Endoscopy is diagnostic
d) Toxigenic strains usually cause ulcer

8. Which of the following correctly describe H.pylori:

a) Gram negative cocci curved **[PGI 05]**
b) Gram positive cocci straight
c) Gram positive bacilli curved
d) Gram negative bacilli straight
e) Gram negative bacilli curved rod

9. H. Pylori true about : **[PGI 04]**

a) Gram +ve spiral organism
b) It is a protozoa
c) Causes chronic gastirtis in adults due reinfection
d) Treatment prevents gastric Lymphoma
e) Duodenal mucosa normal

10. True about H. pylori : **[PGI 04]**

a) It is flagellated
b) Involved in causation of peptic ulcer disease
c) Hypergastrinemia caused by it
d) It is a Gram (–)ve organism

Answer

1. a) Temperature ... 2. c) Anti urease... 3. d) Ureas ... 4. d) Urea, ... 5. b) Culture ...
6. c) Gastric ... 7. a) With ... 8. e) Gram ... 9. c and d 10. a, b, c and d

11. Regarding H. pylori, all are true except :

a) Gram-negative bacillus **[PGI 02]**
b) Strongly associated with duodenal ulcer
c) Associated with lymphoma
d) C-14 urea breath test is used in diagnosis
e) It should be eradicated in all cases whenever detected

12. True about H. pylori : **[PGI 00]**

a) Seen in 85 to 90% cases of gastric ulcer
b) Seen in 20 to 25% cases of duodenal ulcer
c) Transmitted from man to man, feco-orally and by orogastric route
d) Common in adults of developing countries

13. The most sensitive test for H. pylori is :

a) Breath test **[PGI 99]**
b) Rapid urease test
c) Culture of biopsy
d) Microscopy of biopsy

Answer 11. e) It should ... 12. c and d 13. b) Rapid ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is a i.e. Temprature of 42⁰ C and microarophilic *Ref. Jawetz; 24/e, p 275*

Diagnosis of C. jejuni diarrhoea :

Specimen : Stool

Direct microscopy : Dark field or phase contrast microscope shows *gullwing shaped* C. jejuni with characterstic *darting motility.*

Culture : Growth occurs under microaerophilic conditions with added CO2 (10%). Though C. jejuni grows well at 36-37⁰C but incubation at 42⁰C prevents growth of other faecal bacteria and thus helps in selective growth.

Selective media : Skirrows medium

Remember : C. jejuni cause inflammatory diarrhoea (i.e. presence of WBC in stool).

2. Ans. is c i.e. All children in developing countries have immunity by five years of age

Ref. Harrison 16/e, p 886

Prevelance of H. pylori infection	– **30%** in *developed* countries – **80%** in *developing* countries – **50%** in total *world* population
Risk factors of H. pylori infection	– Age - childhood - most infections are acquired in childhood ***but immunity does not develop.*** – Low socioeconomic status – Crowding

3. Ans. is d i.e. Urease activity provides protective environment to the bacilli

Ref. Harrison 17/e, p 947

"Urease produced by H. pylori provide ammonia to buffer acid and helps in maintanance of infections."

Diagnosis of H. pylori

Test	*Advantages*	*Disadvantages*
Invasive (based on endoscopic biopsy)		
Biopsy urease test	Quick, simple	Not fully sensitive before 24h
Histology	May give additional histologic information	Sensitivity dependent on experience & use of special stains
Culture	Permits determination of antibiotic susceptibitlity	Sensitivity dependent on experience
Noninvasive		
Serology	Inexpensive and convenient	Cannot be used for early follow-up;
^{13}C or ^{14}C urea breath test	Inexpensive and simpler than endoscopy; useful for follow-up after treatment	Low-dose irratation in ^{14}C test
Stool antigen test	Inexpensive & convenient; useful for follow-up after treatment; may be useful in children	New test; appears less accurate than urea breath test

Remember : Microbiologic culture are most specific but not gold standard

4. Ans. is d Provides life long immunity *Ref. Harrison 17/e, p 946*

"***Immune response include both production of antibody and cell mediated response but is ineffective in clearing the bacterium."***

Important features of H. Pylori :

- Gram (–)ve cocobacilli motile with lopotrichous flagella.
- **80%** of *duodenal ulcer* and **60%** of *gastric ulcer* are related to H. pylori.
- *Increase the risk of :*
  - Gastric adenocarcinoma
  - Gatric MALT lymphoma
  - Reflux esophagitis
  - Ischemic heart disease
  - Cerebrovascular disease.
- Urea breath test is most consistently accurate test for diagnosis.
- Microbiologic culture is most specific but insensitive.

5. Ans. is b i.e. Culture on Skirrow's medium incubated at 42^{0}C under microaerophillic condition
Ref. Jawetz 24/e, p 274-275

Already explained, refer answer no. 1

6. Ans. is c i.e. Gastric leiomyoma *Ref. Harrison 17/e, p 947*

Already explained, refer answer no. 4

7. Ans. is a i.e. With chronic infection urease breath test becomes negative
Ref. Harrison 17/e, p 948

Urease breath test is most consistently accurate test for diagnosis of H. pylori.
It becomes negative only after treatment and is used to asses outcome of treatment.

Remember :

- Most specific test is microbiologic culture of specimen obtaining by upper GI endoscopic biopsy.
- Major disease associated H. pylori virulence factor are vacuolating cytotoxin (VaCA) and group of genes called *CagPal.*
- *Urea breath test, stool antigen test, and biopsy based tests can all be used to assess the success of treatment.*

8. Ans. is e i.e. Gram negative bacilli curved rod *Ref. Ananthnarayan 7/e, p 407*

"H.pylori is a Gram negative curved spiral rod motile by unipolar tuft of lopotrichous flagella."
Correctly speaking H. pylori is a coccobacilli.

Remember :

Other Gram (–)ve coccobacilli		*All important bacilli are gram positive except*	
– Hemophilus	– Bordetella	– **A**ctinomycetes	– **B**acillus
– Brucella	– Campylobacter	– **C**lostridium	– **C**orynebacterium
– Helicobacter	– Legionella	– **M**ycobacteria	– **L**isteria
– Rickettsiacea	– Chlamydiae	***Mnemonic*** – **ABC CML**	

9. Ans. is c and d i.e. Causes chronic gastirtis in adults due reinfection; and Treatment prevents gastric Lymphoma *Ref. Harrison 17/e, p 1871*

– H. pylori causes type B or antral predominant gastritis.
– MALT lymphoma (associated with H. pylori) remains dependent upon the presence of H. pylori and its eradication is often associated with complete regression of tumor.

Treatment of H. pylori

Symptomatic causes –

First line :				
Regimen 1 -	O C A	7 days	(**O**meprazole , **C**larithromycin, **A**moxicilline)	x 7 days
Regimen 2 -	O C M	7 days	(**O**meprazole**, C**larithromycin, **M**etronidazole)	x 7 days
Second line :	OBTM	14 days	(**O**meprazole, **B**ismuth, **T**etracycline, **M**etronidazole)	x 14 days

Asymptomatic cases – *no treatment*

10. Ans. is a, b, c and d i.e. It is flagellated; Involved in causation of peptic ulcer disease; Hypergastrinemia caused by it; and It is a Gram (–)ve organism *Ref. Harrison 17/e, p 947-948*

H. pylori is associated with hyperacidity.

Other options have been already described.

11. Ans. is e i.e. It should be eradicated in all cases whenever detected *Ref. Harrison 17/e, p 948*

In asymptomatic cases no treatment is given.

Remember :
- The most clear cut indication of H.pylori treatment are H.pylori related duodenal or gastric ulceration or low grade gastric lymphoma.
- Family history of dyspepsia.
- H.pylori treatment may provoke or exacerbate GERD.

12. Ans. is c and d i.e. Transmitted from man to man, feco-orally and by orogastric route; Common in adults of developing countries *Ref. Ananthnarayan 7/e, p 408*

Mechanism of transmission is likely to be oral - oral or fecal-oral.
- 80% of **duodenal** ulcer and 60% of gastric ulcer are associated with H. pylori.
- Prevalance of H. pylori in developing countries is 80%.

13. Ans is b i.e. Rapid urease test *Ref. Harrison 17/e, p 947*

Rapid urease test = Biopsy urease test – most convenient biopsy based test.

Already explained.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. About helicobacter Pylori, all are true except :

a) Is a Gram -ve spiral bacteria **[AIIMS 96]**
b) Uncommon undeveloping Asian countries
c) Urea breath test +ve
d) Associated with duodenal ulcer

[Ref. Harrison 17/e, p 946]

2. Which of the following medically potent urease activity : **[MP 06]**

a) Proteus mirabilis
b) Brucella melitensis
c) Helicobacter pylori
d) Ureaplasma urealyticum

[Ref. Ananthnarayan 7/e, p 408]

Answer 1. b) Uncommon ... 2. c) Helicobacter ...

14 Legionella

- *Gram negative non capsulated, intracellular cocobacilli.*
- *They are motile, aerobic, catalase and oxidase positive.*

Culture

- Not grow on ordinary media.
- Buffered charcoal yeast extract ***'BCYE'*** is selective medium used to grow legionella. It grows best at pH - 6.9 temperature 35^0C and 90% humidity.
- ***MC*** species associated with human infection *is L.pneumophilia,* (***MC*** with ***serogroup 1***).
- Other important species is L.micdadei (Pittsburgh pneumonia agent). It is partial acid fast (AFB).
- ***Natural habitat*** is *aquatic bodies including lakes and streams.* Shows symbiotic relations with algae, amebas, ciliated protozoa.
- Factors enhancing colonisation are warm temperature, stagnation and sediments. It can form microcolonies with in biofilms. Its eradication require disinfectants that can penetrate the biofilm.

Mode of transmission

- ***Aspiration*** is predominant mode of transmission. Other modes include aerosolization, direct instillation in to lungs.
- No man to man transmission occurs.
- Aerosolization by A.C., nebulizer, humidifier and direct instillation into lung are other modes.

Risk Factors and pathogenesis

- Conditions that impair mucocilliary clearance predispose to legionaires disease most commonly cigarette smoking.
- Hairy cell leukemia (not other leukemia) and immunocompromised state are other risk factor.
- Bacteria attach host cell by type IV pili, HSP60 and major outermembrane protein. Legionella binds to CR_1 and CR_3 integrin receptor.
- Cell mediated immunity is primary mechanism of host defense (Role of neutrophill appears to be minimal).
- Humoral immunity plays no role.

Legionellosis

Legionella cause 2 clinical syndromes :

A. Pontiac fever :

- Acute febrile self limited illness. Airbone transmission with high attack rate.
- Pneumonia does not develop. ***MC*** **symptom** - malaise, fatigue and myalgia.

B. *Legionnaires disease :* Designation for pneumonia.

- ***4th MC*** cause of community acquired pneumonia (***MC*** - S.pneumoniae **2nd** ***MC*** - H.influenzae **3rd** ***MC*** Chlamydia pneumoneae). *..... Harrison 17/e, p 929*
- Cause atypical penumonia which is more serious than atypical pneumonia of other agents.
- ***Clinical features suggestive of L. pneumonia :***
  - Diarrhoea
  - High fever
  - Hyponatremia
  - Proteinuria
  - Onset of symptom with in 10 days after discharge from hospital suggest nosocomial logionnaires disease.
- Mostly caused by serotype 1 but serotype 6 is associated more commonly with hospital acquired and has poor prognosis.
- Relative bradycardia is useful diagnostic finding.

Extrapulmonary Legionellosis

- Results from blood borne dissemination from lung.
- ***MC*** extrapulmonary site is **heart.**
- Most cases are hospital acquired.
- ***MC*** neurological **abnormality** are **confusion** or changed mental status.

Diagnosis

Specimen:
- Sensitivity of bronchoscopy specimens is approximately the same as that of sputum. Bronchoalveolar lavage fluid gives higher yield than bronchial wash specimen.

Staining :
- Gram staining usually show numerous leucocytes but no organisms.
- DFA test is rapid and highly specific but less sensitive.

Culture :
- Definitive method of diagnosis.
- Requires 3-5 days to become grossly visible.
- B'CYE media is used.

Antibody detection :
- Requires 12 weeks, so used for retrospective diagnosis or epidemiologic studies.

Urinary antigen :
- Cheap, rapid, second in sensitivity and highly specific.
- Detectable with in 3 days.
- The test is not affected by antibiotic administration.

Radiographic Abnormalities :
- Pleural effusion
- In immunosuppressed distinct round nodular opacity may be seen.

Treatment

- Azithromycin and Respiratory tract quinolones (Levofloxacin, Gemifloxacin, Moxifloxacin) are ***DOC.***
- Quinoliones are preffered antibiotic in transplant recepients.

Prevention

- Disinfection of water by :
  - Superheat and flush method - ***Ideal*** for ***emergency*** situation
  - Copper and silver ionization method
  - ***Superchlorination*** is ***not*** effective.
  - Tap water filters particularly in transplant units.

QUESTIONS

1. A 70 year old patient presents with high grade fever, dry cough and abdominal pain. Sputum sample collected from patient, shows Gram negative organisms that are able to grow only on charcoal yeast extract medium. The most likely organism is : [AI 07; AIIMS 06]

a) H. influenza
b) Leigonella
c) Lesteria monocytogenes
d) M. catarhalis

2. A 60-year old man is diagnosed to be suffering from Legionnaires disease after he returns home from attending a convention. He could have acquired it : [AI 03]

a) From a person suffereing from the infection while traveling in the aero plane
b) From a chronic carrier in the convention center
c) From inhalation of the aerosol in the air conditioned room at convention center
d) By sharing an infected towel with a fellow delegate at the convention

3. Anju, a 28 year female, has diarrhoea, confusion, high grade fever with bilateral pneumonitis. Organism causing this : [AI 00]

a) Legionella
b) Neisseria meningitisdis
c) Streptococcus pneumoniae
d) H.influenza

4. All of the following are true regarding Legionella except : [AIIMS 04]

a) Legionella can be grown on complex media
b) L. pneumophilia setogroup 1 is the most common serogroup isolated from humans
c) Legionella are communicable from infected patient to others
d) L. pneumophila is not effectively killed by polymorphonuclear leukocyte

5. Which of the following is a good media to use for diagnosis of legionnaires disease : [AIIMS 01]

a) Theyer Martin media
b) BCYE agar
c) Bordet Gengu media
d) Chocolate agar

6. Pontiac fever is caused by : [PGI Dec. 07]

a. Legionella
b. Listeria
c. Scrub typhus
d. Leptospira
e. Ricktettsia

7. BCYE. medium is used to culture : [PGI 99]

a) Mycoplasma
b) T pallidum
c) H. pylori
d) Legionella

Answer

1. b) Leigonella
2. c) From ...
3. a) Legionella
4. c) Legionella ...
5. b) BCYE ...
6. a) Legionella
7. a) Mycoplasma

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b i.e. Legionella *Ref. Harrison 17/e, p 929; Jawetz 24/e, p 313*

Dry cough, high grade fever and growth on charcoal yeast medium suggest legionella.

Legionella have fastidious requirements and grow on complex media such as buffered charcoal, yeast extract (BCYE) agar with L. cysteine and antibiotic supplements with 5% CO_2 at pH 6.9, 35^0C and 90% humidity.

2. Ans. is c i.e. From inhalation of the aerosol in the air conditioned room at convention center
Ref. Harrison 17/e, p 928

Important features of Legionella

- Aerobic, Gram negative motile, non encapsulated bacilli .
- Natural habitat are aquatic bodies such as stagnant water, mud, hot springs.
- Out breaks are associated with contaminated water source such as air conditioning cooling to wers.
- Multiple modes of transmission - ***Aspiration (MC)***, Aerosolization, direct instillation.
- ***No man to man transmission,*** no animal reservoir.
- It Causes :

Manifestations	
Pneumonia	**Pontaic fever**
– Atypical pneumonia – Presents with high fever, diarrhoea, pneumonia	– Acute febrile self limiting illness

- ***MC*** extrapulmonary site of Legionella **is heart.**
  - **Selective media** – Buffered charcoal yeast extract **(BCYE) agar.**
  - **Treatment :** - Macrolides and quinolones.
    - β lactams are not effective.

3. Ans. is a i.e. Legionella *Ref. Harrison 17/e, p 930*

Clinical features suggestive of Legionnaire's disease

- **Diarrhea**
- *High fever (>40^0 C or >104^0 F).*
- *Numerous neutrophils but no organisms revealed by Gram's staining of respiratory secretions.*
- *Hyponatremia (serum sodium level of < 131 meq/L).*
- *Failure to respond to β-lactam drugs (penicillins or cephalosporins) and aminoglycoside antibiotics.*
- *Occurrence of illness in an environment in which the potable water supply is known to be contaminated with Legionella.*
- *Onset of symptoms within 10 days after discharge from the hospital.* *.....Harrison 17/e, p 930*

Remember : ***MC*** extrapulmonary site in heart is which it causes myocarditis, pericarditis.

4. Ans. is c i.e. Legionella are communicable from infected patient to others

Ref. Harrison 17/e, p 929 - 930

"Their is no man to man transmission."

- **Modes of transmission** are aerosolization, aspiration and direct instilation of contaminated water into the lung.
- **L. pneumophilia** is *most common* legionella causing human disease.
- Serogroup 1, 4 and 6 are *most commonly* implicated.
- **Cell mediated** immunity is primary mechanism of host defence. Alveolar macrophage readily phagocytose Legionella; many are killed but some proliferate intracellularly until cell rupture.

Risk factors for Legionnaires disease :
– **Cigarette** *smoking and other condition that impair mucociliary clearance*
– Chronic lung disease
– Advance age
– Immunosuppression
– Surgery is predisposing factor in nosocomial infection with transplant recepient at highest risk.

5. Ans. is b i.e. BCYE agar *Ref. Jawetz 24/e, p 313*

- **BCYE agar** is the medium used to grow Legionella.
- This highly enhanced medium contains the ***amino acid L-cysteine*** which is an ***absolute growth requirement*** for Legionella.

6. Ans. is a i.e. Legionella *Ref. Harrison 17/e, p 928*

Already explained, refer answer no. 2

7. Ans. is a i.e. Legionella *Ref. Jawetz 24/e, p 313*

Already explained, refer just above answer.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.

1. True about Legionella pneumoniae is :

a) Acid fast **[DNB 05]**

b) Can be isolated from lung biopsy

c) Gram positive

d) Sputum shows polymorphonuclear leukocytes with organisms

[Ref. Harrison 17/e, p 931]

Answer 1. b) Can be isolated ...

15 Rickettsiaceae & Chlamydiae

CHLAMYDIAE [PLT AGENT]

- **Obligate intracellular** bacteria so *unable* to *grow in cell free media.*
- Lacks enzyme of electron transport chain and require ATP from host cell so called ***energy parasites.***
- Peptidoglycan and N-acetylmuramic acid is absent from its cell wall. Its cell wall contain tetrapeptide linked matrix and relatively high lipid content.
- Show tropism for squamous epithelial cells and lymphnodes.

Growth cycle

Replicate by ***binary fission*** without an eclipse phase.

Chlamydiae occur in 2 forms :

Elementary Body (EB)	*Reticular Body (RB)*
Extracellular Infective form	Intracellular growing and replicative form
Contain rigid trilaminal cell wall	Friable cell wall lacking peptidoglycan
Contain electron dense nucleoid	No electron dense nucleoid
DNA = RNA	RNA > DNA about 4 times

Reticular body undergoes binary fission resulting in chlamydial microcolony called ***inclusion body.*** This whole cycle takes about 24 - 48 hours.

Effect on host cell :

C. trachoma leave host cell with scar while. C. psiticosis leaves host cell severly damages followed by lysis.

Classification

Chlamydiae are divided into three species :

i. C. trachomatis
ii. C. pneumoniae
iii. C. psittaci.

Features	C. trachoma	C. pneumoniae	C.psittaci
Serovars	15	1	≥ 4
Inclusion body	Round vacuolar called *HP bodies	Round dense	Large dense called *LCL bodies
Glycogen in inclusions	+	–	–

Continue .....

Susceptibility to sulfonamide	+	–	–
Plasmid	+	–	+
Natural host	Humans	Humans	Birds
Transmission	Persono to person Mother to infant	Airborne person to person	Airborne bird excreta to humans
Elementary body morphology	Round	Pear shaped, round	Round

*HP = Halberstaedter Prowazek
*LCL = Levinthal - cole - lillie

Antigen

- **Heatstable LPS** – Genus (Group) specific
  – Common to all chlamydia
  – Responsible for complement fixation test (CFT).
- **Envelope surface** – Species specific so classify chlamydiae into trachomatis, psittaci, pneumoniae and pecorum.
- **Major outer membrane protein (MOMP)** – Used for intraspecies typing i.e. for serovar or serotypes.
  – Responsible for Microimmunofluorescence.

Lab diagnosis

- ***Microscopy***
  a. Staining – By Giemsa or castaneda or Ma chiavello particularly in neonatal inclusion conjuctivitis.
  b. Immunofluoroscence – Using monoclonal anti-body
  – More sensitive and specific.
- ***Isolation*** – Cell culture is preferred mode.
  – Can also done by inoculation into embryonated eggs or experimental animals.
- ***Demonstration of antigen***
  a. Microimmunofluoroscence – Commonly used method.
  b. ELISA – Preferred for screening.
  c. DNA probes and amplification texhniques (PCR and LCR) – More sensitive and specific.
- ***Detection of antibody*** – CFT : Can't distinguish species as it is Group = Genus specific.
  – Micro IF : More useful for TRIC (inclusion conjunctivitis).

Remember :
- ***High titre antibody are usually seen only in :***
  – Infant pneumonia – Salpingitis – LGV.
- C.pneumoniae, grows better in HL and HEp - 2 cells than in HeLa 22q or McCoy cells.
- McCoy cells are widely used to culture C. trachomatis.
- Skin hypersensitivity in LGV can be demonstrated by Frie's test.

CHLAMYDIAE TRACHOMATIS

- ***MC*** cause of STD worldwide.
- ***MC*** cause of opthalmia neonatorum.
- 15 serotypes [A to K and L_1, L_2, L_3] are known :
  – A, B, Ba, C - Endemic blinding trachoma.
  – D to K - Inclusion conjuctivitis, Genital infection, Infant pneumonia.
  – L_1, L_2, L_3 Lymphogranuloma venerum.
- C. trachomatis is ***MC*** cause of non gonococcal urethritis, post gonococcal urethritis.

- ***MC*** cause of epididymitis.
- **Inclusion conjuctivitis of *Neonate*** is called ***inclusion blenorrhea*** while *adult* form is called as ***"Swimming pool disease."***
- **LGV - Lymphogranuloma venerum** - Most cases occur due to **L2** serovar
  - ***MC*** **presentation** in heterosexual man is painful lymphadenopathy called inguinal syndrome/Tropical bubo.
  - LGV strains are **more invasive** than the other serovars.
  - ***MC*** LN involved in woman - *Intrapelvic and pararectal.*
  - In women it cause rectal stricture and elephantiasis of vulva (esthiomene).
  - Elementary bodies are known as *Miyagawa's corpuscles.*
- **Reiter's syndrome :**
  - Conjuctivitis, urethritis, arthritis and characteristic mucocutaneous lesions
  - Associated with HLA B - 27.

Diagnosis : ***LCR and PCR are most sensitive*** chlamydial diagnostic test available. *..... Harrison 16/e, p 1014*

Treatment : Azithromycin ***DOC*** for STD.

CHLAMYDIAE PNEUMONAIAE (TWAR STRAIN)

- Distinguished from other 2 species on the basis of DNA morphology.
- Only one serovar identified.
- Associated with increased risk of atherosclerosis, asthma, sarcoidosis.
- HL cells - Most effective cell line for isolation.

Treatment : Erythromycin/Tetracycline

CHLAMYDIAE PSITTACI

- Primarily disease of parrots.
- Acquired in humans by inhalation of dropping or nasal discharge.
- Human infection mostly occupational.
- Consumption of poultry products does not lead to infection.
- Psiticosis is a septicemia, pneumonia is usual manifestation.

Treatment :
- Tetracycline is ***DOC***
- Alternative Erythromycin.

RICKETTSIACEAE

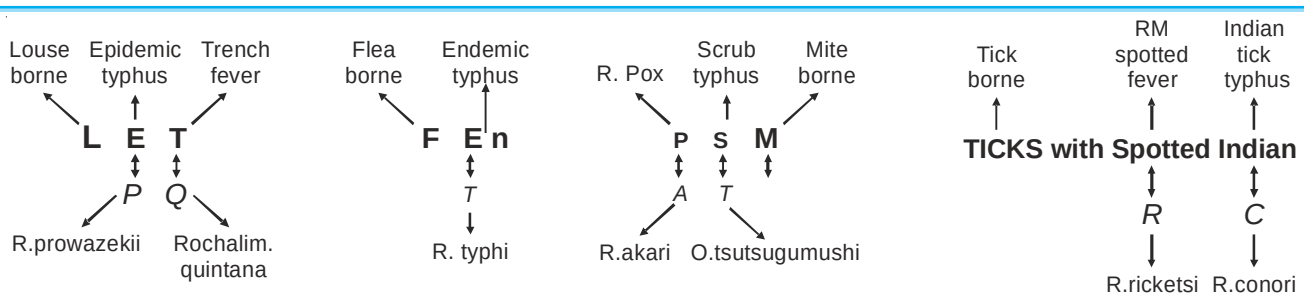
- This family consist of 3 genera - Rickettsia, Orientia and Ehrlichia.
- These are Gram (–)ve obligate intracellular parasite so unable to grow in cell free media, except Rochalimaea, quintana.
- Transmitted by arthropod vectors.
- In humans they infect vascular and reticuloendothelial cells.
- ***Except for louse-borne typhus, humans are incidental hosts.***
- Coxella burnetti is notorious for its ability to survive outside reservoir or vector and for its extreme infectiousnes. ***(Non arthropod air borne rickettsial disease).***
- Severity of Rickettsial disease are enhanced by sulphonamide. Penicillin is also ineffective in rickettsial disease.
- Rickettsia are stained by Giemsa, Castaneda, Machiavello and Giemnez stains.
- Rickettsia grow best in cells that are not metabolizing actively.
- Rickettsia are non motile non capsulated, pleomorphic coccobacilli.

Classification of Rickettsial Cell Disease

	Disease	Agent	Vectors
Typhus group	a. Epidemic typhus or Brill zinsser disease	R. prowazekii	Louse
	b. Murine/Endemic typhus	R.typhi (R. mooseri)	Flea
Spotted fever group	a. Rocky Mountain spotted Fever	R. rickettsii	Tick
	b. R. pox	R. akari	Mite
	c. Fever boutonneuse or Mediterranean spotted fever or Indian tick typhus	R.conorii	Tick
Other	a. Q. fever	Coxiella burnetii	Nil ***[Air Borne]***
	b. Trench fever / Five day fever	Rochalimaea quintana (Bartonella quintana)	Louse
	c. Scrub typhus (Chigger borne typhus)	R. tsutsugamushi or Orientia tsutsuga mushi	Mite
	d. Ehrlichiosis	Ehrlichiae	Tick

- ***Don't go into DETAILS of Individual disease as they are asked very rarely.***

MNEMONIC TO LEARN THIS CONFUSING TABLE



- **Most severe** ricketssial disease is Rocky Mountain Spotted Fever.
- **Most mild** ricketssial disease Rickettsia pox.
- Rickettsial infections are characterized by fever, headache, malaise, prostraton, skin, rash (except in Q fever) and Hepatosplenomegaly.
- Neil - Mooser or tunica reaction positive in R. typhi (R.mooseri), R. conori, R.akari and negative for R. prowazekii.
- **Weil felix reaction** - It is heterophile agglutination test. Based on sharing of alkali stable polysaccharide between typhus rickettsia and some strain of Proteus bacilli. (OX 19, OX - 2, OX K)

  OX 19 - (+++) In Epidemic and Endemic typhus.

  OX 19, OX - 2 - (++) In Rocky Mountain Spotted fever.

  OXK - (+++) in Scrub typhus.

  – *No vlaue in* : a. Q fever b. Trench fever c. Rickettsial pox.
  – *False positive in* Typhoid, liver disease, proteus infection, Pseudomonas, Borrelia, S.typhi.

QUESTIONS

1. A male patient with symptoms of uretheritis. Examination reveals only pus cells without any organism. Most likely cause is : [AI 08; AIIMS 07]

a) Chlamydia trachomatis
b) H. ducreyi
c) Treponema pallidum
d) M. tuberculi

2. Lice are not the vectors of : [AI 07; AIMS 06]

a) Relapsing fever4
b) Q fever
c) Trench fever
d) Epidemic typhus

3. Which of the following is not true regarding chalmydia : [AI 07; AIIMS 06]

a) Has biphasic life
b) Elementary body is metabolically active
c) Reticulate body undergoes binary fission
d) Once it invades into cell it abates phagolysosomal fusion

4. In a patient with UTI; on smear, no bacteria are found on gram stain with abundant pus cells, to demonstrate organism, which of the following is useful : [AI 07; AIIMS 06]

a) Mccoy cell line
b) Thayer martin medium
c) L. J. medium
d) Acid fast staining

5. A patient complained of chills and fever following a louse bite 2 weeks before. He had rashes all over the body and was delirious at the time of presentation to the hospital and subsequently went into coma. A provisional diagnosis of vasculitis due to Rickettsial infection was made. Which one of the following can be the causative agent :

a) Rickettsia typhi **[AI 05]**
b) Rickettsia rickettsiae
c) Rickettsia prowazekii
d) Rickettsia akari

6. Chalmydia trachomatis is associated with the following except : [AI 05]

a) Endemic trachoma
b) Inclusion conjuncitivitis
c) LGV
d) Community acquired pneumoia

7. Which one of the following statements is true regarding Chlamydia pneumoniae : [AI 05]

a) Fifteen serovars have been identified as human pathogen
b) Mode of transmission is by the air borne bird excreta
c) The cytoplasmic inclusions presents in the sputum specimen are rich in glycogen
d) The group specific antigen is responsible for the production of complement fixing antibodies

8. The most sensitive method for detecting cervical Chlamydia trachomatis infection is : [AI 04]

a) Direct fluorescent antibody test
b) Enzyme immunoassay
c) Polymerase chain reaction
d) Culture on irradiated McConkey cells

9. All of the following statement are true regarding Q fever except : [AI 03]

a) It is a zoonotic disease
b) Human disease is characterized by an interstitial pneumonia
c) No rash is seen
d) Weil Felix reactions is very useful for diagnosis

10. Which of the following statements is true about endemic typhus : [AI 03]

a) Is caused by R. rickettsii
b) Is transmitted by bites of fleas
c) Has no mammalian reservoir
d) Can be cultured in chemical defined culture medium

11. Chlamydia does not cause : [AI 00]

a) Q. fever
b) Non gonococcal urethritis
c) Trachoma
d) Salpingitis

12. Which of the following is an obligate parasite:

a) Mycoplasma **[AI 98]**
b) Chlamydia, trachomatis
c) Gram -Ve bacilli
d) Gram +Ve cocci

Answer

1. a) Chlamydia... 2. c) Trench fever 3. b) Elementary ... 4. a) Mccoy cell ... 5. c) Rickettsia ...
6. d) Community ... 7. d) The group ... 8. c) Polymerase ... 9. d) Weil Felix ... 10. b) Is trans ...
11. a) Q. fever 12. b) Chlamydi ...

13. Chalmydia causes all the following disease except : [AI 95]
a) Non-gonococcal urethritis
b) Pneumonia
c) Trachoma
d) Parotitis

14. Scrub typhus is transmitted by : [AIIMS Nov. 07]
a) Reduvid bug
b) Trombiculid mite
c) Enteric pathogens
d) Cyclops

15. It is true regarding Endemic typhus that :
a) Man is the only reservoir of infection **[AIIMS 06]**
b) Flea is a vector of the disease
c) The rash developing into eschar is a characteristic presentation
d) Culture of the etiological agent in tissue culture is a diagnostic

16. All are true regarding chalmydia psittaci except:
a) Endemic in birds **[AIMS 06]**
b) Cause non-gonococcal urethritis
c) Grow in a specified laboratory
d) Tetracycline is trx of choice

17. A 45 year female complains of lower abdominal pain and vaginal discharge. On examination there is cervicitis along with a mucopurulent cervical discharge. The gram smear of the discharge shows presence of abundant pus cells but no bacteria. The best approach to isolate the possible causative agent would be : [AIIMS 05]
a) Culture on chocolatre agar supplemented with Haemin
b) Culture on McCoy cells
c) Culture on a bilayer human blood agar
d) Culture on vero cell lines

18. The following is not a method of isolation of chlamydia from clinical specimes : [AIIMS 05]
a) Yolk inoclation
b) Enzyme immunoassay
c) Tissue culture using irradiated McCoy
d) Tissue culture using irridiated BHK cells

19. The following statements are true regarding Chlamydia except : [AIIMS 05]
a) Erythromycin is effective for therapy of Chalmydial infections
b) Their cell wall lacks a peptidoglycan layer
c) They can grow in cell free culture media
d) The are obligate intracellular bacteria

20. Following is the etiological agent of Rocky Mountain spotted fever : [AIIMS 05]
a) R. rickettsii
b) Rochalimae quintana
c) R. tsutsugamushi
d) Coxiella burnetti

21. Mode of transmission of Q-fever is : [AIIMS 04]
a) Bite of infected louse
b) Bite of infected tick
c) Inhalation of aerosol
d) Bite of infected mice

22. A man present with fever, chills 2 weeks after a louse bite. There was maculopapular rash on the trunk which spread peripherally. The cause of this infection can be : [AIIMS 03]
a) Scrubtyphus
b) Endemic typhus
c) Rickettsiae pox
d) Epidemic typhus

23. A man present to STD clinic with urethritis and urethetral discharge. Gram stain shows numerous pus cells but no microorganism. Culture is negative on routine laboratory media. The most likely agent is : [AIIMS 02]
a) Chlamydia trachomatis
b) H. ducreyi
c) T. pallidum
d) N. Gonorrhoeae

24. Chlamydia trachomatis serovars D-K cause :
a) Arteriosclerosis **[AIIMS 02]**
b) Trachoma
c) Lymphogranuloma venereum
d) Urethritis

25. All are true about Rickettsia except : [AIIMS 99]
a) Obligate intracellular
b) Gram +ve bacillus
c) Arthropods are vector
d) Weil felix test used in diagnosis

26. Which is not transmitted by arthropod :
a) Rickettsia prowazaki **[AIIMS 97]**
b) Coxiella burmeti
c) Rickettsia akari
d) Rickettsia rickettsi

Answer

13.	d) Parotitis	14.	b) Trombiculid ...	15.	b) Flea is a ...	16.	b) Cause non ...	17.	b) Culture ...
18.	b) Enzyme ...	19.	c) They can ...	20.	a) R. rickettsii	21.	c) Inhalation ...	22.	d) Epidemic ...
23.	a) Chlamydia ...	24.	d) Urethritis	25.	b) Gram +ve ...	26.	b) Coxiella ...		

27. Triad of Reiter's syndrome : **[PGI 07]**

a) Conjunctivitis
b) Uveitis
c) Polyarthritis
d) Mucosal lesions
e) Glaucoma

28. Which is caused by Rickettsia : **[PGI 07]**

a) Weil's disease
b) Rocky mountain spotted fever
c) Scrub typhus
d) Lymes disease

29. Chalmydia grows in which of the following cell lines : **[PGI 01]**

a) HeLa
b) HeP2
c) McCoy
d) Human diploid fibroblast series
e) Vero cells

30. Chlamydia causes : **[PGI 00]**

a) Infertility
b) Pneumothorax
c) Pelvic inflammatory disease
d) Congenital malformation in fetus

31. Neill-Mooser reaction is used to diagnose :

a) Rickettsiae **[PGI 99]**
b) Chlamydiae
c) Mycoplasma
d) Herpes

32. Following grows in the cell free medium except :

a) Rickettsia **[PGI 99]**
b) M. leprae
c) Bartonella
d) Syphilis

Answer 27. a, c and d 28. b) Rocky .... 29. a, b and c
30. a and c 31. a) Rickettsiae 32. a, b and d

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is a i.e. Chlamydia *Ref. Harrison 17/e, p 1072; CMDT 08, p 1266*

The patient is suffering from non gonococcal urethritis and *C.trachomatis is the most common cause of non gonococcal urethritis.*

Other causes of NGU :
- Ureoplasma urealyticum
- Mycoplasma genitalium
- Trichomonas vaginalis
- Herpes simplex virus

2. Ans. is c i.e. Trench fever *Ref. Ananthnarayan 7/e, p 414*

"Q fever is air borne disease."

Lice act as vector in following diseases :

Disease	Causative agent
• Epidemic typhus	R. prowazeki
• Relapsing fever	Borrelia recurrentis
• Trench fever	Rochalimaea quintana
• Dermatitis	
• Pediculosis	

Remember : Relapsing fever can be tick borne also.

3. Ans. is b i.e. Elementary body is metabolically active *Ref. AA 7/e, p 423; Jawetz 24/e, p 357*

Reproductive Cycle of Chlamydiae

Elementary body (EB)
- Stable spherical form
- Extracellular phase
- Infectious form
- 200 - 300 nm diameter
- Rigid trilaminar cell wall
- Electron dense nucleoid (contains DNA)
- DNA = RNA

↓

Attach to surface of susceptible epithelial cell near base of microvilli by adhesins (eg. major outer membrane protein); receptors (heparin sulfate like proteoglycans in case of Chl. trachomatis)

↓

Engulfment of EB into host cell either by endocytosis into clathrin coated pits or pinocytosis into non coated pits. Lysosomal fusion is inhibited by unknown mechanism, so EB form of chlamydiae is protected under membrane bound environment.

↓

Reorganisation of EB by spheroplast - like transformation / loss of cross-linking of EB membrane proteins.

↓

Reticulate body (Initial body form)
- Pleomorphic stage
- Intracellular form
- Growing and replicative form
- 500 - 1000 nm size
- No electron dense nucleoid
- RNA > DNA

↓

Within membrane bound vacoule RB divides by binary fission repeatedly to form EB.
↓
Cytoplasmic inclusion bodies form (EB filled vacoule)
↓
This EB liberate from host cell to infect new cells.

4. Ans. is a i.e. Mccoy cell line *Ref. Ananthnarayan 7/e, p 427; Jawetz 24/e, p 361*

"Complant of urethritis with no result on gram staining signifies nongonococcal urethritis."

MC cause of NGU is chlamydia trachomatis urethritis is one of the manifestation of genital chlamydiasis.

Diagnosis of genital chalmydiasis (D-K serovars)

I. Culture :

- Scarpe epithelial cells from 1-2cm deep into endocervix.
- Dacron, cotton,rayon or calcium alginate on plastic shaft should be used to collect specimen.
- Inoculum is centrifuged onto the monolayer of cycloheximde treated McCoy cells.
- This is incubated at 35-37^{0}C for 48-72 hours.
- Monolayers can be increased.
- Examine monolayers by direct IF to see inclusion bodies.
- This method is 80% sensitive but 100% specific.

Remember : HeLa cell culture can also used.

II. Direct cytologic examination (direct fluorescent antibody) and enzyme linked immunoassay.

III. Nucleic acid detection by PCR and LCR are test of choice to diagnose genital C.trachomatis infections.

IV. Serology – Serum antibodies are more common than trachoma because of more antigenicity in genital tract.

Remember : LJ medium is for Mycobacteria tuberculosis. Thayer martin medium is for Neiserria.

5. Ans. is c i.e. Rickettsia prowazekii *Ref. Ananthnarayan 7/e, p 414; Park 18/e, p 241; 19/e, p 253*

Most important point in the given question is "louse borne rickettsial infection" which is only one i.e., Epidemic typhus which is caused by R. prowazekii.

Epidemic typhus

– Also called as louse borne typhus or classical typhus or Gaol fever.
– Usually seen among military and refugee populations and famine areas.
– Humans are only natural vertebrate host.
– **Vector :** Body or head louse (Pediculus humanus) not pubic louse.
– **Causative agent :** R. prowazekii
– **Route of transmission :** Louse feces is rubbed over abraded skin. So, infection is transmitted from man to man by infected louse.
– **Incubation period :** 5 to 15 days
– **Clinical feature :** Fever, chills, rash (starts on trunk and spread over limbs sparing face, palms and soles), stupor and delirium.
– Rickettsia may become latent in lymphoid tissue causing recrudescent typhus or Brill - Zinsser disease.

Remember **:** Trench fever is also transmitted by louse but causative agent is Rochalimaea or Bartonella quintana which is excluded from Rickettsiacea, because it can grow in cell free media.

6. Ans. is d i.e. Community acquired pneumonia *Ref. Harrison 17/e, p 1070-1073; AA 7/e, p 424*

Disease caused by Chalmydia trachomatis

Serotype	Disease
A, B, Ba, C	• Endemic blinding trachoma
DEFGHIJK	• Inclusion conjunctivitis • Genital chlamydiasis • Infant pneumonia
L1, L2, L3	• Lymphogranuloma venerum

Remember : • ***Four most common cause of community acquired pneumonia are :***
- S. pneumoniae
- H. influenzae
- Chlamydia pneumoniae
- Legionella.

7. Ans. is d i.e. The group specific antigen is responsible for the production of complement fixing antibodies *Ref. Jawetz 24/e 359; Ananthnarayan 7/e, p 424*

"Genus or Group specific heat stable LPS antigen is responsible for CFT while serovar specific Major membrane protein is responsible for Microimmunofluorescence."

Characteristic of chlamydiae

Feature	C trachomatis	C penumoniae	C psittaci
Inclusion morphology	Round, vacuolar	Round, dense	Large, variable shape, dense
Glycogen in inclusions	Yes	No	No
Elementary body morphology	Round	Pear-shaped, round	Round
Susceptible to sulfonamides	Yes	No	No
DNA homology to C pneumoniae	<10%	100%	<10%
Plasmid	Yes	No	yes
Serovars	15	1	> 4
Natural host	Humans	Humans	Birds
Mode of trAns.mission	Person to person, mother to infant	Airborne person to person	Airborne bird excreta to humans
Major diseases	Trachoma, STDs, infants pneumonia, LGV	Pneumonia, bronchitis, sinusitis	Psittacosis, pneumonia, fever of unexplained origin

8. Ans. is c i.e. Polymerase chain reaction *Ref. Harrison 17/e, p 1074*

"Amplification assays such as ligase chain reaction and polymerase chain reaction are the most sensitive chlamydial diagnostic method available."

Diagnostic methods for Chalmydia	Accuracy
• Cell culture technique	– Low sensitivity (60 to 80%)
• Direct immunofluoroscent antibody test	– 70 - 80% sensitive and quite specific
• ELISA	– 60 - 80% sensitive
• LCR and PCR	– Most sensitive method available

9. Ans. is d i.e. Weil Felix reactions is very useful for diagnosis

Ref. Jawetz 24/e, p 350; Harrison 17/e, p 1066

Clinical features of Q-fever :

– Headache – Fever – Fatigue
– Interstitial pneumonia – No rash.

- **Rashes seen in :** – Epidemic typhus (no eshar)
  – Endemic typhus (no eschar)
  – Scrub typhus (50% have eschar)
  – RMSF (no eschar)
  – Rickettsial pox (eschar)
  – Fever boutonneuse (tache noire eschar).
- Weil felix reaction is negative in Q fever, R pox, Trench fever.

Remember **:**

Bacterial Zoonotic diseases :

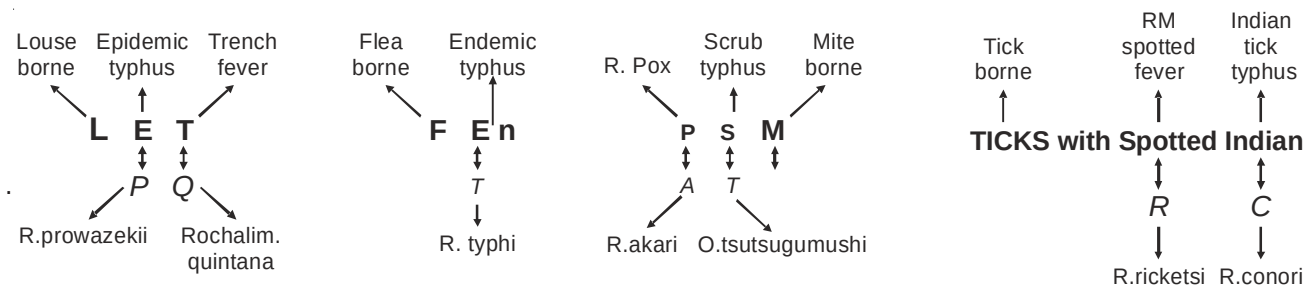
– Q fever – Anthrax
– Brucellosis – Leptospirosis
– TB – Plague

10. Ans. is b i.e. Is transmitted by bite of flea

Ref. Ananthnarayan 7/e, p 414; Park 18/e, p 239 - 240, 19/e, p 252

Endemic typhus or Murine or fleaborne typhus

– Caused by R.typhi or R. mooseri. It is zoonatic disease.
– No direct man to man transmission occur.
– Human acquire infection usually when saliva or feces of infected flea is rubbed over skin.
– Clinical features is similar to epidemic typhus in milder form.
– Its mammalian reservoir is rodents.
– Serology is ***diagnostic test.***
– Human infection is dead end infection.



Remember : Rickettsia can't grow in artifical culture media.

11. Ans. is a i.e. Q. fever *Ref. Ananthnarayan 7/e, p 424*

Human disease caused by chlamydia

Species	Serotype	Disease
C. trachomatis	A. B, Ba, C	Endemic blinding trachoma
C. trachomatis	D - K	Inclusion conjunctivitis, genital chlamydiasis, infant pneumonia
C. trachomatis	L1, L2, L3	Lymphogranuloma venerum
C. psittaci	Many serotype	Psittacosis
C. pneumoniae	Only one serotype	Acute respiratary disease

Remember : Inclusion conjunctivitis include inclusion blenorrhea or opthalmia - neonatorum and swimming pool conjunctivitis.

12. Ans. is b i.e. Chlamydia trachomatis *Ref. Ananthnarayan 7/e, p 423*

"***Chalmydiae are obligate intracellular bacterial parasite."*** *..... Ananthnarayan p 422*

They can be isolated only in cell culture.

McCoy and Hela cell lines are ***MC cell lines*** used to culture chlamydiae.

Remember : Other obligate parasite :
- Rickettsiaceae and coxiella burnetti
- M. Leprae
- Pathogenic treponemes
- Viruses.

13. Ans. is d i.e. Parotitis *Ref. Ananthnarayan 7/e, p 424*

Genital chlamydiasis :

Men – Epididymitis, proctitis.

Women – Bartholinitis, cervicitis, salpingitis, endometritis, PID, Perihepatitis (fitz Hugh syndrome), Infertility, abortion, ectopic pregnancy.

Either sex – Reiter's syndrome, NGU, conjunctivitis.

14. Ans. is b i.e. Trombiculid mute *Ref. Harrison 17/e, p 1064*

Scrub typhus

- Caused by *O.tsutsugamushi*
- **Transmitted** by *tromiculid mite* which also shows transovarian spread
- **Clinical features :** – Fever, headach, myalgia, cough and GI symptoms.
  – Classic case includes an eschar, regional lymphadenopathy and a maculopappular rash.

Diagnosis :

- Serologic assays (IFA, indirect immunoperoxidase and enzyme immunoassays) are main stay of diagnosis.

Treatment : – Rifampin
– Azithromycin and clarithromycin

15. Ans. is b i.e. Flea is a vector of the disease *Ref. Ananthnarayan 7/e, p 414*

Already explained, refer answer no. 5

16. Ans. is b i.e. Cause non-gonococcal urethritis *Ref. Ananthnarayan 7/e, p 428; Jawetz 24/e, p 364*

C. Psittaci

- Causes psittacoses in humans / birds, ornithosis in birds, meningo pneumonitis, feline pneumonitis and other animal diseases.
- Form diffuse intracytoplasmic inclusions that lack glycogen, not stained by I_2 and not inhibited by sulphadiazine or cycloserine. Heat stable group reactive. CF antigen resist proteolytic enzymes so seems to be lipopolysaccharide.
- Psittacosis is disease of human acquired from contact with birds and also includes infection of psittacine birds.
- Ornithosis is infection in all types of domestic birds.
- Infection in birds is usually subclinical (carriers).
- Human infection is usually occupational as is poultry workers, pigeon farmers, pet-shop owners, bird fencers and veterinarian. Usually occur by inhalation of infected dried feces.
- Incubation period about 10 days.
- Manifest as influenza / atypical pneumonia / sepsis.
- Antibodies to species specific antigen can neutralize toxicity and infectivity.
- Diagnosis : Culture is dangerous and if done; than isolation should be attempted only in special laboratories as laboratory infection is serious hazard detection of antigen by direct fluorescent antibody staining or by immunoassay or PCR is preferred serology (confirmatory) by CFT or MIF.
- Treatment : – DOC is tetracycline.
  – Should be continued for 10 days after defervescence to prevent relapse.

17. Ans. is b i.e. Culture on McCoy cells *Ref. Ananthnarayan 7/e, p 427; Jawetz 24/e, p 361*

"Genital Chalmydiasis is suspected if Gram stained smear of urogenital exudates show significant number of neutrophills (> 4/oil immersion field in urethritis, > 30 in cervicitis) in absence of gonococcal bacteria."

For more details, refer answer no. 3

18. Ans. is b i.e. Enzyme immunoassay *Ref. Ananthnarayan 7/e, p 425*

Isolation of Chlamydiae can done by :

a. Inoculation into yolk sac/embryonated eggs of 6 - 8 day old chick embryo which may be pretreated by streptomycin or polymyxin B.

b. Inoculation into experimental animals (mice).

c. Tissue / cell culture :

- *Preferred mode*
- Commonly used cell lines are McCoy and HeLa cells.
- Cell cultures are pretreated by irradiation or chemicals such as 5-iodo - 2 deoxyuridic or cycloheximide to enhance replication and detection of inclusion bodies.
- Pretreatment with DEAE dextrax or centrifugation after inoculation, promotes contact between chalmydiae particles and cell monolayer.

19. Ans. is c i.e. They can grow in cell free culture media *Ref. Ananthnarayan 7/e, p 422*

– Chlamydia are obligate intracellular parasite so, they can not be grow in cell free media.
– Gram negative coccobacilli.
– Chalmydia don't have peptidoglycan cell wall.
– They lack enzymes of electron transport chain. So require ATP from host cells & are called energy parasites.
– ***Drugs effecitve against chlamydiae :*** Doxycycline, Azithromycin, Erythromycin.

20. Ans. is a i.e. R. rickettsii *Ref. Park 18/e, p 239, 19/e 252*

Already explained, refer answer no. 10

21. Ans. is c i.e. Inhalation of aerosol *Ref. Harrison 17/e, p 1066; Jawetz 24/e, p 351*

"Q fever transmitted by inhalation of dust contaminated with rickettsial from placenta, dried feces, urine or milk or aerosols in slaughter houses."

Q fever :

- Caused by coxella burnetti
- A ***zoonotic*** disease
- Primary source of human infection are cattle, sheep and goats
- **Mode of transmission :**

In infected female animal C. burnetti localises uterus
↓
Infection reactivates during pregnancy
↓
High concentration of coxella in placenta
↓
Soil gets contaminated during parturation
↓
Coxella aerosols generates during storms
↓
Human infection

Remember : **Q fever** – Gives negative Weil-felix reaction.
– Also transmitted by infected milk.

22. Ans. is d i.e. Epidemic typhus *Ref. Park 18/e, p 239; 19/e, p 251*

Already explained, refer answer no. 5

23. Ans. is a Chlamidia trachomatis *Ref. Harrison 17/e, p 1072; Ananthnarayan 7/e, p 229*

"Complaint of urethritis with no result on Gram staining signifies Non gonoccoccal urethritis."

Cause of Non-gonococcal urethritis :

- Chlamydia trachomatis ***(MC)***
- Trichomonas vaginalis
- Mycoplasma hominis
- Gardnerella vaginalis
- Candida albicans
- Ureoplasma urealyticum
- Herpes simplex virus
- CMV
- Acinetobacteri Iwoffi, Ac calcoaceticus

24. Ans. is d i.e. Urethritis *Ref. Ananthnarayan 7/e, p 424*

- Urethritis is one of the presentation.
- Genital chlamydiasis, caused by serotype D-K of C. trachomatis.
- C. pneumonia increased the risk of artherosclerosis, asthma, sarcoidosis.

25. Ans. is b i.e. Gram positive *Ref. Ananthnarayan 7/e, p 423*

Rickettsia are Gram negative coccobacilli.

26. Ans. is b i.e. Coxella burnetti *Ref. Harrison 17/e, p 1066*

"Coxella burnetti – Causative agent of Q fever is transmitted through aerosolization"

27. Ans. is a, c and d *Ref. Harrison 17/e, p 1073*

Reiter's syndrome consists of conjunctivitis, urethritis, (or in female patient cervicitis) arthritis and characteristic mucocutaneous lesion.
Pathogenesis is unknown. However more than 80% affected patient belong **to HLA-B-27..**

28. Ans. is b i.e. Rocky Mountain *Ref. Harrison 17/e, p 1059*

Family rickettsiae includes six genera :

- Rickettsia
- Orientia
- Neorickettisa
- Ehrlichia
- Anaplasma
- Coxiella

As question is about disease by rickettsia answer is RMSF (which is caused by *Rickettsia rickettsii*) only as Scrub typhus is caused by *Orientia tsutsugamushi.*

29. Ans. is a, b and c i.e. HeLa; HeP2; and McCoy *Ref. Ananthnarayan 7/e, p 425*

Cell lines for chlamydiae are :
- – McCoy
- – HeLa
- – HEp - 2, HL.

- Human diploid fibroblast series and vero cell lines are used for virus isolation.

30. Ans. is a and c i.e. Infertility; and Pelvic inflammatory disease *Ref. Harrison 17/e, p 1071-1073*

Chlamydial diseases are :
- **In Men** – NGU, Epididymitis
- **In Women** – Cervicitis, Salpingitis, Urethritis, PID, infertility
- **Either sex** – Proctitis, LGV, Reiter syndrome
- **Neonates** (As a result of perinatal infection) – Conjunctivitis, pneumonia

31. Ans. is a i.e. Rickettsiae *Ref. Ananthnarayan 7/e, p 415 - 417*

Neill - Mooser or Tunica reaction – Used to differentiate between R. typhi and R. prowazaki.
- – Male guinea pigs are inoculated intraperitoneally with blood from a case of endemic typhus or culture of R. typhi, they develop fever and characteristic scrotal inflammation. This is called *neill - Mooser reaction.*
- – This is ***negative*** with R. Prowazaki but ***positive*** in R.typi, R.conori and R.akari.

32. Ans. is a, b and d i.e. Rickettsia; M. leprae; and Syphilis *Ref. Ananthnarayan 7/e, p 423*

Already explained, refer see answer no. 12

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. The primary site of multiplication of rickettsial organisms is in the : [Kerala 90]

a) Paranchymal cells of the liver
b) Endothelial cells of small vessels
c) Media of arteries
d) Adventitia of all blood vessels

[Ref. Ananthnarayana 7/e, p 412]

2. Weil felix reaction with OXK antigen indicates infection with : [JIPMER 90]

a) R. tsutsugamushi
b) R. Moseri
c) R. Quintana
d) R. Akari

[Ref. Ananthnarayana 7/e, p 418]

3. Mite transmits : [AI 91]

a) Scrub typhus
b) Trench fever
c) Endemic typhus
d) Epidemic typhus

[Ref. Ananthnarayana 7/e, p 414]

4. Anthro zoonosis are all except : [AI 93]

a) Guinea worm infection
b) Rabies
c) Plague
d) Hydatid cyst

[Ref. Park 19/e, p 88]

5. Most common diagnostic test in LGV is :

a) Fluorescent antibody **[PGI 93]**
b) Complement fixation test
c) Cell culture
d) Frei's test

[Ref. Ananthnarayana 7/e, p 425 - 428]

6. Chlamydia cause all of the following except :

a) Trachoma **[PGI 93]**
b) Non-gonococcal urethritis
c) Pneumonia
d) Parotitis

[Ref. Ananthnarayana 7/e, p 424, 229]

7. Q fever is caused by : [Kerala 94]

a) Rickettsia tsutsugamushi
b) R. prowozekii
c) R. Quintana
d) C. burnetti

[Ref. Ananthnarayana 7/e, p 419]

8. Which is not a zoonotic disease : [UP 96]

a) Giardia
b) Leptospirosis
c) Brucellosis
d) Epidemic typhus *[Ref. Park 19/e, p 642]*

9. The following are zoonotic disease except :

a) R. Pox **[UP 97]**
b) Scabies
c) Leptospirosis
d) Brucellosis

[Ref. Park 19/e, p 642]

10. Chalmydia cause all except : [UP 98]

a) Trachoma
b) Inclusion conjunctivitis
c) Granuloma inguinale
d) on specific urethritis

[Ref. Ananthnarayana 7/e, p 229, 424]

11. Neil Mooser's reaction is given by : [TN 02]

a) Rickettsial infection
b) Chalamydial infection
c) Mycoplasma
d) Pnemococcai infection

[Ref. Ananthnarayan 7/e, p 415]

Answer

1. b) Endothelial ...
2. a) R. tsutsugamushi
3. a) Scrub typhus
4. a) Guinea worm ...
5. c) Cell culture
6. d) Parotitis
7. d) C. burnetti
8. a) Giardia
9. None
10. c) Granuloma ...
11. a) Rickettsial ...

12. Micro organism that does not obey koch's postulates : **[Kerala 02, AI 89]**

a) M. tuberculosis
b) Poliovirus
c) M. leprae
d) Streptococcus

[Ref. Ananthnarayan 7/e, p 3]

13. Rickettsia prowazeki is transmitted by :

a) Fleas **[SRMC 02]**
b) Mites
c) Tick
d) Louse

[Ref. Ananthnarayan 7/e, p 414]

14. All the following statement are true about rickettsial excepts : **[UPSC 02]**

a) These are transmitted by arthropod vectors
b) Eschar is not seen in RMSF
c) Well Felex reaction may be diagnostic
d) Cephalosporin are drug of choice

[Ref. Ananthnarayan 7/e, p 416; Harrison 16/e, p 1000

15. Chlamydia trachomatis, the causative agent for trachoma : **[Kar 2003]**

a) Is a yest
b) Is an intracellular organism
c) Forms extracellular bodies which are diagnostic
d) Is never demonstrable in conjunctival scrapings

[Ref. Ananthnarayan 7/e, p 422, 424]

16 Causative agent of Q fever : **[Kolkata 03]**

a) Ro.quintana
b) R.prowazekii
c) R.typhi
d) Coxiella burnetti

[Ref. Ananthnarayan 7/e, p 419]

18. Reiter's syndrome is due to : **[Jharkhand 04]**

a) Chlamydia
b) Nisseria
c) Mycoplasma
d) Herpes virus

[Ref. Ananthnarayan 6/e, p 229]

19. For all of the following reaction Well Felix reaction is diagnostic except : **[SGPGI 05]**

a) Endemic typhus
b) Scrub typhus
c) Epidemic typhus
d) Q fever

[Ref. Ananthnarayana 7/e, p 418 - 419]

20. Endemic typhus is transmitted by : **[DNB 05]**

a) Rat flea
b) Mite
c) Tick
d) None

[Ref. Ananthnarayana 7/e, p 414]

21. All of the following can be grown in cell free culture media except : **[SGPGI 05]**

a) Mycoplasm
b) Rickettsia
c) Salmonelia
d) Campylobactor

[Ref. Ananthnarayan 7/e, p 413]

22. Which rickettesiae are able to grow in cell free media : **[Jharkhand 05]**

a) R. Quintana
b) R. rickettsi
c) R. typhi
d) R. Tsugatmushi

[Ref. Anantharayan 7/e, p 412]

23. Infectious part of Chlamydia is :

a) Elementary body **[Jharkhand 06]**
b) KP body
c) Reticulate body
d) None

[Ref. Anantharayan 7/e, p 422]

Answer 12. c) M. leprae 13. d) Louse 14. d) Cephalosporin ... 15. b) Is an intra ... 16. d) Coxiella ...
18. a) Chlamydia 19. d) Q fever 20. a) Rat flea 21. b) Rickettsia 22. a) R. Quintana
23. a) Elementary ...

16 Spirochetes

Group comprising : Elongated, motile, flexible bacteria.

Characteristic feature of spirochetes is *presence of varying number of* ***endoflagella*** which are polar flagella situated between outer membrane and cell wall; unlike flagella of other bacteria they *don't protrude outside.*

Pathogenic spirochetes belong to genera :

1. **Treponema**
2. **Borrelia**
3. **Leptospira**

TREPONEMA

- Relatively short spirochetes with fine spiral and **pointed or rounded ends.**
- Pathogenic treponemes **have not been successfully cultivated in** cell free media while the non-pathogenic [which are commensals] can be cultivated.
- **Pathogenic treponemes include :**
  - ***T. pallidum*** (causative agent of endemic and veneral syphilis)
  - ***T. partenue*** (causative agent of yaws)
  - ***T. carateum*** (causative agent of pinta)

  They are identical in their morphology, antigenic structure and other biochemical features, differs only in clinical feature of disease they produce. But recently molecular signatures have been identified that can differentiate the three subspeices of T.pallidum by PCR based methods. *... Harrison 17/e, p 1038*

TREPONEMA PALLIDUM

Morphology

- A thin spiral organism which is actively motile through endoflagella.
- *Seen* by **immunofluorescence staining** or dark field illumination or phase contrast microscope.
- *Stained* by **silver impregnation methods** - Fontana method useful for staining films and Levaditi method for tissue sections.

Cultures and Growth

- Grows only in tissue culture not in artificial culture media as it lack genes required for denovo synthesis of aminoacids, nucleotides and lipids.
- *Reiter strain (T.phagedenis)* - Non pathogenic. treponeme; shows morphological and antigenic similarities with T. Pallidum; can grow in artificial culture.
- T.pallidum is microaerophillic organism grows best in 1-4% O_2.

Antigenic structure

- Treponemal infection induce 3 antibodies :
  - **Reagin antibody :** It is responsible for *Wasermann reaction, kahn test* and ***VDRL.*** In these reactions a hapten called cardiolipin *[extracted from beef heart]* is used as antigen. Chemically cardiolipin is diphosphatidyl glycerol.
  - ***Antibody to group antigen*** which is found in both pathogenic and non pathogenic treponemes.
  - **Antibody to species specific** antigen which is polysaccharide in nature and is positive only with sera of patients infected with pathogenic treponemes.

Clinical manifestations

Natural infection with T.pallidum occurs ***only in*** human beings. It causes :

1. Veneral Syphilis

Acquired by sexual contact **Infectivity** of patient to its sexual partner is maximum during ***1st two years of disease.***

Treponema rapidly penetrates intact mucous membrane or micorspcopic abrasions in skin and with in few hours enters the lymphatics and blood to produce systemtic infection.

Blood from the patient with incubating or early syphilis is infectious.

Natural history fall into ***3 stages :***

Primary syphillis	• Primary lesion of syphilis **is painless hard chancre** at the site of entry of spirochete which heal with out scar in 10 - 40 days. • Cases in which syphilis is acquired ***non venerally*** [as occupationally in doctors] primary chancre is ***extragenital usually on fingers.*** • Cases in which syphilis is transmitted by blood transfusion chancre don't occur. • Persistent or multiple chancres may be seen in HIV infected or other immunodeficient patient.
Secondary syphilis	• 3 months after primary lesion. • *Reseolar or papular skin rashes, mucous patches in oropharynx and condylomata at mucocutaneous junction are characteristic lesions. Spirochetes* are abundant in the lesions. • Patient **is most infectious** during this stage.
Tertiary sphillis	• Consist of **cardiovascular lesions; chronic granuloma *(gummata)*** & **meningovascular manifestations** such as ***tabes dorsalis.***

Remember : **Latent syphilis :** – Period of quiescence between secondary and tertiary stage.
– During this period diagnosis is only possible by serological test.

2. Congenital syphillis

- *Woman with early syphillis is more infective* to her child.
- Transmission across placenta can take place at any time, but lesions of congenital syphillis have their onset after 4th months of gestation. So, adequate treatment of mother before 4th month of pregnancy prevents fetal damage.
- **Earliest sign** of congenital syphillis is rhinitis or snuffles. *....Harrison 17/e, p 1042*
- ***MC*** early **manifestation** are bone changes, hepatosplenomegaly, lymphadenopathy.
- ***Clutton's joint*** *(Bilateral knee effusion),* ***interstitial keratitis*** are late manifestation.
- Residual stigmata of congenital syphilis are :

Hutchinson's teeth	:	Centrally notched, widely placed upper central incisor.
Mulberry molars	:	Sixth year molars with poorly developed cusps.
Rhagades	:	Linear scars at angle of mouth.

Diagnosis

1. ***Demonstration of Organism***
   - **Darkfield microscopic examination of lesion** exudate such as chancre of primary syphillis or more reliably by immunofluoroscence or immunohistochemical method.

2. **Serological test for syphilis**

Nontreponemal test	*Treponemal test*
Detect IgG or IgM *against cardiolipin antigen* • Includes : **RPR** (Rapid plasma reagin) ***[test of choice for rapid diagnosis]*** • **VDRL** ***[test of choice for response to therapy]*** • VDRL is type of slide flocculation test while kahn flocculation is tube test	*Detect specific antibody* against T. pallidum • Includes : Fluoroscent treponemal antibody absorption test **[F-TAABS]** – *Agglutination assays* **(MHATP, TPHA, TPPA)** – TPI (Treponemal pallidum immobilisation) test

Remember : – **FTA-ABS, *TPPA*** are most sensitive test.
– ***TPI*** is most specific serological test.
– **TPPA** has **supplanted** the FTA-ABS test as diagnostic test. *..... CMDT' 06, p 1445*

Diagnosis of neurosyphilis : Examination of CSF for pleocytosis, increase protein concentration, VDRL reactivity.

Diagnosis of congenital syphilis : If both test i.e. **VDRL** and **FTA- ABS IgM** (specific) test are positive in the infant than congenital syphilis should be strongly suspected and the child should be treated.

Treatment

Stage of syphilis	DOC	Patient with penicillin allergy
Primary secondary or early latent	*Penicillin benzathine*	Tetracycline or Doxycycline
Late latent	*Penicllin G*	Tetracycline
Neurosyphilis	*Aqueous penicillin G*	Desensitization and treatment with penicllin
Syphilis in pregnancy	*According to stage*	Desensitization and treatment with pencillin

- Continued susceptibility of treponema to penicillin is due to highly conserved genome.

Jarisch Herxheimer reaction :
– May occur after penicillin therapy.
– Seen in primary; mostly after secondary; early latent syphilis; delayed in neurosyphilis.
– Subsides itself.
– ***Treatment :*** Symptomatic - Antibiotic should not be stopped. Steroids should not be given.

Evaluation of response to therapy :
- Response to treatment is determined by monitoring VDRL or RPR titer.
- Activity ***of neurosyphilis is*** best correlated with CSF pleocytosis.
- Continued susceptibility of treponema to penicillin is due to highly conserved genome.

NON VENERAL TREPONEMATOSIS

Infection usually transmitted by body to body contact. It includes :

A. Endemic syphilis :

- Caused by T. pallidum subspecies endemicum
- Disease is common is young children, primary chancre is not usually seen.
- ***Treatment :*** Same as veneral syphillis.

B. Yaws :

- Caused ***by T.pallidum*** subspecies ***T.pertenue*** which is morphologically and Immunologically identical to T.pallidum. *(Learn Py.)*
- Primary lesion is extragenital papule which enlarges and ulcerate to form an ulcerating granuloma.

C. Pinta :

- *Causative agent T.**c**arateum (Learn Cap).*
- It is not identical but closely related to T.pallidum.
- ***Primary lesion*** is extragenital papule which doesnot ulcerate but develop into lichenoid or psoriatic patch.

Remember : In non veneral treponematosis, yaws ***(always)*** and pinta ***(usually)*** **serological test of syphilis are positive.**

LEPTOSPIRA

Actively motile spirochetes possesing a large number of closely wound spirals and characterstic ***hooked ends.***

Culture : Grow *best* under aerobic condition. For isolation **EMJH** media is used.

Pathogenesis and clinical manifestation :

- Leptospirosis is a **zoonosis** with ***rodents*** being most important reservoir.
- **Transmission** results from ingestion or contact with urine, blood or tissue from infected animal but not from bite. Since leptospires are excreted in urine of infected rat, *water is important vehicle*. Human to human transmission don't occur.
- **Vasculitis is responsible for most clinical manifestation.**
- It mainly infects : Liver *(centritobular necrosis is found)*
  Kidney *(cause interstitial nephritis, tubular necrosis)*
- After formation of antibody, leptospires are eliminated from all sites except *the eye, proximal renal tubules and brain.*
- More than 40% of symptomatic person have mild and anticteric from of leptospirosis.
- Severe leptospirosis is characterized by **profound jaundice, renal dysfunction, hemorrhagic diathesis called as** Weil's syndrome or Icterohemorrhagic fever.

Diagnosis

1. Isolation of organism	– From blood or CSF during 1st 10 days – From urine after 1 week – For ***isolation EMJH medium is useful***
2. Serology	– **Microscopic agglutination test [MAT]** – **ELISA**

Treatment

– ***Mild*** - Doxycycline or Ampicillin.
– ***Moderate / severe*** - Penicillin or Erythromycin.

Chemoprophylaxis : Doxycycline

BORRELIA

- Large, refractile spirochetes which can be ***stained by ordinary method*** and are Gram (–) ve.
- Pathogenic species are :

B.burgodorferi	-	Causes Lyme's disease
B.recurrentis	-	Causes Relapsing fever
B.vincenti	-	Causes Vincent angina

Lymes Disease

- Causative agent ***B.burgodorferi.***
- ***MC*** vector born infection in **Europe. Transmitted by bite of Ixodid ticks.** *.... Harrison 17/e, p 1055*
- **Clinical features**
  - ***Stage I. (Localized infection)***
    - After incubation period of 3 to 32 days EM occurs at the site of bite. EM (Erythema migrans) is not painful.
  - ***Stage II. Disseminated infection***
    - Disseminate hematogenously to produce secondary annular skin lesion, meningitis, carditis (*MC* cardiac finding is fluctuating degree of Atrioventricular heart block).
  - ***Stage III. Persistent infection***
    - Usually present as oligoarticular arthritis (***MC*** knee), encephalopathy, polyneuropathy. Acrodermatitis chronica atrophicans is late skin manifestation.
- **Diagnosis**
  - ELISA followed by western blot is *best investigation.*
  - Culture in BSK medium gives definitive diagnosis but not useful clinically.
  - PCR particularly in persistant infection.
- **Treatment**
  - For **nervous manifestation** and **3^0 heart block** – ***Ceftriaxone*** is ***DOC.*** *..... Harrison 17/e, p 1058*
  - For **skin manifestation, arthritis 1^0 and 2^0 AV block** – ***Doxycycline*** is ***DOC.***

Relapsing Fever

- Causative agent ***B.recurrentis.***
- It is of 2 types **:**
  - *Louse borne* and *Tick borne* the, Borellia causing them are indistinguishable.
  - ***Louse borne*** relapsing fever occur as ***epidemic.***
  - ***Tick borne*** occur as ***sporadic / endemic*** cases.
- **Treatment :** Erythromycin is ***DOC.*** *..... Harrison 17/e, p 1054*

Vincent angina

- Causative agent ***B.vincenti***
- Normal mouth commensal, but when associated with fusiform bacilli (Fusobacterium fusiform) causes ulcerative gingivostomatitis or oropharyngitis called vincent angina.
- **Treatment :** Penicillin and Metronidazole.

QUESTIONS

1. Which is not true about Yaws ? **[AI 08]**

a) Spread by sexual transmission
b) Caused by T.perteune
c) Has cross immunity with syphillis
d) Cannot be differentiated serologically from T. pallidum

2. A bacterial disease with 3 'R's i.e. rats, rice fields and rainfall is : **[AI 05]**

a) Leptospirosis
b) Plague
c) Melioidosis
d) Rodent bite fever

3. A sweeper involved with repair-work of sewers was admitted with fever, jaundice and renal failure. The most appropriate test to diagnose infection of this patients : **[AI 03]**

a) Weil Felix test
b) Paul Bunnel test
c) Microscopic agglutinatiion test
d) Micro immunoflurescence test

4. The following are true regarding Lyme's Disease, except : **[AI 03]**

a) It is transmitted by ixodes tick
b) Erythema chronicum migraines may be a clinical features
c) Borrelia recurrentis is the etiologic agent
d) Rodents act as natural hosts

5. Which of the following is transmitted by Rat urine ? **[AI 02]**

a) Leptospira
b) Listeria
c) Legionella
d) Mycoplasma

6. Congenital syphilis can be diagnosed by :

a) IgM FTA abs **[AI 01, 96]**
b) IgG FTA abs
c) VDRL
d) TPI

7. False +ve VDRL is seen in : **[AI 00, 95]**

a) Lepromatous leprosy
b) Infectious mononucleosis
c) HIV
d) Pregnancy

8. All are true about FTA-ABS Syphilis, except :

a) FTA-ABS becomes negative after treatment
b) Present in secondary syphilis **[AI 00]**
c) It is a sensitive test
d) May be positive in Lyme's disease

9. The following statements are true regarding leptospirosis, except : **[AIIMS 06]**

a) It is a zoonosis
b) Man is the dead end host
c) Man is an accidental host
d) Lice act as reservoirs of infection

10. 'Chancre redux' is a clinical feature of :

a) Early relapsing syphilis **[AIIMS 06]**
b) Late syphilis
c) Chancroid
d) Recurrent herpes simplex infection

11. A 25-year old farmer presented with history of high grade fever for 7 days and altered sensorium for 2 day. On examination, he was comatosed and had conjunctival hemorrhage. Urgent investgations showed a hemoglobin of 11 gm/dl. Peripheral blood smear was negative for malarial parasite. What is the most likely diagnosis ? **[AIIMS 05]**

a) Brucellosis
b) Weil's disease
c) Acute viral hepatitis
d) Q fever

Answer

1. a) Spread by... 2. a) Leptospirosis 3. c) Microscopic ... 4. c) Borrelia ... 5. a) Leptospira
6. a) IgM FTA ... 7. b) Infectious ... 8. a) FTA-ABS ... 9. d) Lice ... 10. ??
11. b) Weil's ...

12. A 23 year old male had unprotected sexual intercourse with a commercial sex worker Two weeks later he developed a painless, indurated ulcer on the glans that exuded clear serum on pressure inguinal lymph nodes in both groins were enlarged and non-tender Most appropirate diagnostic test is : [AIIMS 04]

a) Gram's stain of ulcer discharge
b) Dark field microscopy of ulcer discharge
c) Giemsa stain of lymph node aspirate
d) ELISA for HIV infection

13. Which one of the following microorganisms uses antigenic variation as a major means of invading host defenses : [AIIMS 04]

a) Streptococcus pneumonia
b) Borrelia recurrentis
c) Mycobacterium tuberculosis
d) Listeria monocytogenes

14. 20 year old body has admitted with history of fever, icterus, conjunctival suffusion and hematuria for 20 days. Which of the following serological test can be of diagnostic utility : [AIIMS 04]

a) Widal test
b) Microscopic agglutination test
c) Paul Bunnel test
d) Weil Felix reaction

15. Best indicator for monitoring of syphilis treatment: [AIIMS 02]

a) VDRL
b) FTA-ABS
c) TPI
d) TPHA

16. Spirochaetes among following are : [PGI 06]

a) Syphilis
b) Leptospira
c) Mycoplasma
d) Brucella
e) Borelia

17. Non venereal treponemas is/are : [PGI 04]

a) T. Pertenue
b) T. Carateum
c) T. Palildum
d) T. Cuniculi

18. Lyme disease caused by : [PGI 01]

a) Leptospira
b) Borrelia
c) Treponema
d) Bordetella
e) Arbovirus

19. Dark ground microscopy is used for : [PGI 98]

a) TPI
b) FTA-ABS
c) Kahn's test
d) VDRL

20. Following is true of T. pallidum, except :

a) Can be maintained in rabbit testis [PGI 98]
b) Motile by peritrichate flagella
c) To visualise, dark ground microscopy is used
d) TPI test is very useful

Answer

12. b) Dark field ... 13. b) Borrelia ... 14. b) Microscopic ... 15. a) VDRL 16. a, b and e
17. a and b 18. b) Borrelia 19. a) TPI 20. b) Motile ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is a i.e. Spread by sexual transmission *Ref. Harrison 17/e, p 1047*

Yaws is caused by T. pallidum subspecies pertnue.

- T.pertenue is antigenically identical to syphilitis.

Mode of transmission : Infection is transmitted by direct contact with infectious lesions, often during play or group sleeping.

Clinical features : After 3-4 weeks the first lesion begins as a papule usually on extremity, it is followed by appearance of multiple skin lesion.

Treatment of choice : Benzathine penicililn.

2. Ans. is a i.e. Leptospirosis *Ref. Ananthnarayan 7/e, p 389; Harrison 17/e, p 1048*

Leptospirosis

- ***Dead end infection*** of leptospira characterized by clinical manifestations ranging from inapparent infection to fulminant icterohemmoragic fever ***(Weils's syndrome).***

Modes of transmission :

- **Rodents** are most important reservoir.
- Transmission occur by direct contact with urine, blood or tissue from an infected animal.
- **Water is** an important vehicle of transmission.
- Out breaks mostly occur as a result of heavy rainfall and consequent flooding.

So. guys ***Leptospirosis is associated with :*** – Rats
– Rainfall
– Rice - Rats usually live in rice farms.

Other options – **Heavy rainfall** tends *to protect against plague and Rodent bite fever* by damaging rodent burrows.
– Meliodosis is not associated with Rat.

3. Ans. is c i.e. Microscopic agglutination test
Ref. Harrison 17e, p 1050; Ananthnarayan 7/e, p 392; 6/e, p 362

- The patient is a case of ***Weil's syndrome*** or ***icterohemmorhagic fever*** which is caused by **Leptospira** and manifest as :
  - ***Fever***
  - ***Jaundice***
  - ***Renal failure (Hematuria)***
- Human infection are usually due to occupational exposure to urine of infected animal eg.,
  - *Farmers*
  - *Workers in underground Sewers*
  - *Veterinarians*
  - *Workers in rice field and sugarcane field*
  - *Meat and animal handlers*

Diagnosis	
Isolation of organism	**Serology**
• **EMJH** medium is useful	• Raise in antibody titre (≥ : 100) in ***microscopic agglutination test (MAT).***
• **Dark field examination** of patient blood	• ***Macroscopic agglutination test*** is useful for screening but is ***not specific.***
	• ***IgM enzyme immunosorbant assay (EIA)*** - particularly useful in making an ***early*** diagnosis.

Remember :
- Leptospirosis is most widespread zoonotic disease in world.
- Vasculitis is responsible for most manifestation of Leptospirosis
- Penicillin G is ***DOC*** for Leptospirosis.
- Fletcher medium and Korthof medium can also be used for isolation of leptospira.

4. Ans. is c i.e. Borrelia recurrentis is the etiological agent

Ref. Ananthnarayan 7/e, p 389; 6/e, p 359; Harrison 17/e, p 1055

"Lyme's disease is caused by Borreliea burgdorferi not B. reccurentis."

Lyme's disease
- *Causative agent* – Borellia burgdorferi
- *Vector* – Ixodes tick
- Natural reservoir host – Rodents, deer and other mammals.

Clinical Manifestation
- ***Stage 1*** – After I.P of 3-32 days
  - Erythema migrans occur at the site of tick bite.
  - ***MC*** **site** - Thigh, groin, axilla
- ***Stage 2*** – Disseminate hematogenously to produce :
  - *Secondary annular skin lesion*
  - *Meningitis*
  - *Carditis*
- **Stage 3 (Persistent infection)** – Intermittent attacks of oligoarticular arthritis (***MC*** - Knee).
  Acrodermatitis atrophicans – late skin manifestation.

Diagnosis
- **Serology –** ELISA followed by western blot can't distinguish active and inactive infection.
- **Isolation of organism**
  - B. burgdorferi may be cultured from skin lesions of patient.
  - Grows best in BSK medium at 33^0C.
- Detection of DNA by PCR, particularly in joint fluid.
- Later in infection PCR is greatly superior to culture.

Remember : B.recurrentis is etiological agent of Relapsing fever.

5. Ans. is a i.e. Leptospira *Ref. Ananthnarayan 7/e, p 389; Harrison 17/e, p 1055*

Already explained, refer answer no. 2

6. Ans. is a i.e. IgM FTAbs *Ref. Ananthnaryan 7/e, p 383; Harrison 16/e, p 984*

"Newborn infant of mother with reactive VDRL or FTA-ABS shows (+) ve test irrespective of infection because of transplacental transfer of maternal IgG antibody."

As IgM antibody don't cross placenta, neonatal IgM antibody can be detected in cord or neonatal serum with the syphilis capita M or 195 IgM FTA-ABS test. *..... Harrison 16/e, p 984*

Important points about Congenital syphilis

- Transmission across placenta can take place any time, but lesion appear after 4 month of gestation.
- ***Earliest sign*** of congenital syphilis – Rhinitis, snuffles
- ***Residual stigmata*** of congenital syphilis – Hutchinson's teeth, Mulberry molars, Rhagades
- ***DOC*** of congenital syphilis – Penicillin G.

Caution : According to *Harrison 17/e, p 1045* no commercially available IgM test is recomended for evaluation of infant with suspected cong. syphilis.

7. Ans. is b i.e. Infectious mononucleosis *Ref. Harrison 16/e, p 985; CMDT '08, p 1269*

The modern VDRL and RPR test are 97% to 99% specific and false psotive test are now limited to following condition :

Causes of False Positive VDRL	
Acute false positive reaction <6 months	**Chronic false positive reaction >6month**
– Recent viral illness or immunization	– Aging
– Genital herpes	– Auto immune disorders
– HIV infection	– SLE
– Malaria	– Rheumatoid arthritis
– Parenteral drug use	– Parenteral drug use

Infectious mononucelosis is acute infection of EBV and can give false (+)ve VDRL

- *In CMDT '08, p 1269* Leprosy is also mentioned as cause of false (+)ve VDRL: but with use of newer non-lipoidal VDRL test, leprosy no longer give false positive result.
- ***False negative* VDRL.**
  Seen when very high antibody titre is present **[Prozone phenomenon].**

8. Ans. is a i.e. FTA-ABS becomes negative after treatment *Ref. Harrison 17/e, p 1049*

- *Only VDRL and RPR for syphilis becomes negative after treatment and are recommended for evaluation of therapy. VDRL or RPR titer progressively declines, becomes (–ve) by 12 months in 40-75% of primary cases and in 20-40% of secondary cases.*
- *FTA-ABS and agglutination test remains positive after treatment so these test are not useful in evaluating the response to therapy.*

Diagnosis of syphilis

1. **Demonstration of organism :**
   - ***Darkfield microscopic examination*** of lesion exudate is useful in moist cutaneous lesion such *as chancre* of primary syphilis; *condylomata* of secondary syphilis.

  - A treponamal *concentration of >10^4/ml in* exudate is required for visibility under dark field microscope
- *Direct fluoroscent antibody T. pallidium (DFA-TP) test* – Use fluoroscent conjugated antibody for detection of T. pallidium in fixed culture.

2. Serological test for Syphilis

Non treponemal test	Treponemal test
– Detect antibody against cardiolipin	– Detect specific antibody against T. pallidum antigen
– **Includes** • VDRL (test of choice for response to therapy); RPR (test of choice for rapid diagnosis) • TRUS (Toulidine red unheated serum test)	– **Includes** • FTA-ABS **(most sensitive test)** • Agglutination assays (MHA-TP; TPHA; TPPA) * TPPA has supplanted the FTA-ABS test as as diagnostic test. • TPI - **most specific serological test** (not used now)

9. Ans. is d i.e. Lice acts as reservoir *Ref. Park 18/e, p 232; 19/e, p 244; Harrison 17/e, p 1048*

"Reservoir of leptospirosis are rats not lice." Other wild mammals as well as farm animals may also harbor leptospires.

- Human infection is ***mostly accidental.***
- Transmission occur through direct contact - Leptospira enter the body through skin abrasions or through intact mucous membrane :
  - Ingestion of food and water contaminated with leptospira.
  - Inhalation of droplets of urine of infected animal.

10. Ans. is ?? *Ref. Still searching*

Sorry, Guys for this question, we have searched all books and sites.

Chancre redux is second chancre seen in cases of syphiltic subject, possibly due to an allergic reaction without presence of spirochete. *..... Stedmann's dictionary 27/e, p 327*

This is the only thing that we have found about chancre redux.

11. Ans. is b i.e. Weil's disease *Ref. Harrison 17/e, p 1050*

This is **classic** case of **Weil disease** with :
- Fever
- Jaundice
- Renal failure (increase urea).

12. Ans. is b i.e. Dark field microscopy of ulcer discharge

Ref. Ananthnarayan 7/e, p 380; Harrison 16/e, p 1040

Painless indurated ulcer (Hard chancre) with non tender inguinal lymphadenopathy signifies diagnosis of syphilis.

13. Ans. is b i.e. Borrelia recurrentis *Ref. Ananthnarayan 6/e, p 357; 7/e, p 387*

"Borrelia readily undergoes antigenic variations in vivo and this is beleived to be the reason for relapsing in the disease." *..... Ananthnarayan 7/e, p 387*

Borrelia recurrentis

– Causative agent of relapsing fever
– Antigenic variation occur due to DNA rearrangement in linear plasmids present in Borrelia
– Cause two types of relapsing fever :
  • Louse borne – Occur as epidemic
  • Tick borne – Occur as Sporadic cases

Remember :

- **Other bacteria exhibiting antigenic variation are :**
  – Neisseria
  – Group A streptococci

14. Ans. is b i.e. Microscopic agglutination test *Ref. Harrison 17/e, p 1050; Ananthnarayan 7/e, p 392*

Already explained, refer answer no. 3

15. Ans. is a i.e. VDRL *Ref. Harrison 17/e, p 1043*

Serological test of syphilis

- ***Most sensitive test*** - FTA-ABS
- ***Most specific test*** - TPI (not used now)
- ***Test of choice*** for ***rapid diagnosis*** - RPR
- ***Test of choice*** for ***evaluation*** of ***therapy*** - VDRL
- ***Test of choice*** for ***diagnosis*** of ***congenital syphilis*** - IgM FTA-ABS

Now, TPPA has ***supplanted*** FTA-ABS as ***definitive diagnosis test*** for ***syphilis.*** *..... CMDT '08, 1270*

16. Ans. is a, b and e i.e. Syphilis; Leptospira and Borelia *Ref. See below*

Spirochete	Species	Diseases
Treponema	T. pallidum	– Syphilis
	T. Endemicum	– Bejel / Endemic syphilis
	T. Pertune	– Yaws
Borrelia	T. carateum	– Pinta
	B. Burgdoferi	– Lyme disease
	B. recurrentis	– Relapsing fever
	B. recurrentis	– Vincent's angina
	B. Vincenti	– Vincent's angina
Leptospira	L. interrogans	– Weil's disease
	L. canicola	– Canicola fever

17. Ans. is a and b i.e. T. pertenue; and T. carateum *Ref. Ananthnarayan 6/e, p 355; 7/e, p 385*

Non veneral Treponematosis

• **Endemic syphilis**	– Caused by T. pallidum subspecies endemicum. – Transmitted by body to body contact. – Mainly seen in young children. – Primary chancre is not formed. – ***Treatment*** - penicillin is ***DOC.***
• **Yaws** *(=pian* = Parangi)	– Caused by T. pallidum subspecies T. pertenue. – Primary lesion is extragenital papule which ulcerate to form an ulcerating granuloma.
• **Pinta**	– Caused by T. carateum – Not identical but closely related to T. pallidum – Primary lesion is extragenital papule which does not ulcerate but develop into lichenoid or psoriatic patch.

Remember :

T. pallidum subspecies endemicum and **T. pertenue are morphologically** and **immunologically identical to T. pallidum subspecies pallidum** (causative agent of syphilis), So VDRL is positive.

18. Ans. is b i.e. Borellia *Ref. Ananthnarayan 6/e, p 359; 7/e, p 382*

Already explained, refer answer no. 4

19. Ans. is a i.e. TPI *Ref. Ananthnarayan 6/e, p 352; 7/e, p 382*

"For Treponema pallidum immobilization test dark ground microscopy is required."

- **TPI** is *most specific* test for syphilis, but not performed now, as it requires Treponoma in Tissue culture.
  - In TPI treponema is combined with antibody and complement of patient sample, if it results in immobilization (which is seen in dark ground), infection is confirmed.
- *Kahn test, is* **tube flocculation** test
- *VDRL* is **slide flocculation** test
- ***FTA-ABS*** is an ***indirect immunofluoroscence test***
- ***Organism examine under dark ground microscope are :*** – **L**eptospira – **T**reponema – **V**ibrio cholera – **C**ampylobacter jejuni.

Mnemonic - **L**ocal **T**rain **V**ia **C**handigarh

20. Ans. is b i.e. Motile by pertrichiate flagella *Ref. Ananthnarayan 6/e, p 348; 7/e, p 377*

T. pallidum

- Motile by ***endoflagella*** not peritrichate flagella. Endoflagella are not visible outside.
- Visualized on dark ground microscopy.
- Pathogenic treponemes do not grow in artificial culture media.
- Can be maintained in rabbit testis.
- Have rotational movement, forward - backward movement, flexion of whole body.

Remember : TPI is most specific serologic test for syphilis.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Characteristic of primary chancre : [Kerla 97;
a) Painless punched out ulcer **[AIIMS 87, JIP. 87]**
b) Painless ulcer with over hanging edges
c) Pain less ulcer with irregular raised edges
d) Painfull punched out ulcer
[Ref. Ananthnarayana 7/e, p 379; Harrison 17/e, p 1040; Dasohre, p 105]

2. The following is not true of syphilis : [AIIMS 91]
a) TPI is most specific
b) VDRL is not specific
c) VDRL is negative in secondary syphilis
d) IgM test is specific for congenital syphilis
[Ref. Ananthnarayana 7/e, p 383; Harrison 17/e, p 1043]

3. Which is false about syphilis : [AI 92]
a) TPI gives definite diagnosis
b) TPHA is earliest to be +ve
c) VDRL is +ve 1 week after appearance of chancre
d) Serologically not different from yaws
[Ref. Ananthnarayana 7/e, p 382; Jawetz 24/e, p 335]

4. In syphilis the semen is infective for :
a) 2 weeks **[JIPMER 92]**
b) 4 weeks
c) 4 months
d) 1 year
[Ref. Under consideration]

5. Yaws is caused by : [Kerala 94; TN 89]
a) Pertunae
b) T. pallidum perteroue
c) T. caraetum
d) Hemophilus
[Ref. Harrison 17/e, p 1046]

6. False +ve VDRL test is not seen in : [Kerala 94]
a) Herpes infection
b) Leprosy
c) Malaria
d) SLE
[Ref. Harrison 16/e, 982]

7. Which of the following investigation is very specific for spirochaetal infection ? [Kar 03]
a) Wasermanns test
b) VDRL test
c) Treponema pallidium
d) Fluorescent treponemal antibody absorption test
[Ref. Ananthnarayan 7/e, p 382]

8. Organisms that has not been cultured successfully so far is : [J & K 01]
a) Leptospira
b) Treponema pallidum
c) Bordetella
d) Staphylococcus
[Ref. Ananthnarayan 7/e, p 377]

9. Necrotizing granulomatous lymphadenopathy is caused by : [JIPMER 95]
a) Syphillis
b) Granuloma inguinale
c) Sarcoidosis
d) Tuberculosis
[Ref. Taylor 3/e, p 77, table 5.2]

10. VDRL is a : [TN 95]
a) Slide flocculation test
b) Tube flocculation test
c) Gel precipitation tes
d) Indirect hemaglutination test
[Ref. Ananthnarayana 7/e, p 381, 95]

Answer

1. a) Painless ...
2. c) VDRL ...
3. b) TPHA is earliest ...
4. b) 4 weeks
5. b) T. pallidum ...
6. None
7. d) Fluorescent
8. b) Treponema ...
9. a and d
10. a) Slide ...

11. Which of the following disease is not caused by treponema : [Kar 00]

a) Yaws
b) Bejel
c) Relapsing fever
d) Syphilis

[Ref. Harrison 17/e, p 1052]

12. Treponema palidum is very difficult to demonstrate in : [JIPMER 02]

a) Chancre
b) Maculopapular lesion
c) Gumma
d) Mucosal patch

[Ref. Ananthnarayana 7/e, p 380; Harrison 17/e, p 1042]

13. The most commonly performed test for the serodiagnosis of syphilis is : [Kar 2002]

a) TPHA
b) Wasermann
c) TPI
d) VDRL

[Ref. Ananthnarayan 7/e, p 381]

14. Syphilis was first identified by : [TN 02]

a) Fraenkel
b) Nicolaicu
c) Schaudinn and Hoffman
d) Ogston

[Ref. Ananthnarayana 7/e, p 376]

15. Syphilis is diagnosed all except : [UP 02]

a) TPI
b) FTA-ABS
c) Weil felix
d) VDRL

[Ref. Ananthnarayana 7/e, p 352]

16. Consider the following serological test :

a) TPI **[UPSC 02]**
b) TPHA
c) FTA-ABS
d) VDRL

17. Which of these are specific for diagnostic syphilis? [Bihar 03]

a) 1 only
b) 2 and 4
c) 3 and 4
d) 1, 2, and 3

[Ref. Ananthnarayana 7/e, p 352]

18. Most specific test for syphillis : [Kolkata 03]

a) FTA-ABS
b) TPI
c) VDRL
d) ELISA

[Ref. Ananthnarayan 7/e, p 382]

19. Test used for diagnosis of congenital syphilis :

a) IgMFTA **[MP 05]**
b) VDRL
c) TPI
d) Kahn flocculation test 23rd

[Ref. Ananthnarayana 7/e, p 384; Harrison 16/e, p 984]

20. Leptospira icterohemorrhagica infection is transmitted by : [TN 95]

a) Bats
b) Rats
c) Birds
d) Dogs

[Ref. Ananthnarayan 7/e, p 393]

21. Antigenic variations seen in : [MP 06]

a) Borrelia recurrentis
b) Borrelia burgdorferi
c) Borrelia vincenti
d) None

[Ref. Ananthnarayan 7/e, p 387]

22. The causative agent of Lyme's disease :

a) Borrelia burgdorferi **[SGPGI 07; MP 05]**
b) Borrelia recurrentis
c) Leptospira icterohemorrhagiae
d) Clostridium difficile

[Ref. Ananthnarayana 7/e, p 389]

Answer

11. c) Relapsing ...	12. c) Gumma	13. d) VDRL	14. c) Schaudinn ...	15. c) Weil felix
16. None	17. d) 1, 2, and 3	18. None	19. a) IgMFTA	20. b) Rats
21. c) Borrelia ...	22. a) Borrelia ...			

17 Mycoplasma

- Smallest free living bacteria, bounded by sterols containing soft trilaminar membrane.
- **Lack cell wall** hence show polymorphism and resistance to cell wall active antimicrobial agent such as penicillin, cephalosporin and lysozyme.
- Also called as ***PPLO = Stable L forms.***
- Even cell precursors like muramic acid or diaminopimelic acid are absent.
- Do not possess spores flagella or fimbria. Some species exhibit motility.

Morphology

- Gram negative but better stained *by Giemsa.*
- Can be grown on cell free media. Colony is typically biphasic with **"Fried egg appearance" best studied** after staining *by Dienes* method.
- Some species shows bulbous enlargement with a differentiated tip structure which aids in attachment of organism to host cell carrying neuraminic acid receptor.

Mechanism of Pathogenicity

- Adherence to host cell.
- H_2O_2 production (as in M.pneumonia).
- Ammonia production (as in M.hominis).
- Urease activity to produce ammonia (as in U.urealyticum).
- IgM autoantibodies that agglutinate human group O erythrocyte at 4^0C. This *cold agglutinin* produce anemia.

Classification

- M. pneumoniae – Upper and lower respiratory tract infection.
- M. genitalium and Ureaplasma Urealyticum – Urethritis and other genital condition.
- M. hominis and U.urealyticum – *Part of flora of bacterial vaginosis.*

MYCOPLASMA PNEUMONIA = PRIMARY ATYPICAL PNEUMONIA = WALKING PNEUMONIA

- Cause by M.pneumonia (= Eaton agent) in which pneumonia is classic presentation but **non-pneumonic** infection is more common with prolonged incubation period.
- Interstitial type of pneumonia characterized by paucity of respiratory signs on auscultation with striking radiological abnormalty.
- **Extrapulmonary manifestations** (eg. Erythema multiforme, anemia, coagulopathies) is due to autoantibodies against brain, heart and muscle.

Diagnosis

i. *Isolation* - Throat swab/respiratory secretions are inoculated into medium containing glucose and phenol.

ii. *Serological diagnosis* **Specific test** - Immunofluorescence hemagglutination inhibition and metabolic inhibition are most sensitive test.

Non specific serological test are streptococcus MG (group F) and cold agglutination test.

GENITAL MYCOPLASMAS

- Non-gonococcal Urethritis (NGU) - U.urealyticum and M.genitalium cause most of non-chlamydial cases of NGU.
- U.urealyticum called as **T. strain/T. form of mycoplasma** are able to hydrolyse urea. Hence Urea and cholesterol is essential growth factor.

Treatment : Tetracycline [Doxycycline] is ***DOC*** for treatment of mycoplasma infection.

Cell wall defective bacteria

L phase variants (L forms)

- Wall defective microbial forms that can replicate serially as non rigid cells and produce colonies on solid media.
- *Protoplasts* are such forms usually derived from Gram +ve organisms. They are osmotically fragile.
- *Spheroplasts* are cell wall defective form usually derived from Gram –ve bacteria. They retain outer membrane.
- These L forms results from spontaneous mutation or by the effect of chemicals.
- Reversion of L-form to the parental bacterial form is enhanced by growth in the presence of 15-30% gelatin or 2-5% agar.

QUESTIONS

1. Atypical pneumonia can be caused by the following microbial agents except : [AI 05]

a) Mycoplasma
b) Legionella pneumophilia
c) Human corona virus
d) Kleibsella pneumoniae

2. All are features of Ureplasma urealyticum except:

a) Non gongococcal urethritis **[AI 01]**
b) Salpingitis
c) Epididymitis
d) Bacterial vaginosis

3. The following statements are true with references to Mycoplasma except : [AIIMS 05]

a) They are the smallest prokaryotic organisms that can grow in cell free culture media
b) They are obligate intracellular organisms
c) They lack a cell wall
d) They are resistant to Beta-lactam drugs

4. In reference to mycoplasmas, the following are true except : [AIIMS 05]

a) They are inhibited by penicillins
b) They can reproduce in cell free media
c) They have an affinity for mammlian cell membranes
d) They can pass through fiters of 450 nm pore size

5. The following is true about Mycoplasmas except:

a) Multiply by binary fission **[AIIMS 02, 96]**
b) Are sensitive to beta-lactam gourp of durgs
c) Can grow in cell free media
d) Require sterols for their growth

6. Mycoplasma pneumonia is characterised by all except : [AIIMS 98]

a) Diagnosed by serum cold antibody
b) Treatment is erythromycin
c) Can not be cultured from sputum
d) Raised ESR

7. True about mycoplasma is : [AIIMS 95]

a) Causes lung infection
b) Penicillin is drug of choice
c) Thick cell wall
d) Thallium acetate inhibits the growth

8. Diene's method is used for : [PGI 99, 95]

a) Mycoplasma
b) Chlamydiae
c) Plague
d) Diptheria

9. Cell wall deficient organisms are : [PGI 99]

a) Chlamydia
b) Mycoplasma
c) Streptococcus
d) Anaerobes

Answer

1. d) Kleibsella ...
2. b) Salpingitis
3. b) They are ...
4. b) They ...
5. a) They ...
6. b) Are ...
7. c) Can ...
8. a) Causes ...
9. a) Mycoplasma

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is d i.e. Kleibsella pneumoniae *Ref. Robbin's 7/e, p 751*

Atypical pneumonia is characterized by patchy inflammatory changes in the lung, largely confined to alveolar septa and pulmonary interstitium.

Causes of Atypical pneumonia :

- Mycoplasma ***(MC)***
- Legionella pneumonia
- Francisella tularensis
- Chlamydia psittacosis, chlamydia pneumoniae
- Viruses (influenzae A and B, RSV, Adeno, rhino, rubeola, varicella etc)
- Coxiella burnetti (Q fever)
- Pneumocystii carnii
- H. capsulatum
- Coccidiodis immitis.

Kleibsella is associated with community acquired pneumonia classically in **alcoholics** (also in diabetics and chronic lung disease). It usually affects **upper lobes** producing expansion of lobes (bulging fissure) and Red current jelly sputum.

Remember : Causes of community acquired pneumoniae in decreasing frequency ***Strep. pneumoniae > H. influenza > Chalmydia > Legionella.***

2. Ans. is b i.e Salpingitis *Ref. Harrison 17/e, p 1069; Ananthnarayan 7/e, p 398; CGDT 9/e, p 654*

Ureoplasma urealyticum are T form mycoplasmas which are urease postive.

It causes :

- Nongonococcal urethritis ***MC*** cause is Chalmydia trachomatis also caused by U. urealyticum and M. genitalium.
- Epididymitis **(no role of M. homins).**
- Chorioamnionitis
- Post partum fever
- Proctitis
- Reiter's syndrome
- Acute salpingitis
- Infertility in both men and women
- Late abortion
- Low birth weight infant
- Balanoposthitis
- Cervicitis and vaginitis

... Not given in Harrison and CGDT

- Pneumonia and chronic lung disease in VLBW infants
- PID and bacterial vaginosis : by M hominsis and U.urealyticum
- Bacterial vaginosis (Altered vaginal normal microbial flora) is associated with Gardenella and Hemophilus vaginitis, in which **clue cells** are present and **Amide test** is positive.

If 'none' is given as option than it is more appropriate than 'Salpingitis' as salpingitis is given in 'Ananthnarayan'.

3. Ans. is b i.e. They are obligate intracellular organisms *Ref. See below*

- Mycoplasma is not obligate intracellular bacteria.

- ***Obligate intracellular bacteria :*** – M.leprae
  – Chlamydia
  – Rickettsiaecae and coxiella burnetti
  – Pathogenic treponemes.
- Obligate intracellular bacteria can not grow in cell free media.

4. Ans. is a i.e They are inhibited by penicillins *Ref. Ananthnarayan 7/e, p 395 - 397*

- Mycoplasmas are devoid of cell walls *(but bound by soft trilaminar unit membrane of sterols)* and so they are **resistant to B. lactams (penicillin, cephalosporins, vancomycin, Bacitracin) and lysozmes that act on cell wall.**
- Due to lack of cell wall they are highly pleomorphic and pass through **bacterial filters** of 450 nm since size varies from 50-300 nm in diameter.
- Parasitic mycoplasma requires cholesterol or other sterols as an essential growth factor.
- They have affinity for mammalian cell membrane. *.....Jawertz 24/e, p 344*
- It typically colonizes mucosal surfaces of respiratory, GIT and genitourinary tracts.
- Mycoplasma occur as granules and filaments (shows **true branching).**
- They multiply by asynchronous binary fission producing budding forms and chains of beads.
- Some species get attached to suitable host cells carrying neuraminic acid receptors by bulbous enlargement.
- ***Mycoplasmas (and other organism) grows in cell free media.***
- **Media** of mycoplasma are **enriched with 20% horse** or **human serum** and **yeast extract**
  – Penicillin and thallium are **selective agents.**
  – Colonies is typically biphasic with a **fried egg appearance** and are best studied after staining by Dienes method.
  – Growth of mycoplasma is inhibited by specific antibody.

5. Ans. is b i.e. Are sensitive to beta-lactam gourp of durgs *Ref. Ananthnarayan 7/e, p 395 - 397*

Remember : Doxycycline is drug of choice for mycoplasma.

6. Ans. is c i.e. Can not be cultured from sputum *Ref. Ananthnarayan 7/e, p 398; Harrison 17/e, p 1068*

- Mycoplasma pneumoniae is ***MC*** cause of Atypical pneumonia which characterized by reticulonodular or interstitial infiltration of lower lobes on X-ray with paucity of signs on auscultation.

Diagnosis

- ***Specimen :***
  – Throat swabs, sputum or respiratory secretions.
- ***Microscopy :***
  – It cannot be detected on Gram's stain as it lack cell wall.
  – Gram's stain of sputum shows leucocytes without predominance of any bacteria morphologic type.
- ***Culture :***
  – It can be grown on artificial media but process is difficult as it requires special media and take more than 2 weeks so culture do not provide timely information.

- ***Serology :***
  a. *Specific* : Antibodies are detected by enzyme linked immunoassys, indirect immunofluorescence, or complement fixation test.
  b. *Nonspecific* : Cold agglutinin aids in diagnosis since develops within 7-10 days of infection and can be easily detected.
     – They are IgM autoantibodies which agglutinate human erythorcytes at 4^0C.
     – Cold agglutinin titre > 1:32 supports diagnosis of M. pneumoiae.
     – It can also performed at the bedside.

- ***Antigen Detection test :***
  Include antigen capture, indirect enzyme immunoassays, DNA probing and Multiplex Nucleic acid amplification test.

Treatment

Ambulatory patients with community acquired pneumonia	Hospitalized patients with community acquired pneumonia
• Oral Doxycycline • Oral erythromycin • Oral clarithromycin, azithromycin; levo, Gati, Moxifloxacin	• IV ceftriaxone or IV cefotaxime

7. Ans. is a i.e. Causes lung infection *Ref. Ananthnarayan 7/e, p 395*

Remember : Media for cultivating mycoplasma are enriched with 20% horse or human serum and yeast extract. Penicillin and thallium acetate are added as selective agent.

8. Ans. is a i.e. Mycoplasma *Ref. Ananthnarayan 7/e, p 396*

- Colonies of mycoplasma are typically biphasic, with a fried egg appearance.
- Colonies are best studied after staining by Dienes method :
  – Dienes method : A block of agar containing the colony is cut and placed on slide.
  – It is covered with a coverslip on which has been dried an alcoholic solution of methylene blue and azur.
- Colonies can't be picked by platinum loops.
- Most mycoplasma colonies are hemolytic.

9. Ans. is b i.e. Mycoplasma *Ref. Ananthnaryan 7/e, p 12 - 13, 395 - 399*

Cell wall deficient forms :

a. ***L. forms*** (mycoplasma is stable L form).
b. ***Protoplasts*** (by action of lysozyme on Gram positive bacteria).
c. ***Spheroplasts*** (by action of lysozyme on Gram negative bacteria).
   – Some cell wall material is retained in spheroplast as compared to protoplast.
   – Role of cell wall deficient forms of bacteria is persistence of chronic infections such as pyeloephritis and recurrence of infection.
   – They do not initiate the infection.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. True about Mycoplasma : [UP 97]

a) CO_2 is important for growth
b) Does not cause hemolysis
c) May be commensal in throat
d) Acid fast bacillus

[Ref. Ananthnarayan 7/e, p 600]

2. True about mcyoplasmas is : [MP 98]

a) Not sensitive to antibiotics
b) L. Form is commonest
c) Culture in sarbaroudz media
d) Most common cause of nongonococcal urethritis

[Ref. Ananthnarayan 7/e, p 399]

Answer 1. c) May be comm ... 2. b) L. Form is comm ...

UNIT – II VIROLOGY

1.	**DNA Virus** Herpes virus, Adeno & Pox, Parvo & Papovo	263 – 284
2.	**RNA Virus** Picorna virus, Myxo virus, Rota & other viral gastroenteritis, Arbo, Rhabdoviruses	285 – 319
3.	Slow Virus Diseases	320 – 325
4.	Hepatitis Viruses	326 – 343
5.	HIV & Other Retroviruses	344 – 366

DNA Virus

HERPES VIRUSES

- ***Enveloped*** virus with linear double stranded genome.
- Characterised by their ability to produce latent infection.
- Replicate in host cell ***nucleus*** forming **cowdry type A intranuclear** *(Lipshutz)* inclusion bodies.

Classification of human herpes viruses

Species				
Official name	**Common name**	**Subfamily**	**Cytopathology**	**Site of latent infection**
Human herpesvirus type 1	Herpes simplex virus type 1	alpha	cytolytic	neurons / gasserian or trigeminal ganglia
Human herpesvirus type 2	Herpes simplex virus type 2	alpha	cytolytic	neurons / sacral ganglia
Human herpesvirus type 3	Varicella zoster virus	alpha	cytolytic	neurons / T3 - L3 (***MC***)
Human herpesvirus type 4	Epstein–Barr virus	gamma	lymphoproliferative	lymphoid tissue (B cells)
Human herpesvirus type 5	Cytomegalovirus	beta	cytomegalic	secretory glands Kidneys, (salivary glands and bowel)
Human herpesvirus type 6	Human B cell lymphotropic virus	beta	lymphoproliferative	lymphoid tissues
Human herpesvirus type 7	R K virus	beta	lymphoproliferative	lymphoid tissues
Human herpesvirus type 8		gamma		

- **HH V – 6** cause exanthem subitum / *roseola infantum* or ***sixth disease.***
- Different Herpes virus species don't show any antigenic cross reaction except Herpes simplex type 1 and 2.
- HHV-8 is associated with AIDS / Non AIDS **Kaposi sarcoma.**

HERPES SIMPLEX VIRUS (HSV)

HSV Type 1	HSV Type 2
• Cause lesion in and around mouth	Cause lesion around genital area
• Transmitted by direct contact or droplet spread	Usually transmitted sexually
• Replicate poorly in chick embryofibroblast cell	Replicate well
• Relatively sensitive to antiviral agents	Resistant
• Less neurovirulent	More neurovirulent
• Infectivity is less temperature sensitive	More temperature sensitive

Pathogenesis

- Humans are only natural host.
- ***Source of infection*** Saliva, skin lesion or respiratory secretion.
- On exposure mucosal surfaces or abraded skin permits entry of virus and initiates its replication in epidermis and dermis.
- On entry into neuronal cells the virus is transported intra-axonally (centripetally) to nerve cell bodies in ganglia.
- During initial phase of infection virus replication occur in ganglia, virus then spread to other mucosal surfaces through centrifugal migration of infectious virions via peripheral sensory nerves.
- ***Both*** antibody mediated and cell mediated immunity are important.
- ***CD8 + T cell*** responses are critical for clearance of virus from lesion.

Clinical Features

- **Orofacial infection :**
  - Gingivitis and pharyngitis are most frequent clinical manifestation of first episode of HSV - 1 infection **(primary infection).**
  - Recurrent herpes ***labialis*** is ***MC*** manifestation of ***reactivation*** (occur by stress stimulus).
  - ***Erythema multiforme may*** be associated with HSV infection.
  - HSV -1, Varicella zoster virus (VZV) may cause Bell's palsy.
- **Genital infection (HSV-2) :**
  - Widely placed bilateral lesion (vesicles, pustules, or ***painful*** erythematous ulcer) are characterstic of primary infection.
  - ***Cervix*** and ***urethra*** are most commonly involved **in** women with primary infection.
  - Primary infection in patient who has prior HSV - 1 infection are associated with ***less*** frequent systemic manifestation and faster healing of lesion.
  - A clear mucoid discharge and dysuria are characterstic of symptomatic HSV urethritis.
- **Herpetic Whitlow**
  - HSV infection of finger may occur as a complication of primary oral or genital herpes by inoculation of virus through abraded skin. *Seen in Doctors, dentists.*
- **Eczema Herpeticum**
  - Generalized eruption caused by Herpes infection in children suffering form eczema.
- **Herpes Gladiatorum**
  - Mucocutaneous HSV infection of thorax, ears, face and hands.
  - Seen in wrestlers due to recurrent trauma.

- **Central and Peripheral nervous system manifestation**

  A. Encephalitis – HSV -1 is ***MC*** cause of ***sporadic encephalitis.***

  – Present as acute onset of fever, focal neurologic signs especially of ***temporal lobe.***

  – ***Most sensitive* non invasive** method for early diagnosis of HSV encephalitis is demonstration of HSV DNA in CSF by PCR (Investigation of choice).

  • Demonstration in brain tissue by biopsy is over all most sensitive but ***invasive*** method.

  B. Meningitis

  • HSV is ***MC*** cause of recurrent Lymphocytic meningitis ***(Mollaret's meningitis).***

  • Diagnosed by demonstration of HSV DNA or HSV antibodies in CSF.

- **Visceral infection**

  – **Oesophagitis *MC*** site is **distal oesophagus.**

  – Endoscopically obtained secretion for cytology and culture provide most useful material for diagnosis.

  – Pneumonia in Immuno compromised.

  – Hepatitis – may lead to disseminated intravascular coagulation.

- **Neonatal HSV infection**

  – Infection is usually acquired perinatally *at the time of delivery.*

  – Of all age group, neonates have highest frequency of visceral or CNS infection.

Diagnosis

- Both clinical and Laboratory.
- Scrapings from base of characteristic lesion is taken and stained with Wright's, Giemsa (Tzanck Preparations) to detect giant cell or intranuclear inclusions. Sensitivity is low and this can't differentiate between VZV and HSV.
- HSV infection is best confirmed (specific test) by ***isolation*** of virus in tissue culture.
- ***PCR*** for detection of HSV DNA is most sensitive. *..... Harrison 17/e, p 1100*

Treatment

Acyclovir is most frequently used drug.

VARICELLA - ZOSTER

Causative agents of :

- *Varicella* = Chicken pox (Primary infection)
- *Herpes zoster* = Shingles (Reactivation of latent infection).

Pathogenesis

- Humans are ***only*** known reservoir of VZV.
- **Primary infection** *(Chicken pox)* – Transmitted by respiratory route.
- **Recurrent infection** – (Herpes zoster)- During primary infection virus infect dorsal root ganglia, where it remains latent. When immunity wanes, virus reactivates and travel along sensory nerve to produce zoster lesion on mucosa, or skin supplied by it.

Clinical manifestation

I. Chicken pox – Highly contagious disease (secondary attack rate 90%) affecting 5-9 year children *most commonly.*

- **I.P** – 10 to 21 days
- Patient **is infectious** *48 hours prior to onset of vesicular rash to until all vesicles are crusted.*
- Skin lesions – The hall mark of infection includes maculopapules, vesicles and scabs *in various stage of evolution.*
- Immunocompromised have severe (often hemorrhagic) and long lasting lesion with higher rate of visceral complication and fatality.

- The ***MC*** **site of extracutaneous** involvement in children **is CNS.**
- *Visceral pneumonia is the most serious complication* occuring mostly in adults.
- **Perinatal varicella** is associated with high mortality when maternal disease develop **with in 5 days before delivery or** within 48 hrs **thereafter.**

II. Herpes zoster (Shingles)

- Reactivation of latent infection.
- Age group – 60 and beyond.
- Characterized by ***unilateral*** lesion within a dermatome associated with severe pain. The dermatome from T3 to L3 is most frequently affected.
- Patient with herpes zoster can transmit infection to seronegative individual which will develop chickenpox.
- **Zoster Opthalmicus** – Due to *reactivation* in ophthalmic branch of *trigeminal (gasserian) ganglia.*
- **Ramsay Hunt syndrome** – Due to *reactivation in geniculate ganglion of facial nerve.*
- Most debiliating complication of Shingles is pain associated with acute neuritis and post herpetic neuralgia.
- Patient with Hodgkin's disease and NHL are at greatest risk for progressive Herpes zoster.

Lab diagnosis

- Isolation of VZV from vesicles in tissue culture cell lines or detection of DNA by PCR.
- Serology : Most frequently used are :
  - FAMA (fluoroscent antibody to membrane antigen) test
  - ELISA
  - Immuno adherant hemagglutination.

FAMA test and ELISA are most sensitive.

Treatment

- No antiviral for immunocompetent child.
- *Aspirin should be* **avoided** during episode of chicken pox as it *increase risk of development of Reye's syndrome.*
- **Acylovir** therapy is recomonded for adolescent and adults with chicken pox of < 24 hours duration.
- Herpes zoster – Famciclovir and valacyclovir are more effective than acyclovir.
- **Post herpetic neuralgia** and acute neuritis :
  - Analgesics
  - Gabapentin
  - Amitryptyline
  - Lidocaine patch
  - Glucocorticoid (with concomitent antiviral therapy).
- In immunocompromised patient IV acyclovir should be given.

CMV = SALIVARY GLAND VIRUS

- Characterised by enlargement of infected cell and prominent intranuclear inclusion (Owl's eye appearance).
- ***Largest virus*** of herpes family.
- ***MC*** organism causing intrauterine infection.
- ***MC*** pathogen complicating organ transplantation.

Pathogenesis

- Transmitted by sexual route, transplacental, blood transfusion, organ transplant.
- Once infected, individual carry CMV for whole life.
- Infection usually remains latent, reactivation may occur when cell mediated immunity is compromised.

Clinical feature

I. Congenital infection

- Petechiae, Hepatosplenomegaly, Jaundice are ***MC*** manifestation.
- Intracerebral calcificatiion (usually periventricular) and chorioretinitis, deafness are other important findings.

II. Perinatal infection

- Infection acquire through birth canal at the time of delivery or through breast milk.
- Mostly asymptomatic.
- Interstitial pneumonia in preterm infant.

III. Beyond neonatal period immunocompetant host

- *Heterophile antibody (-)ve infectious mononucleosis is **MC** manifestation.*

IV. Immunocompromised host

a. *Organ transplant patient :* – Period of maximal risk of infection – *Between 1 and 4 month after transplantation.*
– Retinitis is late complication.
– Transplanted organ is particulary vulnerable as a target for CMV infection eg. CMV hepatitis in liver transplant holder.

b. *AIDS patient :* – Cause retinitis *(cottage and cheese appearance / pizza pie retinopathy)* or disseminated disease particulary when CD4 + < 50 - 100 / µl.

Diagnosis

- ***Most sensitive*** method to detect CMV in blood is **PCR.**
- Congenital infection is diagnosed by culture *(best specimen saliva and urine);* PCR.

Treatment

- Ganciclovir or Valganciclovir is ***DOC.***

EPSTEIN - BARR VIRUS

- **Causative agent of Heterophile (+)ve infectious mononucleosis** *(Kissing disease) = Glandular fever.*
- **Associated with :** – Nasopharyngeal Ca
  – Burkitt's lymphoma
  – Hodgkin's disease (mixed cellularity type)
  – B cell lymphoma in patients with immunoficiency
  – CNS lymphoma in AIDS patient
  – Increase risk of Thymoma, tonsillar and gastric carcinoma.

Pathogenesis

- Source of infection is usually salivary secretions so ***kissing*** is predominate mode of transmission.
- The virus infect epithelium of oropharynx and the salivary gland; tonsillar crypts can also be infected directly. Virus then spreads through the blood stream.
- EBV receptor CD21 present on B cell is also receptor for CD3 component of complement; **So EBV infection immortalise B cell.**
- *Memory B cell are* reservoir *of EBV in body.*
- Cellular immunity is more important than humoral immunity in controlling EBV infection.
- If *T cell immunity decreased, infected B cells begins to proliferate hence producing lymphoma.*

Clinical features

- Most EBV infection in infant and young children are asymptomatic.
- In adolescent, most infection present as **infectious mononucleosis.**
  - IP : 4-8 weeks
  - ***MC*** **symptom** sore throat
  - ***MC*** **sign** - Lymphadenopathy (*mostly of posterior cervical nodes*)
  - Erythema nodosum, Erythema multiforme may also occur.

Diagnosis

- Increase TLC; Lymphocytosis with **> 10%** atypical lymphocytes.
  - Atypical lymphocyte are ***mainly CD8 + cells*** which have undergone blast transformation.
- Neutropenia
- Thrombocytopenia
- Serological testing
  - Heterophile test ***(Paul Bunnel test)*** is used for diagnosis of IM in children and adults.
  - EBV specific antibody test : ***IgM antibody to VCA*** is most useful for diagnosis of IM.

Complication

- Most cases are self limited.
- ***Most death*** which occur very rarely are due to ***CNS complications.***
- Coombs (+)ve autoimmune hemolytic ***anemia.***
- Acute EBV may be associated with ***Gullen Baire syndrome, CNpalsy*** **(*MC* - facial nerve).**

Other disease associated with EBV

- Fatal **lymphoproliferative disorder of** Duncan's disease.
- ***Oral hairy leukoplakia*** is an early manifestation of EBV infection in AIDS patient.
- ***Chronic fatigue syndrome.***

POX VIRUS

Largest pathogenic virus of vertebrates

Important pox virus are :
- Variola *(causative agent of small pox)*
- Vaccinia *(Artificial virus which was used as small pox vaccine)*
- Molluscum contagiousum.

Variola

- ***Brick shaped*** virion
- Elementary bodies are called paschen bodies.

Vaccinia

- It is an artificial virus whose genome can accomodate about 25000 foreign base pairs.
- But it is not suitable as a vector for human use due to its pathogenic effects.
- Properties are similar to variola.

Small pox

- On 8th May 1980 WHO anounced Global eradication of small pox.
- In India last case was found in 1975.
  - *Disease had been eradicated, so clinical features etc are not going to be asked.*

Cultivation of Pox virus

- Both Variola and Vaccinia grow on **CAM** producing pocks.
  - Variola pocks are small, shiny, white convex, non necrotic, non hemmorhagic lesions with ***ceiling temperature*** *(highest temperature above which pocks are not produced) of* ***38⁰ C.***
  - Vaccinia pocks are larger, irregular, flat, greyish, hemorrhagic and Necrotic with *ceiling temperature of* ***41⁰ C.***
- **On tissue culture**
  - Cytopathic effect are produced by Vaccinia in 24 - 48 hours and more slowly by Variola.
  - ***Inclusion bodies*** called **Guarnieri bodies** can be seen.

Molluscum Contagiosum

- Usually seen in children and young adults.
- Characterised by ***pink or pearly white nodules*** on skin which show large ***inclusion bodies*** called ***Molluscum bodies.***
- Virus ***can not be grown in*** eggs, tissues culture or animals.

ADENOVIRUS

- Space vehicle (Hexagonal shape) shaped, non enveloped virus containing ds DNA.
- They have capacity to carry DNA upto 7 kb **so, are potential vectors of gene therapy.**

Classification

- There are about 50 serotype which are pathogenic to humans. *..... Ananthnarayan, p 486*
- Human adenovirus have been divided into 6 subgenera on the basis of DNA homology.

Clinical manifestation – *MC* is upper respiratory tract infection

Syndrome	Principal serotype
Respiratory disease in children	1, 2, 5, 6
Sore throat, febrile cold, pneumonia	3, 4, 7, 14, 21
ARD in military recruits	4, 7, 21
Follicular (swimming pool) conjunctivis	3, 7
Epidemic keratoconjunctivitis (shipyard eye)	8, 19, 37
Diarrhea (by enteric type adeno)	40, 41
Hemorrhagic cystitis	11, 21
Generalized exanthem, Mesenteric adentitis and intussusception	

Lab diagnosis

- Isolation of virus from throat, eye, urine or feces.
- It grow only in tissue cultures of human origin eg. human embryonic kidney, HeLA or HEP-3.
- All mammalian adenovirus share a common complement fixing antigen which is detected by immunofluorescence or ELISA.

Adeno Associated virus – (Dependovirus)

- These are virus which can multiply only in cells infected with adenovirus as they lack enough DNA.
- It is classified under family parvoviridae.

PARVO VIRUS

- Non enveloped ***SS DNA*** virus
- Most parvo virus are pathogenic to Animals. Human pathogen is **B-19,** the causative agent of **fifth disease.**

Pathogenesis and Clinical Manifestation

- Most of the severe manifestation of B19 viremia are due *to its ability to lyse erythroid precursor.*
- **Erythema Infectosum (fifth disease)**
  - ***MC*** manifestation of B19 infection.
  - Child present with facial rash *(slapped cheek appearance)* which is preceded by low grade fever.
- **Arthropathy** – In *adults* B-19 infection *most commonly* present *as acute arthralgia* and arthritis which is symmetrical and *involves wrist most often.*
- **Transient aplastic crisis**
  - B-19 infection is *the* ***MC*** **cause of** ***transient aplastic crisis*** ***in patient*** with chronic hemolytic disease.
  - Unlike patient with erythema infectosum or arthropathy, these patient can readily transmit B-19 infection to other people.
- **Immunodeficient patient**
  - ***MC*** manifestation is chronic anemia.
- Fetal and congenital infection
  - Maternal B-19 infection usually do not adversely affect fetus but can rarely cause non immuno hydrops fetalis if infection occur in first 20 weeks of pregnancy.

Diagnosis

- Most commonly relies on B-19 specific IgM and IgG antibodies.

PAPOVA VIRUS

- Nonenveloped, Icosahedral DNA, tumor viruses
- Family contains 2 genera :
  1. ***Polyoma virus*** – which contains SV 40, polyoma viruses.
  2. ***Papillomavirus*** – which contain human and animal papilloma virus.

HUMAN PAPILLOMA VIRUS (HPV)

- HPV ***selectively infect*** the epithelium of skin and mucous membrane and may immortalize the keratinocyte leading either asymptomatic infection or warts or neoplasia.
- Genome consist of :
  - Early (E) region
  - Late (L) region
  - Upstream regulatory region (URR).
- Product of E genes **(E6; E7)** are related to immortalization or malignant transformation of keratinocytes by interfering with **P53, Rb gene** respectively.
- HPV ***infect only*** human skin and ***grows only*** in organ cultures of human skin.

Clinical features

- Replication of HPV begins with the infection of ***basal cells.***
- ***Koilocytes*** appear in granular cells.
- ***It causes :***
  - Common Warts (verruca vulgaris) – Type 1, 2, 3, 4
  - Condyloma accuminata (anogenital warts) – Type 6, 11
  - Cervical intraepithelial neoplasia – Type 6, 11 (low risk)
  - Cervical cancer – 16,18,31, 33, 45 (high risk type)
  - Plantar warts (verruca plantaris)
  - Respiratory papillomatosis
  - Flat warts (verruca plana) – ***MC*** among children
  - Also associated with Sq cell carcinoma and dysplasia of penis, anus, vagina and vulva; epidermodysplasia verruciformis (type 5, 8).

Diagnosis

- The ***most sensitive*** and ***specific*** method of diagnosis is PCR or hybrid capture assay to detect HPV nucleic acids and to identify specific virus type.

Treatment

- ***Cryosurgery*** is initial *treatment of choice* for condyloma accuminatum.
- Topically – Podophyllum, podofilox
  - Interferon (IFN)
  - IFN inducer imiquimod.

QUESTIONS

1. The following diseases are associated with Epstein - Barr virus infection, except : [AI 06]
a) Infectious mononucleosis
b) Epidermodysplasia veruciformis
c) Nasopharyngeal carcinoma
d) Oral Hairy leukoplakia

2. Epstein Barr (EB) virus has been implicated in the following malignancies except : [AI 04]
a) Hodgkin's disease
b) Non-hodgkin's lymphoma
c) Nasopharyngeal carcinoma
d) Multiple myeloma

3. Epstien Barr virus causes all the following except:
a) Infectious mononucleosis **[AI 02; AIIMS 99]**
b) Measles
c) Nasopharyngeal carcinoma
d) Non Hodgkins lymphoma

4. Infectivity of chicken pox last for :
a) Till the last scab falls off **[AI 02, AIIMS 00]**
b) 6 days after onset of rash
c) 3 days after onset of rash
d) Till the fever subsides

5. Virus causing hemorrhagic cystitis, diarrhea and conjunctivitis is : [AI 01]
a) RSV
b) Rhinovirus
c) Adenovirus
d) Rotavirus

6. A patient with sore throat has a positive Paul Bunnel test. The causative organism is : [AI 00]
a) EBV
b) Herpes virus
c) Adeno virus
d) Cytomegalovirus

7. Herpes - zoster is caused by : [AI 99]
a) Herpes-simplex type I
b) Herpes-simplex type II
c) Epstein-barr virus
d) Varicella

8. Viral enterotoxin is detected as a possible mechanism of pathogenesis in : [AI 98]
a) Adeno virus
b) Rota virus
c) Calcivirus
d) Astrovirus

9. All of the following are true about Herpes group virus excpt : [AI 98]
a) Ether-sensitive
b) May cause malignancy
c) HSV II involves below diaphragm
d) Burkitt's lymphoma involves T-cells

10. Varicella are classified under : [AI 96]
a) Enterovirus
b) Retrovirus
c) Poxvirus
d) Herpes virus

11. EB virus belongs to which group : [AI 95]
a) Retrovirus
b) Herpes virus
c) RNA virus
d) Pox virus

12. All of the following are true about the papovavirus except : [AI 95]
a) They are non-enveloped icosahedral viruses
b) Produce papilloma
c) RNA virus
d) SV-40 is oncogenic

13. Which of the following does not establish a diagnosis of congenital CMV infection in a neonate? [AI 95]
a) Urine culture of CMV
b) IgG CMV antibodies in blood
c) Intra-nuclear inclusion bodies in hepatocytes
d) CMV viral DNA in blood by polymerase chain reaction

14. Parvovirus B19 does not cause : [AIIMS 08]
a. Roseola infantum
b. Aplastic anemia in sickle cell
c. Fetal hydrops
d. Collapsing FSGS

15. Epstein Barr virus is associated with :[AIIMS 04]
a) Carcinoma larynx
b) Carcinoma bladder
c) Carcinoma nasopharynx
d) Carcinoma maxilla

16. All of the following statement are true regarding CNS infection except : [AIIMS 04]
a) Measles virus is causative agent of subacute sclerosing panecephalitis
b) Cytomegalo virus cause bilateral temporal lobe hemorrhagic infarction
c) Prion infection cause spongiform encephalopathy
d) JC virus is causative agent of progressive multifocal leucoencephalopathy

Answer

1. b) Epidermodyspl ...	2. d) Multiple ...	3. b) Measles	4. b) 6 days ...	5. c) Adenovirus...
6. a) EBV	7. d) Varicella	8. b) Rota ...	9. d) Burkitt's ...	10. d) Herpes ...
11. b) Herpes ...	12. c) RNA ...	13. b) IgG ...	14. a) Roseola ...	15. c) Carcinoma ...
16. b) Cytomegalo				

17. The most common cause of sporadic viral encephalitis is : **[AIIMS 04]**
a) Japnese B encephalitis
b) Herpes simplex encephalitis
c) HIV encephalitis
d) Rubeola encephalitis

18. A 40 year old man underwent kidney transplantation. Two month after transplantation, he developed fever and feature suggestive of bilateral diffuse interstitial pneumonia. Which of the following is most likely etiologic agent :
a) Herpes simplex virus **[AIIMS 03]**
b) Cytomegalovirus
c) Epstein-barr virus
d) Varicella - zoster virus

19. A neonate develops encephalitis without any skin lesions most probable causative organism is :
a) HSV I **[AIIMS 02]**
b) HSV II
c) Meningococci
d) Streptococci

20. A patient has undergone a renal transplantation 2 months back and now presented with difficult breathing. X-ray showed bilateral diffuse interstitial pneumonia. The Probable etiologic agent would be : **[AIIMS 02]**
a) CMV
b) Histoplasma
c) Candida
d) Pneumocystic carinii

21. Encephalitis is caused by : **[AIIMS 98]**
a) HSV-I
b) EBV
c) Infectious mononucleosis
d) CMV

22. Parvo virus causes : **[PGI 07]**
a. Aplastic anemia
b. Erythema infectiosum
c. Roseola infantum
d. Arthritis

23. In parvovirus infection what is common in adult :
a. Bone marrow **[PGI 07]**
b. PRCA
c. Erythema infectiosum
d. Arthropathy

24. Which of the following pair is correct ? **[PGI 05]**
a) RSV – Brochiolitis
b) HHV5 – Infectious mononucleosis
c) Parvovirus Exanthem subitum
d) HHV - 6 - Kaposi sarcoma
e) VZV – Chicken pox

25. Which of the following statement is correct :
a) Viral warts usually resolve spontaneously
b) Plantar warts should not be excised **[PGI 05]**
c) Callosity are formed occupationally
d) Corn's are viral in etiology
e) Plantar warts are painless

26. Renal involvement is seen in which of the following infections : **[PGI 03]**
a) Cytomegalovirus
b) Polyoma virus
c) Human papilloma virus
d) HIV
e) HBV

27. EBV associated with : **[PGI 03]**
a) Ca tonsil
b) Nasopharyngeal Ca
c) Anal Ca
d) Infectious mononucleosis

28. True about Herpes Virus : **[PGI 03]**
a) HSV encephalopathy is treated with acyclovir
b) Oropharyngeal involvement is common in HSV-1
c) Recurrent genital involvement is seen in HSV-2
d) Recurrence is rare in HSV-1

29. Disease caused by Epstein Barr virus are :
a) Infectious mononucleosis **[PGI 02; 01]**
b) Burkitt's lymphoma
c) Kaposi sarcoma
d) Nasopharyngeal Ca
e) Herpangina

30. Regarding HSV-2 infection True is / are : **[PGI 02]**
a) Primary infection is usually widespread
b) Recurrent attacks are due to reactivation of latent infection
c) Encephalitis can be caused by HSV-2
d) Newborn may acquire infection via the birth canal at the time of labour
e) Treatment is with acylovir

31. Vaccine preparation requires which virus as vector: **[PGI 01]**
a) Rhinovirus
b) Vaccinia
c) Adenovirus
d) Ebola
e) Hepatitis B

32. EBV does not cause : **[PGI 98]**
a) Nasopharyngeal Ca
b) Inverted papilloma
c) Burkitt's lymphoma
d) Infectious mononucleosis

33. Immunocompromised patient due to transplantation is suffering from pyrexia and neutropenia. Most likely cause is : **[PGI 97]**
a) HSV
b) CMV
c) Gram '-' ve organism
d) Gram '+' ve organism

Answer

17. b) Herpes ...	18. b) Cytomega ...	19. b) HSV II	20. a) CMV	21. a) HSV-I
22. a, b and d	23. d) Arthropathy	24. a, b and e	25. a, b and c	26. a, d and e
27. a, b and d	28. a, b and c	29. a, b and d	30. a, b, c, d and e	31. b) Vaccinia
32. b) Inverted ...	33. b) CMV			

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b i.e. Epidermodyplasia verruciformis *Ref. Harrison 17/e, p 1107-1108*

Epidermodyplasia verruciformis is a rare inherited disease with numerous flat warts on the hand and feet. These individuals have defect in cell mediated immunity and increased susceptibility to human papilloma virus infection.

Disease caused by EBV	
Neoplastic	**Non Neoplastic**
– Burkitts lymphoma – Postorgan transplant lymphoma – Primary CNS diffuse large B cell lymphoma (type of NHL) – Hodgkins disease (particularly mixed cellularity type) – Nasopharyngeal Ca – T-cell lymphoma – Gastric Ca, Tonsilliar Ca } In some cases	– Infectious mononucleosis - ***MC*** cause of infectious mononucleosis is EBV. – Oral Hairy leukoplakia - White corrugated lesion on tongue in HIV patient (early stage). – Chronic fatigue syndrome.

Remember : ***Multiple Myeloma is associated with Human herpes virus 8*** in some cases not with EBV.

2. Ans. is d i.e. Multiple Myeloma *Ref. Harrison 17/e, p 1107-1108*

Already explained, refer answer no. 1

3. Ans. is b i.e. Measles *Ref. Harrison 17/e, p 1107-1108*

Already explained, refer answer no. 1

4. Ans. is b i.e. 6 days after rash *Ref. Park 18/e, p 123; 19/e, p 125*

"Period of communicability of varicella range from 1 to 2 days before the appreance of rash, and 4 to 5 days there after." *..... Park 18/e, p 123*

The patient ceases to be infectious once the lesions have crusted.

Scabs are not infective

So, ***option "a"*** is wrong.

Important features of chicken pox

Causative Agent - Varicella zoster virus (HHV type 3)
Incubation period - 14 to 16 days
Secondary attack rate - 90%
Rash

	Chicken pox	Small pox
–	Superficial	Deep seated
–	Pleomorphic	Only one stage of rash at 1 time
–	Centripetal	Centrifugal
–	Unilocular	Multilocular
–	Dew drop like appearance	Umblicated
–	Inflammation (+)nt	No area of inflammation around vesicle
–	Mostly flexor surface	Mostly extensor surface

5. Ans. is c i.e. Adenovirus *Ref. Ananthnarayan 7/e, p 488*

Disease caused by Adenovirus	
Disease	**Principal Serotype**
• Respiratory disease in children	1, 2, 5, 6
• Acute respiratory disease in military recruits (***MC*** presentation in adult)	4, 7, 21
• Epidemic keratoconjuctivitis (Shipyard eye)	8, 19, 37
• Diarrhoea	40, 41
• Pharyngoconjunctival fever	3, 7

6. Ans. is a i.e. EBV *Ref. Ananthnarayan 7/e, p 484*

- Paul Bunell test is the *standard diagnostic procedure* of infectious mononucleosis which is caused by EBV.
- Paul Bunell test detects heterophile antibody.

Paul Bunell test

- In this test inactivated serum (56^0 C for 30 minutes) in doubling dilutions is mixed with equal volumes of a 1% suspension of sheep erythrocytes.
- An agglutination titre of 100 or above is suggestive of infectious mononucleosis.
- For confirmation, differential absorption of agglutinins with guineapig kidney and ox red cells is necessary
- The Paul Bunell antibody develops early during the course of infectious mononucleosis, and disappears within two months.
- ***False positive :*** In patient with lymphoma hepatitis, malaria connective tissue disease

Remember :
– ***MC*** *cause* of ***heterophile antibody (+)ve*** infectious mononucleosis is **EBV.**
– ***MC*** cause of ***heterophile antibody (–) ve*** infectious mononucleosis is **CMV.**
– Heterophile (–) ve IM also caused by toxoplasmosis, Listeria, non-infectious stimuli.

7. Ans. is d i.e. Varicella *Ref. Ananthnaryan 7/e, p 480*

"Herpes zoster is reactivation of latent chicken pox virus (varicella zoster virus) from the dorsal root ganglia."

Characteristic features of Herpes zoster

– Unilateral vesicular eruption within a dermatome often associated with severe pain. The dermatome from ***T3*** *to* ***L3*** *are most frequently* involved.
– *Ramsay hunt syndrome* : Rare form of herpes zoster affecting the facial nerve with eruption on tympanic membrane and external auditary canal with ipsilateral facial palsy.
– ***Most debiliating complication*** of herpes zoster in both the normal and immunocompromised host is pain.

8. Ans. is b i.e. Rotavirus *Ref. Harrison 17/e, p 1207*

Mechanism of Rotavirus diarrhea :

a. Rotavirus destroy mature enterocytes of proximal small intestine.
   - Loss of absorptive villi and proliferation of secretory crypt cells
     – *Secretory diarrhea*
   - Brush border enzymes are reduced so unmetabolized disaccharides accumulates resulting.
     – *Osmotic diarrhea*

b. **NSP_4 =** enterotoxin which alteres epithelial cell function and permeability causing secretory diarrhea.

c. Virus evoke fluid secretion by the activation of enteric nervous system in intestinal wall.

9. Ans. is d i.e. Burkitt's lymphoma involves T cells *Ref. Ananthnarayan 7/e, p 474; Robbin's 7/e, p 671*

Burkitt's lymphoma = ALL L3.

- ALL are tumors of relatively mature ***B cells.***

Feature of Herpes Virus

– Enveloped Ds DNA virus, nucleocapsid is icosahedral.
– As enveloped so are susceptible to fat solvent like ether, alcohol, bile salts.
– Replicate in nucleus, forming **cowdry type A** intranuclelar (lipschutz) inclusion bodies.
– Some herpes virus have been implicated with malignancies.
– ***EBV*** - *Mentioned in ans. 2*
– ***HSV - 2*** - Carcinoma cervix
– ***HHV-8*** - Kaposi sarcoma, Multiple myeloma.

10. Ans. is d i.e. Herpes virus *Ref. Ananthnarayan 7/e, p 475*

Members of Human Herpes (HHV) family

Features	Common name	Disease
HHV-1	Herpes simplex virus type 1	Herpes (usually above the waist)
HHV-2	Herpes simplex virus type 2	Herpes (usually genital)
HHV-3	Varicella zoster virus	Chicken pox / Herpes zoster
HHV-4	Epstein-Barr virus	Infectious mononucleosis and tumors
HHV-5	CMV	Heterophile antibody (–)ve infectious mononucleosis
HHV-6	Human B-cell lymphotrophic virus	Exanthum subitum (roseola infantum or sixth disease)
HHV-7	RK virus	No disease yet found
HHV-8		Kaposi sarcoma; multiple myeloma

11. Ans. is b i.e. Herpes virus *Ref. Ananthnarayan 7/e, p 475*

Already explained, refer see answer no. 10

12. Ans. is c i.e. RNA virus *Ref. Ananthnaryan 7/,e p 562*

Papova virus are non enveloped; Icosahedral human virus containing **Ds DNA** as genetic material.

Family Papova virus contain 2 generas :

1. ***Papilloma virus*** – Contain humans and animal papilloma virus
2. ***Polyoma virus*** – Contain SV-40 polyoma viruses

Other papova virus are :

- JC virus – Isolated from patient of Hodgkin's disease and progressive multifocal leucoencephalopathy.
- BK virus – Isolated from urine of patient with kidney transplant.
- SV 40 – Produce malignant tumors when inoculated into new born mice or hamsters.

13. Ans. is b i.e. IgG CMV antibodies in blood *Ref. Nelson 17/e, p 1068*

"IgG antibody test is of little diagnostic value as positive results also reflects maternal antibodies" although its absence exclude the diagnosis of congenital CMV infection. *..... Nelson*

Diagnosis of congenital CMV infection

- **Virus isolation**
  - Definitive and best method.
  - Culture : Urine and saliva are best specimen for culture although it can be isolated from buffy coat (blood), bronchoalveolar washing.
  - PCR
- **Antibody assay**
  - IgG test are not diagnostic as positive results reflects maternal antibodies.
  - IgM test lacks sensitivity and specificity and are unreliable for diagnosis of congenital infection.
- **Detection in amniotic fluid**
  - Fetal infection can be confirmed by viral isolation from amniotic fluid.
  - Detection of viral genome by PCR in amniotic fluid is equally sensitive (Viral genome > 10^5 genome is a predictor of symptomatic congenital infection).

Remember : CMV infected cells contain large intranuclear and smaller intracytoplasmic inclusions which are pathognomic for CMV infection.

14. Ans. is a i.e. Roseola infantum *Ref. Harrison 17/e, p 1112, 1116*

Roseola infantum or exanthem subitum is caused by HHV 6 and HHV-7 (rarely).

Diseases caused by Parvo virus :

- Erythema infectosum
- Seronegative arthritis
- Aplastic crisis in hemolytic anaemia
- Fetal infection leads to non-immunohydrops fetalis
- Chronic anaemia in immunocompromised
- Hemophagocytic syndrome
- Severe anaemia in malarial patients.

15. Ans. is c i.e. Carcinoma Nasopharynx *Ref. Harrison 17/e, p 1108*

Already explained, refer see answer no. 1

16. Ans. is b i.e. CMV virus causes B/L temporal lobe infarction *Ref. Harrison 17/e, p 1111*

CNS manifestatin of CMV :

– CMV rarely cause CNS infection.
– Two forms of CMV encephalitis are seen :
  1. Resemble HIV encephalitis and present as progressive dementia.
  2. Ventriculoencephalitis - Characterized by cranial nerve deficit, nystagmus and ventriculomegally.
– In immunocompromised patient CMV can also cause subacute progressive polyradiculopathy.

No where is given that CMV can cause temporal lobe infarction : *Hence answer*

Other options :

- **Subacute sclerosing pan encephalitis**
  – It is a rare chronic progressive demyelinating disease of CNS associated with a chronic permissive infection of brain tissue with measles virus.
- **Progressive Multifocal leucoencephalopathy**
  – Progressive disorder characterised pathologically by multifocal areas of demyelination of varying size distributing throughout the CNS caused by JC virus.
- **Spongiform encephalopathy**
  – Caused by prion infection; HIV infection.

17. Ans. is b i.e. Herpes simplex encephaitis *Ref. Harrison 17/e, p 2630*

"The most common virus causing sporadic cases of encephalitis in immunocompetant adult are HSV-1, VZV, EBV and less comonly enterovirus."

Remember : Epidemic of encephalitis are caused by Arbovirus which include :
1. Alphaviruses 2. Toga viruses 3. Bunyaviruses

Neurological manifestation of Herpes

CNS manifestation		ANS manifestation	PNS manifestation
Encephalitis	Involving temporal lobe especially	• ANS dysfunction especially of sacral region leading to numbness, tingiling of the buttocks or perineal areas.	• Bell's palsy
Meningitis	HSV is ***MC*** cause of recurrent lymphocytic meningitis ***(mollaret's meningitis)***	• Urinary retention, constipation, impotence.	• Cranial polyneuritis
		• Gullen barre syndrome	

18. Ans. is b i.e. Cytomegalovirus *Ref. Harrison 17/e, p 1111*

- It is a case of diffuse interstitial pneumonitis due to CMV.

Remember :
- **CMV is** the ***MC*** infection complicating organ transplantation.
- **CMV is** ***MC*** cause of intrauterine infection.
- Risk of post transplant CMV infection is greatest 5-13 weeks after transplant.

Infections after Kidney Transplantation

Period after transplanatation			
Infection Site	**Early (< 1 month)**	**Middle (1 - 4 months)**	**Late (> 6 months)**
Urinary tract	Bacteria (Escherichia coli, Klebsiella, Enterobac-teriaceae, Pseudomonas, Enterococcus) associated with bacteremia and pyelonephritis, Candida	Cytomegalovirus fever alone is common)	Bacteria; late infections usually not associaed with bacteremia
Lungs	Legionella	***CMV diffuse interstitial pneumonitis***, Pneumocystis, Aspergillus, Legionella	Nocardia, Aspergillus, Mucor
Central nervous system		Listeria meningitis, CMV encephalitis, Toxoplasma gondii	CMV retinitis, Listeria meningitis, cryptococcal meningitis, Aspergillus, Nocardia

19. Ans. is b i.e. HSV-II *Ref. Harrison 17/e, p 1100*

Although skin lesion are the most common recognized feature of disease, many infant do not develop lesion until well into the course of disease.

Most cases of neonatal infection are due to HSV-2.

So, now it is clear that initially skin lesions may not be present in case of HSV -2 encephalitis.

Meningococci do not cause encephalitis in neonates.

Remember : ***Of all HSV infected individual, neonates have highest frequency of visceral and / or CNS infection."***

Neonatal infection is usually acquired perinatally from contact with infected genital secretions at the time of delivery

20. Ans. is a i.e. CMV *Ref. Harrison 17/e, p 1111*

Already explained, refer see answer no. 18

21. Ans. is a i.e. HSV-1 *Ref. Harrison 17/e, p 2630; 16/e, p 2480*

Virus causing encephalitis

- ***Common :*** – Arbovirus – Enterovirus – EBV
  – HSV-1 – Mumps – VZV
- ***Less common :*** – CMV, HIV, measles.
- ***Rare :*** – Adenovirus, influenza virus, para influenza virus, rabies, rubella

So we can see : – HSV-1, EBV, CMV, all cause encephalitis
– ***But commonest among these is HSV-1,*** *Hence Answer.*

22. Ans. is a, b and d i.e. Aplastic anemia; Erythema infectiosum; and Arthritis

Ref. Harrison 17/e, p 1116

Already explained, refer answer no. 14

23. Ans. is d i.e. Arthropathy *Ref. Harrison 17/e, p 1116*

Arthropathy is commonest manifestation of parvo-virus in adults.

- Erytheia infectosum is seen in infants
- Bone marrow aplasia is seen in patients of chronic hemolytic anaemia.

24. Ans. is a, b and e i.e. RSV – Brochiolitis; HHV5 – Infectious mononucleosis; and VZV – Chicken pox

Ref. Ananthnarayan 7/e, p 475

Remember : **RSV** is *most common* cause of bronchiolitis.

Other causes are :
- – Parainfluenza virus
- – Adenovirus
- – Influenza virus
- – Mycoplasma pneumoniae

25. Ans. is a, b and c i.e. Viral warts usually resolve spontaneously; Plantar warts should not be excised; and Callosity are formed occupationally

Ref. Harrison 17/e, p 1118; Short case by S. Das 2/e, p 20

Warts are patches of hyperkeratotic overgrow skin.

- Three types of warts can be seen :
  a. Common wart
  b. Veneral wart
  c. Senile wart
- Common wart can be :
  a. Verruca vulgaris = ***MC*** *type*
  b. Verrucaplana = Flat wart - ***MC*** *type in children*
  c. Plantar wart = Verrucaplantaris - *painfull*
- **HPV *is the etiological agent of these warts.***

Treatment

- – Most HPV lesion resolve spontaneously.
- – Cryosurgery is treatment of choice.
- – Surgical excision is not recommended as it leads to scarring and recurrence rate is quite high.

Other options

- ***Callosity*** – Superficial circumscribed yellowish white flat thickened patch of hyperkerotic material. Etiology is mostly occupational.
- ***Corn*** – Localised hyperkeratosis of skin.
  – Usually occurs at the site pressure eg. on sole, foot and toes.

26. Ans. is a, d and e i.e. Cytomegalo virus; HIV and HBV *Ref. Harrison 17/e, p 1789 - 1791, 1796*

Virus causing Glomerular Disease

Disease	Virus
• Focal segmental glomerulosclerosis	HIV, HBV, Parvo virus, Cox sackie
• Membrane proliferative glomerulonephritis	HBV, HCV, HIV, CMV, EBV
• Diffuse proliferative glomerulonephirits	Cox sackie virus
• Membraneous nephropathy	HBV; HCV
• Endocapillary proliferative GN	Measles, Dengue
• Mesangioproliferative GN	Parvo virus, Mumps

Remember: Other infectious causes of Membraneous GN-Syphilis, Malaria, Schistosomiasis, Filariasis, Leprosy

27. Ans. is a, b and d i.e. Ca Tonsil; Nasopharyngeal Ca; and Infectious mononucleosis
Ref. Harrison 17/e, p 1108

Already explained, refer answer no 1

28. Ans. is a, b and c i.e. HSV encephalopathy is treated with acylovir; Oropharyngeal involvement is common in HSV -1; and Recurrent genital involvement is seen in HSV-2
Ref. Harrison 17/e, p 1097 - 1098

Difference between HSV 1 and HSV 2 are as follows :

HSV Type 1	HSV Type 2
• Cause lesion in and around mouth	Cause lesion around genital area
• Transmitted by direct contact or droplet spread	Usually transmitted sexually
• Replicate poorly in chick embryofibroblast cell	Replicate well
• Relatively sensitive to antiviral agents	Resistant
• Less neurovirulent	More neurovirulent
• Infectivity is less temperature sensitive	More temperature sensitive

Remember :
– Genital HSV-2 infection is twice as likely to reactivate and recurs 8 to 10 times more frequently than genital HSV-1 infection.
– Similarly oral - labial HSV-1 infection recurs more frequently than oral - labial HSV-2 infection.

Treatment of **CNS infection :** *HSV encephalitis :* IV acyclovir for 10 days.

29. Ans. is a, b and d i.e. Infectious mononeucleosis; Burkitt's lymphoma; and Nasopharyngeal Ca
Ref. Harrison 17/e, p 1107

Remember : Herpangina is caused by coxsackie virus A, coxsackie virus B and Echovirus.

For more details, refer answer no. 1

30. Ans. is a, b, c, d, e i.e. (All are correct options) *Ref. Harrison 17/e, p 1097 - 1098*

Characteristic of HSV-2 infection :
• Usually (but not absolutely) cause lesion below waist.

- First episode of primary genital herpes is characterised by fever, headache, malaise, myalgia.
- Widely, spaced bilateral lesions on external genitalia are characteristic.
- Cervical and urethral involvement seen in >80% woman in 1st episodes.
- The 12 month recurrence rate among patient with first episode HSV-2 and HSV-1 infections are 90% and 55% respecitvely.
- **Neonatal HSV infection :** Usually acquired perinatally at the time of delivery**.**
- **Treatment :** Acyclovir is most commonly used drug.

31. Ans. is b i.e. Vaccinia *Ref. Ananthnarayan 7/e, p 469*

- Vaccinia virus is unique is that it is an artificial virus and does not occur in nature as such.
- It is used as a vector for development of recombinant vaccines.
- Its genome can accomodate 25,000 foreign base pairs.
- Genes encoding antigens of HBV, HIV, rabies and neuropeptides are inserted in it.

32. Ans. is b i.e. Inverted papilloma *Ref. Ananthnarayan 7/e, p 576*

Note : Inverted papilloma is the ***MC*** neoplasm of nose and sinuses of unknown aetiology.

33. Ans. is b i.e. CMV *Ref. Harrison 17/e, p 1111*

- **CMV is the *MC* pathogen complicating organ transplantation.**
- Period of maximum risk is between **1 and 4 month after transplantation.**
- In transplant recepient ***CMV produces :***
  - Fever
  - Hepatitis
  - Gastritis
  - Retinitis (late complication)
  - Leukopenia
  - Pneumonitis
  - Colitis.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Most sensitive test for diagnosis of infectious mononucleosis : [Kerala 90]

a) Monospot test
b) Paul Bunnet test
c) Lymphocytosis in peripheral smear
d) Culture of the virus

[Ref. Harrison 17/e, p 1108]

2. Herpes simplex virus is : [AI 91]

a) Single stranded DNA
b) Double stranded DNA
c) Single stranded RNA
d) Double stranded RNA

[Ref. Ananthnarayan 7/e, p 446]

3. Which of the following is not a pox virus :

a) Cow pox **[AIIMS 92]**
b) Molluscum contagiosum
c) Small pox
d) Chicken pox

[Ref. Ananthnarayan 7/e, p 468, 473]

4. Which is not a useful method of diagnosis of herpes infection : [JIPMER 93]

a) DNA analysis
b) Serology
c) Tissue culture
d) Microscopy

[Ref. Ananthnarayan 7/e, p 477-478]

5. Ebstein Barr virus causes all except : [Kerla 97]

a) Burkitt's lymphoma
b) Infectious mononucleosis
c) Nasopharyngeal carcinoma
d) Carcinoma cervix

[Ref. Ananthnarayan 7/e, p 483]

6. Herpes virus infection causes : [UP 98]

a) Intracytoplasmic inclusion bodies
b) Syncytial formation
c) Heat stable
d) White shiny necrotic pocks

[Ref. Ananthnarayan 7/e, p 475]

7. EB virus affects : [UP 99]

a) T cells
b) Monocytes
c) B cells
d) Lymphocytes

[Ref. Ananthnarayan 7/e, p 483]

8. Infectious mononucleosis, true is A/E : [UP 99]

a) Caused by EBV
b) Also called kissing disease
c) Diagnosed by paul bunnel test
d) None of the above

[Ref. Ananthnarayan 7/e, p 482-484]

9. True about virus is : [UP 00]

a) HSV-I cause encephalitis
b) EBV affects T lymphocyte
c) CMV is always symptomatic
d) Herpeszoster is not reactivated

[Ref. Ananthnarayan 7/e, p 477]

10. Which virus remains dormant but reactivate is :

a) Herpes simplex **[UP 00]**
b) Herpes zoster
c) EB virus
d) CMV

[Ref. Ananthnarayan 7/e, p 478]

11. Kaposi-sarcoma is caused by : [UP 01]

a) EBV
b) Parvovirus
c) Herpes virus
d) Rotavirus

[Ref. Ananthnarayan 7/e, p 485]

Answer

1. a) Monospot ... 2. b) Double ... 3. d) Chicken pox 4. None 5. d) Carcinoma ...
6. b) Syncytial ... 7. c) B cells 8. d) None of the ... 9. a) HSV-I cause ... 10. b) Herpes ...
11. c) Herpes ...

12. Virus B 6-7 is causative agent in : [UP 01]

a) Carcinoma cervix
b) Carcinoma endometrium
c) Clear cell carcinoma
d) Focal encephalitis

[Ref. Ananthnarayan 7/e, p 485]

13. The causative organism for infectious mononucleosis is : [Jharkhand 03]

a) EB virus
b) Coxasackie virus
c) Varicella virus
d) Parovo virus

[Ref. Ananthnarayan 7/e, p 483]

14. Which virus reactivate and involves the eyes :

a) Herpes-Zoster **[Jharkhand 04]**
b) CMV
c) EM virus
d) Enterovirus - 70

[Ref. Ananthnarayan 7/e, p 480]

15. All are true regarding cytomegalovirus Except :

a. It is DNA virus **[Kolkata 05]**
b. Most commonly infected in the last trimester
c. Diagnosed by increased IgA in fetal blood
d. Most common cause of congenital viral infection

[Ref. Ananthnarayan 7/e, p 299]

16. The Epstein Barr Virus is implicated in all of the following except : [DNB 05]

a) Nasopharyngeal Ca
b) Burkitt's lymphoma
c) Infectious mononucleosis
d) Leukemia

[Ref. Harrison 17/e, p 1106]

17. The following about epstien barr virus are true except : [MP 06]

a) It is a member of Herpes virus family
b) It infects epithelial cells of oropharynx
c) The main target of the virus is T-cells lymphocytes
d) It is implicated in nasopharyngeal carcinoma

[Ref. Harrison 17/e, p 1106]

18. Patient present in your clinic. On physical examination, there is bilateral lymphadenopthy, which is tender on palpation. He gave history of sexual contact. He is truck driver by profession. The probable causative agent is : [MP 06]

a) Herpes
b) LGV
c) H. ducreyi
d) Treponema

[Ref. Harrison 17/e, p 832]

19. Epstein barr virus causes all except : [MP 06]

a) Nasopharyngeal carcinoma
b) Burkitt's lymphoma
c) Hodgkin's disease
d) Heterophile negative mononucleosis

[Ref. Harrison 17/e, p 1106-1108; Ananthnarayan 7/e, p 484]

20. African burkitts lymphoma is cuased by :

a. Cytomegala virus **[UP 06]**
b. EB virus
c. Herpes zoster
d. Infectious mononucleosis

[Ref. Harrison 17/e, p 1106]

21. Erythema infectosum is caused by : [Kar 06]

a. Human parvovirus is B19
b. Papova virus
c. Human herpes virus type 8
d. Measles virus

22. Most common extra skin manifestation of varicella is involvement of : [UP 07; SGPGI 05]

a) CNS
b) Lungs
c) Kidneys
d) CVS

[Ref. Harrison 17/e, p 1103]

Answer 12. d) Focal ... 13. a) EB virus 14. a) Herpes ... 15. c) Diagnosed ... 16. d) Leukemia 17. c) The main ... 18. a) Herpes 19. d) Heterophile ... 20. b) EB virus 21. a) Human ... 22. a) CNS

2 RNA Virus

PICORNA VIRUSES

Icosahedral, non enveloped RNA viruses, divided into two :

Enterovirus (acid resistant parasites of enteric tract)	**Rhinovirus (sensitive to acids infect nasal mucosa)**
Polio vrius Type 1, 2, 3 Cox-sachie virus A and B ECHO virus or ORPHAN virus Entero virus Type 70 Acute hemorrhagic conjunctivitis Type 72 HAV	↓ • ***MC*** cause of common cold which is ***MC*** infectious disease of human • Isolated by inoculating into Monkey Kidney tissue culture.

POLIO VIRUS

- SS positive sense RNA virus, which doesn't survive lyophilization.
- ***MC*** type and most epidemic is caused by **Type 1.**
- Epidemic caused by Type 1 and 3 while endemic is by Type 2.
- Vaccine induced paralysis is caused by mutated **Type 3.**
- Most **antigenic strain** - Type **2.**
- Two antigen – D or Native (N) antigen and C or heated (H) are identified.
- Anti D antibody is protective and used for measuring potency of injectable vaccine in terms of D antigen units.
- Transmitted by **feco-oral** route.
- **Earliest change** is the degeneration of Nissel bodies **(chromatolysis)** seen mostly in anterior homs of spinal cord (Signs of **lower motor neuron paralysis**).

Clinical features

- I.P 7-14 days. Manifest as :
  a. Inapparent **(subclinical)** infection – ***MC*** manifestation (95%).
  b. Abortive polio or minor illness.
  c. Non paralytic polio - Mimics aseptic meningitis (~1%)
  d. Paralytic polio - Least common manifestation (<1%)

- Predominant sign - **Descending;** asymmetric; **proximal** more than distal; flaccid paralysis of **legs (*MC*),** arms, abdominal, thoracic or bulbar muscles.
- **Objective sensory** testing usually yields **normal** results.
- ***MC*** muscle affected **-** *Quardriceps*
- ***MC*** muscle which undergoes complete paralysis - *Tibialis anterior*
- ***MC*** muscle affected in hand - *opponens pollicis*
- Common deformity at hip is flexion, abduction and external rotation.
- **At knee** - flexion deformity is common but in severe cases *triple deformity* consist of flexion, posterior subluxation and external rotation occurs.
- Post polio syndrome is due to progressive dysfunction and loss of motor neurons that compensated for the lost neurons during original infection (not due to persistent / reactivation of virus).
- **Risk of paralytic polio is increased by :**

– Tonsillectomy	– Intramuscular injection	– Tooth extraction
– Adenoidectomy	– Strenous physical exercise	– Fatigue
– Cortisone adminstration		

COX-SACKIE VIRUS, ECHO VIRUS AND OTHER ENTEROVIRUSES

- ***MC*** clinical **manifestation of enterovirus** infection - Non specific febrile illness. *(Summer Grippe)*
- ***MC*** cause of **aseptic** meningitis – *Enterovirus* (ECHO is ***MC***)
- ***MC*** cause of **rubelliform** rash – *Echovirus 9*
- Transplacental Transmission occur in coxsackie virus.

	Serotype of Virus		
Manifestation	**Cox sackievirus**	**Enterovirus**	**Echo**
i. Acute hemorrhagic conjunctivitis (characteristic subconjuctival hemorrhage)	A-24	Ent. 70	–
ii. Aseptic meningitis	Most group A, all B	Ent	E
iii. Encephalitis	A, B	Ent	E
iv. Exanthem	A, B	Ent	E
v. Generalized disease of newborn	B_{2-5}	–	E
vi. Hand, foot and mouth disease	A, B (commonly by A)	Ent 71	–
vii. Herpangina	A, B (commonly by A)	Ent 71	E
viii. Myocarditis, pericarditis	A, B (Commonly B)	–	E
ix. Paralysis	A, B (commonly A)	Ent	E
x. Pleurodynia (Bornholm disease)	A, B (commonly B)	–	E
xi. Pneumonia	A, B	Ent	E
xii. Juvenile diabetes	B-4	–	–
xiii. Orchitis	Coxasackie	–	–
xiv. Post viral fatigue syndrome	B	–	–

Diagnosis of Enterovirus (Including polio)

- ***MC* procedure** for diagnosis of infection - *Isolation* of enterovirus *in cell culture.*
- Isolation of virus from nasopharyngeal, throat sample, stool is not specific but isolation from throat is more specific than from stool.
- Culture of CSF, serum, fluid from body cavities or tissues - less sensitive but specific.
- If CSF culture is negative than stool culture is done within first 2 weeks after onset of symptoms to confirm diagnosis.

- PCR of CSF - Highly sensitive and specific and rapid than culture.
- PCR of serum - Done for disseminated disease.
- Cox-sackievirus may require inoculation into special cell - culture lines or into suckling mice.

Treatment

- IV / Intrathecal or intraventircular Ig for chronic enterovirus meningoencephalitis and dermatomyositis in patient with hypo or aggamaglobulinemia.
- ***Pleconaril.***
- Glucocorticoids are contraindicated.

MYXOVIRUS

- Myxovirus is enveloped RNA virus, characterized by ability to adsorb on to mucoprotein receptors on erythrocytes causing hemagglutination.
- It is divided into two families - Orthomyxoviridae and Paramyxoviridae.

Distinguishing features of Orthomyxo and Paramyxovirus

Features	*Orthomyxoviridae*	*Paramyxovridae*
i. *Genome*	Segmented (8 pieces)	Single linear RNA
ii. *Site of synthesis of Ribonucleo protein*	Nucleus	Cytoplasm
iii. *Genetic Reassortment*	Present	Absent
v. *Antigenic Stability*	Variable	Stable
vi. *Members*	Influenza virus	Measles (Morbillivirus) Mumps, Parainfluenza (Paramyxovius), Respiratory syncytial virus (pneumovirus)

INFLUENZA

- Typically spherical virus divided into 3 subtypes (A,B,C) which are antigenically distinct. It has two types of antigens :
  a. Internal antigen - Type specific i.e. (A, B, C) and stable.
     – Consist of RNP or soluble (S) antigen and M protein antigen.
     – It also includes envelope lipid antigen which is host specific.
  b. Surface / Viral or V antigen – Strain specific and show antigenic variations. (A > B) and C doesn't show antigenic variation.

- Antigenic variation is of 2 types :
  ii ***Major antigenic variation or antigenic shift*** – It is due to *genetic recombination that is genetic reassortment* between animal & human virus and is **responsible for** *major epidemics or pandemic. Only* shown by type ***A***
  ii. ***Minor antigenic variation or antigenic drift*** – It is due to *point mutation* and **is repsonsible for** *periodical epidemic.*
     – Shown by type *A* and *B.*

- *V antigen* composed of at least 2 virus coded protein.
  i. ***Hemagglutinin (H) :*** Cause hemagglutination.
  Anti hemagglutinin is protective.
  ii. ***Neuraminidase (N)*** – is receptor destroying enzyme (RDE) so cause elution.
     – Anti-neuraminidase antibody is not as effective in protection as that of hemagglutinin.
     – It may contributes to limit the infection.

- In world, three types of influenza virus are circulating - A (H_1N_1), A(H_3N_2), and B viruses.
- *New* influenza virus : A (H_5N_1), causative agent of bird flu.
- ***Source of Infection*** – Usually a case or subclinical.
- *Portal of entry* – Respiratory route
- *Incubation period* – 18-72 hours.

Clinical Features

- There is *no* viremia.
- Respiratory symptoms are prominent but abdominal pain and vomiting may occur in type B infections.
- ***MC*** complication is *pneumonia.*
- **Most serious** complication of influenza ***B virus*** is *Reye's syndrome [also occur in influenza A and VZ virus].*
- Cardiac, neurological complication and gastric flu (with type B) may occur.
- ***MC*** **secondary** bacterial pneumonia in influenza - *Strep pneumoniae.*

Lab-Diagnosis

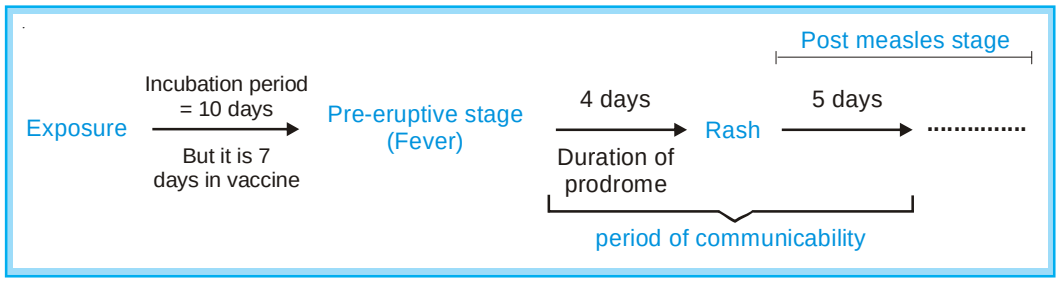
- Virus isolation – **Best** specimen is *nasopharyngeal* secretions
  – Detected by Indirect fluorescent antibody.

Prevention

1. **Best** is immunization. Vaccine is recommended only in certain selected population. Vaccine is of following types.
   a. *Killed vaccine* :
   Most commonly used vaccine :
   – *Contains H, N antigens*
   – *Usually one dose given but in patient with no previous immunological experience 2 dose given*
   – *Immunity last for only 3 - 6 month.*
   – *Vaccine can produce very rarely Guillain Barre syndrome (ascending paralysis).*
   b. *Live attenuated vaccines* :
   Administered as nose drops so induce both local and systemic immunity
   c. *Newer vaccines* :
   Split virus vaccine (sub -virion vaccine), Neuraminidase specific vaccine (sub-unit vaccine contain only N antigen); Recombinant vaccine
2. Antiviral drugs :
   – For type A virus : Amantadine and rimantidine (used in treatment also).
   – For both A and B : Zamamivir, Oseltamivir.

MEASLES (RUBEOLA)

- RNA paramyxovirus, having *only one* serotype.
- *It cannot* survive outside the human body.
- *Carriers* are *not* known to occur. But subclinical cases occurs.
- Secondary attack rate > *80%.*
- Immunity after vaccination and infection is life long.
- Multinucleated giant cells with inclusion bodies in the nucleus and cytoplasm ***(Warthin - Finkeldey Cells)*** are pathognomic for measles.



Clinical features

i. ***Prodromal / Pre-eruptive stage :*** A day or two before the appearance of rash **Koplik's spot** (*bluish white with erythematous halo)* appear on the buccal mucosa opposite the first and second upper molars.
   - It is **pathognomonic enanthem** of measles.
   - It disappear after the onset of rash.

ii. ***Eruptive stage :*** Rash appear on 4th day from fever. It begins at hairline and behind the ear and spread downward rapidly. Characteristically it is erythematous, non-pruritic and maculpapular.

iii. ***Post measles stage***

Remember : Modified measles occur in individual with pre-existing partial immunity induced by active or passive immunization.

Complication :

- ***MC*** complications are - measles associated diarrhoea, pneumonia and *otitis media* (***MC*** complication **in young children).**
- More *serious* are neurological complication (febrile convulsions, encephalitis and sub-acute sclerosing pan encephalitis i.e. SSPE). Most cases result from immune mediated response to myelin proteins (post infectious encephalomyelitis) and not directly from viral infection.

Remember : Atypical measles occur in person who received formalin inactivated measles vaccine in which rash begins peripherally and moves centrally.

Prevention

1. **Measles Vaccination :** *Live attenuated, tissue culture; freeze dried vaccine of HDC - Edmonston - Zagreb strain;* given to child as single subcutaneous dose of 0.5 ml as close to the age of 9 month.
   - Reconstituted in Distilled water and should be used within one hour.
   - There is no spread of virus from vaccines to contacts.
   - Immunity develop in 11 to 12 days after vaccination.
   - One dose of vaccine give 95% protection.
   - Susceptible contacts may be protected by giving vaccine within 3 days of exposure.
   - Toxic shock syndrome occurs if vaccine is used after 4 hours of opening the vial.
   - Pregnancy is contraindication.

2. **Immunoglobulin**

Remember : ***Eradication*** is achieved when immunization coverage is at least 96%.

MUMPS VIRUS = MYXOVIRUS PAROTIDITIS

- Paramyxovirus having predilection for glandular and nervous tissue.
- It has only one serotype.
- ***Maximum infectivity*** is just before and at the onset of parotitis.

- It spreads mainly by droplet infection.
- One attack (clinical or subclinical) induce life long immunity.
- **Incubation Period –** Usually 18 days.

Clinical Features

- *Mumps* is the **most frequent** cause of *parotitis in children* in the age group 5-15 years.
- Usually bilateral parotitis occurs. Submandibular and sublingual gland can also involved.
- Some patient develops pre-sternal edema.
- Other than parotitis, *orchitis* is the ***MC*** manifestation among *post- pubertal males.*
- *Aseptic meningitis* is a common manifestation in both children and adults.
- Glucose level in CSF may be abnormally low and this raise suspicion of bacterial meningitis.
- In pregnancy, it does not lead to premature birth or fetal malformation.

Prevention

- Single dose of live-attenuated vaccine primarily in susceptible adults especially males who have not had mumps.
- Combined vaccine - MMR : at the age of 12-15 month and again at 4-12 years of age. *....Harrison 16/e, p 1155*

PARAINFLUENZA VIRUS

- First parainfluenza virus to be discovered - Sendai virus or Hemagglutinating virus of Japan (HVJ) or influenza virus type D.
- It ranks second only to RSV as cause of lower respiratory tract illness.
- It has 4 types - 1, 2, 3, 4.

Clinical Features

- **Most serious** clinical disease is *croup (laryngotracheobronchitis).*
- Para-influenza **type 1** is ***MC*** cause of croup in children.
- **Type 3** is important cause of lower respiratory disease (bronchitis, bronchiolitis and pneumonia) in infants.
- In older children and adults, most frequent symptom - common cold or hoarsenss.
- This virus confined to respiratory tract unlike mumps which is a systemic disease.

Diagnosis

Isolation of virus from throat and nasal swabs by inoculating in primary monkey kidney cell cultures or continous monkey kidney cell line (LLC-MK2) with trypsin.

RESPIRATORY SYNCYTIAL VIRUS (RSV)

- ***MC*** cause of *lower respiratory tract disease.*
- ***MC*** cause of *bronchiolitis seen* among infants between 1 and 6 month of age peaking between 2 and 3 months of age.
- ***MC*** manifestation **in infants** rhinorrhea.
- **In adults *MC*** symptom are *common cold* with *rhinorrhea*, sore throat and cough.
- Immunity is not long lasting.
- Nasal IgA is more protective than serum antibody.
- RSV is transmitted primarily by close contact with contaminated fingers or fomites.
- It produce fine rales; rhonchi, emphysematous change (that is hyperexpansion on chest X-ray) and atelectasis.

Diagnosis

- Specific diagnosis – by isolation of RSV from respiratory secretions (sputum, throat swab, nasopharyngeal wash).

Treatment

- ***Oxygen :*** mainstay of therapy.
- ***Ribavirin :*** for infants who are severely ill or who are at high risk of complications of RSV infection (premature infants and those with bronchopulmonary dysplasia, congenital heart disease and immunosuppression).

ROTAVIRUS AND OTHER VIRAL GASTROENTERITIS

- ***MC*** cause of diarrheal disease in infants and children : ***Rotaviurs***
- ***MC*** agent among older children and adults : Norovirus *(Norwalk like viruses)*

ROTAVIRUS

- Non enveloped, icosahedral virus with **segmented ds RNA (Character of Reovirus family)** so it exhibits *genetic reassortment.*
- VP-6 is major structural protein, is the target of commercial immunoassays and determines the group specificity of rotaviruses.
- **Human illness** is caused *primarily* by **group A** and to a much lesser extent by group B and C.
- Adult diarrhea rota virus (ADRV) belong to **group B** while **group C** cause pediatric gastroenteritis.
- 10 G serotypes of group A are identified in humans but 5 types ***(G1 through G4 and G9)*** are common.

Pathogenesis

1. It infect and destroy mature enterocytes in villous epithelum of proximal small intestine causing :
   a. Secretory diarrhea by ↓ villous epithelum + ↑ secretory crypt cells.
   b. Osmotic diarrhea – by ↓ brush border enzymes causing accumulation of unmetabolized disaccharides.
2. Secretory diarrhea also result by :
   a. Enterotoxin (=NSP4) which alter epithelial cell function and permeability.
   b. Activation of enteric nervous system in the intestinal wall.

Clinical features

- It infects all children by 3-5 years. May also infect neonates.
- Peak age - 4 to 23 months of age.
- Occurs predominantly during the cooler fall and winter months.
- Transmitted predominantly through fecao-oral route. Also transmitted by respiratory secretion, person to person, contaminated environmental surface.
- ***Severity of dehydration :*** Rotavirus > Norovirus > Sapovirus
- ***Vomiting*** frequently ***precedes*** the diarrhea.
- Stools are characteristically loose and watery and only infrequently contain red or white cells.
- Rotaviurs associated with respiratory and neurologic features, sudden infant death syndrome, necrotizing enterocolitis, intussusception and diabetes mellitus type I.
- Its infection produces virus specific secretory IgA in intestine and IgA, IgM, IgG in serum which increase with each reinfection, so severe disease is ***MC*** in young children with first or second infections.

Diagnosis

- As virus is shed in large quantities (10^7-10^{12}/g) in stool, the diagnosis is ***confirmed by*** detecting viral antigen in feces by Enzyme immunoassays and by detecting viral RNA (by gel electrophoresis, probe hybridization or PCR).
- Human rotaviurs does ***not grow*** readily in cell culture.

Treatment

- Rehydration therapy is given.
- Antibiotics and antimotility agents avoided.
- In immunocompromised children - oral immunoglobulin or colostrum given.

Prevention

- Vaccine was withdrawn since it cause intussusception.

OTHER VIRAL GASTROENTRITIS

1. Norwalk and Related human calciviruses

- Norovirus is the ***MC*** infectious agent of mild gastroenteritis in the community and affect all age groups whereas sapoviruses primarily cause gastroenteritis in children.
- Noroviruses are the major cause of epidemics of gastroenteritis worldwide.

Pathogenesis

- It is attached on carbohydrates (similar to human histoblood group antigens) of duodenal epithelium of individuals with the secretor phenotype (genetic predisposition to illness).
- Reversible lesion in upper jejunum e.g. broadening and blunting of villi, shortening of microvilli etc.
- Malabsorption of carbohydrates and fats and decreased brush border enzymes.
- Adenylate cyclase activity is not altered.
- Gastric motor function is delayed but histological changes are absent in stomach and colon.

Clinical features

- Transmission occurs predominantly by fecal-oral route but virus is also present in vomitus.
- Also transmitted by aerosolization, contact with contaminated fomites, person to person contact.
- Shellfish harvested from fecally contaminated water pose a special risk.
- ***Vomiting*** is more common among children where adults usually develop ***diarrhea.***
- Constitutional symptoms are common.
- ***Stool*** are characteristically loose and watery without blood, mucus or leukocytes.
- There is paradoxic inverse association between level of antibody and protection from disease that is person with higher level of pre-existing antibody are more susceptible to illness.

Diagnosis

- PCR for detection of virus in stool and vomitus.
- EIA (Enzyme immunoassays) for detection of virus in stool and serologic response to specific viral antigen.
- It has not yet been propagated in cell cultures.

Treatment : Generally not required since it is self limited.

2. Adenovirus : Enteric adenovirus (40 and 41) are difficult to cultivate in cell lines.

3. Astrovirus : Serotype 1 is ***MC.***

4. Torovirus : Cause less vomiting and more bloody diarrhea.

5. **Picobirnaviruses :**
   - Bi-segmented ***double stranded RNA*** virus.
   - Cause gastroenteritis ***in HIV*** infected adults.

6. **SARS-Cov :** (Severe acute respiratory syndrome associated coronavirus).

7. **Hendra and Nepah viruses :**
   Classified under paramyxoviridae family. Cause gastroenteritis in persons in contact with pigs.

8. **Enteroviruses, reoviruses, pestiviruses, parvovirus B.**

ARBOVIRUSES = ARTHOPOD BORNE VIRUSES

- The most important arbovirus vectors are mosquitoes followed by ticks.
- Most arbovirus agglutinate red cells (Hemagglutination) but spontaneous elution does not occur.
- Arboviruses have been placed in Toga, Flavi, Bunya, Reo and Rhabdovirus families.
- Arboviruses known to be prevalent in India are :

Group A	Group B	Others	
(Alphaviruses)	(Flaviviruses)	Umbre	Chandipura
Sindbis	Dengue	Sathuperi	Chittor
Chikungunya	Kyasanur Forest disease	Ganjam	Minnal
	Japenese encephalitis	Venkat puram	Dhori
	West Nile	Kaisodi	Sandfly fever
		Vellore	African horse sickness

- ***Clinical syndromes of Arbovirues :***
  - **Febrile group :** - ***MC*** group
    - No rash and arthralgia seen
    - eg. Sindbis, Chikungunya, dengue (Types 1-4), Westnile, Sandfly fever, Rift valley fever.
  - **Hemorrhagic fevers (HF)**
    Dengue, chikungunya, kyasanur forest disease, lassa fever, yellow fever, marburg or ebola HF, hantavirus pulmonary syndrome, HF with renal syndrome, rift valley fever, crimean congo HF, omsk HF.
  - **Encephalitis :** eg. West Nile, Japanese encephalitis.

RHABDOVIRIDAE

- **Bullet shapted**, enveloped viruses with SS RNA genome are known as Rhabdovirus.
- Rhabdoviridae contains two genera : i. Vesiculovirus containing vesicular stomatitis virus, chandipura virus.
  ii. Lyssavirus containing Rabies virus, Lagos bat, Mokola, Duvenhage.
- **Rabies virus (*Lyssavirus serotype 1*)** is a unsegmented, linear negative, **Neurotropic**, RNA virus which causes direct zoonosis of **warm blooded animals** (particularly carnivorous such as dogs, cats, jackals and wolves) including man called as RABIES.
- Serotype 2, 3, 4 are *rabies related virus.*
- It has two major antigen - glycoprotein (G Protein) and internal nucleoprotein antigen.
- Glycoprotein seems to be the only antigen capable of inducing the formation of virus neutralizing (protective) and hemagglutination - inhibiting antibodies.
- Virus excreted in the saliva of rabid animals is called as 'street virus' which is pathogenic for all mammals and has long **variable** incubation period.

- Serial brain - to - brain passage of Street Virus modifies it to convert into fixed virus which has following characteristics :
  - Short, fixed and reproducible incubation period.
  - Not form Negri bodies and not multiply in extraneural tissues.
  - Used in the preparation of anti - rabies vaccine.
  - It is pathogenic under certain conditions eg. when inadequately inactivated for vaccine production.
- Rabies is only communicable disease of man that is *always fatal.*

Remember : Rabies is dead end infection.

Type of Rabies

i. ***Urban rabies –*** maintained by the dog and is responsible for 99% of human cases in India.
ii. Sylvatic or wild life rabies.
iii. Bat rabies.

Remember :
- In *most* of the world, dog is the most important vector.
- Maldives is the only country which does not have human or animal rabies.
- In India, rabies occur in all parts except Lakshadweep and Andman and Nicobar Islands
- *Most effective* natural barrier to rabies - water.

Mode of transmission :
- *Animal bites* - ***MC***
- Licks on abraded skin and abraded or unabraded mucosa.
- Respiratory (aerosol) transmission.
- Person to Person - rare
- Also by corneal and organ transplants.

Incubation period : Highly variable depending on the site of bite (i.e. actual distance that the virus has to travel to reach to CNS), severity of bite etc.

Clinical features

- Virus spreads ***centripetally*** from site of infection (striated muscle) than ascends through nerve associated tissue space, and than spreads ***centrifugally*** in peripheral autonomic nerves to many tissues.
- Salivary gland invasion is ***crucial*** for transmission of virus.
- Most characteristic pathologic finding in CNS is the formation of cytoplasmic inclusions called ***Negri Bodies*** *(composed of finely fibrillar matrix and rabies virus particles)* within neurons of Ammons horn, cerebral cortex, brain stem, hypothalmus, purkinje cells of the cerebellum and dorsal spinal ganglia.
- It has four stages :
  a. *Prodromal period* : Specific symptom is complaint of paresthesia / fasciculation at or around the site of inoculation of virus.
  b. *Encephalitic phase* : Abnormalities of automatic nervous system. Aerophobia (pathognomic) and Hydrophobia (pathognomic and absent in animals) may seen.
  c. ***Manifestation of brain stem dysfunction*** : The prominence of early brain stem dysfunction distinguish it from other viral encephalitidis.
  d. *Death or* in rare cases recovery occurs.

Remember : It may be also present as ascending paralysis resembling GBS most frequently among persons given post-exposure prophylaxis after being bitten by vampire bats.

Diagnosis : Confirmed by antigen detection using immunofluorescence of infected tissue (corneal impression smear, skin biopsy or brain) and by virus isolation from saliva and other secretions.

Prevention

Types of Vaccine :

i. Nervous tissue vaccine (NTV)
   - From adult animal tissues (eg sheep) : Simple type
   - From suckling mouse brain

ii. Duck embryo vaccine (DEV) – Not available in India

iii. Cell culture vaccine :

Human diploid cell (HDC) vaccine In India it is used for both pre and post exposure prophylaxis (PEP)	*"Second generation" tissue culture (animal cell) vaccines* i.e. of Non human origin eg. chick embryo fibroblast, vero cells. The WHO recommended that culture of HDC line should be replaced by culture of animal cell line.

Types of Prophylaxis :

1. *Post - exposure prophylaxis* – Combined administration of single dose of antirabies serum with a course of vaccine, and local treatment of wound is the *best* specific prophylactic treatment after exposure of man to rabies.
   - **Indication of anti-rabies Treatment :**
     a. If animal shows sign of rabies within 10 days
     b. Biting animal can't traced
     c. Unprovoked bites
     d. Laboratory test (fluorescent rabies antibody test or test for negri bodies) of brain of biting animal are positive.
     e. All bites by wild animals
   - **Classification of exposures :**

Class I (slight risk) :	*Class II (Moderate risk)*	*Class III (severe risk)*
– Licks on healthy unbroken skin – Consumption of unboiled milk of suspected animal – Scratches without oozing of blood	– Licks on fresh cuts – Scratches with oozing of blood – All bites except on head, neck, face, palm, fingers – Minor wounds less than 5 in number	– All bites or scratches with oozing of blood on neck, head, face, palm, fingers – Lacerated wounds on any part of body – Multiple wounds 5 or more in number – Bites from wild animals

   - **Standard WHO intramuscular regimen –** 0, 3, 7, 14, 28, days and booster on 90 day.

2. *Preexposure prophylaxis* – given to laboratory staff working with rabies virus, veterinarians etc.
   - Cell culture vaccines on 0, 7, 28 days.
   - If titre of neutralizing antibody in serum taken after 1 month of 3rd dose, is less than 0.5 iu/ml than administer booster until antibodies become demonstrable.

3. *Post exposure treatment of persons who have been vaccinated previously* –
   - If titre of antibody > 0.5 iu/ml and bite is not severe – 2 doses (days 0, 3).
   - If titre of antibody is unknown or bite is severe - 3 doses of HDC on 0, 3, 7 days.

QUESTIONS

1. Which of the following is not true about measles:
a) High secondary attack **[AI 08]**
b) Only one strain causes infection
c) Not infectious in prodromal period
d) Infections confer life long immunity

2. H5N1 is : **[AI 08]**
a) Bird flu virus
b) Vaccinefor HIV
c) Causative agent of Japanese encpehalitis
d) An eradicated virus

3. The most common etiological agent for acute bronchiolitis in infancy is : **[AI 06]**
a) Influenza virus
b) Parainfluenza virus
c) Rhinovirus
d) Respiratory syncytial virus

4. With reference to mumps which of the following is true : **[AI 06]**
a) Meningoencephalitis can precede parotitis
b) Salivary gland involvement is limited to the parotids
c) The patient is not infectious prior to clinical parotid enlargement
d) Mumps orchitis frequently leads to infertility

5. All of the following statement are true about congenital Rubella except : **[AI 05]**
a) It is diagnosed when the infant has IgM antibodies at birth
b) It is diagnosed when IgG antibodies persist for more than 6 month
c) MC congenital defects are deafness, cardiac malformation and cataract
d) Infection after 16 weeks of gestation result in major congenital defects

6. Laboratory diagnosis of viral respiratory tract infections can be established by all of the following tests except : **[AI 04]**
a) Detection of virus specific IgM antibodies in single serum specimen
b) Demonstration of viral antigens by indirect immunofluorescence assay in nasopharyngeal washings
c) Isolation of viruses using centrifugation enhanced culture
d) Detection of viral hemagglutination inhibiting (HAI) antibodies in a single serum specimen

7. All of the following statements are true regarding poliovirus except : **[AI 04]**
a) It is transmitted by feco-oral route
b) Asymptomatic infections are common in children
c) There is a single serotype causing infection
d) Live attenuated vaccine produces herd immunity

8. All of the following clinical features are associated with Enteroviruses except : **[AI 04]**
a) Mycocarditis
b) Pleurodynia
c) Herpangina
d) Hemorrhagic fever

9. Commonest complication of Mumps is : **[AI 00]**
a) Orchitis and Oophritis
b) Encephalitis
c) Pneumonia
d) Myocarditis

10. True statement about Influenza A virus : **[AI 04]**
a) It has a double stranded segmented RNA
b) Pandemics are caused by antigenic drifts
c) Nucelocapsid antibody is not specific
d) Hemaglutinin and neuraminidase are strain specific

11. Acute hemorrhagic conjunctivitis is caused by :
a) Enterovirus **[AI 97]**
b) Adenovirus
c) Poliovirus
d) Hepadna virus

12. Reverse transcriptase polymerase chain reaction can aid in diagnosis of all of the following viral infection except : **[AI 97]**
a) Adenovirus
b) Astrovirus
c) Rotavirus
d) Poliovirus

13. All of the viruses cause pneumonia except :
a) Cytomegalovirus **[AI 95]**
b) Mumps
c) Measles
d) Retrovirus

Answer

1. c) Not .... 2. a) Bird flu .... 3. d) Respiratory ... 4. a) Meningoencep ... 5. d) Infection ...
6. d) Detection ... 7. c) There is a ... 8. d) Hemorrhagic ... 9. a) Orchitis ... 10. d) Hemaglutinin ...
11. a) Enterovirus 12. a) Adenovirus 13. b) Mumps

14. True about polio : **[AIIMS 08]**

a) Paralytic polio is most common
b) Only one type exist
c) Increased muscular activity leads to increased paralysis
d) Polio drop given only in <3 years

15. Regarding mumps which is true :

a) Causes SSPE **[AIIMS Nov. 07]**
b) Mumps causes aseptic meningitis in children
c) Sublingual gland is invlved commonly
d) All

16. All are false regarding polio virus except :

a) Most case are symptomatic **[AIIMS Nov. 07]**
b) Inactivated vaccine given IM
c) Inactivated polio vaccine are given to child less than 3 year of age
d) Only one type exists

17. Which of the following is the 'Least common' complication of measles ? **[AIIMS 06]**

a) Dirrhoea
b) Pneumonia
c) Otitis media
d) SSPE

18. Risk of the damage of fetus by maternal rubella is maximum if mother gets infected in :

a) 6-12 weeks of pregnancy **[AIIMS 05]**
b) 20-24 weeks of pregnancy
c) 24-28 weeks of pregnancy
d) 32-36 weeks of pregnancy

19. All are true about polio virus except : **[AIIMS 02]**

a) Type 1 is responsible for most epidemics
b) Very difficult to eliminate type 1
c) Type I is responsible for vaccine induced paralytic poliomyelitis
d) Type I most commonly associated with paralysis

20. Rota virus is detected by : **[AIIMS 02]**

a) Antigen in stool
b) Antibody in serum
c) Demonstration of virus
d) Stool culture

21. Enterovirus causes all except : **[AIIMS 01]**

a) Hemorrhagic fever
b) Pleurodynia
c) Herpangina
d) Aseptic meningitis

22. A 11 month old child presents with complaints of respiratory distress. On examination there is bilateral crepitation and wheezing. Which of the following is the most likely cause : **[AIIMS 00]**

a) Pneumonia
b) Adenovirus
c) Respiratory syncitial virus
d) Rhinovirus

23. Rota virus is diagnosed by : **[AIIMS 99]**

a) IgM specific antibody in stool
b) ELISA demonstrates antibody in stool
c) Immunoflorescence antigen in stool
d) Culture of rota virus

24. Segmented double stranded RNA virus is seen in:

a) Reovirus **[AIIMS 98; PGI 97]**
b) Myxovirus
c) Rabies
d) Parvo virus

25. Conjunctivitis is cause by all except :

a) CMV **[AIIMS 98]**
b) Enterovirus 70
c) Coxsackie A 24
d) Adenovirus

26. All are true about Rota virus except : **[AIIMS 97]**

a) Causes diarrhoea in man and children
b) Rota B can be grown in cell culture
c) Rota C can cause diarrhoea in children
d) Culture can not be done

27. All are cultivable virus except : **[AIIMS 97]**

a) Rota virus
b) Entero virus
c) ECHO virus
d) Coxsackie virus

28. Segmented RNA is found in : **[AIIMS 97, PGI 00]**

a) Influenza virus
b) Rabies virus
c) Herpes virus
d) Molluscum contagiosum virus

29. Vaccination causing intussuception :

a) Rota virus **[PGI Dec. 07]**
b) Parvo virus
c) Inactivated polio
d) BCG
e) Measles

Answer

14. c) Increased... 15. b) Mumps ... 16. b) Inactivated ... 17. d) SSPE 18. a) 6-12 ...
19. c) Type I ... 20. a) Antigen ... 21. a) Hemorrhagic ... 22. c) Respiratory ... 23. c) Immunoflore ...
24. a) Reovirus 25. a) CMV 26. b) Rota B ... 27. a) Rota ... 28. a) Influenza ...
29. d) Rota virus

30. Vaccines prepared by embryonated Hen's egg are: [PGI 04]
a) Mealses
b) Rabies
c) Rubella
d) Varicella

31. All are included in picorna group of viruses except: [PGI 04]
a) Encephalo myocarditis
b) HEV
c) Foot and mouth virus
d) Polio virus

32. Choose the correct matches : [PGI 02]
a) Mumps-RA 27/3 strain
b) Rubella-Jeryl-Lynn strain
c) Measles - Edmonston zagreb strain
c) BCG-Danish 1331 strain

33. Micro-Organism used as weapon in biological terrorism : [PGI 02]
a) Small pox Virus
b) Rabies Virus
c) Ebola Virus
d) Influenza C Virus
e) Human parvovirus

34. Incubation period less than 10 days seen :
a) Influenza [PGI 02]
b) Cholera
c) Plague
d) Chickenpox
e) Rabies

35. Organism (s) causing, bronchiolitis in infant :
a) RSV [PGI 00]
b) Rhino virus
c) Parainfluenza
d) Influenza
e) H. influenzae

36. Lipid envelope is found in which virus :
a) Reo [PGI 98]
b) Herpes
c) Picorna
d) All of the above

ARBO AND RHABDO

37. Soft tick transmits : [AI 08]
a) Relapsing fever
b) KFD
c) Tick typhus
d) Tularemia

38. Negre body is seen in : [AI 07]
a) CMV
b) Rabies
c) Inclusion of herpes simplex
d) EBV

39. Which of the following viral infections is transmitted by tick : [AI 05]
a) Japanese encephalitis
b) Dengue fever
c) Kyasanur forest disease (KFD)
d) Yellow fever

40. For the treatment of case of class III dog bite, all of the following are correct except : [AI 05]
a) Give Ig for passive immunity
b) Give ARV
c) Immediately stitch wound under antibiotic coverage
d) Immediately wash wound with soap and water

41. Class II exposure in animal bites includes the following : [AI 03]
a) Scratches without oozing of blood
b) Licks on a fresh wound
c) Scratch with oozing of blood on palm
d) Bites from wild animals

42. Which of the following statement is true about rabies virus : [AI 03]
a) It is double stranded - RNA virus
b) Contains a DNA-dependent RNA polymerase
c) RNA has a negative polarity
d) Affects motor neurons

43. Which is true about arboviral disease : [AI 00]
a) Yellow fever is endemic in India
b) Dengue virus have only one serotype
c) KFD is transmitted by ticks
d) Japanese encphalitis is transmitted by Aedes

Answer

30. a) Mealses
31. b) HEV
32. c and d
33. a and c
34. a, b and c
35. a, c and d
36. a) Reo
37. c) Relapsing ...
38. b) Rabies
39. c) Kyasanur ...
40. c) Immediately ...
41. b) Licks on ...
42. c) RNA ...
43. c) KFD is ...

44. Regarding Rabies, true is : [AI 00]

a) Incubation period depends on the site of bite
b) Diagnosis is by eosinophilic intranuclear inclusion
c) It is a DNA virus
d) Caused only by dogs

45. All of the following rabies vaccines are commercially available except : [AI 99]

a) Killed sheep brain vaccine
b) Human diploid cell vaccine
c) Vero continous cell vaccine
d) Recombinant glycoprotein

46. True statement about rabies is : [AI 97]

a) Rabies infection cause life long immunity
b) Rabies vaccine is always live attenuated
c) Rabies has various strains
d) Rabies is best diagnosed by immuno-florescence study

47. Negri bodes are found in : [AI 96]

a) Hypothalamus
b) Hippocampus
c) Midbrain
d) Medulla

48. Mark true in following : [AIIMS 08]

a) Hanta virus pulmonary syndrome is caused by inhalation of rodent urine and feces
b) Kyansur forest disese is caused by bite of wild animal
c) Lyssa virus is transmitted by ticks
d) Chikugunya is caused by anophales

49. A 25 year old girl has admitted to hospital with provisional diagnosis of rabies. The most suitable clinical sample that can confirm the antemortem diagnosis is : [AIIMS 04]

a) Serum for antivirus IgG antibody
b) Corneal impression smear for immuno-fluorescence stain
c) CSF sample for viral culture
d) Giemsa stain on smear prepared from salivary secretions

50. All are true regarding hantana virus except : [AIIMS 96]

a) DNA virus
b) Carried by rodents
c) Causes recurrent respiratory infection
d) Hemorrhagic manifestation may occur

51. New infectious agents are : [PGI 07]

a) Nipah virus
b) Pneumocystis jeruveci
c) Corona virus
d) SARS
e) Prion

52. Following are Arboviral disease : [PGI 03]

a) KFD
b) West Nile Fever
c) Ganjam virus
d) RSV
e) Puumala virus

53. True about hanta virus : [PGI 02]

a) Hantavirus pulmonary syndrome
b) Transmitted by arthopod
c) Transmitted by rodents
d) Hemorrhagic fever with renal failure
e) Hantavirus pulmonary symdrome acquired from person to person

54. In Japanese Encephalitis pigs acts as : [PGI 00]

a) Amplifier
b) Definitive host
c) Intermediate host
d) Any of the above

55. Rabies virus inactivated by : [PGI 97]

a) Phenol
b) UV radiation
c) BPL (Beta propiolactone)
d) All

56. Negri bodies are characteristic of viral infection by : [PGI 97]

a) Rabies
b) Toxoplasmosis
c) Polio
d) Herpes simpex infection

57. Hantan virus : [PGI 96]

a) Is a DNA virus
b) Causes Hemorrhagic fever with renal involvement
c) Belong to Retroviridae family
d) Person to person transmission

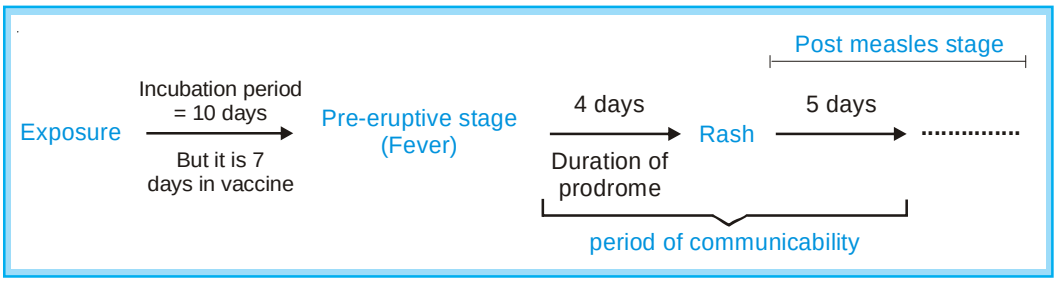
Answer

44. a) Incubation ... 45. d) Recombinant ... 46. d) Rabies is ... 47. b) Hippoca ... 48. a) Hanta virus ...
49. b) Corneal ... 50. a) DNA ... 51. a, c and d 52. a, b, c and e 53. a, c and d
54. a) Amplifier 55. d) All 56. a) Rabies 57. b) Causes ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is c i.e. Not infectious in prodomal period *Ref. Park 19/e, p 127*

"Measles is highly infectious during the prodomal period and the stage of rash."



2. Ans. is a i.e. Bird flu virus *Ref. Park 19/e, p 133*

H5N1 is a type of new influenza virus which is a causative agent of bird flu.

- Majority of avian influenza do not infect humans. However avian H5N1 is a strain with pandemic potential since it ultimately adapt in to a strain that is contagious among humans.

3. Ans. is d i.e. Respiratory syncytial virus *Ref. O.P Ghai 6/e, p 352; Nelson Pediatrics17/e, p 1076*

- RSV is the *most common* cause of bronchiolitis.
- RSV is the *most common* cause of viral pneumonia in infants.

RSV
- RNA virus belonging to family paramyxoviridae.
- In infants ***MC*** maifestation is ***bronchiolitis.***
- In adults ***MC*** manifestation is ***common cold.***

Remember :

Treatment of Bronchiolitis :
- In uncomplicated cases, treatment is symptomatic.
- Humidified oxygen is usually indicated for hospitalized infant.
- Epinephrine may be given, however corticosteroids are not indicated.
- Antiviral drug ribavirin has moderate efficacy.

4. Ans. is a i.e. Meningoencephalitis can precede parotitis *Ref. Nelson 17/e, p 1035 - 1036*

Complications of Mumps

- ***Meningoencephalomyelitis***
  - ***MC*** complication in childhood.
  - Males are affected *more commonly.*
  - May be either due to primary infection of neuron or post infectious encephalitis with demyelination.
  - In primary infection it occurs before parotitis while in post infectious form, it follows parotitis.

- ***Orchitis and Epididymitis***
  - Parotitis may be absent in some cases.
  - CSF shows lymphocytic pleocytosis.
  - These complication are rare in prepubscent age group, while common in adolescent and adults.
  - Infertility is rare even with bilateral orchitis.
- Pancreatitis, myocarditis, arthritis, thyroiditis.
- Measles associated deafness, Dacryoadenitis are other complication.

5. Ans. is d i.e. Infection after 16 weeks of gestation result in major congenital defects

Ref. Park 18/e, p 128 - 129; 19/e, p 130 -131; Harrison 17/e, p 1218

Important features of Rubella virus

- Rubella is RNA virus of ***togavirus*** family.
- No known carrier state for postnatally acquired rubella.
- Infectivity is greatest when rash is erupted.
- Rubella (german measles) is mainly a disease of childhood particularly 3-10 years.
- One attack results ***life long immunity***
- It cause two types of disease :

a. Postnatally Acquired Rubella

- Virus is shed from pharynx during prodromal phase and continue for about a week after onset.
- It is invariably self limited.
- ***Foremost symptoms***
  - Posterior auricular, cervical and suboccipital lymphadenopathy; fever and rash (begins on face and spreads down the body).
- Petechial enathem on soft plate called Forschheimer spots may seen.
- **Complications :**
  - Arthiritis (***MC*** in fingers, wrist or knees) almost exclusively in women.
  - Hemorrhage due to thrombocytopenia and vascular damage.
  - Encephalitis.
- **Diagnosis :**
  - Throat swab culture for virus isolation
  - Serology :
    - Most widely used serological test is hemagglutination inhibition test (HAI).
    - 4 fold rise in HI antibody titre in paired sera or presence of IgM in single sera obtained 2 weeks after the rash is **diagnostic** of recent rubella infection.

b. Congenital Rubella Syndrome

- Infectivity as well as severity is more in early pregnancy *(first trimester of <11 weeks).*
- ***Classic*** *triad of patent ductus arteriosus (cardiac malformation), cataract* and *deafness* is seen.
- Infection in 2nd trimester - may be deafness only.
- >16wk – no major abnormalities
- **Diagnosis**
  - Isolation of virus in cell cultures of throat samples, urine or other secretions.
  - Detection of IgM in single serum sample shortly after birth.
  - Persistance of Rubella IgG antibodies serum beyond 1 year or rising antibody titre anytime during infancy in an unvaccinated child.

– Biopsy of tissues/ blood / CSF fluid for viral antigen by monoclonal antibodies.
– Detection of Rubella RNA by in situ hybridization and PCR.

- **Prevention**
  – **Rubella vaccine :** Live attenuated RA 27/3 vaccine
  – **Strategy :** - Immunize all infants at 12-15 mth with MMR and second dose in early childhood
    - Also administer to anyone who is thought to be susceptible to infection and is not pregnant.
  – **Contraindication :** Pregnancy

Remember : ***Pregnancy should be avoided for atleast 3 months after rubella vaccination.***

6. Ans. is d i.e. Detection of viral hemagglutination inhibiting (HAI) antibodies in a single serum specimen

Ref. Ananthnarayan 7/e, p 456; 457; Harrison 17/e, p 1079

Laboratory Diagnosis of Viral Disease

- ***Microscopy :*** By electron microscopy (for viral diarrhea); Fluorescent antibody technique (eg Rabies) etc.
- ***Demonstration of virus antigen :*** by counterimmunoelectrophoresis, radioimmunoassay, ELISA, precipitation in gel Immunofluorescence.
- ***Isolation of virus :*** by inoculation into animals, eggs or tissue culture.
  As most viruses are heat labile, refrigeration is essential during transport.
- ***Serological diagnosis :*** by neutralization, complement fixation, ELISA, Hemagglutination inhibition tests, immunofluorescence.
  – It is essential to examine paired sera (acute and Convalescent).
  – Examination of single sample of serum for antibodes is meaningful only when IgM, specific test are done.
  – Serological diagnosis is based on greater than fourfold rise in IgG in convalescent sera when acute and convalescent serum are analyzed at the same time. A simultaneous fall in IgM confirms recent primary viral infection.
  – Paired sera with rising titres of antibody to virus specific antigens and shift from IgM to IgG are generally accepted as diagnostic of acute viral infection.
  – Hemadsorption and hemagglutination assay measure the ability of serum antibodies to inhibit RNA virus induced erythocyte adsorption or agglutination.

7. Ans. is c i.e. There is a single serotype causing infection

Ref. Park 19/e, p 167-169; Ananthnarayan 7/e, p 493 - 496

Important features of Polio virus

- Polio virus, causative agent of Polio, is SS positive sense RNA virus having 1, 2 and 3 serotypes.
- ***MC*** serotype - *Type 1*
- ***MC*** cause of epidemic - Type 1 (epidemics is also caused by Type 3 while endemics is by Type 2)
- ***MC*** type associated with paralysis - *Type 1*
- Most difficult to eradicate Type -1
- Most antigenic - Type 2
- ***MC*** cause of vaccine induced paralysis ***- mutated Type - 3***

- **Modes of transmission**
  - *Main route* : Faeco-oral route directly or indirectly.
  - *Droplet infection* : may occur in acute phase of disease.
- **Clinical Spectrum**
  - Most vulnerable age is between 6 month and 3 years.
  - M.C clinical presentation – Inapparent / subclinical infection.
  - Most rare clinical presentation – Paralytic polio.
  - Usual cause of death – respiratory insufficiency.
  - Progressive paralysis, coma or convulsions usually indicate cause other than polio.
- **Prevention**
  - Two type of vaccine :
    i. Inactivated (salk) injectable polio vaccine.
    ii. Oral (sabin) live attenuated vaccine - It provides both local immunity (by producing intestinal IgA) and systemic immunity.
      - Vaccine progeny is excreted in feces and secondary spread occurs to house hold contacts so non immunized person are immunized by replacing wild strain by vaccine strain.
      - It results in herd immunity even if only about **66%** of community is immunized.

Mnemonic **= For Live Attenuated Vaccine (TIPS BYE C_2MMR)**

T	**I**	**P**	**S**
Typhoid oral	Influenza	Plague	Sabin
B	**Y**	**E**	
BCG	Yellow Fever	Epidemic typhus	
C2	**M**	**M**	**R**
Chicken pox Cholera	Measles	Mumps	Rubella

8. Ans. is d i.e. Hemorrhagic fever *Ref. Ananthnarayan 7/e, p 499*

See manifestation of enterovirus in theory of our book.

9. Ans. is a i.e. Orchitis and Oophoritis *Ref. Harrison 17/e, p 1220; Park 19/e, p 132*

- ***MC*** manifestation of mumps - bilateral parotitis.
- It can also involve submaxillary and sublingual glands but never involved alone.
- ***MC*** manifestation (other than parotitis) in post pubertal males is orchitis (sterility is rare). Seen in 20% of cases.
- Oophoritis is far less common than orchitis in males. It also not lead to sterility.
- ***MC*** manifestation (other than parotitis) in children : Aseptic meningitis which may develop before, during or in absence of parotitis.
- **Period of communicability –** Usually 4-6 days *before onset of symptoms and a week or more* thereafter. Period of maximum infectivity is just before and at onset of parotitis.

- ***Complications :***

– Encephalitis (rarely)	– Cerebral ataxia
– Facial palsy	– Transverse myelitis
– Gullen barre syndrome	– Acqueductal stenosis (Hydrocephalous)
– Pancreatitis	

10. Ans. is d i.e. Hemagglutinin and neuraminidase are strain specific

Ref. Ananthnarayan 7/e, p 504 - 505

Antigenic structure of Influenza Virus

Surface / viral or V antigen	Internal antigen
• Strain specific • Shows antigenic variation • Two types a. Hemagglutination - Antibody against this is protective b. Neuraminidase - Antibody against this is not protective	a. Envelop antigen (nucleocapsid) - Host specific b. Membrane (M) antigen - Type specific i.e. A, B or C c. Ribonucleoprotein (RNP) or soluble (s) antigen • Type specific • Stable i.e. not show antigenic variation

Antigenic variation

Antigneic drift or Minor antigenic variation	Antigenic shift or Major antigenic variation
• Due to point mutation • Responsible for epidemic • Shown by A, B	• Due to genetic reassortment • Responsible for pandemics • Only shown by type A

Remember : **Ds RNA** – Reoviridae family (reo, orbi, rota virus), Picobirnaviruses
SS DNA – Parvoviridae

11. Ans. is a i.e. Enterovirus *Ref. Ananthnarayan 7/e, p 499, Khurana Ophtha. 2/e, p 95*

Acute epidemic hemorrhagic conjunctivitis or apollo conjunctivitis is caused by :

- Pneumococci
- Adeno virus
- Coxsackie virus type A - 24
- Enterovirus type 70 ***(MC)*** ***Mnemonic -*** **PACE**

12. Ans. is a i.e. Adenovirus *Ref. See below*

RT - PCR is used to detect RNA viruses. Adenovirus is a DNA Virus.
So, it can not be detected RT - PCR.

13. Ans. is b i.e. Mumps *See below*

Causes of Viral pneumonia :

i. Adenovirus	ii. CMV
iii. Herpes simplex virus	iv. HIV (Retrovirus)
v. Influenza virus	vi. Measles virus
vii. Respiratory syncytial virus	viii. Varicella
ix. Enterovirus	x. Rhinoviruses
xi. Coronoviruses	

14. Ans. is c i.e. Increased muscular activity..... *Ref. Ghai 6/e, p 210; Park 19/e, p 172*

Predisposing factors for paralytic polio

- Tonsillectomy
- Adenoidectomy
- Cortisone adminstration
- Intramuscular injection
- Strenous physical exercise
- Tooth extraction
- Fatigue

- Oral polio vaccine is recommended to all children below 5 years.
- For eradication it is essential to immunize all infants below 6 months.

15. Ans. is b i.e. Mumps causes *Ref. Harrison 17/e, p 1220*

Already explained, refer answer no. 9

16. Ans. is b i.e. Inactivated vaccine is given IM *Ref. Park 19/e, p 171, 169*

Inactivated poliovaccine or IPV (salk type) is given subcutaneously or IM.

Other options

Option a

Most cases of polio are asymptomatic

Option c

- Dose schedule of IPV
- First dose when infant is 6 weeks old
- Additional doses are recomended prior to school entry and then every five years until the age of 18.

Option d

- These are three serotypes of apolio.
- Most out breaks of paralytic polio are due to type 1.

17. Ans. is d i.e. SSPE *Ref. Harrison 17/e, p 1215*

Complication of Measles

Otitis media	Very common in infants with measles
Pneumonia	May be primary viral pneumonia or bacterial superinfection; frequent reason for hospitalization of adults; measles rash sometimes lacking in immunocompromised patients with measles pneumonia. Primary giant cell *(Hecht's)* pneumonia is seen in immunocompromised
Croup	Occasionally severe
Gastroenteritis	Diarrhea can be life theratening in infants

Cervical adenitis	Due to lymphoid hyperplasia as host response to virus; common
Acute encephalitits	May be mild to severe / fatal; occurs in 1 in 1000 cases of mesles
Subacute sclerosing panencephalitis (SSPE)	In 1 in 100,000 cases of measles, usually when measles occured in infancy; seen 5 - 10 years later.

18. Ans. is a i.e. 6-12 week of pregnancy *Ref. Park 19/e, p 131; Harrison 17/e, p 1219*

Already explained, refer see answer no. 3

19. Ans. is c i.e. Type I is responsible for vaccine induced paralytic polio myelitis
Ref. Park 19/e, p 169

Already explained, refer see answer no. 7

20. Ans. is a i.e. Antigen in stool *Ref. Ananthnarayan 7/e, p 573; Harrison 17/e, p 1207*

Diagnosis of Rotaviurs diarrheoa

1. Stool examination

- Genotyping of rotavirus nucleic acid by PCR is most sensitive method.
- As virus is shed in large quantities (10^7-10^{12}g) in stool, diagnosis is ***confirmed by*** detecting *virus in faeces* by enzyme immunoassay or viral RNA can be detected by gel electrophoresis, probe hybridization, or PCR.
- Viral shedding detectable by EIA usually subsides within a week but may persist for >30 days in immunocompromised while PCR detect viral shedding for longer periods.
- Electron microscopy / immunoelectronmicroscopy is used to see virus in faeces.

2. Serology

- IgM or IgG antibodies in the blood are increased.

21. Ans. is a i.e. Hemorrhagic fever *Ref. Ananthnarayan 7/e, p 499*

See manifestation of enterovirus in theory of our book.

22. Ans. is c i.e. Respiratory syncytial virus *Ref. Ghai 6/e, p 352 - 353*

"Child of 11 month (infant) with respiratory distress, bilateral crepitation and wheezing is a typical presentation of Bronchiolitis."

- Cause of **Bronchiolitis :**
  - **Respiratory syncytial virus *(MC)***
  - Parainfluenza 3, 1, 2
  - Adenovirus
  - Influenza virus
  - Mycoplasma pneumonia *(Rarely)*.

***Mnemonic* - My PAIR**

23. Ans. is c i.e. Immunofluorescence antigen in stool *Ref. Ananthnarayan 7/e, p 573*

Already explained, refer answer no. 15

24. Ans. is a i.e. Reovirus *Ref. Ananthnarayan 7/e, p 448; Harrison 17/e, p 1080*

Segmented RNA virus are : *..... Harrison 17/e, p 1208*

P	– **P**icobirna viruses	→ Ds RNA
A	– **A**rena viridae	→ Ss RNA
R	– **R**eoviridae	→ Ds RNA
B	– **B**unyaviridae	→ Ss RNA
O	– **O**rthomyxoviridae (Influenza)	→ Ss RNA

***Mnemonic* = PARBO**

25. Ans. is a c i.e. CMV *Ref. Ananthnarayan 7/e, p 488, 499; Khurana 2/e, p 94*

Viral Causes of conjunctvitis

- **Adenovirus** : – Follicular (swimming pool) conjunctivitis : 3, 7, type
  – Epidemic keratoconjunctivitis (shipyard eye) : 8, 19, 37 type
- **Cox Sackie A. 24** : – Acute hemorrhagic conjuncitivitis
- **Enterovirus 70** : – Acute hemorrhagic conjunctivitis
- **Herpes simplex**
- **Herpes zoster**
- **Pox virus**
- **Myxovirus**
- **ARBO virus**
- **New castle virus.**

26. Ans. is b i.e. Rota B can be grown in cell culture
Ref. Ananthnarayan 7/e, p 572; Harrison 17/e, p 1207; Jawetz 23/e, p 507

– ***MC*** cause of Rotavirus diarrhea : ***Group A***
– Rotavirus (group A) is ***MC*** cause of diarrheal disease in infants and young children.
– ***Group B*** cause gastroenteritis in adults so called **ADRV** (adult diarrhea rotavirus).
– ***Group C*** cause small proportion of **pediatric** gastroenteritis.
– Rota virus can't be grown in cell culture but most group A human rotaviruses can be cultivated if pretreated with trypsin which facilitates uncoating.
– Very few non group A rotavirus have been cultivated.

27. Ans. is a i.e. Rota virus *Ref. Ananthnarayan 7/e, p 473, 572 - 573*

Non cultivable viruses :
- Rotavirus
- Norwalk virus
- Mollascum contagiosum.

28. Ans. is a i.e. Influenza virus *Ref. Harrison 17/e, p 1080*

Already explained, refer answer no. 24

29. Ans. is d i.e. Rota virus *Ref. Harrison 17/e, p 1207*

- The first rotavirus vaccine was introduced in 1998 and withdrawn because it was linked with intussuception.
- In 2006 two new rotavirus vaccine have been introduced, one of this is a multivalent bovine human reassortant rotavirus preparation. Second one is a single attenuated rotavirus strain.

30. Ans. is b i.e. Rabies *Ref. Ananthnarayan 7/e, p 439, 458*

- **Vaccine that grow in embryonated eggs :**
  - Influenza
  - Yellow fever (17 D strain)
  - Rabies (Flury strain)
  - ***Mumps*** *..... Ananthnarayan 7/e, p 514*
- Varicella vaccine grown in chick embryo fibroblast culture.
- Rubella – RA 27/3 vaccine produced in human diploid fibroblast. *..... Park 19/e, 131*
- No eggs culture vaccine measles are produced at all today. All are tissue culture vacciine, either check embryo or human diploid cell line. *..... Park 19/e, p 120*

31. Ans. is b i.e. HEV *Ref. Ananthnarayan 7/e, p 447, 491*

Picorna viruses		
Enterovirus	Rhinoviruses	Hepatoviruses
↓ Polio, ↓ Coxasackie, ↓ Echo, ↓ Other enteroviurses		• HAV (enterovirus 72)

Foot and mouth disease is manifestation of entero virus and coxsackie.

32. Ans. is c and d i.e. Measles - Edmonston zogreb strain; and BCG-Danish 33 strain
Ref. Ananthnarayan 7/e, p 514

Vaccine	Strain
Mumps	Jeryl-Lynn strain
Chicken Pox	OKA strain
Measles	HDC-Edmonston Zagreb strain
Rubella	RA 27/3
BCG	'Danis 1331' Strain
Cholera	CVD. 103 - HgR strain
Typhoral	Ty 21-a strain
Yellow fever 17-D	Asibi strain

33. Ans. is a and c i.e. Small Pox Virus; and Ebola virus *Ref. Harrison 17/e, p 1343*

Bioterrorism agents

- **Category A :**
  - Anthrax *(Bacillus anthracis)*

- Botulism *(Clostridium botulinum toxin)*
- Plague *(Yersinia pestis)*
- Smallpox *(Variola major)*
- Tuleremia *(Francisella tularensis)*
- Viral hemorrhagic fevers :
  - Arenaviruses : Lassa, New World (Machupo, Junin, Guanarito, and Sabia).
  - Bunyaviridae : Crimean Congo, Rift Valley
  - Filovirdiae : Ebola, Marbugh
  - Flaviviridae : Yellow fever, Omsk fever, Kyasanur Forest.

- **Category B :**
  - Brucellosis *(Brucella spp.)*
  - Epsilon toxin of *Clostridium perfringens*
  - Food safety threats *(e.g., Salmonella spp., Escherichia coli 0157 : H7, Shigella)*
  - Glanders *(Burkholderia mallei)*
  - Melioidosis *(B. Pseuodmallei)*
  - Psittacosis *(Chalmydia psittaci)*
  - Q fever *(Coxiella burnetii)*
  - Ricin toxin from *Ricinus communis* (castor beans)
  - Staphylococcal enterotoxin B
  - Typhus fever *(Rickettsia prowazekii)*
  - Viral encephalitis [alphaviruses (e.g. Venezulean, eastern, and western equine encephalitis)]
  - Water safety threats *(e.g. Vibrio cholerae, Cryptosporidium parvum).*

- **Category C :**
  - Emerging infectious diseases threats such as Nipah, hantavirus and SARS coronoavirus.

34. Ans. is a, b and c i.e. Influenza; Cholera; and Plague *Ref. Ghai 6/e, p 352 - 353*

Disease	Incubation Period
Pertussis	7 - 14 days
Chicken pox	14 - 16 days
Polio	7 - 14 days
Rubella	2 - 3 weeks (average 18 days)
Mumps	usually 18 days
Influenza	18 - 72 hrs
Diptheria	2 - 6 days
Menigococcal meningitis	usually 3 - 4 days
Cholera	few hours upto 5 days (commonly 1 - 2 days)
Rabies	highly variable, commonly 3 - 8 weeks (vary from 4 days to many years)
Plague-Bubonic plague	2 - 7 days
- Septicemic plague	2 - 7 days
- Pneumonic plague	1 - 3 days
Tetanus	usually 6 - 10 days
Leprosy	average 3 - 5 years or more

35. Ans. is a, c and d i.e. RSV; Parainfluenza; and Influenza *Ref. Ghai 6/e, p 352 - 353*

Already explained, refer answer no. 17

36. Ans. is a i.e. Herpes *Ref. Ananthnarayan 7/e, p 446*

Enveloped DNA viruses :
- *Herpesviridae*
- *Hepadnaviridae (HBV)*

All RNA viruses are **enveloped** *except* **PARC** (Picorna, astro, Reo, Calciviridae).

ARBO AND RHABDO

37. Ans. is a i.e. Relapsing fever *Ref. Park 19/e, p 635*

Tick borne diseases are :

Hard tick
- Tick typhus
- Tularemia
- Human Babesiosis
- Viral encephalitis
- Tick paralysis
- Q fever (usually air borne disease)
- Viral encephalitis *(not Japenese encephalitis which is transmitted by culex)*
- Viral haemorrhagic fever *(eg Kyasanur forest disease)*

Soft tick
- Relapsing fever

38. Ans. is b i.e. Rabies *Ref. Harrison 17/e, p 1222*

- Negri bodies are the intracytoplasmic inclusions of rabies virus in the CNS.
- Negri bodies are distributed throughout the brain particularly in Ammon's horn, the cerebral cortex, the brain stem, the hypothalamus, purkinje cells of cerebellum and the dorsal root spinal ganglia.
- They are not seen in about 20% cases of rabies and their absence does not rule out the diagnosis.

Inclusion Bodies

It is of following types :

a. Intracytoplasmic eosinophilic inclusions :
- ***Negri bodies*** – rabies
- ***Guarnieri bodies*** – variola (small pox), vaccinia
- ***Bollinger bodies*** – fowlpox
- ***Henderson - peterson bodies*** – molluscum contagiosum

b. Intranuclear acidophilic inclusion bodies :
- ***Cowdry type A*** – herpes, chicken pox, CMV, yellow fever
- ***Torres bodies*** – yellow fever
- ***Cowdry type B*** – polio virus

c. Both Nuclear and cytoplasmic :
- ***Warthin Finkeldey*** – measles

d. Intranuclear basophilic inclusion bodies :
- ***Cowdry type B*** – adenovirus

39. Ans. is c i.e. Kyasanur Forest disease *Ref. Park 19/e, p 622, 634*

Already explained, refer answer no. 37

40. Ans. is c i.e. Immediately stitch wound under antibiotic coverage *Ref. Park 19/e, p 229-230*

"Immediate stitching is contraindicated."

- **Combined administration of :**
  - Single dose of antirabies serum
  - Anti rabies (ARV) vaccine and;
  - Local treatment of wound is the *best* specific prophylactic treatment after exposure of man to rabies (especially in all severe cases i.e. class III exposures and in all cases of unprovoked bites by wild animals).
- **Anti Rabies Serum *(Passive immunity)*** should be given as promptly as possible after sensitivity test, irrespective of interval between exposure and begining of treatment.
  - It prolongs I.P if administered soon after exposure to rabies so it is particularly important in class III bites.
  - It is given either as Horse antirabies serum (40 IU) or Human rabies immunoglobulin (20 IU) in which part of the dose given around the wound and rest by IM in gluteal region.
- **Local Treatment of wound :**
  - It can reduce the chances of developing rabies by upto 80%. It consist of :
    a. Cleansing with plenty of soap and water, preferably under a running tap for at least 5 minutes.
    b. Chemical treatment by virucidal agents either alcohol, tincture 0.01% of aqueous solution of iodine or povidone iodine (not use savlon, cetavlon, carbolic or nitric acid).
    c. ***Suturing - Not done immediately*** but should be done 24 - 48 hours later.
    d. Antirabies serum.
    e. Observe the animal for 10 days.

41. Ans. is b i.e. Licks on Fresh wound *Ref. Park 19/e, p 231*

Classification of exposures

Class I (slight risk) :	*Class II (Moderate risk)*	*Class III (severe risk)*
– Licks on healthy unbroken skin – Consumption of unboiled milk of suspected animal – Scratches without oozing of blood	– Licks on fresh cuts – Scratches with oozing of blood – All bites except on head, neck, face, palm, fingers – Minor wounds less than 5 in number	– All bites or scratches with oozing of blood on neck, head, face, palm, fingers – Lacerated wounds on any part of body – Multiple wounds 5 or more in number – Bites from wild animals

42. Ans. is c i.e. RNA has a negative polarity *Ref. Ananthnarayan 7/e, p 535 - 536*

Rabies virus are :

- ***Bullet*** shaped

- Belong to rhabdoviridae-serotype 1 (Lyssavirus type - 1) [Serotype 2, 3 and 4 are rabies related viruses].
- Lipoprotein envelope carry glycoprotein spikes.
- Core consist of helically arranged ribonucleoprotein and ***RNA dependent RNA transcriptase.***
- Genome is unsegmented, linear, negative sense RNA ***[Other -ve sense RNA viruses - Ortho, paramyxoviridae].***
- Virus is inactivated by phenol, formalin, betapropioplactone, ultraviolet, irradiation, sunlight.
- Virus has hemagglutinating activity due to spikes.
- Virus spreads centripetally from site of inoculation *(within striated muscle),* than ascends throgh nerve associated tissue space and than spreads centrifugally in peripheral autonomic nerves to many tissues including salivary glands. Thus pathogenesis does not show that it has affinity for motor neurons.

43. Ans. is c i.e. KFD is transmitted by ticks *Ref. Park 18/e, p 227 - 228, 602; 19/e, p 622*

- List of tick transmitted disease is already mentioned in question no. 32
- ***Yellow fever*** is an exotic disease for India i.e. disease which may be imported in India or India is yellow fever 'receptive' area that is "an area in which yellow fever does not exist but where condition would permit its development if introduced".
- Dengue virus has at least 4 serotypes not one.
- Japanese encephalitis is transmitted by culex not Aedes.

Remember : *Other culex transmitted diseases are :*
- Bancroftian filariasis
- West Nile fever
- Viral arthritis (epidemic / polyarthritis).

44. Ans. is a i.e. Incubation period depends on the site of bite
Ref. Park 18/e, p 218; 19/e, p 219; Ananthnarayan 7/e, p 449, 539

- **Incubation period of Rabies depends on the :**
  - Site of bite
  - Number of wounds
  - Species of biting animal
  - Severity of bite
  - Amount of virus injected
  - Protection provided by clothing and treatment undertaken.
- I.P is shorter in :
  - Severe exposures
  - Bites by wild animals.
  - Bites on face, head, neck and upper extremities
- In India most of human rabies cases have resulted from dog bites but it ***also occurs by bite of cat, monkey, horse, Jackals, fox-hyena etc.***
- Also transmitted by licks on abraded skin and mucosa; aerosols; corneal and organ transplants.
- Characteristic of rabies is Negri Body which is ovoid eosinophilic intracytoplasmic inclusion bodies.
- Rabies is bullet shaped SS negative sense RNA virus.

45. Ans. is d i.e. Recombinant glycoprotein vaccine *Ref. Park 18/e, p 219; 19/e, p 229*

Rabies Vaccines

- **Vaccine currently in use are of three types**
  a. ***Nervous tissues vaccine :*** BPL inactivaed Adult sheep (Semple type) and Suckling mouse brain vaccine.

b. ***Duck embryo vaccine :*** Not available in India.

c. ***Cell culture vaccine -***

– Human diploid cell vaccine (HDCV) used in India for both pre and post exposure immunzation.

– Second generation tissue culture vaccine eg. Chick embryo fibroblast, vero continous cell vaccine etc it is recommended by WHO.

46. Ans. is d i.e. Rabies is best diagnosed by immunoflorescence study
Ref. Ananthnarayan 7/e, p 539; Park 18/e, p 217; 19/e, p 227

Diagnosis of Human Rabies

– ***Specimen***

Antemortem Corneal smears, skin biopsy from face or neck, saliva.

Postmortem : Brain

– Method *most commonly used* for diagnosis is the demonstration of rabies virus ***antigens by immunofluorescence*** (direct or using monoclonal antibodies).

– Demonstration of negri bodies in the brain or spinal cord.

– ***Isolation*** of virus by intracerebral inoculation in mice; from the brain, CSF, saliva, urine.

– Rapid isolation is done by tissue culture cell lines.

– High titre rabies specific ***antibodies in CSF*** (Not seen after immunization) by Fluorescent antibody test.

– Detection of rabies virus RNA in saliva by Reverse transcription PCR.

Remember :

- Rabies infection terminates in death, not life long immunity.
- Rabies virus has single serotype i.e. Lyssavirus type 1.
- Rabies vaccine is killed inactivated vaccine.
  – Inactivation is commonly done by phenol or Betapropiolactone.

47. Ans. is b i.e. Hippocampus *Ref. Harrison 17/e, p 1222*

Sites of Negri bodies

- Cerebellum and hippocampus *.....Ananthnarayan 7/e, p 539*
- Neurons of Ammon horn, cerebral cortex, brain stem, hypothalmus, purkinje cells of cerebellum and dorsal spinal ganglia. *.... Harrison 16/e, p 1157*

48. Ans. is a i.e. Hanta virus pulmonary syndrome is caused by inhalation of rodent urine *Ref. Jawetz 24/e, p 525; Park 19/e, p 240 - 241*

Hantavirus are classified in the hantavirus genes of the Bunyaviridae family. It cause two serious and often fatal disease.

– Hemorrhagic fever with renal syndrome.

– Hanta virus pulmonary syndrome.

- Hantavirus are natural pathogen of rodents. Viremia is present in infected rodents and the virus is shed in urine, feces and saliva in high titres. *Transmission from rodent to rodent and rodent to human* is primarily respiratory by inhalation of virus contained in dried excreta.

Other options :

- KFD is a febrile disease caused by an arbovirus and transmitted to man by bite of infective tick.
- *Chikugunya fever* - Dengue like disease caused by chikugunya virus and transmitted by Aedes, Culex and Mansonia mosquito.

49. Ans. is b i.e. Corneal impression smear for immunofluoresence stain
Ref. Ananthnarayan 7/e, p 539

Already explained, refer answer no. 39

50. Ans. is a i.e. DNA virus *Ref. Ananthnarayan 7/e, p 533*

- Hantaan virus is a RNA virus belong to genus Hantavirus and family Bunya viridiae.
- It causes two syndromes :

a. Hemorrhagic fever with renal syndrome (HFRS) or Manchurian epidemic HF or rodent bome nephropathy

– It occur in two forms : i. Epidemic nephritis - milder form
ii. Epidemic hemorrhagic fever-serious form.
– Resembles typhoid, leptospirosis and scrub typhus clinically.
– Genus hantavirus contain 4 species- Hantaan, Seoul, puumala and Hill virus.
– They are natural pathogen of rodents so consider robovirus and not stirctly an arbovirus infection.
– ***Major host*** for hantaan : Field mice
– Transmission from rodent to rodent and rodent to human is primarily respiratory, by inhalation of virus contained in dried excreta.
– ***Diagnosis :*** Demonstrating IgM by ELISA or of rising titre of immune adherence hemagglutinating antibodies in paired sera.

b. Hantavirus pulmonary syndrome

– Caused by new H-antavirus the *Sin Nombre* (meaning nameless) virus which is associated with deer mouse and other rodents.
– ***No arbovirus*** is linked in transmission.
– Transmission occur by inhalation of virus areosol in dried rodent feces.

51. Ans. is a, c and d i.e. Nipah virus; Corona virus; and SARS *Ref. Harrison 17/e, p 1743*

Already explained, refer answer no. 33 (category C)

52. Ans. is a, b, c and e i.e. KFD; West Nile fever; Ganjam virus; and Puumala virus
Ref. Ananthnarayan 7/e, p 522

Family	Genus	Important species
Togaviridae	Alphavirus	Chikungunya, Sindbis and Venezuelan equine encephalitis viruses
Flaviviridae	Flavivirus	Japaness encephalitis, West Nile, Yellow Fever, Dengue types 1, 2, 3, 4, Kyasanur Forest Disease, Omask hemorrhagic fever
Bunyaviridae	Bunyavirus	California encephalitis
	Phlebovirus	Sandfly fever viruses, Rift valley fever virus
	Nairovirus	Crimean Congo hemorrhagic fever viruses, Ganjam virus
	Hantavirus	Hantan, Seoul, Puumala, Prospect Hill, Sin Nombre viruses
Reoviridae	Orbivirus	Colorado tick fever, African horse sickness, Blue tongue viruses
Rhabdoviridae	Vesiculovirus	Vesicular stomatitis virus, Chandipura virus

53. Ans. is a, c and d i.e. Hantaviurs pulmonary syndrome; Transmitted by rodents; and Hemorrhagic fever with renal failure *Ref. Ananthnarayan 7/e, p 533*

Already explained, refer answer no. 50

54. Ans. is a i.e. Amplifier *Ref. Park 18/e, p 228 - 229; 19/e, p 239*

Japanese encephalitis

- **Vector :** – Culex tritaneorhynchus (most important)
  – C. vishnvi
  – C. gelidus.
- Man is an incidental ***'dead end'*** host.
- Animal host :

  Pigs – major vertebrate host.
  – not manifest any symptoms so acts as as an amplifiers.

  Cattles and buffaloes – act as mosquito attractants.

  Horses – only domestic animals which shows signs of encephalitis.
- Birds host – Pond herons (reservoir host), Cattle egrets, poultry and ducks.
- Incubation period in man – 5 - 15 days.
- Average period between onset of illnes and death is about 9 days.

Remember :

Killed mouse brain vaccine is available by which immunity develops after one month of second dose.

55. Ans. is d i.e. All *Ref. Ananthnarayan 7/e, p 536*

- **Inactivating agent of rabies virus :**
  – Phenol
  – Formalin
  – Betapropiolactone
  – UV irradiaction
  – Sunlight.
- Thermal inactivation occurs in one hour at 50^0C and 5min at 60^0C.

56. Ans. is a i.e. Rabies *Ref. Ananthnarayan 7/e, p 499; Harrison 17/e, p 1222*

Already explained, refer answer no. 38

57. Ans. is b i.e. Causes Hemorrhagic fever with renal involvement *Ref. Ananthnarayan 7/e, p 533*

Already explained, refer answer no. 50

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Man is the only reservoir of : **[AIIMS 90]**

a) Rabies
b) Measles
c) Typhoid
d) Japanese B encephalitis

[Ref. Park 19/e, p 127]

2. Which of the following statemtn is/are true of all paramyxoviruses : **[DNB 90]**

a) They contain a single-standed RNA genome of negative polarity
b) Envelopes are dervied from the hostcells plasma membrane
c) They have a cytoplasmic site of replication
d) They enter the body by the respiratory route

[Ref. Ananthnarayan 7/e, p 431, 437, 512]

3. Negri Bodies are commonly seen in :

a) Hippocampus **[AIIMS 90, 92; AI 88]**
b) Hypothalamus
c) Mamillary bodies
d) Cerebrum
e) Pons

[Ref. Ananthnarayan 7/e, p 539]

4. Which of the following vaccine [s] should not be given to an immunodeficient patient : **[DNB 90]**

a) Influenza vaccine
b) Rubella vaccine
c) Pneumococcal vaccine
d) Trivalent oral polio vaccine

[Ref. Park 19/e, p 97]

5. In india, human infections has been reported dengue virus type : **[AP 91]**

a) Types I and 1
b) Types 1 and 3
c) Types 2 and 4
d) Type 1 only
e) All 4 types

[Ref. Park 19/e, p 206]

6. KFD is transmitted by : **[AI 91]**

a) Fleas
b) Mite
c) Tick
d) Mosquito

[Ref. Ananthnarayan 7/e, p 531]

7. Which of the following is not common in India :

a) Japnese B encphalitis **[AI 91]**
b) Lassa fever
c) KFD
d) Dengue

[Ref. Park 19/e, p 238]

8. Neurological complications following Rabies vaccines is common with : **[Jipmer 91]**

a) HDC Vaccine
b) Chick embryo vaccine
c) Semple vaccine
d) Duck egg vaccine

[Ref. Park 19/e, p 219]

9. Acute epidemic keratoconjuctivitis is caused by :

a) Herpes virus **[AI 91]**
b) Echo 51
c) Enterovirus 70
d) Enterovirus 72

[Ref. Ananthnarayan 7/e, p 499]

10. The following is true of Rota virus : **[AI 92]**

a) Easily grown in cell culture
b) Double stranded DNA
c) Terminal ileum villi destroyed
d) Adult and old people account for 60% of infection

[Ref. Ananthnarayan 7/e, p 572; Harrison 17/e, p 1207]

Answer

1. c) Typhoid
2. a, b and d
3. a) Hippocampus
4. b and d
5. e) All 4 types
6. c) Tick
7. b) Lassa ...
8. c) Semple ...
9. c) Enterovirus ...
10. c) Terminal ...

11. Which of the following does not cause conjuctivitis:
a) Adeno virus **[JIPMER 92]**
b) Entero virus
c) Coxasackie virus
d) Herpes virus
[Ref. Ananthnarayan 7/e, p 477, 488, 499]

12. Negri bodies are located in : [Bihar 91; DNB 92]
a) Astrocytes
b) Oliogodendroglia
c) Neurons
d) Microglia
[Ref. Ananthnarayan 7/e, p 539]

13. All are true of rabies Except : [AIIMS 92]
a) 100% mortality
b) Spreads from periphery
c) Infects only the brain
d) Prophylactic immunisation of people at Risk
[Ref. Ananthnarayan 7/e, p 537]

14. Diarrrhoea in Rota virus infection is due to :
a) Increased intestinal hypermotility **[PGI 93]**
b) Decreased absorption by villi
c) Increased Secretion by villi
d) None of the above
[Ref. Harrison 16/e, p 1142]

15. Virus causing chicken pox belongs to : [AI 93]
a) Pox virus
b) Herpes virus
c) Coxsackie virus
d) Adeno virus
[Ref. Ananthnarayan 7/e, p 479]

16. Latent infection is seen in : [AI 93]
a) Small pox
b) Adeno virus
c) Chicken pox
d) Measles
[Ref. Ananthnarayan 7/e, p 474]

17. Japanese B encephalitis virus is transmitted by :
a) Aedes aegypti **[JIPMER 86, NIMHANS 87,**
b) Culex fatigans **Kar. 94]**
c) Culex tritaeniorynchus
d) Hard tick
e) Soft tick
[Ref. Ananthnarayan 7/e, p 526]

18. Negri bodies are seen in : [Kerala 94]
a) Rabies
b) Small pox
c) Trachoma
d) Lymphogranuloma venerum
[Ref. Ananthnarayan 7/e, p 539]

19. Virus causing pneumonia are all except :
a) Cytomegalo virus **[JIPMER 95]**
b) Mumps
c) Herpes
d) Mealses
[Ref. Harrison 17/e, p 109]

20. Which ARV has been recommended by WHO as the most effective : [TN 95]
a) Duck cell vaccine
b) Chick fibroblast vaccine
c) HDCV
d) Sheep brain vaccine
[Ref. Park 19/e, p 229]

21. The staining useful for antemorten diagnosis of rabies is : [Karn. 95]
a) Seller
b) Macchiavillo
c) Giemsa
d) Fluorescent
[Ref. Ananthnarayan 7/e, p 539]

22. Post exposure immunization is done for :
a) Measles **[JIPMER 95]**
b) Polio
c) Rabbies
d) Chicken pox
[Ref. Park 19/e, p 129, 229]

23. Subacute sclerosing panencephalitis is associated with : [Delhi 96]
a) Chicken pox
b) Rabies
c) Measles virus
d) Polio virus
[Ref. Ananthnarayan 7/e, p 568]

24. In which of the following virus is shed in stool :
a) Herpangina **[UP 96]**
b) Influenza
c) Varicella
d) Small pox
[Ref. Ananthnarayan 7/e, p 497]

Answer

11. None	12. c) Neurons	13. c) Infects only ...	14. b) Decreased ...	15. b) Herpes ...
16. c) Chicken ...	17. c) Culex ...	18. a) Rabies	19. b) Mumps	20. b) Chick ...
21. d) Fluorescent	22. a and c	23. c) Measles ...	24. a) Herpangina	

25. Which viral infection always causes clinical disease in human beings : **[Kerala 96, 97]**

a) Rubella
b) Poliomyelitis
c) Measles
d) Chicken pox
e) Rabies

[Ref. park 19/e, p 127, 228]

26. Strain used in measles vaccine is : **[UP 99]**

a) Salk
b) Sabin
c) TAF
d) Edmonston jagreb

[Ref. Park 19/e, p 129]

27. RSV causes : **[UP 99]**

a) Bronchiolitis
b) Mumps
c) Croup
d) Bronchitis

[Ref. Ananthnarayan 7/e, p 516]

28. True about influenza A is : **[UP 00]**

a) Double strained segmented RNA
b) Pandemic are caused by antigenic drift
c) Nucleocapsid antibody is specific
d) Hexaminidase and Neuraminidase is type specific

[Ref. Ananthnarayan 7/e, p 504-505]

29. True about picorna virus are A/E : **[UP 00]**

a) OPV provides herd immunity
b) Immunity in poliomyelitis is type specific
d) Best method of isolation is tissue culture
d) Passive immunization of human immunoglobulin has more value

[Ref. Ananthnarayan 7/e, p 491 - 492; Park, 19/e, p 170]

30. Which of the following viruses is composed of two distinct capsids enclosing the double stranded RNA? **[Kar 00]**

a) Adenovirus
b) Reovirus
c). Herpes virus
d) Myxovirus

[Ref. Jawetz 24/e, p 502]

31. The vector for Japanese encephalitis is :

a) Lice **[Kar 00]**
b) Tick
c) Culex mosquito
d) Sandfly *[Ref. Park 19/e, p 238]*

32. Type of vaccine available commercially for rabies are all except : **[UP 00]**

a) Inactivated sheep brain vaccine
b) Genetically engineered glycoprotein vaccine
c) Duck embryo cultured vaccine
d) Human diploid cell vaccine

[Ref. Park 19/e, p 229]

33. All enveloped helical RNA viruses belong to one large group, which includes all of the following except : **[Kar 01]**

a) Influenza
b) Parainfluenza
c) Mumps
d). Herpes

[Ref. Ananthnarayana 7/e, p 475, 501]

34. Rotaviruses are responsible for : **[Kar 01]**

a) Acute nonbacterial gastroenteritis in adults
b) Infantile diarrhea
c) Teratogenic effects
d) Respiratory tract infection in immunocompromised individuals

[Ref. Harrison 17/e, p 1206]

35. Epidemic hemorrhagic conjunctivtis is caused :

a) HSV **[UP 02]**
b) HZV
c) HIV
d) Picorna virus

[Ref. Ananthnarayansa 7/e, p 499; Table 54.2]

36. The congenital rubella syndrome : **[DNB 02]**

a) May be prevented by vaccination in early pregnancy
b) Causes intra uterine growth retardation
c) Causes cataracts
d) Causes deafness only if acquired before 16 weeks of gestation

[Ref. Park 19/e, p 130-131]

37. Rubella vaccination is contra indicated in all except : **[JIPMER 02]**

a) Patient on immunosuppressant
b) Girl with Leukemia
c) Girls between 11-14 years
d) Pregnancy

[Ref. Park 19/e, p 131]

Answer

25. c and e	26. d) Edmonston ...	27. a) Bronchiolitis	28. d) Hexaminidase ...	29. d) Passive ...
30. b) Reovirus	31. c) Culex ...	32. b) Genetically ...	33. a and d	34. b) Infantile ...
35. d) Picorna ...	36. b and c	37. c) Girls ...		

38. Pre-exposure cell culture vaccine used in Rabies
a) 3 doses **[UP 02; AI 90]**
b) 4 doses
c) 5 doses
d) 6 doses
[Ref. Park 19/e, p 233-234]

39. Break bone fevers caused by which virus :
a) Variola **[Bihar 03]**
b) Coxsackie
c) Arbo
d) Adeno virus
[Ref. Anantharayan 7/e, p 530]

40. Epidemic of polio is due to : **[Kolkata 03]**
a) Type I virus
b) Type II virus
c) Type III virus
d) Combine of type II and type III virus
[Ref. Park 19/e, p 168]

41. Recommended vaccines for rabies : **[Kar 04]**
a) DPT
b) MMR
c) BCG
d) HDCV
[Ref. Park 19/e, p 229]

42. About rabies true is : **[SGPGI 05]**
a) Vaccine causes life long immunity
b) Multiple strains are found
c) CNS infention occurs through viremia
d) Bullet-shaped nonenveloped, double stranded RNA virus
[Ref. Ananthnarayan 7/e, p 535 - 537]

43. Which of the following is associated with acute hemorrhagic conjunctivitis ? **[Bihar 05]**
a) Rhabdovirus
b) Enterovrus
c) Calcivirus
d) Echovirus
[Ref. Ananthnarayan 7/e, p 499]

44. Enteroviruses cause : **[Bihar 05]**
a) A. hemorrhagic conjunctivitis
b) Ac. follicular conjunctivitis
c) Posterior follicular conjunctivitis
d) Epidermic kerato conjunctivitis
[Ref. Ananthnaryan 7/e, p 499]

45. Break one fever is caused by which virus :
a) Varioloa **[Bihar 05]**
b) Coxsackie
c) Dengue
d) Adenoa virus
[Ref. Anathnarayan 7/e, p 530]

46. Commonest cause of Bronchiolitis is : **[UP 05]**
a) RSV
b) Adenovirus
c) Influenza
d) Herpes virus
[Ref. Ghai 6/e, p 352]

47. Which of the following is true regarding influenza:
a) It is caused by an enveloped DNA virus
b) Laboratory studies may show neutropenia early in the course of disease **[MP 06]**
c) Primary infectious pneumonia is less common than secondary bacteria pneumonia
d) Antiviral agents is given early prevents complications
[Ref. Harrison 17/e, p 1129]

48. Virus lacking hemagglutinin and nuraminidase but have membrane fusion protein is :
a) RSV **[Jharkhand 06]**
b) CMV
c) HSV
d) Ebestein Barr virs
[Ref. Anantharayan 7/e, p 516]

49. Negri bodies are seein in infections due to :
a) Polio virus **[Kar 06]**
b) Rabies virus
c) Herpes virus
d) Aenovirus
[Ref. Ananthnarayan 7/e, p 539]

50. A vaccine for rabies was first developed by :
a) Louis psteur **[Kar 06]**
b) Robert koch
c) Edward jenner
d) Landsteiner
[Ref. Ananthnarayan 7/e, p 2]

51. Coxsackie group A commonly causes : **[TN 01]**
a) Conjunctivitis
b) Aseptic meningitis
c) Hepatitis
d) Myocarditis
[Ref. Ananthnarayan 7/e, p 497]

Answer
38. a) 3 doses 39. c) Arbo 40. None 41. d) HDCV 42. b) Multiple ...
43. b) Enterovrus 44. a) A. hemorrhagic ... 45. c) Dengue 46. a) RSV 47. c) Primary ...
48. a) RSV 49. b) Rabies ... 50. a) Louis ... 51. b) Aseptic...

3 Slow Virus Diseases

Slow virus infections have the following characteristics :

– Incubation periods range from months to year.
– Course of illness lasting for months or years with remissions and exacerbations.
– Predilection for involvement of central nervous system.
– Absence of immune response or an immune response that does not arrest the disease but may actually contribute to pathogenesis.
– Genetic predisposition.
– Invariable fatal termination.

Remember : ***MC prion disorder*** in humans is **sporadic** form of **CJD.**

Classification

I. ***Group A***

- Infections of sheep caused by lentiviruses
  – Eg visna maedi

II. ***Group B*** = *Subacute Spongioform viral encephalopathies*

- Comprise of prion (infectious protein) diseases.
- These are chronic progressive degenerative diseases of CNS.
- Pathology consists of progressive vacuolation in the dendritic and axonal process of neurons and extensive astroglial hypertrophy and proliferations which leads to spongiform degeneration in the grey matter. There is no sign of any inflammation or immune response.
- **Mechanism**
  – Proliferation of an abnormal prion protein (PrPse) which is derived from the normal prion protein PrPe.
  – PrPse is not simply a misfolded protein but it is an alternatively folded molecule with a function.

Disease	***Mechanism of Pathogenesis***
Human	
a. Kuru (meaning tremor)	Infection through ritualistic cannibalism
b. Iatrogenic Creutzfeldt Jakob disease (CJD)	Infection from prion contaminated human growth hormone, duramater graft, corneal transplant
c. Variant (CJD)	Infection from bovine prion (Eating BSE infected beef)

Continue .....

d.	Familial CJD	Germline mutation in PRNP
e.	Sporadic CJD	Somatic mutation or spontaneous conversion of P_rP^c into P_rP^{sc}
f.	Fatal familial insomania	Germline mutation in PRNP
g.	Gestmann strausster Scheinker	Germline mutation in PRNP

Animal prion disease eg.

a. Scrapie
b. Mink encephalopathy
c. Bovine spongiform encephalopathy (BSE, 'mad cow disease).

III. *Group C* *- eg.*

a. Subacute sclerosing panecephalitis (SSPE)
   - It is delayed sequel to infection with defective measles virus.
   - Virus cannot be isolated in routine culture but only by co-cultivation of infected brain cells with susceptible cells of non neural origin.
   - Antibody is regularly found in CSF and is **pathognomonic.**
   - ***SSPE also seen in rubella infection.***

b. Progressive multifocal leucoencephalopathy (PML)
   - Seen in elderly persons whose immune proces is impaired by malignancy or HIV etc.
   - Caused by JC virus (papovavirus).

Remember : JC virus also cause Hodgkins disease of brain.

QUESTIONS

1. Prion are : **[AI 08]**

a) Infectious proteins
b) Made up of bacteria and virus particles
c) Nuclear material
d) Can be cultured in cell free media

2. Prions consists of : **[AIIMS 07]**

a) DNA and RNA
b) DNA, RNA and proteins
c) RNA and proteins
d) Only proteins

3. Which of the following is not prion associated disease : **[AIIMS 03]**

a) Scarpie
b) Kuru
c) Creutzfedt - Jakob disease
d) Alzheimer disease

4. True about Prion disease is all except :

a) Myoclonus is seen in 10% of the patients
b) Caused by infectious protein **[AIIMS 01]**
c) Brain biopsy is diagnostic
d) Commonly manifests as dementia

5. Fatal familial insomnia is associated with :

a) Prion disease **[AI 99]**
b) Degenerative disease
c) Neoplastic disease
d) Vascular disease

6. Creutzfeld Jakob disease is caused by :

a) Prion **[PGI 99]**
b) JC virus
c) Genetic factors
d) Nutritional deficiency

Answer 1. a) Infectious ... 2. d) Only ... 3. d) Alzheimer ... 4. a) Myoclonus is ... 5. a) Prion ... 6. a and c

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is a i.e. Infectious proetin *Ref. Jawetz 24/e, p 2, 581*

Prions are infectious protein devoid of nucleic acid.

- Prions are usually resistant to standard means of inactivation. They are resistant to treatment with formaldehyde, urea, dry heat, boiling. However they are sensitive to phenol, ether, autoclaving.
- Prions infect and propagate by refolding abnormally into a structure which is able to convert normal molecule of protein in to the abnormally structure form.

2. Ans. is d i.e. Only protein *Ref. Jawetz 24/e, p 581*

Already explained, refer answer no. 1

3. Ans. is d i.e. Alzheimer disease *Ref. Harrison 17/e, p 2647*

Various prion are as follows :

- Kuru
- Fatal familial insomnia (FFI)
- Sporadic fatal insomnia (SFI)
- Transmissible mink encephalopathy
- Chronic wasting disease
- Exotic ungulate encephalopathy
- Creutzfeldt Jakob disease (CJD)
- Gerstmann - Straussler - Scheinker disease (GSS)
- Scrapie
- Bovine spongiform encephalopathy (mad cow disease)
- Feline spongiform encephalopathy

4. Ans. is a i.e. Myoclonus is seen in 10% of the patients *Ref. Harrison 17/e, p 2646 - 2650*

- Prion is proteinaceous infectious particle that lacks nucleic acid and causes slow virus disease.
- ***MC*** human prion disease is sporadic **CJD.**
- **Clinical Features of CJD :**
  - Most patient present with deficits in higher cortical function which almost always progress to dementia.
  - 90% patienty exhibit myoclonus which persist during sleep in comparison of other involuntary movements.
  - Also present with visual impairment or cerebellar gait, coordination deficit, extrapyramidal dysfunction, pyramidal signs, seizures.
- **Diagnosis :**
  1. Constellation of dementia, myoclonus and peirodic electrical burst in an afebrile 60 year old patient generally indicates CJD.
  2. ***Only specific diagnostic test for CJD is measurement of P_rP^{sc}***
  3. In humans the diagnosis of CJD as established by brain biopsy if p_rp^{sc} is detected.
     - There is no abnoramlity on gross examination of brain.
     - Pathologic hallmarks are spongiforms degeneration (in cerebral cortex, putamen etc) and Astrocytic glycosis.
     - 10% of CJD patient have amyloid plaques.

4. CT may be normal or show cortical atrophy.
5. Sequencing the PRNP gene.
6. CSF is nearly always normal but may show minimal protein elevation.

5. Ans. is a i.e. Prion disease *Ref. Ananthnarayan 7/e, p 567*

Already explained, refer answer no. 1

6. Ans. is a and c i.e. Prion; and Genetic factors *Ref. Harrison 17/e, p 2649*

- **Genetic factors are involved in familial form of CJD.**
- **Missense mutation** and expansions in the octapeptide repeat region of the gene are ***responsible for familial forms of prion disease.***

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Mad cow disease is due to :

a) Slow virus **[Culcutta 2K, UPGMEE 97]**
b) Mycoplasma
c) Bacteria
d) Fungus

[Ref. Ananthnarayan 7/e, p 567]

2. "Human cannibalism" is associated with :

a) Q fever **[UP 06]**
b) Sleeping sickness
c) Trachoma
d) Kuru

[Ref. Ananthnaranayan 7/e, p 567]

Answer 1. a) Slow virus 2. d) Kuru

4 Hepatitis Viruses

Comparative Features of Viral Hepatitis

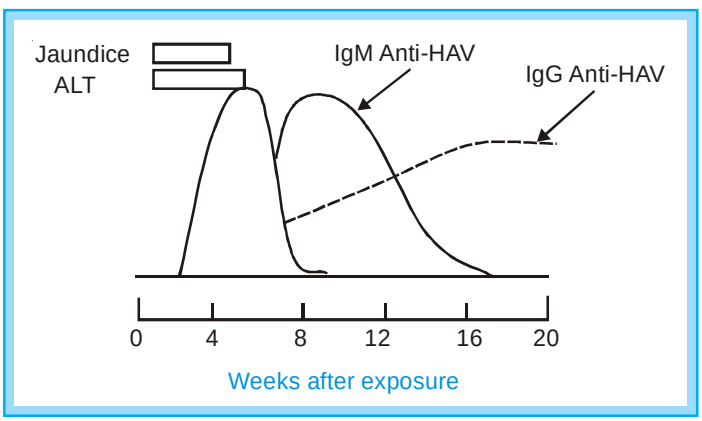
Feature	HAV	HBV	HCV	HDV	HEV
Family	Picornavirus	Hepadnavirus	Flavivirus	Defective virus	Calcivirus/ Alphavirus
Incubation (days)	15-45, mean 30	30-180, mean 60-90	15-160, mean 50	90-180 mean 60-90	14-60, mean 40
Onset	Acute	Insidious or acute	Insidious	Insidious or acute	Acute
Transmission					
Fecal-oral	+++	–	–	–	+++
Percutaneous	Unusual	+++	+++	+++	–
Perinatal	–	+++	±	+	–
Sexual	±	++	±	++	–
Clinical					
Severity	Mild	Occasionally severe	Moderate	Occasionally severe	Mild
Fulminant	0.1%	0.1-1%	0.1%	5-20%	1-2%
Progression to *chronicity*	None	Occasional (1-10%) **(90% of neonates)**	Common	Common	None
Carrier	None	0.1-30%	1.5-3.2%	Variable	None
Cancer	None	+	+	±	None
Prognosis	Excellent	Worse with age, debility	Moderate	Acute : good Chronic : poor	Good
Prophylaxis	IG Inactivated vaccine	HBIG Recombinant vaccine	None	HBV vaccine (none for HBV carriers	Unknown
Therapy	None	Interferon Lamivudine Adefovir	Pegylated interferon plus ribavirin	Interferon ±	None

HEPATITIS - A

- ***Non enveloped RNA virus*** belonging to picorna family.
- Originally called as enterovirus 72.
- Resistant to ether, acid and heat but sensitive to chlorination.
- ***Only*** hepatitis virus that can be cultivated in vitro.
- ***MC*** cause of acute hepatitis in children.
- ***Only*** viral hepatitis which can cause spiky fever.

Diagnosis :

- Detection of ***IgM anti HAV*** antibody during late incubation period which reaches peak level in *2 - 3 weeks.*



Clinical and laboratory features of viral hepatitis

Treatment

- Symptomatic *no specific antiviral* drug is given.

Prevention

– ***Formalin inactivated tissue culture vaccine*** is effective.
– Given IM
– Vaccine should be given in age > 2 years.
– Provides immunity after 4 weeks of vaccination.
– Immunity last for approx 20 years.

HEPATITIS - B

Most widespread and important type of hepatitis virus.

- ***DNA virus belonging to hepadnaviruses family.***

Viral Proteins and Particles

Three particulate form can be seen by electron microscopy :

1. 22 nm spherical or filament form (***MC***). Represent *excess viral envelop protein.*
2. 42 nm double shelled spherical particles - Represent intact HBV virion.
3. Smaller spherical or tubular particle - Represent hepatitis B surface antigen **(HBS Ag = Australia Antigen).**

HBV Genes and Gene Products

Genes	*Regions*	*Gene products*
S	S	Major protein (S)
	S+Pre-S2	Middleprotein (M) HBs Ag
	S+Pre-S1 and S2	Large protein (L)
C	C	HbcAg
	C+Pre-C	HbeAg
P (Largest gene)		DNA polymerase
X		HBx ***Ag (contributes to carcinogenesis)***

Mutants of HBV

Two types of mutant are found :

- ***Hbe Ag Negative phenotype (MC mutant) :*** Results in severe chronic infection with detectable HBV DNA and anti HBe Ag but HBe Ag is not detectable.
- ***Escape mutant :*** Due to change in HBs Ag. Vaccine is not effective against them.

Pathogenesis and Clinical features

1. **Acute hepatitis**
   - Low grade fever, jaundice, splenomegaly and tender hepatomegaly is found in all acute viral hepatitis.
   - Non of hepatitis virus is known to be directly cytopathic to hepatocyte, it is immunologic response which cause cell injury.

2. **Chronic hepatitis**
   - Persistence of ***HBeAg*** *beyond* 3 month or Persistance of ***HBsAg*** *beyond* 6 months after acute hepatitis.

3. **Perinatal transmission**
   - Occurs primarily in infants born to ***HBSAg carrier mothers or mothers with acute hepatitis B*** during third trimester.
   - Likelihood of perinatal transmission of HBV **correlates with presence of HBeAg;** 90% of HBeAg positive mothers but only 10 to 15% of anti HBe positive mother transmit infection.
   - Most infection are transmitted at the time of delivery and are not related to *breast feeding.*

     ..... Harrison, 17/e, p 1940
   - Mostly acute infection in neonate is clinically asymptomatic, but the child is very likely to become HBs Ag carrier.

4. **Extrahepatic manifestation of HBV**
   - Glomerulonephritis
   - Polyarteritis nodosa
   - Essential mixed cryoglobulinemia.

5. **Carrier stage**

   Carriers are more common in patients of :
   - Down's syndrome
   - Leukemia
   - Polyateritis nodosa
   - Infection drug users
   - Lepromatous leprosy
   - Hodgkins disease
   - Chronic renal disease

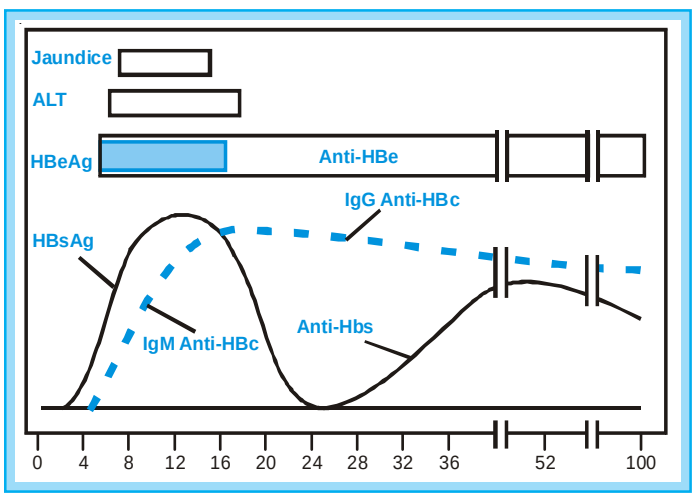
   – ***Carriers of HBs Ag particularly those infected in infancy have high risk of hepatocellular Ca.***

Serology and Diagnosis

A. Serology

- ***First virologic marker*** detectable is HBsAg.
- **Diagnostic *marker*** of ***acute*** hepatitis B infection IgM anti HBc.
- HBc Ag is sequestered in HBs Ag coat so, it is not routinely detectable.
- Diagnosis in window period is made by AntiHBc.
- **Marker of infectivity -** HBe Ag
- *Titre of HBs Ag bears inverse relationship with the degree of cell damage i.e. titre is very low in acute fulminant hepatitis.*

Scheme of typical and laboratory features of acute viral Hepatitis



Weeks after exposure

- **Markers of replicative phase :**
  - HBe Ag - *Qualitative marker.*
  - HBV DNA - *Quantitative marker.*
- Anti HBS Ag - **Protective antibody**
  - Anti HBS Ag with out Anti HBc **signifies vaccination.**
  - Anti HBs Ag in presence of IgG Anti HBc signifies recovery of infection.

B. *Liver function test* (done in all case of acute hepatitis).

- ↑ ALT and AST (Level doesn't correlate with degree of cell damage).
- ↑ Bilirubin
- PT - **Prolonged value** signify hepatocellular necrosis and indicate worse prognosis.

Treatment

- Acute – Antiviral therapy is not used usually.
- In severe acute hepatitis B-Treatment with nucleoside analogue such as lamivudin can be given.

Prevention

- **Genetically engineered vaccine** from yeast consisting of non glycosylated HBsAg particles.

Dose : – 3 IM dose (in deltoid not in gluteal)
– Injections are recommended at O, I and 6 month.
– *Pregnancy is not contraindication to vaccine.*

- ***Post exposure prophylaxis*** **:** Combination of HBIG and Hepatitis B vaccine.
- ***Perinatal exposure :***
  – *Single dose of HBIG 0.5 ml IM at birth followed by complete 3 dose of Hepatitis B vaccine.*
  – First dose of vaccine should be given within 12 hours of life.

Remember : As Hepatitis B can lead to hepatocellular carcinoma, vaccination makes ***HCC the only human cancer which is vaccine preventable.***

HEPATITIS D VIRUS = DELTA VIRUS

Defective virus that require helper function of HBV for its replication.

- HDV is formalin sensitive SSRNA virus.
- Delta core of HDV is encapsidated by an outer envelop of HBsAg, so it require cooperative function of HBV.
- Intracellular replication of HDV RNA can occur without HBV but liver injury require the presence of HBV.
- HDV can cause either :

Features	Superinfection	Coinfection
Definition	• In patient already infected with HBV	• Infection simultaneously with HBV
Course	• Grave course • More chance of Fulminant hepatitis and chronic infection	• Comparatively mild course
Serology	IgM Anti HDV + IgM Anti HBc	Ig M Anti HDV + Ig G Anti HBC

HDV antigen in liver and HDV RNA in serum and liver can be detected during HDV replication.

HEPATITIS C VIRUS

- Linear **SS RNA virus.**
- Belongs to gene hepacivirus of family flavivirus.
- ***MC*** **virus** associated with transfusion related hepatitis.
- **Cause fatty change in liver.**
- HCV is associated with ***Cryoglobinemia; porphyra cutania tarda; Idiopathic pulmonary fibrosis; membrane proliferative glomerulonephritis.***

Genome

- Envelope protein coded by hypervariable region varies from isolate to isolate and allow the virus to invade host immunity.
- Because of divergence of HCV isolates within a genotype or subtype and within the same host, these intragenotypic differences are referred to *as* quasi-species.

Serology and Diagnosis

- Assays of ***HCV RNA*** are the most sensitive test for HCV infection and represent the ***gold standard for diagnosis*** of hepatitis C *(HCV RNA detection has supplanted RIBA in most clinical settings).*

- 2 types of Amplification techniques can be used to detect HCV RNA.
  - ***Branched chain complementary DNA (b DNA) assay.***
  - ***Reverse transcriptase PCR or TMA :*** It is more sensitive than b DNA assay.
- Anti HCV antibody not be detectable in acute phase and are not sensitive.
- **Anti HCV are** not protective so chance of chronicity is very high.

Treatment

- In typical case of hepatitis C recovery is rare; *progression to chronic hepatitis is the rule.*
- Antiviral therapy with interferon alpha reduce the rate of chronicity.
- ***Duration of infection*** is the single most important variable which determine interferon responsiveness.

CHRONIC HEPATITIS - C

Clinical features :

- *Fatigue* is ***MC*** symptom Jaundice is rare.
- Extrahepatic manifestations may be seen.

Lab features :

- Aminotransferase fluctuate between high to high normal value.
- ALT and AST - increase with ALT > AST .
- But when cirrhosis develop AST becomes greater than ALT
- ***LKM1 - Antibody may be seen in cases of HCV.***

Treatment :

- Combination therapy of pegylated interferon plus Ribavirin is now standard therapy.
- **Liver transplantation -** When cirrhosis develops.

Remember :

- ***Chronic hepatitis C is MC indication of*** liver transplantation.
- ***Best prognostic*** indicator in chronic Hepatitis C is liver histology.

..... Harrison, 17/e, p 1963

HEPATITIS - E VIRUS

- Epidemic *hepatitis or enterically transmitted non A non B hepatitis.*
- ***SS RNA*** virus belonging to Alpha virus family.
- Hepatitis of hepatitis E. virus is characteristically *associated with cholestasis.*
- *Most important* ***cause of fulminant hepatitis in pregnancy.***

HEPATITIS G VIRUS

- Blood borne RNA virus.

Important points about Chronic Hepatitis

Type of Hepatitis	Diagnostic Test (s)	Autoantibodies	Treatment
Chronic hepatitis B	HBsAg, IgG anti-HBc, HBeAg, HBV DNA	Uncommon	IFN-α, lamivudine
Chronic hepatitis C	Anti-HCV, HCV RNA	Anti-LKMI	PEG-IFN-α Plus ribavirin
Chronic hepatitis D	Anti-HDV, HDV RNA, HBsAg, IgG anti-HBc	Anti-LKM3	IFN-α

QUESTIONS

1. Serology of a young man shows HBsAg however HBeAg is negative with normal levels of AST and ALT. He is asymptomatic. What is the next line of management ? **[AI 08]**

a) Wait and watch
b) Antivirus
c) Immunoglobulins
d) Liver transplant

2. A young pregnant woman presents with fulminant hepatic failure. The most likely aetiological agent is : **[AI 04]**

a) Hepatitis B virus
b) Hepatitis C virus
c) Hepatitis E virus
d) Hepatitis A virus

3. Which of the following hepatitis virus have significant perinatal transmission : **[AI 03]**

a) HEV
b) HCV
c) HBV
d) HAV

4. A pregnant woman from Bihar presents with hepatic encephalopathy. The likely diagnosis :

a) Hepatitis E **[AI 01, 95]**
b) Hepatitis B
c) Sepsis
d) Acute fatty liver of pregnancy

5. HCV is associated with : **[AI 00]**

a) Anti LKM-1 antibody
b) Scleroderma
c) Cryoglobulinemia
d) Polyarteritis nodusa

6. Chronic liver disease is caused by : **[AI 00]**

a) Hepatitis B
b) Hepatitis A
c) Hepatitis C
d) Hepatitis E

7. Non - parenteral hepatitis is : **[AI 00, AIIMS 96]**

a) Hepatitis A
b) Hepatitis B
c) Hepatitis C
d) Hepatitis D

8. Reverse transcriptase of HBV is coded on following gene : **[AI 00]**

a) C gene
b) S gene
c) P gene
d) X gene

9. A blood donor is not considered for safe transfusion, if he has : **[AI 00]**

a) Anti HBS Ab+ve
b) Anti HBS Ab and HBc Ag+ve
c) HbS Ag +ve and IgM anti HBC+ve
d) Anti HBe+ve

10. During epidemic of hepatitis E, fatality is maximum in : **[AI 00]**

a) Pregnant women
b) Infants
c) Malnourished male
d) Adolescents

11. Acute infection with HBV is characterized by :

a) HBs Ag **[AI 99, AIIMS 96]**
b) Anti HBs Ag
c) IgM anti HBc Ag and HBs Ag
d) Anti HBc Ag

12. Marker for acute hepatitis B is : **[AIIMS 07]**

a) HBV DNA
b) IgM anti-HBc
c) Core antgen (HbcAg)
d) Anti-HbsAg

13. In a patient of active chronic hepatitis B all are seen except : **[AIIMS 07]**

a) HbsAg
b) IgM anti HbcAg
c) HbeAg
d) Anti-HbsAg

14. Which of the following Hepatitis virus is cultivable:

a) Hepatitis A **[AIIMS 07]**
b) Hepatitis B
c) Hepatitis D
d) Hepatitis E

Answer

1. a) Wait and watch	2. c) Hepatitis ...	3. c) HBV	4. a) Hepatitis E	5. a and c
6. c) Hepatitis C	7. a) Hepatitis A	8. c) P gene	9. c) HbS ...	10. a) Pregnant ...
11. c) IgM ...	12. b) IgM anti...	13. b) IgM anti...	14. a) Hepatitis A	

15. With which of the following of viral hepatitis infection in pregnancy, the maternal mortality the highest : **[AIIMS 06]**

a) Hepatitis A
b) Hepatitis B
c) Hepatitis C
d) Hepatitis E

16. A 30 year old patient presented with history of jaundice for 10 days. His liver function tests showed bilirubin of 10mg/dl, SGOT/SGPT - 1100/1450, serum alkaline phosphatase - 240 IU. He was positive for HbsAg. What should be the confirmatory test to establish acute hepatitis B infection ? **[AIIMS 06]**

a) IgM Anti-HBc antibody
b) HbeAg
c) HBV DNA by PCR
d) Anti-HBc antibody

17. A 30 year old lady delivered a healthy baby at 37 week of gestation. She was a known case of chronic hepatitis B infection. She was positive for HBsAg but negative for HBcAg. Which of the following is the most appropriate treatment for the baby ? **[AIIMS 05]**

a) Both active and passive immunization soon after birth
b) Passive immunization soon after birth and active immunization at 1 year of age
c) Only passive immunization soon after birth
d) Only active immunization soon after birth

18. Hepatitis C virus is a : **[AIIMS 04, PGI 98]**

a) Togavirus
b) Flavi virus
c) Filovirus
d) Retrovirus

19. The best diagnostic test for recent hepatitis B is:

a) HBs Ag **[AIIMS 03, 01, 00**
b) IgM anti HBc Ag **PGI 99, 97]**
c) Anti HBe
d) Anti HBs

20. Which of the following Hepatitis virus is a DNA virus : **[AIIMS 02]**

a) Hepatitis C virus
b) Hepatitis B virus
c) Delta agent
d) Hepatitis E virus

21. A mother is HBs Ag positive at 32 weeks of pregnancy. What should be given to the newborn to prevent neonatal infection : **[AIIMS 02]**

a) Hepatitis B vaccine + immunoglobulins
b) Immunoglobulins only
c) Hepatitis B vaccine only
d) Immunoglobulins followed by vaccine 1 month later

22. A thirty year man presented with nausea, fever and jaundice of 5 days duration. The biochemical tests revealed a bilirubin of 6.7 mg/dl (conjugated 5.0 mg/dl) with SGOT/SGPT (AST/ALT) of 1230/900 IU/ml. The serological tests showed presence of HBs Ag,Ig M anti HBc and HBe Ag. The most likely diagnosis : **[AIIMS-02]**

a) Chronic hepatitis B infection with high infectivity
b) Acute hepatitis B infection with high infectivity
c) Chronic hepatitis B infection with low infectivity
d) Acute hepatitis B infection with low infectivity

23. Hepatitis B vaccination is given to a patient. His serum will reveal : **[AIIMS 02]**

a) HBsAg
b) Anti-HBsAg
c) IgM Anti-HBc Ag and HBS Ag
d) IgM and IgG Anti-HBc Ag

24. Commonest hepatotropic virus causing increased chronic carrier state is : **[AIIMS 97, 01]**

a) HEV
b) HAV
c) HBV
d) HCV

25. Acute hepatitis B can be earliest diagnosed by :

a) IgM anti HBc ab **[AIIMS 01, 95]**
b) HBs Ag
c) IgG anti HBc Ab
d) Anti HBs Ab

26. Which of the following is calcivirus : **[AIIMS 01]**

a) HEV
b) HBV
c) HCV
d) HAV

27. Best epidemiological tool for investigation of hepatitis B is : **[AIIMS 00; AI 97]**

a) Anti HBs Ag
b) Anti HBc Ag
c) Anti HBe Ag
d) HBc Ag

Answer

15. d) Hepatitis E
16. a) IgM ...
17. a) Both active...
18. b) Flavi ...
19. b) IgM ...
20. b) Hepatitis ...
21. a) Hepatitis ...
22. b) Acute ...
23. b) Anti-HB...
24. d) HCV
25. b) HBs Ag
26. a) HEV
27. b) Anti HBc ...

28. In a patient only anti HBs Ag is positive in serum all other viral markers are negative. This indicates

a) Acute hepatitis **[AIIMS 00]**
b) Chronic active
c) Persistent carrier
d) Hepatitis B vaccination

29. Hepatitis C virus true finding is : **[AIIMS 98]**

a) Spreads along fecooral route
b) Antibody to HCV may not be seen in acute stage
c) Does not cause chronic hepatitis
d) It cannot be cultured

30. If a patient was immunzed with hepatitis B vaccine, which of the following is seen in serum:

a) HbeAg **[PGI 06]**
b) HbSAg
c) anti Hbs antibody
d) Anti Hbe antibody
e) Anti Hbc antibody

31. HCV is : **[PGI 05]**

a) Enveloped RNA virus
b) Unenveloped RNA virus
c) Unenveloped positive strand RNA
d) Unenveloped negative strand RNA
e) DNA virus

32. Transmission of hepatitis A virus occurs :

a) One week before and one week after onset of symptom **[PGI 99]**
b) 2 weeks before onset of symptom
c) 2 week after onset of symptom
d) 2 week after onset of symptom

33. HBV all true, except : **[PGI 98]**

a) It is a DNA virus
b) Spreads by blood transfusions
c) HBs Ag marker of infectivity
d) Least chance of chronicity

Answer

28. d) Hepatitis ...
29. b) Antibody ...
30. c) Anti Hbs...
31. a) Enveloped ...
32. b and d
33. c and d

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is a i.e. Wait and Watch *Ref. Harrison 17/e, p 1946*

In hepatitis B, among previously healthy adult who present with clinically apparent acute hepatitis recovery ocurs in 99% therefore, antiviral therapy is not likely to improve the rate of recovery and is not required.

In this case patient is virtually asymptomatic, so no treatment is required.

2. Ans. is c i.e. Hepatitis E virus *Ref. Harrison 17/e, p 1941; COGDT 9/e, p 439*

Learn the following characteristics :

HAV	– Cause spiky fever
HBV	– Only hepatitis virus which is DNA virus, may cause cytopathic effect
HCV	– Cause fatty change
HDV	– Defective virus
HEV	– Cause fulminant hepatitis in pregnant woman; Associated with cholestasis.

Remember :

HEV – SS RNA virus belonging to Alpha virus family. Transmitted faeco-orally.
– Secondary person to person transmission is rare *(C/F to other enteric born infection).*

3. Ans. is c i.e. HBV *Ref. Harrison 17/e, p 1940*

Perinatal transmission of various hepatitis virus				
HAV	HBV	HCV	HDV	HEV
–	+++	±	+	–

- **HBV is *MC* hepatitis virus that is transmitted perinatally.**
- *Most important* **factor** that determine perinatal transmission is HBe Ag (risk 90%).
- ***MC* time** of perinatal transmission is at the **time of delivery.**
- ***MC* presentation** in neonate is asymptomatic **HBs Ag carrier.**
- *Most effective* **treatment** of neonatal infection is HBIg immediately after delivery followed by complete 3 dose immunization by HBs Ag vaccine. First dose within first 12 hours of life.

4. Ans. is a i.e. Hepatitis. E *Ref. COGDT 9/e, p 439*

MC cause of ***fulminant hepatitis*** in pregnancy - ***Hepatitis E.***
MC cause of ***hepatic encephalopathy*** in pregnancy is - ***Hepatitis E.***

5. Ans. is a and c i.e. Anti LKM antibody; and Cryoglobulinemia *Ref. CMDT '06, p 655*

See, the following line.

"HCV is a pathogenic factor in cryoglobulinemia and membranoproliferative GN. and may be related to lichen planus, Autoimmune thyroiditis; Lymphocytic sialedinitis; Idiopathic pulmonary fibrosis; Porphyria cutanea tarda; Monoclonal gammopathies and lymphoma, Increase risk of Type II diabetes mellitus." *.... CMDT' 06, p 655*

Now see *Harrison 17/e, p 1963*

"Some patient with serologically confirmable chronic hepatitis C have circulating anti LKM-1. The occurrence of anti LKM may result from partial sequence homology between the epitope recognized by anti LKM -1and 2 segments of HCV polyprotein."

So, inspite of wasting time for 1 answer switch over to next question.

Remember :

LKM 1 antibody	–	Hepatitis C
LKM 2 antibody	–	Drug induced hepatitis
LKM 3 antibody	–	Hepatitis D

6. Ans. is c i.e. Hepatitis C *Ref. Harrison 17/e, p 1939*

Decreasing order of progression to chronicity

	HCV >	**HDV**	**> HBV**	**> HAV = HEV**
Frequency of Chronicity	50-70%	5-20%	1-10% **90% of neonates**	None

Remember :

- **HCV** is ***MC*** cause of **chronic hepatitis.**
- **Chronic hepatitis C** is ***MC*** indication of **liver transplantation.**

7. Ans. is a i.e. Hepatitis A *Ref. Harrison 17/e, p 1939*

Transmission	
Parenterally	**Faeco oral**
Hepatitis B	Hepatitis A
Hepatitis C	Hepatitis E
Hepatitis D	
Hepatitis G	

- ***MC*** **hepatitis associated with blood transfusion hepatitis C.**

8. Ans. is c i.e. P gene *Ref. Anantnarayan 7/e, p 552*

HBV Genes and Gene Products			
Genes	**Regions**	**Gene products**	
S	S	Major protein (S)	
	S+Pre-S2	Middleprotein (M)	HBs Ag
	S+Pre-S1 and S2	Large protein (L)	

C	C	HbcAg
	C+Pre-C	HbeAg
P (Largest gene)		DNA polymerase
X		HBxAg

DNA polymerase of HBV has 2 activities :
- DNA dependent DNA polymerase.
- RNA dependent Reverse transcriptase.

9. Ans. is c i.e. HBs Ag + ve and Ig M anti HBc + ve *Ref. Harrison 17/e, p 1943*

- **HBS Ag + ve and IgM anti HBc + ve suggest acute viral hepatitis.**
- So, transfusion from this donour contraindicated.

10. Ans. is a i.e. Pregnant women *Ref. Jawetz p 24/e, p 471 ; COGDT 9/e, p 439*

Already explained, refer answer no. 2

11. Ans. is c i.e. IgM anti HBc Ag and HBs Ag *Ref. Harrison 17/e, p 1943*

Types	Serological Markers of HBV
Acute hepatitis B	Ig M anti HBc Ag + ve ; HBs Ag + ve
Chronic hepatitis B	Ig G anti HBc Ag + ve ; HBs Ag + ve
Marker of vaccination	Anti HBs Ag (+) ve Alone
Marker of remote infection (*Used for epidemiological purposes*)	IgG Anti HBc
Marker of infectivity	*HBe Ag* ***(If present indicate high infectivity)***

12. Ans. is b i.e. IgM anti HBC *Ref. Harrison 17/e, p 1934, 1942*

- Diagnosis of acute hepatitis B infection is made by detection of HBsAg in serum. In cases where HBsAg level are low, diagnosis can be established by presence of IgM anti HBc.
- Anti HBC of the IgM class predominates during the first 6 months after acute infection, where as IgG anti HBc beyond 6 months.

13. Ans. is b i.e IgM antiHBC *Ref. Harrison 17/e, p 1943*

IgM antiHBcAg is seen in acute hepatitis not in chronic active.
Marker of chronic hepatitis : HBsAg+, IgG antiHBcAg, HBVDNA+, HBeAg+

14. Ans. is A i.e. Hepatitis A *Ref. Harrison 17/e, p 1932*

"HAV can be cultivated reproducibly in vitro."

Remember :
- HAV is the hepatitis virus :
  - That causes spiky fever
  - With no perinatal transmission

15. Ans. is d i.e. Hepatitis E *Ref. Harrison 17/e, p 1941*

Already explained, refer answer no. 1

16. Ans. is a i.e. IgM Anti-Hbc *Ref. Harrison 17/e, p 1934 - 1935*

- Test diagnostic of acute infection – IgM anti Hbc
- Test diagnostic of chronic infection – IgG anti Hbc + HbsAg
- Test for determining infectvity – HbeAg.

17. Ans. is a i.e. Both Active and Passive immunization *Ref. Harrison 17/e, p 1948*

Perinatal Transmission of Hepatitis B

- Likelyhood of perinatal transmission of HBV *correlates* with ***presence of HBeAg.*** 90% of HBeAg +ve and only 10-15% of anti HBe +ve mother transmit infection.
- Most infection are transmitted at the time of delivery.
- Acute infection in neonate is clinically asymptomatic but the child is likely to become HBs Ag carrier and have *high risk of developing hepatocellular carcinoma.*

Treatment of perinatal exposure :

For all infant born to HBsAg positive mother.

– *A single dose of HBIG* should be given intramuscularly in thigh *soon after birth.*

– Followed by complete course of three injections of recombinant *hepatitis B vaccine* with first dose *to be given with in the* ***first 12 hour of life.***

– Subsiquent dose of active immunization should be given after 1 month and 6 month.

18. Ans. is b i.e. Flavivirus *Ref. Harrison, 17/e, p 1934*

Remember

Hepatitis **A**	–	**P**icorna virus
Hepatitis **B**	–	**H**epadna virus
Hepatitis **C**	–	**F**lavivirus
Hepatitis **D**	–	**D**efective virus
Hepatitis E	–	Hepeviridae

Mnemonic : ABCD – ***pH Fall Dangerous***

HEV although resembling calcivirus appears to be sufficiently distinct from any known agent to merit a new classification of its own as a unique gene hepevirus with in the hepeviridae family.

..... Harrison 17/e, p 1937

So, *if question comes on* **HEV** *go with* **hepeviridae** *not* ***with calcivirus.***

19. Ans. is b i.e. IgM anti HBc Ag *Ref. Harrison, 17/e, p 1934 - 1935*

Remember

- **Best marker for diagnosing Acute hepatitis B is IgM anti HBc** as it is found only in acute phase of hepatitis B (In chronic hepatitis IgG anti HBc is found).
- First marker after Acute hepatitis B infection is HBs Ag but as it can be found in chronic infection too so, it is not reliable of acute infection.

So, Guys be clear :

– **Diagnostic marker of Acute Hepatitis B-** IgM anti HBc
– **Earliest marker of Acute Hepatitis B** - HBsAg.

20. Ans. is b i.e. Hepatitis B virus *Ref. Harrison 17/e, p 1932*

HCV is a positive strand RNA virus

Virus	Morphology and genome	Family
HAV	Non enveloped RNA SS^+	Picorna virus
HBV	DNA	Hepadna virus
HCV	Enveloped RNA SS^+	Flavivirus
HDV	Enveloped RNA SS^-	Defective virus
HEV	Nonenveloped RNA SS^+	Alphavirus group

$^+$ = Positive strand - = Negative strand

21. Ans. is a i.e. Hepatitis B vaccine + immunoglobulins *Ref. Park 19/e, p 179*

Already explained, refer answer no. 17

22. Ans. is b i.e. Acute hepatitis B infection with high infectivity
Ref. Harrison 17/e, p 1944

See the following table, **Don't try to learn it, just try to understand.**

Commonly Encountered Serologic Patterns of Hepatitis B Infection

HBsAg	Anti-HBs	Anti-HBc	HBeAg	Anti-HBe	Interpretation
+	–	IgM	+	–	Acute hepatitis B,high infectivity +
+	–	IgG	+	–	Chronic hepatitis B, high infectivity
+	–	IgG	–	+	1. Late acute or chronic hepatitis B, low infectivity 2. HBeAg-negative (precoremut ant) hepatitis B (chronic or, rarely, acute)
+	+	+	+/-	+/-	1. HBsAg of one subtype and heterotypic anti-HBs (common) 2. Process of sroconversion from HBsAg to anti-HBs (rare)
–	–	IgM	+/-	+/–	1. Acute hepatitis B 2. Anti-HBc "window"
–	–	IgG	–	+/–	1. Low-level hepatitis B carrier 2. Hepatitis B in remote past
–	+	IgG	–	+/–	Recovery from hepatitis B
–	+	–	–	–	1. Immunization with HBs Ag (after vaccination) 2. Hepatitis B in the remote past (?) 3. False - positive

23. Ans. is b i.e. Anti HbsAg *Ref. Harrison 17/e, p 1944*

Already explained, refer just above to find answer.

24. Ans. is d i.e. HCV *Ref. Harrison 17/e, p 1939*

Already explained, refer answer no. 5

25. Ans. is b i.e. HBs Ag *Ref. Harrison 17/e, p 1933*

Here question is about the earliest diagnostic marker, **which is no doubt HBsAg.**

- HBsAg in absence of IgM anti HBc or IgG anti HBc indicates early acute infection. *....Jawetz 24/e, p 480*
  So, go with **HBsAg.**

Remember :
- **Dignostic** marker of Acute hepatitis B – ***IgM anti HBC***
- **Earliest** marker of Acute hepatitis B – ***HBsAg.***

26. Ans. is a i.e. HEV *Ref. Ananthnarayan, 7/e, p 559*

According to Ananthnarayan 7/e, p 557
"HEV has been classified in genus hepesvirus under family calciviridae."
***But according to** Harrison 17/e, p 1937*
"HEV has classification of its own with in hepeviridae family."
In this question there is no dispute but if you have to choose among calciviridae and hepeviridae go with nepeviridae.

27. Ans. is b i.e. Anti HBc Ag *Ref. Harrison 17/e, p 1934*

Already explained, refer answer no. 11

28. Ans. is d i.e. Hepatitis B vaccination *Ref. Harrison, 17/e, p 1944*

Already explained, refer answer no. 22

29. Ans. is b i.e. Antibody to HCV may not *Ref. Harrison, 17/e, p 1937, 1943*

Serology of HCV : 3rd generation immunoassays which detect antibody against NS-5 region detect Anti HCV earlier than 1st and 2nd generation assay. These antibody may never been detectable in 5-10% of patient
.....Harrison, p 1943

So, ***option "b"*** is correct.

Other options
- Only hepatitis virus that can be cultured in vitro is HAV. *.....Harrison, 17/e, p 1932*
  But other hepatitis virus can be cloned in E col.

- In ***option "d"*** it is not clear whether they are asking culturability in vitro or in vivo (clonability) so, this option may be partially correct.
- HCV is transmitted parenterally.

30. Ans. is c i.e. AntiHbs Antibody *Ref. Harrison 17/e, p 1944*

Already explained, refer answer no. 22

31. Ans. is a i.e. Enveloped RNA virus *Ref. Harrison 17/e, p 1934*

Already explained, refer answer no. 20

32. Ans. is b and d i.e 2 week before onset of symptom; and 1 weeks after onset of symptom
Ref. Park, 19/e, p 174

"The risk of transmitting HAV is greatest from 2 week before to 1 week after the onset of Jaundice."

33. Ans. is c and d i.e. HBs Ag marker of infectivity; and Least chance of chronicity
Ref. Harrison, 17/e, p 1934

- ***Marker of infectivity is HBeAg not HBsAg.***
- ***Least chance of chronicity are in Hepatitis A and Hepatitis E.***

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.

1. Which of the following acute viral hepatitis infections has the highest risk of progression to chronicity ? **[Kar 03]**

a) Hepatitis C
b) Hepatitis B
c) Hepatitis A
d) Hepatitis E

[Ref. Harrison 17/e, p 1939]

2. Which hepatitis virus is notorious for causing a chronic hepatitis evolving cirrhosis ? **[Kar 04]**

a) Hepatitis C virus
b) Hepatitis B virus
c) Hepatitis E virus
d) Cytomegalo virus

[Ref. Harrison 17/e, p 1973]

3. A potent vaccine is available for : **[AI 90]**

a) Hepatitis A
b) Hepatitis B
c) Malaria
d) Respiratory syncitial virus

[Ref. Ananthnarayan 7/e, p 549, 556]

4. Hepatitis A is transmitted by : **[AI 90]**

a) blood route
b) Inhalation
c) Feco-oral route
d) All

[Ref. Harrison 19/e, p 1539]

5. HAV is not destroyed by : **[AIIMS 91]**

a) 0.5 ppm chlorine
b) 1:4000 formalin
c) UV radiation
d) Biolling at 100^{0}C for 5 minutes

[Ref. Ananthnarayan 7/e, p 548]

6. The commonest cause of viral hepatitis in India :

a) Hepatitis type A virus **[DNB 92]**
b) Hepatitis type B virus
c) Enterically transmitted NANB virus
d) Parenterally transmitted NANB virus
e) Delta virus

[Ref. Ananthnarayan 7/e, p 559]

7. The serological marker of accute Hepatitis B infection is : **[AI 92]**

a) HBSAg + HBeAg
b) HBsAg + Core antibody (IgM)
c) HBsAg
d) HBcAG

[Ref. Ananthnarayan 7/e, p 1823]

8. Presence of HBe Ag in patients with hepatitis indicates : **[AIIMS 92]**

a) Simple carriers
b) Late convalescence
c) High infectivity
d) Carriers status

[Ref. Harrison 17/e, p 1942]

9. Anti HBs Ab indicates : **[AIIMS 92]**

a) Resistance to Hepatits B
b) Acute infections
c) Good prognosis
d) Hepatocellular Carcinoma

[Ref. Harrison 17/e, p 1943]

10. Most common route of spread of Hepatitis E is :

a) Sex **[AI 93]**
b) Feco-oral
c) Blood tranfusion
d) IV injections

[Ref. Ananthnarayan 7/e, p 559]

Answer

1. a) Hepatitis C ...
2. a) Hepatitis C virus
3. a and b
4. c) Feco-oral ...
5. a) 0.5 ppm ...
6. c) Enterically ...
7. b) HBsAg + ...
8. c) High infectivity
9. a) Resistance ...
10. b) Feco-oral

11. Hepatitis B is not transmitted by : [AIIMS 93]

a) Blood transfusion
b) Pasteurised albumin
c) Cryoprecipitate
d) Sexual contact

[Ref. Harrison 17/e, p 709, Table (286.2)]

12. Which of the following hepatitis has poor prognosis : [UP 05]

a) Hepatitis A
b) Hepatitis B
c) Non-A Non-B type
d) Hepatitis C

[Ref. Ananthnarayan 7/e, p 56]

13. Carrier state does not axis for : [Kerala 99]

a) Hepatitis B virus
b) Hepatitis A virus
c) Non A non B Hepatitis
d) Delta agent

[Ref. Harrison 17/e, p 1939, Table (285-2)]

14. Chronic hepatitis is seen in : [Kerala 99]

a) Hepatitis C
b) Hepaitits D
c) Hepatitis A
d) Hepatitis E

[Ref. Harrison 17/e, p 1939]

15. HBV is associated with all of the following except:

a) Hepatic cancer **[SGPGI 05]**
b) Chronic hepatitis
c) Hepatic adenoma
d) Cirrhosis

[Ref. Ananthnarayan 7/e, p 533]

16. Route of transmission of Hepatitis E virus is :

a) Skin **[DNB 04]**
b) Faeco oral
c) Blood
d) Sexual contact

17. Serological markers of infectivity of Hepatitis B :

a) HBsAg **[Kerala 06]**
b) HBeAg
c) IgM anti Hbc
d) HbcAg

[Ref. Harrison 17/e, p 1942]

18. Which hepatitis virus had been called as enterovirus : [MP 07]

a) Hepatitis A
b) Hepatitis B
c) Hepatitis C
d) Hepatitis E

[Ref. Ananthnarayan 7/e, p 548]

Answer 11. b) Pasteurised ... 12. b) Hepatitis B 13. b) Hepatitis A ... 14. a) Hepatitis C 15. c) Hepatic ... 16. b) Faeco oral 17. b) HBeAg 18. a) Hepatitis A

5 HIV & Other Retroviruses

- Causative agent of **AIDS** = Slim disease.
- Belongs to *family* **retroviridae;** *subfamily* **lentiviridae.**
- Two types are found HIV 1 and HIV 2. ***HIV 1 is most common*** cause of ***AIDS in world.***
- *Pan troglodytes troglodytes species of chimpanzees are natural reservoir of HIV-1*

Morphology and Replication cycle

- Spherical ***enveloped*** virus. Nucleocaspid has ***icosahedral*** structure.
- Virus contain *external spikes formed by the* ***two major envelope protein*** - *the external gp - 120* and *transmembrane gp - 41.*
- Genome is composed of two identical single stranded positive sense RNA copies.
- ***Main genes are :***

  gag – Determines *the core and shell of virus.* Codes for precursor protein p55 which is cleaved into three proteins p15, p18 and p24.

  env – Determines *the synthesis of envelope glycoprotein.* gp- 160 which is cleaved in to gp 120 and gp 41.

  pol – Codes for *polymerase reverse transcriptase* and other viral enzymes.

  Other genes are : tat, rev, jej, vif, vpu, vpx, vpr, LTR.

  – The major difference between genomes of **HIV 1** and **HIV 2** is HIV 2 lacks vpu gene and has vpx gene which is not present in HIV -1.
- Replication begins with the high affinity binding of gp120 with CD-4 (Present on CD4+ T cells and monocyte macrophage lineage cells). After binding with CD-4, gp120 undergoes conformational change that facilates binding of corecepter. The major corcepter for HIV-1 are CCR-5 and CXCR-4.
- After fusion, HIV genome RNA is uncoated and internalized into target cell. The reverse transcriptase catalyze the reverse transcription of RNA to DNA. DNA so formed intergrates with host cell chromosome through the action of virus encoded enzyme integrase.

Antigenic variation and molecular heterogenity

- ***HIV is highly mutable virus.***
- The variability of HIV is believed to be due to error prone nature of reverse transcription.
- There are three groups of HIV -1.

  Group M - ***(Most of infection), Group O and Group N.***

  There are *nine subtypes* of M group. *..... Harrison 17/e, p 1141*

Subtype C is *most prevelant* **world wide.**

In India and china *subtype* **C *is*** *most prevelant.*

Modes of Transmission

A. Sexual transmission

- The *most common* **mode** of transmission world wide is **heterosexual transmission.**

  ...Harrison 17/e, p 1142
- Chance of infection from *male to female* is **twice** as from *female to male.*
- Anal intercourse has higher risk of transmission.

B. Transmission by blood and blood products :

- Transmission of whole blood. Packed red cells, platelets, leucocytes and plasma are all capable of transmitting HIV infection.
- Hyperimmuno globulin, hepatitis B immunoglobulin, plasma derived heptatitis B vaccine and Rh immunoglobulin *have not been* associated with transmission of HIV infection.
- Risk of gettng HIV infection from **transfusion of a unit of infected blood is > 95%.**

C. Maternal fetal transmission - Risk is 30%

- Occurs ***most commonly*** in perinatal period.
- Cesarean section decrease risk of transmission.
- Risk of infection is high if the mother is newly infected or if she has already developed AIDS.
- Vitamin A deficiency increase risk of transmission.
- Exclusive breast feeding carries lower risk of transmission than mixed feeding. *..... Harrison 17/e, p 1146*
- Presence of mastitis, low maternal CD4+ T cells counts and maternal vitamin A deficiency increase risk of transmission.

D. Transmission by other body fluids :

- HIV can be isolated in low titres from saliva, but *saliva can not transmit* HIV infection *due to presence* of endogenous antiviral factors of which most important ***is secretory leucocyte protease inhibitor (SLPI).***

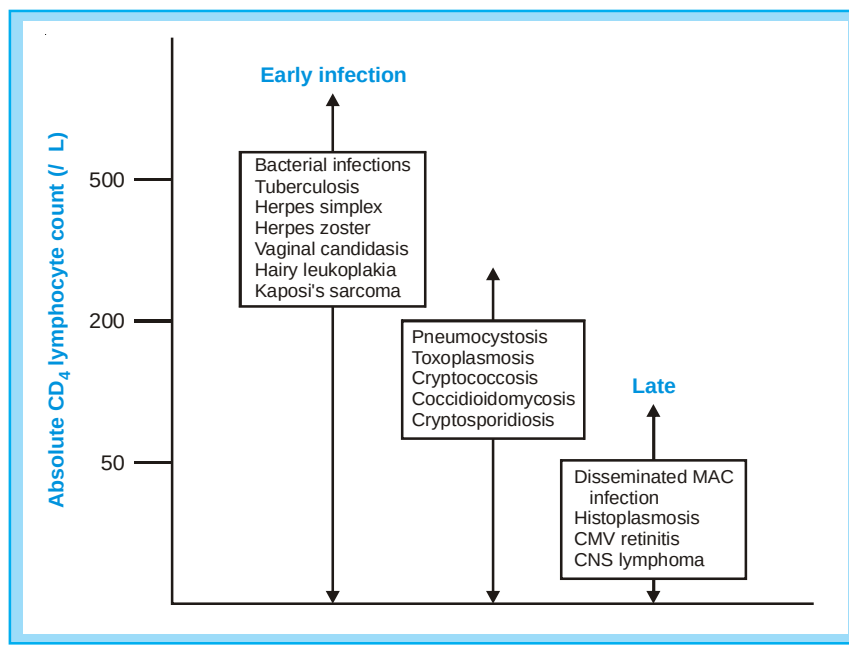
Pathogenesis

- The hallmark of HIV disease is a profound immunodeficiency due to quantitative and qualtitative deficiency of helper or inducer T cells (CD4 - Tcells).
- ***Primary HIV infection and Intial Viremia :***
  - Dendritic cells play an important role in the initiation of HIV infection due to presence of lectin called DC-SIGN which binds with high affinity to HIV envelope.
- ***Chronic and Persistant Infection :***
  - Establishment of chronic infection is due to the ability of virus to mutate.
  - Evolution of mutants that escape control by CD8 + cytolytic T lymphocytes is critical for progression of HIV infection.
  - Another mechanism is the down regulation of HLA class 1 molecules resulting in lack of ability of CD8 + CTL to kill the infected target cell.
- ***Cellular target of HIV :***
  - **CD 4 + = Helper = Inducer T cell** *(Primary target)*
  - Monocye - Macrophages (10 - 15%)
  - Dendritic, langerhans cells
  - Few B cells (5 - 10%).

Clinical features

- **Acute HIV infection** with in 3-6 weeks of infection.
  - Infectious mononucleosis like symptoms.
  - In most patient it is followed by prolonged period of clinical latency.
- **Asymptomatic stage** = Latent infection :
  - Median time of asymptomatic stage is ~ *10 years.*
  - Rate of *disease progression* is directly correlated with *HIV RNA levels.*
  - During this stage rate of CD4 + Tcell decline is ~ 50 µl/yr.
  - ***Any HIV infected individual with CD4 + Tcell count ∠ 200/µl has AIDS by definition.***
- **Symptomatic Disease**

Opportunistic Infection in AIDS



A. Disease of Respiratory System

- **Sinusitis** - *Most commonly* maxillary sinus is involved. ***MC*** causative organism are ***H.influenzae*** and ***Streptococcus.***

- **Pulmonary manifestation**
  - ***MC*** pulmonary manifestation is pneumonia. The *most common* cause of pneumonia is ***p.carinii.***
  - ***MC*** *bacterial cause of pneumonia in HIV patient are H.influenzae, streptococci.*
  - Tuberculosis - HIV increase risk of developing active TB by factor of 100.

* *In India mycobacterium tuberculosis is **MC** oppurtinistic infection in **AIDS** patient.*

Atypical mycobacterial infection – ***MC*** are M.avium or M.intracellulare species (MAC) occur ***when CD - 4 < 50/µl.***
  - *Mostly present as disseminated infection.*

  - Fungal infection - Coccidiodes immunitis; Aspergillosis; Histoplasmosis.
  - *Idiopathic interstitial pneumonia* - Lymphoid interstitial pneumonia (LIP) and nonspecific intestinal pneumonitis.

B. Disease of CVS

It includes :
- *HIV associated cardiomyopathy* - Dilated cardiomyopathy associated with CHF due to direct consequence of HIV infection.
- *Lipodystrophy syndrome* - Due to adverse effect of antiretroviral therapy.

C. Disease of Oropharynx and GIT

Oral lesions
- Thrush - Due to candida
- Hairy leukoplakia - Due to EBV *(not premalignant condition)*
- Apthous ulcer.

Esophagitis - Causative organism are :
- – Candida
- – CMV - Single large ulcer
- – HSV - Multiple small ulcer.

Intestinal infection – *Causes of diarrhoea in AIDS patient.*
- Bacterial – Salmonella, Shigella, Campylobacter jejuni.
- Fungal – Histoplasmosis, Coccidiodomycosis and Pencillosis cause fever and diarrhoea.

D. Disease of Hematopoetic system

- *Anemia* - ***MC*** hematologic abnormality.
- *Thrombocytopenia* - Due to platelet specific antibody or as a direct result of HIV on megakaryocytes.
- *Lymphadenopathy and Leucopenia.*

E. Dermatologic disease

- Dermatologic problems occur in >90% of patients with HIV infection.
- Folliculitis is the most prevalent dermatologic disorder in patients with HIV infection. Seen when CD4 + T cell counts < 200 cells/µl.
- Seborrheic dermatitis occurs in up to 50% of patient with HIV infection.
- Psoriasis and icthyosis, though not increased in frequency, if occurs severity is more than normal population.

F. Neurologic Manifestations

MC opportunistic infection that involve CNS are Toxoplasmosis; Cryptococcus.
- *Meningitis* - ***MC*** cause Cryptococcus neoformans.
- *HIV encephalopathy* = AIDS dementia complex. Subcortical dementia due *to direct effect of HIV.*
- *Seizures* - ***MC*** cause Toxoplasmosis.
- *Myelopathy* - Associated with CMV infection.
- *Peripheral neuropathy.*
- *Myopathy* - Due to direct effect of HIV or due to drugs.

G. Ophthalmologic disease

- ***MC*** fundoscopic finding is cotton wool spot due to retinal ischemia.
- ***MC*** cause of **blindness** in HIV patient is CMV retinitis *(charcteristic appearance - perivascular hemorrhage and exudate)* - occurs when CD-4 < 50/µl.
- Acute retinal necrosis syndrome = Progressive Outer retinal necrosis (PORN) - Due to HSV and varicella zoster.

H. Neoplastic Disease

- *Kaposi Sarcoma* – Multicentric neoplasm of vascular origin appearing in skin, mucous membranes and viscera.
- *Non Hodgkin lymphoma* : – Immunoblastic lymphoma (***MC*** lymphoma in HIV patient)

– Burkitt's lymphoma
– Primary CNS - Usually associated with EBV.

- *AIDS increase incidence of* :

Hodgkin disease	***Multiple myeloma***	
Leukemia	Melanoma	Cervical Ca
Brain tumor	Anal Ca	Oral Ca
Lung Ca	Testicular Ca	

Pediatric AIDS

- Recurrent bacterial infections are more common in children.
- Pneumonia caused by pneumocystis carinii is the ***MC*** **AIDS** defining diagnosis in childen with unrecognised *HIV infection.*
- Tumor *most commonly* associated are ***Non Hodgkin Lymphoma.***

DIAGNOSIS OF HIV INFECTION

Clinical

I. WHO case definition for AIDS surveillance :

Any individual (>12 years of age) is considered to have AIDS if at least 2 of the following major signs are present in combination with at least 1 minor sign.

Major signs :
- Weight loss ≥ 10% of body weight.
- Chronic diarrhoea for more than 1 months.
- Prolonged fever for more than 1 month (intermittent or constant).

Minor signs :
- Persistent cough for more than 1 month.
- Generalized pruritic dermatitis.
- History of herpes zoster.
- Oropharyngeal candidiasis.
- Chronic progressive or disseminated herpes simplex infection.
- Generalized lymphadenopathy.

The presence of either generalized Kaposi sarcoma or cryptococcal meningitis is sufficient for the diagnosis of **AIDS** for surveillance purposes.

II. Expanded WHO case definition for AIDS surveillance :

For the purposes of **AIDS** surveillance and adult or adolescent (>12 years of age) is considered to have **AIDS** if a test for HIV antibody gives a positive result and one or more of the following conditions are present :

- ≥ 10% body weight loss or cachexia, with diarrhoea or fever, or both, intermittent or constant, for at least 1 month, not known to be due to a condition unrelated to HIV infection.
- Cryptococcal meningitis.
- Pulmonary or extra-pulmonary tuberculosis.
- Neurological impairment that is sufficient to prevent independent daily activities, not known to be due to a condition unrelated to HIV infection.
- Candidiasis of the oesophagus.
- Clinically diagnosed life-threatening or recurrent episodes of pneumonia, with or without aetiological confirmation.

Laboratory diagnosis	
Demonstration of Antibody	**Demonstration of HIV or its components**
– ELISA ***(sensitive and best screening test)***	– ***Antigen detection*** *p-24 is earliest virus marker to appear in blood*
– Western blot (specific) (demonstrate antibody to products of all major HIV gene)	– ***Virus isolation -*** By cultivation of patient lymphocyte with uninfected lymphocyte in present of IL-2
– Modern 4th generation EIA kit combines antibody detection with p24 antigen assay	– PCR - Gold standard for diagnosis in all stages of HIV • DNA PCR; RNA PCR, RT - PCR - RT PCR is most sensitive and best

* ***RT PCR is used as a diagnostic and prognostic tool and has become an technique for studies of sequence diversity and microbial resistance to antiretroviral agents.***

* ***Nucleic acid amplification detection : Reverse transcriptase PCR, branched DNA (b DNA) and nucleic acid sequence based amplification.***

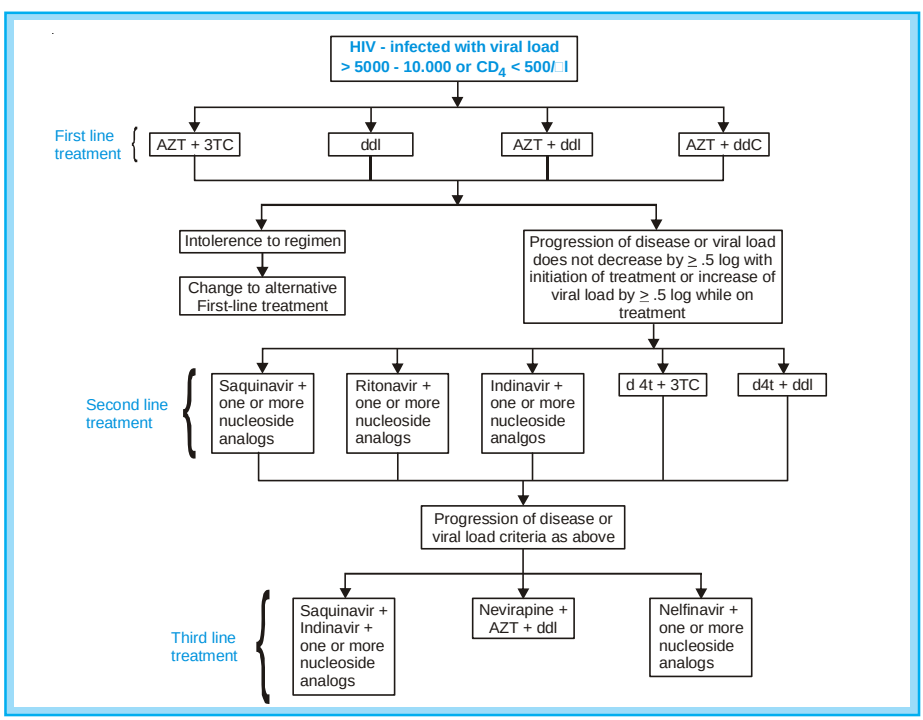
Diagnosis of HIV infection in new born

- The presence of anti HIV antibody (ELISA) is not diagnostic of infection until after 18 month of age.
- Diagnosis during first few month of life is made by detection of HIV DNA with PCR (Best).
- Other methods are : – p-24 antigen detection
  – HIV culture.

Lab monitoring of patient with HIV infection

- *CD4 + Tcell count* – Best indication of immediate state of immunologic competence of patient with HIV infection.
- *HIV RNA determination* – By RT PCR and bDNA assay. ***Determine disease progression. Should be monitored every 3-4 months.***
- *HIV resistance testing*.

Treatment



Nucleoside analogues	*Protease inhibitors*	*Nonnucleoside reverse transcriptase inhibitors*
AZT = zidovudine	Saquinavir	Delaviridine
ddI = didanosine	Ritonavir	
ddC = zalcitabine	Indinavir	
d4T = stavudine	Nelfinavir	
3TC = lamivudine	**RIN shakti**	

Post exposure prophylactic treatment

- Antiretroviral drugs started with hours following accidental exposure following regimen is recommonded.
- A combination of two nucleoside analogese reverse transcriptase inhibitor ***(mostly zidovudine + lamuvidine)*** for 4 weeks for routine exposure.
- For high risk exposure or if the source individual has advanced AIDS protease inhibitor nelfinavir should be added.
- Clinically all cases are considered high risk and high risk regimentis given to all cases.
- If the source individual has failed on Zidovudine + Lamuvidine combination than stavudine + didinosine should be used instead of AZT + Lamuvidine.

OTHER RETROVIRUS

Human Tcell lymphotrophic virus 1 (HTLV - 1) :

- Causative agent of :
  - Adult Tcell lymphoma
  - Tropical spastic paraperisis.

Human Tcells lymphotrophic virus II (HTLV - 2) :

- Thought to be as a virus searching for disease.
- Associated with some cases of T-cell varient of hairy cell leukema.

QUESTIONS

1. HIV can be detected and confirmed by : [AI 05]
a) Polymerase chain reaction (PCR)
b) Reverse transcriptase - PCR
c) Real time PCR
d) Mimic PCR

2. An HIV patient complains fo visual disturbances. Fundal examination shows bilateral retinal exudates and perivascular hemorrhages. Which of the following viruses are most likely to be responsible for this retinitis : [AI 04]
a) Herpes simplex retinitis
b) Human herpes virus
c) Cytomegalovirus
d) EBV

3. Which one of following is true regarding HIV infection : [AI 04]
a) Following needle stick injury infectivity is reduced by administration of nucleoside analogues
b) CD 4 counts are the best predictors of disease progression
c) Infected T cells survive for a month in infected patients
d) In latent phase HIV has minimal replication

4. HIV virus has : [AI 02]
a) Single stranded DNA
b) Single stranded RNA
c) Double stranded DNA
d) Double stranded RNA

5. Regarding HIV which of the following is not true:
a) It is a DNA retrovirus [AI 02]
b) Contains Reverse Transcriptase
c) May infect host CD 4 cells other than T lymphoctyes
d) Causes a reduction in host CD 4 cells at late stage of disease

6. CMV retinitis in HIV occurs when the CD - 4 counts fall below : [AI 02]
a) 50
b) 100
c) 200
d) 150

7. Regarding HIV infection, not true is : [AI 01]
a) p24 is used for early diagnosis
b) Lysis of infected CD4 cells is seen
c) Dendritic cells do not support replication
d) Macrophage is a reservoir for the virus

8. Reverse transcriptase sequence in HIV is best described as : [AI 00]
a) RNA - DNA - RNA
b) DNA - RNA
c) DNA - RNA - DNA
d) RNA - DNA

9. Multifocal tumour of vascular origin in a patient of AIDS : [AI 00]
a) Kaposi sarcoma
b) Astrocytoma
c) Gastric carcinoma
d) Primary CNS lymphoma

10. A patient with HIV has diarrhoea with AFB +ve organism in stool. The most likely organism is :
a) Mycobacterium avium intracellulare [AI 00]
b) Mycobacterium TB
c) Mycobacterium leprae
d) Mycoplasmas

11. A patient comes to hospital with a history of sore throat, diarrhoea and sexual contact 2 weeks before the best investigation to rule out HIV is :
a) p24 antigen assay [AI 00]
b) ELISA
c) Western blot
d) Lymphnode biopsy

12. AIDS involves primarily : [AI 98]
a) T-helper cells
b) T-suppressor cells
c) T-5 cytotoxic cells
d) B-cells

13. When compared to the Western blot technique, ELISA test is : [AI 96]
a) More sensitive, less specific
b) More sensitive, more specific
c) Less sensitive, less specific
d) Less sensitive, more specific

Answer

1. b) Reverse ... 2. c) Cytomega ... 3. a) Following ... 4. b) Single ... 5. a) It is a ...
6. a) 50 7. c) Dendritic cells ... 8. a) RNA - ... 9. a) Kaposi ... 10. a) Mycobacterium ...
11. a) p24 antigen ... 12. a) T-helper ... 13. a) More sensitive ...

14. All of the following viral genes associated with HIV infection code for structural proteins except:
a) Gag gene **[AI 95]**
b) Env gene
c) Pol gene
d) Tat gene

15. Which of the following is a marker of HIV infection in blood : **[AI 95]**
a) DNA polymerase
b) RNA polymerase
c) Reverse transcriptase
d) DNA isomerase

16. All the following are true about HIV infection except : **[AI 95]**
a) Caused by an enveloped RNA virus
b) Rate of killing is directly proportional to T4 molecules on cell surface
c) Increased release of acid labile interferon
d) Decreased delayed hypersensitivity activity reaction

17. In HV window period indicates : **[AIIMS 07]**
a. Time period between infection and onset of symptoms
b. Time period between infection and detection of antibodies against HIV
c. Time between infection and treatment
d. Time between treatment and death

18. A known HIV positive patient is admitted in an isolation ward after an abdominal surgery following an accident. The resident doctor who changed his dressing the next day found it to be soaked in blood. Which of the following would be the right method of choice of discarding the dressing :
a) Pour 1% hypochlorite on the dressing material and send it for incineration in a appropriate bag
b) Pour 5% hypochlorite on the dressing material and send it for incineration in a appropriate bag
c) Put the dressing material directly in an appropriate bag and send for incineration **[AIIMS 05]**
d) Pour 2% lysol on the dressing material and send it for incineration in a appropriate bag

19. Tissue of origin of Kaposi sarcoma is :
a) Lymphoid **[AIIMS 05]**
b) Vascular
c) Neural
d) Muscular

20. Which of the following lesion is associated with HIV infection : **[AIIMS 04]**
a) Hairy leukoplakia
b) Erythroplakia
c) Oral lichen planus
d) Bullous pemphigoid

21. All of the following methods are used for the diagnosis of HIV infection in a 2 month old child except: **[AIIMS 03]**
a) DNA PCR
b) Viral culture
c) HIV ELISA
d) p24 antigen assay

22. A resident doctor sustained a needle stick injury while sampling blood of patient who is HIV positive. A decision is taken to often him postexposure prophylaxis. Which one of the following would be the best recommendation : **[AIIMS 03]**
a) Zidovudine + Lamivudine for 4 weeks
b) Zidovudine + Lamivudine Nevirapine for 4 weeks
c) Zidovudine + Lamivudine + Indinavir for 4 weeks
d) Zidovudine + Stavudine + nevirapine for 4 weeks

23. HIV infects most commonly : **[AIIMS 00]**
a) CD 4 + helper cells
b) CD 8 + cells
c) Macrophage
d) Neutrophil

24. A HIV mother delivers a baby. All are true except:
a) Risk of HIV in the baby is up to 90%
b) HIV infection cannot be diagnosed in the baby with available methods **[AIIMS 99]**
c) AIDS can be transmitted from mother to child during delivery
d) Breast feeding can transmit AIDS

25. Which of the following is not seen in HIV Patient with CD4 count less than 100/µl, who has non productive cough : **[AIIMS 99]**
a) Mycobacterium tuberculosis
b) Pneumocystis carinii
c) Mycoplasma pneumonae
d) Cryptococcal infection

26. Which infection is not common in HIV patients :
a) Cryptosporidiosis **[AIIMS 97]**
b) Atypical mycobacterial infection
c) Aspergillosis
d) Candidiasis

Answer
14. d) Tat ... 15. c) Reverse ... 16. c) Increased ... 17. b) Time period ... 18. c) Put the ...
19. b) Vascular 20. a) Hairy ... 21. c) HIV ... 22. c) Zidovudine ... 23. a) CD 4 + ...
24. a) Risk of ... 25. c) Mycoplasma ... 26. c) Aspergillosis

27. Which of the following gene is present in HIV genome : [PGI 06]

a) Gag
b) Tat
c) p500
d) Kinase
e) P24

28. Fungal infection associated with AIDS patient are

a) Pueumocystis carini **[PGI 03]**
b) Penicillium marneffei
c) Candida
d) Cryptococcus
e) Cryptosporidium

29. HIV infection is associated with : [PGI 02]

a) A glandular fever like illness
b) Generalized lymphadenopathy
c) Gonococcal septicemia
d) Sinus disease
e) Presenile dementia

30. Which of the following is HIV gene : [PGI 02]

a) gag
b) tat
c) p2500
d) kinase
e) p24

31. Which of the following is an AIDS defining criteria according to WHO: [PGI 01]

a) Generalised lymphadenopathy
b) Fever, weight loss and fatigue
c) Pneumocystis carinii pneumonia
d) Mycobacterium avium infection
e) Persistent diarrhoea

32. In diagnosis of AIDS, criteria include the following except : [PGI 01]

a) CD 4 < 200
b) CD 8 < 500
c) CD 4 : CD 8 = 1
d) Presence of any of the opportunistic infections tuberculosis, pneumocystis carinii, cytomegalovirus
e) Western blot is positive

33. Persistent diarrhoea in AIDS is caused by A\E :

a) Microsporidia **[PGI 01]**
b) Cryptosporidium parvum
c) Cryptococcus
d) Isospora belli
e) Giardia lambia

34. Important features of AIDS are : [PGI 01]

a) Follicular tonsillitis
b) Lichen planus
c) Oral candidiasis
d) Hairy leukoplakia

35. HIV gene is/are : [PGI 01]

a) Gp73
b) p24
c) Gp120
d) Gp5

36. True about HIV : [PGI 00]

a) Not transmitted through semen
b) More chances of transmission during cesarean section than normal labour
c) More infectious than hepatitis B
d) Male to female transmission > female to male

37. In India most common cause of T.B. in HIV :

a) Myco. Tuberculosis **[PGI 00]**
b) Myco. Avium intracellulare
c) M. bovis
d) M. scrofulaceum

38. Oppurtunistic infection in HIV patient are :

a) P. carrnii **[PGI 96]**
b) M. avium
c) Pseudomonas
d) Mycoplasma

Answer

27. a and b
28. a, b, c and d
29. a, b, c and e
30. a and b
31. a, b, c, d and e
32. a and c
33. c and e
34. c and d
35. None
36. d) Male to ...
37. a) Myco. ...
38. a and b

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b i.e. Reverse transcriptase PCR *Ref. Harrison 17/e, p 1166*

Diagnosis of HIV Infection	
Detection of Antibody	***Direct detection of HIV or its component***
– ELISA (sensitive and best screening test – Western blot (specific and confirmatory test)	– *Virus isolation* - By cultivation of patient lymphocyte with uninfected lymphocyte in presence IL-2 – *Detection of antigen* - p24 is the earliest viral marker to appear in blood – *Detection of viral nucleic acid :* a. *PCR* - Gold standard of diagnosis in all stages of HIV includes DNA PCR, RNA PCR, RT PCR b. *Branched DNA (bDNA)* assay c. Nucleic acid sequence based assay (NASBA)

RT - PCR is used both as diagnostic and prognostic test.

2. Ans. is c i.e. Cytomegalovirus *Ref. Harrison 17/e, p 1185*

Ophthalmologic manifestations of HIV infection

- The ***MC*** abnormal finding on fundus examination are "cotton wool spots". They represent area of retinal ischemia secondary to microvascular disease. These lesions are not associated with visual loss.
- **CMV Retinitis :**
  - ***MC cause of vision loss in*** AIDS ***patient.***
  - Usually occurs when CD-4 <50/µl.
  - Usually present as painless progressive of vision, patient may also complain of floaters and scintillations.
  - The *characteristic* appearance is that *of perivascular hemorrhage and exudate.*
  - It may be complicated by rheumatogenous retinal detachment.
  - *Treatment* - oral valganciclovir, IV ganciclovir - ***DOC***
- **Acute retinal necrosis syndrome = Progressive outer retinal necrosis (PORN) :**
  - Caused by herpes simplex virus, varicella zoster virus.
  - Associated with pain, keratopathy iritis.
  - Ophthalmologic examination show widespread pale grey lesions.
  - ***DOC*** is intravenous acyclovir.
- **Other secondary infections include :**
  - P.carnii - Cause lesion of choroid.
  - Toxoplasmosis - Cause chorioretenitis.

3. Ans. is a i.e. Following needle stick injury infectivity is reduced by administration of nucleoside analogues

Ref. Harrison 17/e, p 1201; Park 18/e, p 279; 19/e, p 294

"Four week treatment with AZT monotherapy after needle stick exposure to HIV among health care worker decreases the chance of their becoming infected by 79%." *..... Park 19/e, p 294*

Guideliness for post exposure prophylaxis :

- A combination of two nucleoside analogue reverse transcriptase inhibitors for 4 weeks for less severe exposures.
- A combination of two nucleoside analogue RT inhibitor plus a third drug given for 4 weeks for more severe exposure.

Factor associated with increased risk of occupational transmission :

- Deep injury.
- Presence of visible blood on the instrument causing the exposure.
- Injury with the device that has been placed in vein or artery of source patient.
- Terminal illness of source patient.
- Lack of post exposure antiretroviral therapy in exposed health are worker.
  - *Best Predictor to disease progression is HIV RNA estimation not CD 4 + count.* *... H - 17/e, p 1167*
  - CD 4 + count are the *best* indicator of immediate state of immunologic competence.

So, ***option 'b'*** is wrong.

- **Clinical latency versus microbial latency**
  - Clinical latency should not be confused with microbial latency since virus replication is present in most patient.

So, ***option 'd'*** is wrong.

Remember :

- **Test for monitoring of patient with HIV infection :**
  - CD 4 + T cell count
  - HIV RNA determination - Best by RT - PCR
  - HIV resistance testing.

4. Ans. is b i.e. Single stranded RNA *Ref. Ananthnarayan 7/e, p 583*

Classification of HIV (= HTLV III)

Family	–	*Retroviridae*
Subfamily	–	*Lenti virus*
Genome	–	*SS RNA positive sense.*

- Viron contain ***lipoprotein envelope*** and nucleocapsid is icosahedral in shape.
- ***Characteristic feature of retrovirus*** is presence of reverse transcriptase enzyme.
  - Viral RNA is transcribed by this enzyme first in to SS DNA then to ds DNA which gets integrated with host cell.
  - Thus in contrast to central dogma flow of information is RNA → DNA → RNA

5. Ans. is a i.e. It is DNA retrovirus *Ref. Ananthnarayan 7/e, p 583*

HIV is RNA retrovirus (not DNA virus)

- It primarily infect CD 4 + T cells but can infect other cells also which bear CD4 receptor on their surface *[Harrison 16/e, p 1093]*. These include circulating dendritic cells; epidermal langerhan's cells; monocytes.

6. Ans. is a i.e. 50 *Ref. Harrison 17/e, p 1185*

Already explained, refer answer no. 2

7. Ans. is c i.e. Dendritic cell do not support replication

Ref. Ananthnarayan 7/e, p 586; Harrison 17/e, p 1157

- **Cellular target of HIV**
  - CD 4^+ lymphocyte and CD 4 + cells of monocyte and macrophage lineage are principal target of HIV.
  - Circulating dendritic cells - play important role in initiation of HIV infection.
  - Epidermal langerhans cells.
  - 5 - 10% of B lymphocyte. *..... Ananthnarayan, 7/e, p 586*
- Degree of cytopathicity of HIV for cells of the monocyte lineage *is low,* and HIV can replicate extensively in cells of monocyte lineage. Hence play a role in dissemination of HIV in the body and can serve as reservoir of HIV infection. *..... Harrison, 17/e, p 1159*
- **p24 is the earliest virus marker** to appear in blood and is the one tested for. *..... AA 7/e, p 590*

8. Ans. is a i.e. RNA - DNA - RNA *Ref. Ananthnarayan 7/e, p 583; Harrison 17/e, p 1132*

Already explained, refer answer no. 4

9. Ans. is a i.e. Kaposi sarcoma *Ref. Harrison 17/e, p 1162, 1186*

"Kaposi sarcoma is a multicentric neoplasm of vascular origin consisting of multiple vascular nodules appearing in skin, mucous membrane and viscera."

Feature of Kaposi sarcoma :

- Can develop at any stage of HIV infection, even in presence of normal CD-4 count.
- It is a manifestation *of* excess proliferation of spindle cells that are believed to be vascular origin. *..... Harrison 17/e, p 1162*
- Development of KS is associated with Human herpes virus 8 or HHV - 8 is etiologic agent of KS.
- Clinically KS often appear in sun exposed areas, particularly tip of nose. The initial lesion is a small raised reddish purple nodule on skin. *(**MC** appear as raised nodules).*
- LN involvement does not signify poor prognosis.

Treatment :

- *Observation and optimization of antiretroviral therapy.*
- *Single or limited number of lesions :*
  - Radiation
  - Intralesional vinblastine and Cryotherapy.

- *Extensive disease :* – Initial therapy : - Interferon - a (if CD 4 + T cells > 150/µl)
  - Liposomal daunorubicin.
  – Subsequent therapy : - Liposomal doxorubicin
  - Paclitaxel and Radiation treatment.
  – Combination chemotherapy
  – Radiation treatment.

10. Ans. is a i.e. Mycobacterium avium intracellulare *Ref. Harrison 17/e, p 1173*

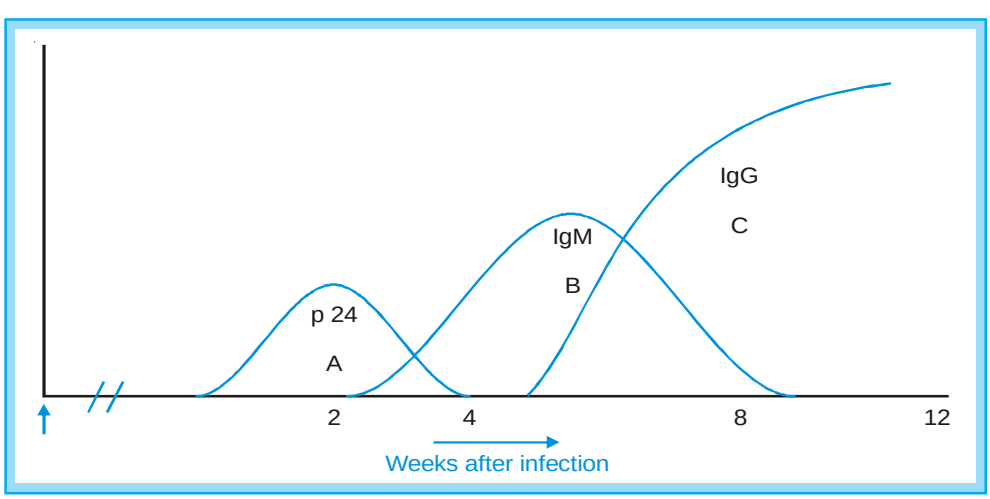
MAC infection in AIDS patients

- MAC infection is the late complication of HIV infection occur when CD 4 < 50/µl.
- ***MC*** presentation is disseminated disease with fever weight loss and night sweats other clinical features are : – Abdominal pain
  – Diarrhoea
  – Lymphadenopathy.
- Diagnosis is made by demonstration of long, slender AFB in sputum, stool, blood or bone marrow.
- **Treatment** : *Clathiromycin + Ethambutol is treatment of choice.*

11. Ans. is a i.e. p24 antigen assay *Ref. Ananthnarayan 7/e, p 590, 594*

"The major core antigen p24 is the earliest virus marker to appear in blood and is the one tested for."

p24 antigen assay is the most useful screening test for acute HIV syndrome as p24 antigen assay can detect those in windows period also.



12. Ans. is a i.e. T-helper cells *Ref. Ananthnarayan 7/e, p 586; Harrison 17/e, p 1157*

Already explained, refer answer no. 7

13. Ans. is a i.e. More sensitive less specific *Ref. Park 17/e, p 277; 19/e, p 293*

Remember : – Screening tests is *more sensitive* and *less specific.*
– Diagnostic tests is *more specific* and *less sensitive.*

For more details, refer answer no. 1

14. Ans. is d i.e. Tat gene *Ref. Harrison 17/e, p 11140-1141; Ananthnarayan 7/e, p 584*

GENES OF HIV
Genes coding for structural protein
• *gag gene* – determine the core and shell of virus • *pol gene* – codes for reverse transcriptase and other enzymes endonuclease • *env gene* – encodes the envelope glycoprotein
Regulatory gene
tat gene – enhance expression of all viral gene *nef gene* – down regulating viral replication *rev gene* – enhancing expression of structural protein *vif gene* – influence infectivity of viral particle *vpu gene* – (present only in HIV - 1) *vpx gene* – (present only in HIV - 2) } enhance maturation and release of progeny *vpr gene* – stimulate promoter region of virus *LTR sequence* - Giving promoter, enhancer, integration signal

15. Ans. is c i.e. Reverse transcriptase *Ref. Harrison 17/e, p 1132*

Reverse transcriptase is characterstic enzyme of family retroviridae.

Retroviriae includes

• ***Oncoviridae (oncogenic viruses)*** –	RNA tumor virus group (HTLV 1, HTLV 2 Rous sarcoma virus).
• ***Lentiviridae***	– HIV 1, HIV 2 – Visna virus – Feline immunodeficiency virus
• ***Spumavirinae foamy virus***	– Simian foamy virus – Human foamy virus

16. Ans. is c i.e. Increased release of acid labile interferon *Ref. Ananthnarayan 7/e, p 587 - 588*

"Infected T-4 cells do not appear to release normal amount of IL-2, IFNγand other lymphokines."

γ Interferon is acid stable in contrast to other interferons.

Immunological abnormalities in HIV infection
I. Features that characterize AIDS
• Lymphopenia • Selective T cell deficiency - Reduction in number of T4 (CD4) cells, Inversion of T4 : T8 ratio. • Decreased delayed hypersensitivity on skin testing • Hypergammaglobulinemia - predominantly IgG and IgA; and IgM also in children. • Polyclonal activation of B cells and increased spontaneous secretion of Ig.

Continue .....

II. Other consistently observed features
• Decreased in vitro lymphocyte proliferative response to mitogens and antigens. • Decreased cytotoxic response by T cells and NK cells • Decreased antibody response to new antigens. • Altered monocyte/macrophage function. • Elevated levels of immune complexes in serum.

17. Ans. is b i.e. Time period *Ref. Harrison 17/e, p 1164*

Window period is the period between infection to antibody detection.

- This period is 3-4 weeks for antibody detection.
- Detection by p24 antigen has decreased this to 16 days and subsequently to 12 days with nucleic acid testing.

18. Ans. is c i.e. Put the dressing material directly in an appropriate bag and send for incineration
Ref. Park 18/e, p 599; 19/e, p 648

This type of waste belongs to category 6 of biomedical waste Disposal method for this category is direct incineration without chemical treatment.

Categories of Bio-Medical Waste in India

Option	Waste Category	Treatment and disposal
Category No.1	Human Anatomical Waste (Human tissues, organs body parts)	incineration[2] / deep burial
Category No. 2	Animal Waste (animal tissue, organs, body parts blood and experimental animals used in research, waste generated by veterinary hospitals colleges.	Incineration[2] / deep burial
Category No. 3	Microbiology and Biotechnology Waste (waste from laboratory cultures, stock or specimens of micro-organisms, live or attenuated vaccines, human and animal cell culture used in research and infectious agents from research and industrial laboratories, waste from production of biologicals, toxins, dishes and devices and for transfer of cultures)	Local autoclaving / microwaving / incineration
Category No. 4	Waste sharps (needle, syringes,scar pels, blades, glass, etc. that may cause puncture and cuts. This includes both used and unused sharps)	Disinefction (chemical treatment @ autoclaving/microwaving and mutation / shredding)
Category No. 5	Discarded medicines and Cytotoxic drugs (wastes comprising of outdated, contaminated and discarded medicines)	Incineration @ destruction and drugs disposal in secured landfills

Category No. 6	Solid waste (items contaminated with blood, and fluids including cotton, dressings, soiled plaster casts, linen, beddings, other material contaminated with blood)	Incineration @ autoclaving/ microwaving
Category No. 7	Solid waste (wastes generated from disposable items other than the waste sharps such as tubings, catheters, intravenous sets etc.)	Disinfection by chemical treatment @@ autoclaving /microwaving and mutilation / shredding ##
Category No. 8	Liquid waste (waste generated from laboratory and washing, cleaning, housekeeping and disinfecting activities)	Disinfection by chemical treatment @@ and discharge into drains
Category No. 9	Incineration ash (ash from incineration of any bio-medical waste)	Disposal in municipal landfill
Category No. 10	Chemicals used in production of biologicals, chemicals used in disinfection, as insecticitdes, etc.	Chemical treatment @@ and discharge into drains for liquids and secured landfill for solids.

@@	*Chemical treatment using at least 1% hypochlorine solution or any other equipment chemical reagent. It must be ensured that chemical treatment ensures disinfection.*
##	*Multilation / shredding must be such so as to prevent unauthorized reuse.*
@	*There will be no chemical pretreatment before incineration. Chlorinated plastics shall not be incinerated.*
2	*Deep burial shall be an option available only in towns with population less than lakhs & in rural areas.*

Remember :

Colour coding and type of container for disposal of bio-medical wastes.

Colour coding	Type of container	Waste category
Yellow	Platic bag	Cat. 1, Cat. 2, and Cat. 3, Cat. 6
Red	Disinfected container/plastic bag	Cat. 3, Cat. 6, Cat. 7
Blue / White translucent	Plastic bag / puncture proof container	Cat. 4, Cat. 7
Black	Plastic bag	Cat. 5 and Cat. 9 and, Cat. 10 (solid)

19. Ans. is b i.e. Vascular origin *Ref. Harrison 17/e, p 1162*

Already explained, refer answer no. 9

20. Ans. is a i.e. Hairy leukoplakia *Ref. Harrison 17/e, p 1174*

Oral lesions in AIDS patient

1. Hairy leukoplakia	– Caused by ***EBV*** – White frond like lesion along lateral border of tongue – ***Not a premalignant condition*** – ***Treatment :*** Topical podophylin or systemic acyclovir.

2. Thrush	– Caused by ***Candida*** – White chessy exudate on erythematous mucosa in post. oropharynx – ***Most commonly*** seen on soft palate – Diagnosed by direct examination of scraping for pseudohyphal elements.
3. Apthous ulcer	– Painful ulcer of unknown etiology on post oropharynx – Thalidomide is an effective treatment.

21. Ans. is c i.e. HIV ELISA *Ref. CPDT 16/e, p 55*

"HIV ELISA is not usefull for diagnosing HIV infection in newborn because IgG antibody of mother which has been transfered to neonate gives false positive result."

Diagnosis of HIV in new born :
1. Detection of HIV DNA or RNA by PCR (Most effective)
2. HIV culture
3. HIV p24 antigen assay.

22. Ans. is c i.e. Zidovudine + Lamivudine + Indinavir for 4 weeks *Ref. Harrison 17/e, p 1201*

Post exposure prophylaxis
- ↓ transmission by 79%.

Guide lines

A. For routine exposure :
- Combination of two nucleoside analogue reverse transcriptase inhibitors daily for 4 weeks.

B. For high risk or complicated exposure
- Combination of two nucleoside analogue reverse transcriptase inhibitor plus a protease inhibitor.

- ***Most clinician administer the later regimen in all cases.***

So, the treatment is : ***Zidovudine + Lamuvidine + Indinavir***

23. Ans. is a i.e. CD4 + Helper cells *Ref. Harrison 17/e, p 1157; Ananthnarayan 7/e, p 586*

Already explained, refer answer no. 7

24. Ans. is a i.e. Risk of HIV in baby is upto 90%
Ref. Harrison 17/e, p 1145; Park 18/e, p 275; 19/e, p 289; Ghai 6/e, p 220

"In the absence of prophylactic antiretroviral treatment the probability of transmission of HIV from mother to fetus ranges from 15 to 25% in developed country and 25 to 35% in developing countries."

..... Harrison, p 1145

Relative proportion of mother to child transmission were :

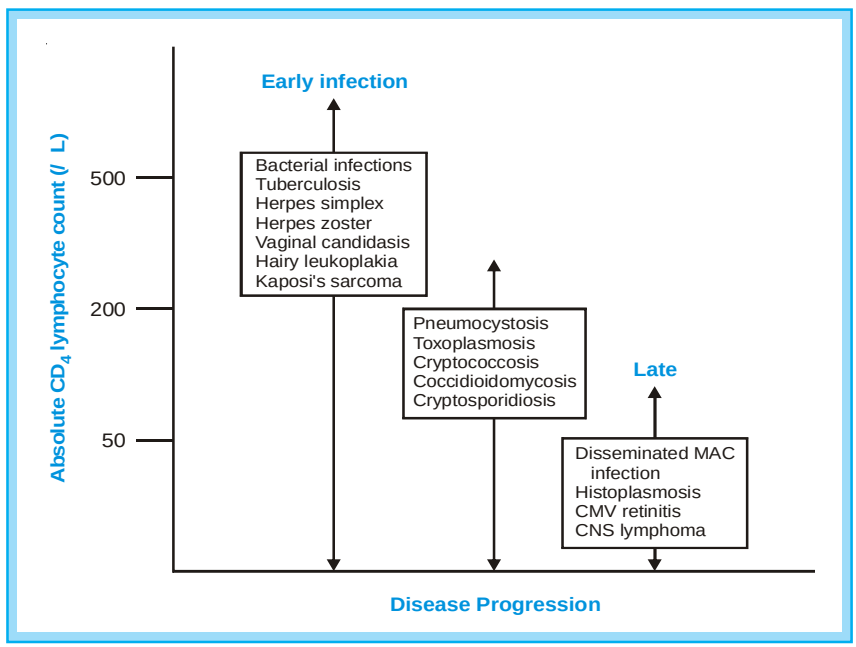
23 to 30% – In utero
50 to 65% – During birth
12 to 20% – Breast feeding.

Maternal fetal transmission

- Risk of transmission is 30%.
- *Most common at the time of delivery.*
- CS decrease risk of transmission.
- Risk is more if mother has advanced AIDS or Acute HIV syndrome.
- First born twin has more risk of getting infection than 2nd born.
- *Breast feeding can transmit infection,* but exclusive breast feeding caries lower risk than mixed feeding.
- Presence of mastitis, Vitamin A deficiency increase risk of transmission via breast feeding.

25. Ans. is c i.e. Mycoplasma pneumonae *Ref. Ananthnarayan 7/e, p 592; Park 18, p 276*

Oppurtinistic infection in HIV patient



Relationship of CD4 count to development of opportunistic infection

26. Ans. is c i.e. Aspergilosis *Ref. Harrison 17/e, p 1170-71*

All of the following organism can cause opportunistic infection in AIDS patient. But Invasive aspergillosis is generally not seen in patient with **AIDS** in the absence of neutropenla or administration of glucocorticoids. Aspergillosis also given in list of oppurtunistic infection but it is not *much common,* hence is best option.

27. Ans. is a and b i.e. Gag and Tat *Ref. Ananthnarayan 7/e, p 584*

Already explained, refer answer no. 14

28. Ans. is a, b, c and d i.e. Pueumocystis carini; Penicillium marneffei; Candida; and Cryptococcus
Ref. Harrison 17/e, p 1172-1173

Fungal infection in AIDS patient are :

- ***Pneumocytis carnii (MC oppurtinstic infection in HIV patient)***
- ***Cryptococcus neoformans (MC cause of meningitis in HIV patient)***
- Histoplasma
- Penicillium marneffei
- Coccidiodes immitis
- Aspergillosis (pseudomembraneous bracheobronchitis in AIDS patient).
- Sporothrix.

Note : Cryptosporidium is a parasite not a fungus.

29. Ans. is a, b, c and e i.e. A glandular fever like illness; Generalized lymphadenopathy; Gonococcal septicemia; and Presenile dementia

See below

Gonococcal septicemia is seen in terminal complement deficiency not in HIV patient.

I do not think that I should explain whole clinical feature here again. Just revise them from theory portion.

30. Ans. is a and b i.e. Gag; and Tat *Ref. Harrison 17/e, p 1140*

Already explained, refer answer no. 14

31. Ans. is a, b, c, d and e i.e. All are correct options *Ref. Park 18/e, p 277; 19/e, p 291*

Guys, please see Diagnosis of AIDS from theory portion.

32. Ans. is b and c i.e. CD 8 < 500; and CD 4 : CD 8 = 1 *Ref. Harrison 16/e, p 1104*

Any HIV infected individual with a CD-4 + T cell count of < 200/µl has AIDS by definition regardless of symptom or oppurtinstic infection.

33. Ans. is c and e i.e. Cryptococcus; and Giardia lambia *Ref. Harrison 17/e, p 1169*

Cause of diarrhoea in HIV patient		
Bacterial	**Fungal**	**Parasitic**
– Shigella	– Histoplasmosis	– Cryptosporidia
– Salmonella	– Penicillosis	– Microsporidia
– Campylobacter	– Coccidioidomycosis	– Isospora belli

34. Ans. is c and d i.e. Oral candidiasis; and Hairy leukoplakia *Ref. Harrison 17/e, p 1174*

Already explained, refer answer no. 20

35. Ans. is None *Ref. Harrison 17/e, p 1140; Ananthnarayan 7/e, p 584*

The options given are not gene but their protein products.

36. Ans. is d i.e. Male to female transmission > female to male *Ref. Harrison 17/e, p 1142*

Modes of transmission of AIDS

- ***Sexual Transmission :***
  - ***MC*** mode of HIV transmission is heterosexual transmission.
  - Chances of HIV infection from male to female is twice
  - Anal intercourse carries higher risk of transmission.
  - Presence of STD increase risk of transmission.
  - Adloscent girl and women above 45 are more prone to get HIV infection.
- ***Transmission by Blood and Blood products :***
  - Transfusion of whole blood, packed RBC, platelets, leukocytes and plasma are all capable of transmitting HIV infection.
  - Hyperimmune gamma globulin, hepatitis B immunoglobulin, plasma derived hepatitis B Vaccine and Rh immunoglobulin have not been associated with transmission of HIV infection.
- ***Maternal fetal transmission***
  - Risk of transmission is 30%.
  - *Most common at the time of delivery.*
  - *CS* decrease risk of transmission.
  - Risk is more if mother has advanced AIDS or Acute HIV syndrome.
  - First born twin has more risk of getting infection than 2nd born.
  - *Breast feeding can transmit infection,* but exclusive breast feeding caries lower risk than mixed feeding.
  - Presence of mastitis, Vitamin A deficiency increase risk of transmission via breast feeding.

37. Ans. is a i.e. Mycobacterium tuberculosis *Ref. Harrison 17/e, p 1172*

- HIV infection increase risk of developing active TB by a factor of 15 to 30.
- In developing countries where M. tuberculosis infection is most frequent, HIV infected individual have primary and secondary infection with the usual way.
- Oppurtunistic infection with M.avium intra cellulare is ***MC*** oppurtunistic infection in west.

So, it is clear that in developing countries like India MC mycobacterial infection is M. tuberculosis.

38. Ans. is a and b i.e. P. carrnii; and M. avium *Ref. Park 18/e, p 276; 19/e, p 292*

Already explained, refer answer no. 2 and 10

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.

1. In the heterosexual trasmission (from ifective partner to non-infective partner) of HIV : [Kar 03]

a) There is greater risk of transmission from man to woman
b) There is greater risk to transmission from woman to man
c) Risk is equal in neither ways
d) HIV infection is not transmitted by heterosexual act

[Ref. Park 19/e, p 289]

2. In India, maximum cases of tuberculosis in AIDS patients are due to : [Bihar 03]

a) M.tuberculosis
b) M. avium intracellulare
c) M.scrofulaceum
d) M.akari

[Ref. Ananthnarayan 7/e, p 589]

3. AIDS involves : [Jharkhand 04]

a) T-helper cells
b) T-suppressor cells
c) T-cytotoxic cells
d) B-cells

[Ref. Ananthnarayn 7/e, p 586]

4. Which of the following gene is associate with encoding of reverse transcriptase ?

a) Pol **[Bihar 05]**
b) Env
c) Gag
d) p–24

[Ref. Ananthnarayan 7/e, p 584]

5. Geg gene encodes for : [Bihar 05]

a) Reverse transcriptase
b) Core antigen
c) Envelope
d) Gene activation

[Ref. Ananthnarayan 7/e, p 584]

6. The most common HIV subtype in India is :

a) D **[Kar 06]**
b) H
c) E
d) C

[Ref. Harrison 17/e, p 1142; Fig 182-7]

7. AIDS virus is : [Kerala 94]

a) RNA virus
b) DNA virus
c) Retro virus
d) Entero virus

[Ref. Ananthnarayan 7/e, p 582]

8. Following is the marker of HIV infection in blood :

a) Reverse Transcriptase **[AIIMS 94]**
b) DNA polymerase
c) RNA polymerase
d) None

[Ref. Ananthnarayan 7/e, p 583]

9. Incidence of AIDS transmission from infective to noninfective partner is more with : [NIMS 96]

a) From a male to a female partner increased risk
b) From a female to a male partner increased risk
c) Equal risk to both
d) No risk of heterosexual transmission

[Ref. Park 19/e, p 289]

10. The gene coding for core of HIV is : [Kerala 96]

a) GAG
b) ENV
c) POL
d) TAT

[Ref. Ananthnarayan 7/e, p 584]

11. Commonest mode of AIDS tranmission in India is by : [Karn. 96]

a) Vertical transmission
b) I.V. drug abuse
c) Heterosexual promiscuity
d) Homosexual promiscuity

[Ref. Harrison 17/e, p 1142]

Answer

1. a) There is greater ...
2. a) M. tuberculosis
3. a) T-helper cells...
4. a) Pol
5. b) Core antigen
6. d) C
7. c) Retro virus
8. a) Reverse ...
9. a) From a male ...
10. a) GAG
11. c) Hetero ...

12. The HIV virus can be destroyed in vitro by which of the following : **[Karn. 96]**
a) Boiling
b) Ethanol
c) Cidex
d) All of the above
[Ref. Ananthnarayan 7/e, p 585, 586]

13. During the window period of patient with AIDS :
a) ELISA is -ve **[NIMS 96]**
b) Western Blot is -ve
c) Both are -ve
d) PCR is -ve
[Ref. Ananthnarayan 7/e, p 591]

14. Risk of HIV transmission is not seen with :
a) Whole blood **[NIMS 96]**
b) Platelets
c) Plasma derived Hepatitis B vaccine
d) Leucocytes Vaccines
[Ref. Harrison 17/e, p 1144]

15. AIDS is not transmitted by : **[Kerala 97]**
a) Blood transfusion
b) Cryoprecipitate
c) Breast milk
d) Plasma
[Ref. Harrison 17/e, p 1144]

16. All the following are true about HIV except :
a) A DNA virus belonging to lentivirus **[TN 99]**
b) Attacks CD4 lymphocytes
c) CD4 : CD8 ratio is reversed
d) Mostly spread by heterosexual contact
[Ref. Ananthnarayans 7/e, p 582]

17. Commonest helminthic infection in AIDS is :
a) Trichuris -Trichuria **[UP 00]**
b) Strongyloidis
c) Enterobius
d) Necator americana
[Ref. Ananthnarayan 7/e, p 592]

18. Following cells are infected by HIV : **[Karn. 02]**
a) CD8 + T lymphocytes
b) CD4 + T lymphocytes
c) B Cells
d) Macrophages
[Ref. Harrison 17/e, p 1149]

18. Which is not increased in HIV infection :
a) CMV **[ST JOHN'S O2]**
b) Kaposi sarcoma
c) Mycobacterial infection
d) Pneumococcal infection
[Ref. Ananthnarayan 7/e, p 592 Table (62.5)]

20. Full blown imunodeficiency syndrome is :
a) High viral titres with low CD4 count **[SGPGI 03]**
b) Low viral titres with low CD4 count
c) Low viral titres with high CD4 count
d) High viral titres with high CD4 count
[Ref. Harrison 17/e, p 1169]

21. All are true about AIDS except : **[UP 03]**
a) Seen in heterosexual only
b) Caused by reterovirus
c) Candidiases is also common feature
d) Retrovirus is thermolabile
[Ref. Ananthnarayan 7/e, p 586]

22. Reverse Transcriptase is : **[UP 04]**
a) DNA polymerase
b) DNA dependant RNA polymerase
c) RNA dependant DNA polymerase
d) None
[Ref. Ananthnarayan 7/e, p 583]

23. Most common mode of transmission of HIV world wide is : **[SGPGI 04]**
a) Heterosexual
b) Homosexual
c) IV drug abuse
d) Contaminated blood products
[Ref. Harrison 17/e, p 1142]

24. Screening test for AIDS : **[MP 05]**
a) ELISA
b) PCR
c) Western blot
d) CD-4 count
[Ref. Park 19/e, p 293]

25. HIV virus has predilection for infecting :
a) CD4 + T cells **[DNB 05]**
b) CD8 cells
c) Macrophages
d) Plasma cells
[Ref. Harrison 17/e, p 1149]

26. Most frequent species of Mycobacterirum associated with HIV infection in India is : **[MP 06]**
a) M. Avium intracelulare
b) M. Fortuitum
c) M. tuberclosis
d) M. Bovis

27. Which of the following is not a HIV gene :
a) Gag **[Kerala 06]**
b) Opl
c) Env
d) Rb
[Ref. Ananthnarayan 7/e, p 584]

Answer

12. d) All of the ... 13. c) Both are -ve 14. c) Plasma ... 15. b) Cryoprecipitate 16. a) A DNA virus ...
17. b) Strongyloidis 18. b) CD4 + T ... 19. d) Pneumo ... 20. a) High viral ... 21. a) Seen in ...
22. c) RNA ... 23. a) Heterosexual 24. a) ELISA 25. a) CD4 + T cells 26. c) M. tuberclosis
27. d) Rb

UNIT – III MYCOLOGY

1.	Dermatophytes	369 – 372
2.	**Yeast & Yeast like Fungus** Cryptococcus, Candida, Pneumocystii carinii	373 – 387
3.	Aspergillus & Mucormycosis	388 – 392
4.	Dimorphic Fungi	393 – 399

1 Dermatophytes

- Filamentous fungi (Mold) that infect only superficial keratinized tissues – skin, hair and nail.
- Causative agent of *Ringworm or Tinea or Dermatophytoses*.
- Not involve living Tissues.
- ***It has 3 genera –*** Trichophyton, Microsporum , Epidermophyton.
- ***In lesion,*** it form *hyphae* and *arthospores.*
- ***In culture*** it form *septate hyphae* and *asexual* spores (micro and macroconidia) with powdery and pigmented colonies.
- They are *differentiated* mainly by *nature of macrocondia.*

Clinical features

- Local inflammation is due to irritation by fungal products and hypersensitivity reaction.
- Transmission occurs from *infected to uninfected person often by brushes, combs and towels.*

Features	Trichophyton	Microsporum	Epidermophyton
Site	Infect hair, skin and nail	Hair and skin only	Skin and Nail only
Colony	Powdery, pigmented	Cotton like pigmented	Powdery greenish yellow
Spores			
• **Microconidia**	Abundant	Relatively scanty	Absent
• **Macroconidia**	Pencil or Cylindrical shaped, relatively scanty	Multicellular Spindle or fusiform shaped and is predominant spore	Club shaped or pear shaped multicellular

- Clinically ringworm is classified depending on the site involved eg. Tinea capitis infect scalp and hair.
- ***MC*** **species** infecting human being – ***T. rubrum.***

QUESTIONS

1. T. capitis (endothrix) is caused by : **[PGI 00]**

a) Epidermophyton
b) T. tonsurans
c) T. violaceum
d) Microsporum

2. Kerion is caused by : **[PGI 98]**

a) Candida
b) Streptococcus
c) Dermatophytes
d) Herpes

3. Tinea cruris is caused by : **[PGI 97]**

a) Epidermophyton
b) Trichophyton
c) Microsporum
d) Candida

Answer 1. b and c 2. c) Dermatophytes 3. a and b

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b and c i.e. T. tonsurans; and T. violaceum *Ref. Ananthnarayan 7/e, p 616*

Dermatophytoses	Common causative agents
Tinea captis	Microsporum, Trichophyton most species
Favus	T. schoenleinii T. violaceum, M. gypseum
Tinea barbae	T. rubrum, T.mentagrophytes, T. verrucosum
Tinea imbricata	T. concentricum
Tinea corporis	T. rubrum and any other dermatophyte
T. cruris	E. floccosum, T. rubrum
T pedis	T. rubrum, E. floccosum
Ectothrix hair infection	Microsporum species, T. rubrum
Endothrix hair infection	T. schoenleinii, T. tonsurans, T. violaceum

2. Ans. is c i.e. Dermatophytes *Ref. Dashore Manual of Skin, p 26*

Kerion

- The fungal infection of scalp caused by *microsporum or trichophyton* species ***not by epidermophyton.***
- Inflammatory boggy swelling covering small or large areas of scalp in which hair are loose and fallout or can be easily epilated.
- Commonly caused by zoophilic dermatophytes like T. mentagrophytes and T. verruco sum.
- Follicular scarring and partial alopecia is common after severe kerion.

Favus

- Chronic type of ringworm in which dense crusts (scutula) develop in hair follicles leading to alopecia and scarring

Remember : Both kerion and favus are type of Tinea captis.

3. Ans. is a and b i.e. Epidermophyton; and Trichophyton *Ref. Ananthnarayan 7/e, p 616*

Already explained, refer answer no. 1

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Dermatophytes are fungi infecting : **[Delhi 93]**

a) Subcutaneous tissues
b) Systemic organs
c) Nails, hair and skin
d) Superficial skin and deep tissue

[Ref. Ananthnarayan 7/e, p 613]

2. Dermatophytosis is caused by : **[Delhi 02]**

a) Herpes simplex
b) Papilloma virus
c) Trichophyton
d) Candida

[Ref. Ananthnarayan 7/e, p 613]

Answer 1. c) Nails, hair ... 2. c) Trichophyton

2 Yeast & Yeast Like Fungus

CRYPTOCOCCUS NEOFROMANS

Only yeast which is pathogenic. Also called as Eurpoean blastomycosis.

Characterized by a thick polysaccharide capsule which is stained by India Ink.

Morphology

- **Cell wall** is gram positive.
- C. neoformans differs nonpathogenic species of Cryptococcus by its ability to grow at 37^0C and the production of phenol oxidase and urease.

  There are four serotypes [A, B, C, D] and 3 varieties of C. neoformans :

  a. C. neoformans var grubii (serotype A)

  b C. neoformans var gatti (serotype B or C) : Cause disease is immunocompetent.

  c. C. neoformans var neoformans (serotype D).

Pathogenesis and Pathology :

- ***MC*** *predisposing factor* for cryptococcosis : **AIDS** (risk increase when CD4 <200/ul).
- Most infections in immunocompromised patient are caused by serotype A.
- Infection is acquired by inhalation of the fungus in to lung which is frequently asymptomatic but in immuno-compromised state there is hematogenous spread from lung to brain which leads to meningoencephalitis.
- Cryptococci are best seen in tissue by staining with *methenamine silver or periodic acid* schiff.
- Infection can occur by pigeon dropping or eucylyptus tree.

Clinical Manifestation

- Most patient present with meningoencephalitis.
- C.neoformis is ***MC*** cause of *meningitis in* **AIDS** patient.
- C.meningitis may not show meningismus, which is seen in bacterial meningitis and it may be associated with sudden vision loss.
- Focal lesions called cryptococcomas are *more common* in previously normal patient.
- These lesions are located ***MC*** at **basal ganglia** or the head of caudate nucleus. *..... Harrison 16/e, p 1184*
- Cryptococcomas are *best* seen with *MRI.*
- Cryptococcus in **AIDS** patient has less sign and symptoms.
- Headache is ***MC*** symptom.

Diagnosis

- Lumbar puncture is single most useful ***diagnostic test.***
- *Indian Ink preparation* is the *method of choice for detecting cryptococci in CSF.*
- *Latex agglutination* – Approx 90% of patient with cryptococcal meningitis including all AIDS patient, have capsular antigen detectable in CSF. However this is less useful in diagnosis of pulmonary disease.

Treatment

Type of disease	Preferred treatment	Alternative
i. Disease in AIDS Patient	Amphotericin B	Itraconazole
ii. Disease in non AIDS Patient		
– Meningitis	Amphotericin B	Switch over to fluconazole when patient condition has improved
– Pulmonary disease		
• Immunocompromised Patient	Amphotericin B	Switch over to Fluconazole when patient condition has improved
• Normal	Fluconazole	Itraconazole

CANDIDA

Candidiasis is ***MC*** systemic mycosis.

- ***MC*** agent responsible is candida albicans.
- All pathogenic candida are commensals of humans particularly in mouth, stool and vagina.

Morphology

Gram positive fungi

They grow as budding yeast cells but they can also form pseudohypahe (except C. glabrata which doesn't) both in culture and in tissues.

- Candida albicans is dimorphic as it also forms true hyphae *[other species of candida are not dimorphic].*

  ... Jawetz 24/e, p 643
- C. albicans is identified on basis of their ability to form of large thick walled spores *(diagnostic)* called *chlamydospores* on nutritionally deficient media or corn meal agar at 20^0C.
- C. albicans form germ tubes *[Reynods Braude Phenomenon].*
- *Accurate identification* of Candida species other than C.albicans require biochemical tests.

Pathogenesis

- Invasive candidiasis is usually preceded by ↑ colonization in mouth, vagina due to broad spectrum antibiotics.
- Majority of non.albicans vagina speices enter the blood through intravascular catheterisation.

Clinical manifestation

I. *Cutaneous and Mucosal candidiasis -*

- **Risk factors** association with superficial candidiasis are :
  - AIDS
  - Pregnancy
  - **Diabetes *(MC)***
  - Infants and elders
  - Oral contraceptives
  - Trauma
- ***It includes -***
  - **Oral thrush :**
    - Painless discrete and confluent adherent white plaques on the oral and pharyngeal mucosa common in AIDS at CD4 <50/μl.
    - Cutaneous candidiasis may be **intertriginous** (erythematous scaling or moist lesion) or **paronychial** (seen in occupation that lead to frequent immersion of hands in water).

- **Esophageal candidiasis :** Most lesion are in distal 3rd of oesophagus. Diagnosed by biopsy.
- **Vulvovaginal candidiasis :** Mostly in 3rd trimester of pregnancy.
- ***Chronic mucocutaneous candidiasis :*** Mostly onset in early childhood and association with cellular immunodeficiencies and endocrinopathy. Present as hyperkeratotic skin lesion, partial alopecia, and both oral and vaginal thrush.

II. ***Deeply Invasive (systemic) candidiasis*** **:**

- Hematogenous seeding (candedemia) is common to retina, kidney, spleen, liver.
- ***In immunocompetent patient –*** U/L or B/L white retinal exudates appear within 2 weeks of onset of candedemia. Most cases of ocular involvement occur in non neutropenic patient.
- ***Hepatosplenic candidiasis*** (Chronic disseminated candidiasis) usually occur in patient with acute leukaemia. originates from intestinal seeding of portal and venous circulation. Mostly occur in neutropenic patient.
- Candida can cause arthritis of knee in patient who have received *chronic glucocorticoid* injections in joint.
- Endocarditis in previously damaged or prosthetic valve.

Diagnosis

i. ***Superficial candidiasis*** **:** Demonstration of pseudohyphae or hyphae on wet smear with confirmation by culture or staining (Gram's, PAS, Methenamine silver).

ii. ***Invasive candidiasis*** **:** Diagnosed by histologic section of biopsies or by culture of CSF, blood, joint fluid.

Treatment

Type	Preferred	Alternative
i. Mucocutaneous		
• Cutaneous	Topical azoles	Topical nystatin
• Vulvovaginal	Azole cream or oral Fluconazole	Nystatin suppository
• Oropharyngeal	Clotrimazole or Fluconazole	Nystatin
• Esophageal	Fluconazole or itracon azole	
ii. Deeply invasive		
• Non neutropenic	• Fluconazole or amphotericin B	
• Neutropenic	• Amphotericin B	
iii. Candida endophthalmitis	• IV polyene + flucytosine	

PNEUMOCYSTIS INFECTION

- Opportunistic fungal pulmonary pathogen, lacks ergosterol so not susceptible to antifungal which inhibit ergosterol synthesis.
- Human isolate – P. jiroveci; P.carnii is found in rats. *... Harrison 17/e, p 1267*
- **Most prominent antigen :** Major surface glycoprotein which shows antigenic variation and facilitates its adherence.
- Other important antigen is 35-55kDa - which acts as marker of infection.

Pathogenesis and Pathology

- Defects in CMI and humoral immunity predispose for its infection eg In HIV infection occur when CD4 + <200/µl.
- Principal host effector cells – alveolar macrophage.
- Transimission – Airborne; person to person.

- **In alveoli :** – It attach to type I cells (extracellular), damage it.
  – Hypertrophy of type II cells occur causing, surfactant abnormalities.
  – Increase IL-8 and neutrophil in BAL fluid.
  – Alveoli filled with typical foamy vacuolated exudate.
- **Severe disease :**
  Mild mononuclear cell (ever plasma cell) interstitial infiltrate seen so called *Interstitial plasma cell pneumoniae.*

Risk factors for Pneumocystis Pneumonia

– HIV
– Immunosuppressive therapy particularly glucocorticoids for cancer
– Organ transplantation and other disorders
– Children with primary immunodeficiency disease and premature malnourished infants.

Clinical feature

- **Symptom** – Dyspnea, fever, non productive cough.
- **Sign** – Tachypnea tachycardia and cyanosis but lung auscultation reveals few abnormalities.
- Risk for extrapulmonary spread increase with : Administration of aerosolized pentamidine.
- ***MC*** extrapulmonary site : **Lymph node**, spleen, liver, bone marrow.
- Most widely used prognostic factor is degree of hypoxemia.

Diagnosis

1. **Definitive diagnosis by histopathologic detection by :**
   a. Staining – Methenamine silver, toludine blue stain cell wall while *Wright-Giemsa stain the nuceli.*
   – Immunoflurescence with monoclonal antibodies; more sensitive.
   b. DNA amplification by PCR – *most sensitive*

2. **Specimen collection**
   a. ***Fiberoptic bronchoscopy with BAL*** which is more sensitive than sputum induction, is the mainstay of diagnosis.
   b. ***Transbronchial biopsy and open lung biopsy*** – *only when* diagnosis can't be made by BAL.

3. **CXR –** Classic finding **:** - B/L diffuse infiltrate in perihilar region.
   - Nodular densities, cavitary lesion, Pneumothorax can also occur.
   - ↑ *Frequency of upper lobe infiltrate in patient who take aerosolized pentamidine.*

4. **Reduced arterial O_2 pressure (PaO_2);** increase alveolar arterial O2 gradient (PAO_2-PaO_2); respiratory alkalosis.

Treatment

- ***DOC cotrimaxazole*** for all forms of pneumocystosis including extrapulmonary disease.
- Alternative for mild to moderate case – Trimethoprim + dapsone and clindamycin + primaquine.
- Alternative for moderate to severe – Pentamidine slow IV.
- Adjunctive therapy – Glucocorticoid in HIV patient with moderate to severe pneumocystosis whose pulmonary function deteriorates on taking anti pneumocystis drugs.

Prophylaxis

- ***DOC*** for HIV primary and secondary (both HIV and Non HIV) prophylaxis is cotrimoxazole.
- Alternative Dapsone
- In HIV prophylaxis given when : – CD_4 + <200/µl
  – History of oropharyngeal candidiasis.

QUESTIONS

1. Pneumocystis Jeroveci : **[AI 08]**
a) Associated with CMV
b) Diagnosis is by sputum microscopy
c) Seen only in immunocompromised patients
d) Always associated with pneumatocele

2. The capsule of Cryptococcus neoformans in a CSF sample is best seen by : **[AI 05]**
a) Gram's stain
b) Indian ink preparation
c) Giemsa stain
d) Methanamine - silver stain

3. The M.C organism amongst the following that cause acute meningitis in an AIDS patient is :
a) Streptococcus pneumoniae **[AI 05]**
b) Streptococcus agalactiae
c) Cryptococcus neoformans
d) Listeria monocytogenes

4. M.C fungal infection in febrile neutropenia is :
a) Aspergillus niger **[AI 01]**
b) Candida
c) Mucormycosis
d) Aspergillus fumigatus

5. Latex agglutination test of the antigen in CSF helps in the diagnosis of : **[AI 00]**
a) Cryptococcus
b) Candidiasis
c) Aspergillosis
d) Histoplasmosis

6. Cryptococcus-neoformans is a : **[AI 99]**
a) Protozoa
b) Fungus
c) Parasite
d) Mycoplasma

7. True about cryptococcus neoform is all except :
a) Capsular antigen is detected in CSF **[AIIMS 96]**
b) Common in immuno compromised patient
c) Anticapsular antibody prevents recurrence
d) Strongly positive mucicarmine stain of the organism in tissue is diagnostic

8. Which is false regarding Cryptococcus neoformans : **[AI 95]**
a) Grows at 5^0C and 37^0C
b) It has 4 serotypes
c) Urease negative
d) Causes superficial skin infection

9. Cryptococcus is least likely to cause infection of:
a) Skin **[AI 95]**
b) Bone
c) Brain
d) Kidney

10. Which dye is most suitable for fungus demonstration in biopsy : **[AIIMS 06]**
a) Alizharian red
b) Verihoff dye
c) Mason's trichome
d) PAS

11. In HIV infected individual Gram stain of lung aspirate shows yeast like morphology. All of the following are the most likely diagnosis except :
a) Candida tropicalis **[AIIMS 05]**
b) Cryptococcus neoformans
c) Penicillium marneffi
d) Aspergillus fumigates

12. HIV positive female presents with an indurated ulcer over the tongue Laboratory findings show growth in cornmeal agar at 20C, microscope by showing hyphae and growth in human serum at 370C show budding yeast Probable cause is :
a) Candida albicans **[AIIMS 01]**
b) Histoplasmosis
c) Blastomycosis
d) Coccidioidomycosis

13. Which fungal infection is commonest in neutropenia : **[AIIMS 99]**
a) Candida
b) Histoplasma
c) Aspergillus niger
d) Aspergillus fumigatus

14. All are yeast like fungus except : **[AIIMS 97]**
a) Cryptococcus
b) Candida
c) Trichophyton
d) None of the above

Answer

1. b) Diagnosis is ... 2. b) Indian ... 3. c) Cryptococcus ... 4. b) Candida 5. a) Cryptococcus
6. b) Fungus 7. c) Anticapsular ... 8. c) Urease ... 9. d) Kidney 10. d) PAS
11. d) Aspergillus ... 12. a) Candida ... 13. a) Candida 14. c) Trichophyton

15. Candida infection is predisposed by all, except :
a) Menstruation **[AIIMS 96]**
b) Diabetes
c) Mini pill users
d) Combined pill users

16. An HIV positive female has an indurated ulcer over the tongue. Laboratory findings show growth in cornmeal agar at 20 Degrees, microscopy showing hyphae and growth inhuman serum at 37 degrees show budding yeasts. The probable cause is : **[PGI 06]**
a) Candida albicans
b) Histoplasmosis
c) Blastomycosis
d) Coccidiodomycosis
e) Mucormycosis

17. Endemic fungal infection is caused is by all of the following except : **[PGI 05]**
a) Coccidiodes immitus
b) Cryptococcus
c) Penicillium
d) Aspergillus
e) Blastomyces

18. Which of the following are difficult to isolate from culture : **[PGI 03]**
a) Candida
b) Dermatophytes
c) Cryptococcus
d) Malassezia furfur
e) Coccoidiodomycosis

19. Cryptococcus can be readily demonstrated by :
a) Albert's stain **[PGI 02]**
b) India ink stain
c) Giema's stain
d) Gram's stain
e) Z-N stain

20. Neurotrophic fungus is/are : **[PGI 02]**
a) Cryptococcus neoformans
b) Histoplasmosis
c) Trichophyton
d) Candida
e) Aspergillosis

21. Pneumocystis carini is a fungus because :
a) rRNA, mitochondrial protein gene sequence and presence thymiylate synthase **[PGI 00]**
b) Cell wall contains glucans
c) Antifungals are effective against P. carini
d) Commonest infection in AIDS

22. Cryptoccoccal meningitis is common in :
a) Renal transplant recipient **[PGI 00]**
b) Agammaglobulinemia
c) Neutropenia
d) IgA deficiency

23. Eucalyptus camaldulensis is associated with the transmission of : **[PGI 99]**
a) Blastomyces dematitidis
b) Histoplasma
c) Cryptococcus
d) Coccidiodes immitis

24. Fungi that possess a capsule is : **[PGI 99]**
a) Candida
b) Aspergillus
c) Cryptococcus
d) Mucor

25. Cryptococcus has predilection for : **[PGI 98]**
a) Lungs
b) Meninges
c) Liver
d) GIT

26. Fungi without sexual cycle are classified as :
a) Fungi imperfecti **[PGI 97]**
b) Phycomyces
c) Ascomycetes
d) Basidiomycetes

Answer
15. a) Menstruation
16. a) Candida albi...
17. b, c and d
18. d) Malassezia ...
19. b) India ...
20. a, b, d and e
21. a and b
22. a) Renal ...
23. c) Cryptococcus
24. c) Cryptococcus
25. a and b
26. a) Fungi ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b i.e. Diagnosis *Ref. Harrison 17/e, p 1267*

Pneumocystis Jiroveci

- Human isolate of Pneumocystis which is associated with severe pneumonia in immunocompromised state particularly AIDS (PcP).
- P.jiroveci is an extracellular pathogen. Growth in the lung is limited to surfactant layer above alveolar epithelium.
- Serologic evidence suggest that most individuals are infected in early childhood (thus ***option "c"*** is wrong) but the pneumonia is seen only in immunocompromised state.
- Diagnosis is made by detection of organism in proper specimen.
- **Specimen for PcP**
  - Sputum - quick and non invasive.
  - Broncho-alveolar lavage (BAL) fluid - ***Main stay*** of pneumocystis diagnosis.
  - Transbronchial biopsy - If diagnosis can not be made by BAL.
- The overt infection is an ***acute interstitial plasma cell pneumonia*** that occurs with high frequency among two groups :
  - As epidemic of primary infection among premature or debilated or marasmic infant of hospital wards in underdeveloped countries.
  - As sporadic cases among older children and adults who have an abnormal cellular immune status.

2. Ans. is b i.e. Indian Ink preparation *Ref. Ananthnarayan 7/e, p 621; Harrison 17/e, 1252*

- Cryptococcus neoformans is the only pathogenic yeast.
- Within the host and on certain culture media, it is surrounded by a large polysaccharide capsule.
- Capsule stands out in ***India Ink preparation.*** *... Ananthnarayan 7/e, 621*
- ***Indian Ink smears remains the method of choice for detecting cryptococcus in "CSF".*** *... Harrison 17/e, p 1252*

* Cryptococci are best seen in tissue by staining with methamine silver or periodic acid schiff (They stain the fungus itself not capsule).

* Muciramine staining of tissue is diagnostic but demonstrable only in few cases.

3. Ans is c i.e. Cryptococcus neoformans *Ref. Harrison 17/e, p 1251 - 1252*

- C. neoformans is ***MC*** cause of meningitis in AIDS patient.
- Generally occurs when CD4+ T cell count **<100/µl.**
- Diagnosis is made by identification of C. neoformans by India Ink or by detection of cryptococcal antigen by latex agglutination test.
- Strongly (+)ve result on muciarmine staining of tissue is ***diagnostic.***

Other important features of cryptococcal meningitis :

- ***MC*** cause of meningitis in AIDS patient
- Predisposing factors : – HIV infection – Solid organ transplantation – Hodgkins disease
  – Sarcoidosis – Corticosteroid therapy.

- Intra cerebral mass lesion (cryptococcomas) and obstructive hydrocephalus may complicated the course.

Treatment : Patient with AIDS and high risk patient : I.V Amphotericin B followed by Fluconazole for maintainance.

4. Ans. is b i.e. Candida *Ref. CMDT '08, p 1106*

Neutropenia ↑ chance of Following Infection. *..... CMDT '08; p 1106*

Bacterial	Fungal	Viral
Gram (-)ve enteric pathogens ***(MC)***	Candida ***(MC)***	Herpes zoster
Pseudomonas	Aspergillus	CMV
Gram (+)ve cocci (particularly Staph. aureus; Staph epidermidis, and viridans streptococci)	Pneumocystis carnii	Respiratory syncytial virus Influenza virus

Thus as **candida** *is given* **before** *aspergillus it would be taken as more common.*

Organism cause infection in granulocytopenic Patients *..... Harrison 17/e, p 535*

- ***Gram-positive cocci***
  - Staphylococcus epidermidis
  - Staphylococcus aureus
  - Viridans Streptococcus
  - Enterococcus faecalis
  - Streptococcus pneumoniae
- ***Gram-positive bacilli***
  - Diphtheroids
  - JK bacillus
- ***Gram-negative bacilli***
  - Escherichia coli
  - Klebsiella spp.
  - Non-aeruginosa Pseudomonas spp.
  - Enterobacter spp.
  - Serratia spp.
  - Acinetobacter spp.
  - Citrobacter spp.
- ***Fungi***
  - Candida spp.

5. Ans. is a i.e. Cryptococcus *Ref. Harrison 16/e, p 1184; CMDT '08, p 1334*

"90% of patient with cryptococcal meningoencephalitis have capsular antigen detectable in CSF or serum by latex agglutination." *... Harrison 16/e, p 1184*

Diagnosis of cryptococcal disease

Meningoencephalitis	*Pulmonary cryptococcus*	*Cutaneous cryptococcus*
– Lumbar puncture is **most useful** test – India ink smear of CSF reveals encapsulated yeast in more than half of cases – 90% of patient have capsular antigen detectable in CSF by latex agglutination – CSF culture is definitive diagnostic test	– Mimics malignancy – Biopsy is required for diagnosis	– Biopsy

6. Ans. is b i.e. Fungus *Ref. Ananthnarayan 6/e, p 574; 7/e, p 620*

Cryptococcus is the only pathogenic yeast.

7. Ans. is c i.e. Anticapsular antibody prevents recurrence *Ref. Harrison 17/e, p 1252*

Cryptococcal Infection

Antibodies are neutralized rapidly by the large amount of capsular antigen released during infection so capsular antigen is not protective. Rather cellular immunity play role in protection.

Remember : **Virulence factors of cryptococcus**

- Polysaccharide capsule
- Ability to make melanin
- Elaboration of enzymes (phospholipase, urease)

8. Ans. is c i.e. Urease negative *Ref. Ananthnarayan 7/e, 621*

Characteristic features of C. neoformans

- It is Urease positive fungus.
- Only pathogenic yeast.
- Presence of polysaccharide capsule which is stained with India Ink.
- Cell wall is gram positive.
- Differs from non pathogenic C. neoformans by :
  - Ability to grow at 37^0C
  - Production of phenol oxidase and urease.
- It has four serotypes A, B, C and D.
  - Most infection are caused by ***serotype A*** which is found in excreta of wild and domestic birds pigeon.
  - *Serotype B occur around Eucalyptus tree.* So, infection occur more in countries with large number of Eucalyptus tree.

9. Ans. is d i.e. Kidney *Ref. Harrison 17/e, p 1252*

Manifestation of C. neoformans (in decreasing order of frequency).

Common	Rare
• Menignoencephalitis ***(MC)***	• Prostitis
• Pulmonary cryptococcusis	• Endopthalmitis
• Cutaneous cryptococcusis	• Hepatitis
• Osteolytic lesion (present as cold abscess)	• Pericarditis
	• Endocarditis
	• Renal abscess

10. Ans. is d i.e. PAS *Ref. Ananthnarayan 7/e, p 611*

"The periodic acid schiff (PAS) and methanamine silver are valuable methods for the demonstration of fungal elements in tissue or biopsy section."

Remember :
- Sabauraud's glucose agar (pH - 5.4), czapek - Dox medium and corn meal agar are most commonly used media in mycology.
- GMS (Gomorris methanamine silver) stain is best fungal stain for biopsy section.

11. Ans. is d i.e. Aspergillus fumigates *Ref. Harrison 17/e, p 1256, 1266*

Aspergillus is a mould with septate hyphae (not have yeast like morphology).

Another confusing option is ***option "c".***

Penicillum marneffi :

- It is a dimorphic fungi, appearing as small yeast cells in tissue and as a mould in culture.
- It is a leading cause of opportunistic infection in patients of late stage HIV.

Candida is a group of yeast like fungus except C. albicans which is dimorphic.

Respiratory Infection in AIDS patients		
Bacterial	**Fungal**	**Viral**
S. pneumoniae ***(MC)***	P.carnii ***(MC)***	CMV
H.influenzae	Penicillium marneffi	
M.tuberculosis	Aspergillus	
Mycobacteria avium complex	Histoplasmosis Candida and Cryptococcus	

12. Ans. is a i.e. Candida Albicans *Ref. Harrison 17/e, p 1254*

This is a case of oral thrush due to candida albicans.

Oral thrush mostly present as discrete and confluent white plaques on the oral and pharyngeal mucosa, particularly in the mouth and on the tongue.

Characteristic feature of Candida

– Candidiasis is ***MC*** *systemic* mycosis.
– ***Gram positive*** fungi characterized by their ability to form *pseudohyphae.*
– Grows rapidly at 25 to 37^{0}C.
– Candida *albicans* (not other species) can also form true hyphae so is dimorphic.
– Candida albicans is identified on the basis of their ability to form germ tubes in serum or by formation of thick walled spores called *chlamydospores* on nutritionally deficient media.

13. Ans. is a i.e. Candida *Ref. CMDT '08; p 1106*

Already explained, refer answer no. 4

14. Ans. is c i.e. Trichophyton *Ref. Chakraborty 2/e, p 611, 622; Harrison 7/e, p 1266*

Trichophyton is dermatophyton which comes under mould.

Morphological Classification of Fungi

Yeast – Cryptococcus neoformans.

Yeast like fungi (Grow partly as yeast and partly as chain of elongated budding cells forming pseudohyphae) Candida.

Moulds (Filamentous fungi)- Forms true hyphae	*Dimorphic fungi* (Grows either as yeast or as filament)
– Dermatohyphyte	– **S**porothrix schenckii
– Aspergillus	– **B**lastomyces dermatitides
– Zygomycetes	– **H**istoplasma capsulatum
– Penicillium	– **C**occidiodes immitis
– Malassezia furfur	– **P**aracoccidiodes brasiliensis
– Madurella species	– **P**enicilium marneffi
– Pseudoallescheria species	– **C**andida albicans (not other spices of candida)
– Philaphora species	***Mnemonic* – SBH Ca Powerful Personal Computer**

15. Ans. is a i.e. Mensturation *Ref. CMDT '08, p 1329*

Risk factor of superficial candidiasis	Risk factor for invasive candidiasis
– *AIDS*	– *Prolonged neutropenia*
– *Pregnancy*	– *Recent surgery*
– ***Diabetes (MC)***	– *Broad spectrum antibiotic therapy*
– *Infants and Elders*	– *Presence of intravascular catheters*
– *Oral contraceptives*	– *Intravenous drug use*
– *Trauma*	
– *Steroids*	

16. Ans. is a i.e. Candida albicans *Ref. Harrison 17/e, p 1254*

"This is a case of oral thrush secondary to candidiasis"

- C. albicans is a dimorphic fungi which occur both as yeast and moulds (with hyphae).
- In HIV oral thrush occurs when CD4 <50/µl.

17. Ans. is b, c and d i.e. Cryptococcus; Penicillium; and Aspergillus *Ref. Jawetz 24/e, p 634*

Endemic mycosis includes fungal infection which are restricted to specific geographical area.

It includes :
- Histoplasmosis (U.S.A)
- Coccidioidomycosis (U.S.A)
- Blastomycosis *(North American blastomycosis)*
- Paracoccidomycosis *(South American Blastomycosis).*

Fungal disease in MAN

Superficial Mycoses	Sub cutaneous Mycoses	Systemic Mycoses
– Dermatophytes (includes trichopyton, Microsporum, Epidermophyton	– Mycotic mycetoma – Chromoblastomycosis – Sporotrichosis – Subcutaneous phycomycosis	– Blastomycosis – Coccidiomycosis – Paracoccidiod mycosis – Histoplasmosis – Oppurtunistic infections (cryptococcus Aspergillus etc.)
– Candida		
– Ptyriasis/Tinea versicolor		
– Tinea nigra		

18. Ans. is d i.e. Malassezia furfur *Ref. Harrison 17/e, p 1263*

- Malassezia furfur (causative agent of Tinea versicolor) is not usually cultured in the clinical Laboratory.
- Cryptococcus, candida, dermatophytes and Coccidiodes are culturable.

Other important feature of Malassezia infection

– Part of normal flora of Human skin.
– Causative agent of Tinea versicolor and Catheter associated sepsis (particularly in infants receiving I.V. lipid).
– On inspection with ***woodlight*** lesion either do not fluoroscence or appear yellow green.

19. Ans. is b i.e. Indian Ink Stain *Ref. Harrison 17/e, p 1252*

Already explained, refer answer no. 2

20. Ans. is a, b, d and e i.e. Cryptococcus neoformans; Histoplasmosis; Candida; and Aspergillosis
Ref. Harrison 16/e, p 2492

Fungus causing CNS infection :

– *Cryptococcus*	– *Coccidiodomycosis*
– *Aspergillus*	– *Histoplasmosis*
– *Blastomycosis*	– *Candidiasis*
– *Sporothrix schenckii*	

21. Ans. is a and b i.e. rRNA, mitochondrial protein gene sequence and presence of thymdiylate synthase; and Cell wall contains glucans *Ref. Harrison 17/e, p 1267; Jawetz 24/e, p 648*

– Molecular studies have clearly placed P. carnii among the fungi with a close relationship to ascomycetis.
– The classification is based on analysis of gene sequences for ribosomal RNA, mitochondrial proteins, and major enzymes.
– The cell wall of P. carnii contain B glucon similar to other fungi.
– In contrast to most fungus P. carnii lacks ergosterol and is not susceptible to ergosterol inhibiting antifungal drugs.

Remember : P. carnii (now P called P.jeroveci) is ***MC oppurtunistic infection*** in AIDS patient.

22. Ans. is a i.e. Renal Transplant recipient *Ref. Harrison 17/e, p 1251*

Predisposing factors of Cryptococcus :

- *AIDS*
- *Solid organ transplant recipient*
- *Sarcoidosis.*
- *HodgkinHematological malignancy*
- *Cortiocosteroid therapy*

23. Ans. is c i.e. Cryptococcus *Ref. Harrison 17/e, p 1252*

Already explained, refer answer no. 8

24. Ans. is c i.e. Cryptococcus *Ref. Ananthnarayan 7/e, p 620*

Already explained, refer answer no. 8

25. Ans. is a and b i.e. Lungs; and Meninges *Ref. Harrison 17/e, p 1252*

Remember : – Meningoencephalitis is ***MC*** manifestation of cryptococcus infection.
– Pulmonary involvement is seen in 40% of patient.

26. Ans. is a i.e. Fungi imperfecti *Ref. Ananthnarayan 7/e, p 611; Chakraborty 2/e, p 613*

Fungi imperfecti :

It is a provisional group of fungi comprising all those of which the sexual or perfect state is not known.
They are also called deutromycetes = Hyphomycetes
Most pathogenic fungi belong to this group.

Ascomycetes – Form sexual spores called ascospores.
Basidomycetes – Form sexual spores called basidiospores.

Remember :
- *Fungi imperfecti, Ascomycetes, Basidomycetes produce septate hyphae.*
- *Phycomycetes - fungi with non septate hyphae.*

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Germ tube test is diagnosis for : **[Kar 04]**

a) Candida albicans
b) Cryptococcus neoformans
c) Histoplasma capsulum
d) Cocciodiodomycosis

[Ref. Ananthnrayana 7/e, p 617]

2. Pneumocystis carnii is : **[SGPGI 03]**

a) Bacteria
b) Fungus
c) Virus
d) Parasite

[Ref. Harrison 17/e, p 1267]

3. Pneumocystis carinii is diagnosed by :

a) Sputum examination for trophozoites and cyst under microscope **[Kerala 01]**
b) Culture
c) Positive serology
d) Growth on artificial media

[Ref. Harrison 17/e, p 1268]

4. All of the following are yeast like fungi except :

a) Canidida **[AIIMS 91]**
b) Geotrichum
c) Cryptococcus
d) Trichophyton

[Ref. Chakorvarty 2/e, p 611]

5. What is the probabale site of entry of a Aspergillus: **[DNB 91]**

a) Puncture wound
b) Blood
c) Lungs
d) Gastrointestinal tract

[Ref. Harrison 17/e, p 1257]

6. Pneumocystis carinii is diagnosed by :

a) Silver nitrate staining **[Kerala 91]**
b) Leishmann staining
c) Fontana staining
d) Acid fast staining

[Ref. Harrison 17/e, p 1268]

7. Pneumocystis carinii is diagnosed by :

a) Silver nitrate staining **[AIIMS 92]**
b) Leishmann staining
c) Fontana staining
d) Acid fast staining

[Ref. Harrison 17/e, p 1268]

8. Blastomycosis is characterized by all except :

a) Yeast like fungus **[Delhi 92]**
b) Commonly involves lung and skin
c) Dimorphic fungus
d) Common in South America

[Ref. Ananthnarayan 7/e, p 624]

9. The following is not true of Candida albicans :

a) Yeastlike fungus **[AI 92]**
b) Forms chlamydosopores
c) Blastomers seen in isolates
d) Causes meningtis in immuno compromised

[Ref. Ananthnarayan 7/e, p 616]

10. Which is not true of cryptococcus neoformans :

a) Grows at 37^0C **[JIPMER 92]**
b) Grows on sabourauds agar
c) Polysaccharide capsule
d) Urease negative

[Ref. Ananthnarayan 7/e, p 621]

11. Candida is most often implicated in causation :

a) Conjunctivitis **[Delhi 93]**
b) Tneacapitis
c) Desert rheumatism
d) Thrush

[Ref. Ananthnarayan 7/e, p 616]

Answer 1. a) Candida albicans 2. b) Fungus 3. a) Sputum ... 4. d) Trichophyton 5. c) Lungs 6. a) Silver nitrate ... 7. a) Silver nitrate ... 8. d) Common in ... 9. c) Blastomers ... 10. d) Urease ... 11. d) Thrush

12. Arc-C-5 in Countercurrent electrophoresis of Serum is diagnostic of : **[JIPMER 93]**

a) Cysticercosis
b) Cryptococcosis
c) Hydatidosis
d Brucellosis

[Ref. Paniker 6/e, p 154]

13. Candiasis is frequently associated with all except: **[PGI 93]**

a) OCP user
b) IUCD user
c) Diabetes
d) Pregnancy

[Ref. CMDT 08/e, p 1328]

Answer 12. c) Hydatidosis 13. b) IUCD user

3 Aspergillus & Mucormycosis

ASPERGILLUS

- Mold with septate hyphae with characterstic dichotomous branching and irregular outline.
- ***MC*** cause of aspergillosis : *A fumigatus.*
- Out of many species of Aspergillus, only those species that grow at 37^0C can cause invasive infection.

... Harrison 17/e, p 1256

Types of Aspergillosis

A. Respiratory disease

1. *In healthy person* : Self limited pneumonitis by massive inhalation of spores.
2. *With underlying lung disease* :
   - Allergic bronchopulmonary aspergillosis in patient with asthma, cystic fibrosis : present with wheeze, central bronchiectasis etc.
   - Endobronchial saprophytic pulmonary aspergillosis (Aspergilloma = fungus ball) in cyst or cavity of TB, sarcordosis, bronchiectasis, histoplasmosis.
   - Often present with hemoptysis. There is no invasion.

B. Superficial infection

- Sinusitis, otomycosis (usually by A.niger, A. fumigatus), keratitis etc.
- Otomycosis is ***MC*** human disease caused by Aspergillus.

C. Disseminated (invasive) Aspergillosis

- ***Lung invasion confined almost entirely to immunosuppresed patients :*** granulocyte count <500/ml *[**MC** risk factor : acute leukemia and recipients of tissue transplants].*
  - Invasion in neutropenic is characterized by hypheal invasion of blood vessels, thrombosis, necrosis and hemorhagic infarction.
  - **Earliest CT finding** : One or more small pulmonary nodules; *Halo sign* (Hazy rim around infarcted tissue), *Cresecent* sign (seen when Bone marrow function recovers) can be seen.
- In HIV patient, ***MC*** site of aspergilioisis : **lung**
- Occur in HIV when **CD_4+<50/ml,** characterized by B/L diffuse or focal infiltrate with a tendency to cavitate.

Diagnosis

1. Microscopy :

Even a single isolate of Aspergillus in KOH mount of sputum of neutropenic patient or hematopoietic stem - cell transplant recipient with pneumonia particularly child or non-smoker suggest diagnosis of invasive disease.

PAS stain biopsy of lung, nose, paranasal sinus or sites of dissemination can also be used.

2. Culture :

Velvety to powdery surface of colony. Ability of A.fumigatus to grow at 45^0C helps to distinguish it from other species.

Culture may be negative or few colonies in aspergilloma or invasive disease.

Treatment

Type of disease	Preferred treatment
• Fungus ball	Lobectomy
• Allergic bronchopulmonary aspergillosis	Short course of glucocorticoids
• Invasive aspergillosis	Voriconazole, Amphotericin B

QUESTIONS

1. In a patient, corneal scraping reveals narrow angled septate hyphae. Which of the following is the likely etiologic agent : [AI 02]

a) Mucor
b) Aspergillus
c) Histoplasma
d) Candida

2. Which of the following is the most common etiological agent in paranasal sinus mycoses ?

a) Aspergillus spp. **[AIIMS 06]**
b) Histoplasma
c) conidiobolus coronatus
d) Candida albicans

3. An early diabetic has left sided orbital cellulitis CT scan of paranasal sinus shows evidence of left maxillary sinusitis. Gram stained smear of the orbital exudate shows irregularly branching septate hyphae. The following is most likely etiological agent : [AIIMS 03]

a) Aspergillus
b) Rhizopus
c) Mucor
d) Candida

4. Branched septate hyphae found on corneal smear in a case of corneal ulcer is : [AIIMS 00]

a) Candida
b) Mucor
c) Aspergillus
d) Histoplasma

5. Mucor mycosis : [PGI 02]

a) Angio-invasion
b) Lymph invasion
c) Septate hyphae
d) Long term deferoxamine therapy is predisposing factor
e) It may lead to blindness

6. Common fungus causing corneal ulcer : [PGI 01]

a) Aspergillus
b) Mucor
c) Fusarium
d) Sporthrix

Answer

1. b) Aspergillus
2. a) Aspergillus ...
3. a) Aspergillus
4. c) Aspergillus
5. a, d and e
6. a and c

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b i.e. Aspergillus *Ref. Ananthnarayan 7/e, p 625; Harrison 17/e, p 1257*

- Aspergillus is mold with septate hyphae with branching at 45^0.
- Asexual conidia are arranged in chain, carried on elongated cells called sterigmata borne on expanded ends of conidiophores.
- *Aspergillus fumigatus* ***is MC*** *cause of* **aspergillosis.**
- *Commonest human disease caused by* **aspergillosis** *is otomycosis.*
- *Aspergillus infection is characterized by hyphae invasion of blood vessel, thrombosis, necrosis, and hemorrhagic infarction.*

Other options :
- *Mucor* – Broad nonseptate hyphae in tissue
- *Histoplasma* – Dimorphic fungi
- *Candida* – Characterised by presence of pseudohyphae.

Remember : ***Aspergillus is MC cause of fungal corneal ulcer.***

2. Ans. is a i.e. Aspergillus *Ref. Dhingra 3/e, p 241*

Many different fungal species are found to involve the paranasal sinuses the more common being Asprgillus; Alternaria; Mucor or Rhizopus.

Varieties of fungal infection of sinuses.

• Fungus ball	– Implantation of fungus in a healthy sinus – Maxillary sinus is most commonly involved – Treatment is surgical removal with no antifungal therapy.
• Allergic fungal sinusitis	– There is no invasion of sinus mucosa by fungus – CT shows mucosal thickening with hyperdense area – Treatment is endoscopic surgical drainage with pre and post operative systemic steroids.
• Chronic invasive	– Fungus invades in to sinus mucosa – CT shows thickened mucosa with opacification of sinus and bone erosion – Treatment is endoscopic surgical removal followed by antifungal therapy.
• Fulminant fungal sinusitis	– Acute presentation mostly seen in immunocompromised or diabetic individuals – *Most common* fungus associated are mucor and aspergillosis.

3. Ans. is a i.e. Aspergillus *Ref. Ananthnarayan 7/e, p 625; Harrison 17/e, p 1257 - 1258*

"Presence of branched septate hyphae in a patient of orbital cellulitis (occur as complication of sinusitis) suggest Aspergillus."

Aspergillus Sinusitis occur in three forms :

1. Ball of hyphae may form in chronically obstructed paranasal sinus, without tissue invasion.
2. A chronic fibrosing granulomatous inflammation begin in sinus and spread slowly to the orbit and brain.
3. Allergic fungal sinusitis

- **Mucor and Rhizopus belong to family Zygomycetes and have non septate hyphae.**

4. Ans. is c i.e. Aspergillus *Ref. Ananthnarayan 7/e, p 625; Harrison 17/e, p 1257*

Already explained, refer answer no. 1

5. Ans. is a, d and e i.e. Angio-invasion; Long term deferoxamine therpay is predisposing factor; and It may lead to blindness

Ref. Harrison 17/e, p 1261; CMDT '08; 1336

Causative agent of Mucormycosis :

- Rhizopus
- Rhizomucor
- Cunninghamella.

They are molds and have non septate hyphae.

Predisposing factors :

- Recepient of organ transplant
- Hematologic malignancy
- Who are receiving long term desferoxamine therapy
- Diabetics
- Treatment with steroid or cytotoxic drugs
- Chronic renal failure.

Important features of Mucormycosis :

- Vascular invasion by hyphae is a prominent feature.
- Ischemic or hemorrhagic necrosis is foremost histologic findings.
- *Nose and paranasal sinus infection :*
  - Present with bloody nasal discharge with low grade fever and sinus pain followed in few days by double vision.
  - On examination nasal turbinate of involved side may be dusky red or necrotic.
  - Fungal invasion of ophthalmic artery or orbit may lead to blindness.
  - Coma may occur by direct invasion.
- *Pulmonary mucormycosis :*
  - Manifest as progressive severe pneumonia.
  - Hematogenous spread to other areas.
- *GI invasion :* Present as one or more ulcer which tends to perforate.

Treatment : Wide surgical debridement and intravenous amphotericin B is indicated.

5. Ans. is a and c i.e. Aspergillus; and Fusarium *Ref. Khurana 2/e, p 123*

Fungi causing corneal ulcer are :

- *Aspergillus* ***(MC)***
- Candida
- Fusarium.

4 Dimorphic Fungi

- **Dimorphic fungus occur in 2 forms :**
  1. **Yeast form = parasitic phase**
     In host tissues and on cultures at 37^0C (enriched agar).
  2. **Spores and filamentous (mold) form = saprophytic phase**
     In soil and culture at 22-25^0C or Sabourads agar at room temperature.
- Disease by all of them are restricted to specific areas of endemicity.
- **Dimorphic fungus are : C**andida albicans, **H**istoplasma, **S**porothrix schencku, **B**lastomycosis, **C**occidioidomycosis, **P**aracoccidiodomycosis, **P**enicillium marneffi.

> ***Mnemonic*** = ***SBH Ca PC = Senior Boys Hostel Ca Powerful Personal Computer.***

HISTOPLASMA CAPSULATUM

Non capsulated intracellular (in macrophages) fungus with septate hyphae. Cause primarily a disease of reticuloendothelial system.

Source of infection

Inhalation of spores present in moist surface alkaline soil enriched by dropping of birds and bats.

Pathology

It forms 2 types of asexual spores large tuberculate macroconidia and smaller elliptical microconidia. Microcondia reach the alveoli and initiate granulomatous reaction.

Clinical features

1. Majority of infections are asymptomatic or mild (acute primary pulmonary histoplasmosis).
   - Cough, fever, malaise, and chest X-ray finding of hilar adenopathy due to caseation necrosis or calcification (which mimics TB) with or without 1 or more areas of pneumonitis are typical features.
2. In small proportion of patient (who lack history of acute primary pulmonary disease) develop progressive disease in either form :
   - Chronic pulmonary histoplasmosis or chronic fibrocavitary pneumonia.
   - Disseminated disease : Among immunosuppresed and user of TNF α antagonist infliximab.
     It mimics disseminated TB.

Diagnosis

Preffered method :

Culture : • *Tuberculate spore is diagnostic*

- Sputum culture – For chronic pulmonary Histoplasmosis.
- Culture of bone marrow, mucosal lesion, liver and BAL fluid are diagnostically usefull in disseminated histoplasmosis.
- Blood culture are best performed by lysis centrifugation method.

Treatment

Disease	Preferred treatment	Alternative
Acute pulmonary	None	
Chronic pulmonary	Itraconazole	Amphotericin B
Disseminated	Itraconazole	Amphotericin B
Severe illness	Amphotericin B	
• CNS involvement		
• Immunocompromised		

BLASTOMYCOSIS (=NORTH AMERICAN BLASTOMYCOSIS)

B.Dermatitides is Dimorphic fungi with septate hyphae forming *conidiophores bearing single globose* to piriform conidia and broad based yeast with single buds usually.

Source of infection : Inhalation of conidia from soil, decomposed vegetation or rotting wood.

Clinical features :

It has marked predilection for lungs, skin and bone.

- Majority of patient, has chronically progressive course and minority has self limited pneumonia.
- Cutaneous disease is usually on the face or other exposed parts of the body in the form of elevated ulcerative lesions.

Diagnosis : Demonstration of fungus in culture of sputum, pus or urine.

Treatment :

- Rapid progression or severe illness → Amphotericin B
- CNS disease → Amphotericin B
- Mild to moderate and no CNS disease. → Itraconazole.

COCCIDIOIDOMYCOSIS

- C. imimitis is Dimorphic fungi with septate hyphae forming barrel shaped (arthospores) or arthroconidia and non-budding spherules with endospores (tissue form).
- It is present in soil and rodents.
- Infection is acquired by inhalation of dust containing arthospore.
- Majority of person develop asymptomatic respiratory infection.
- Some develop self limited influenza like fever known as valley fever or desert rheumatism.
- Very few develops coccidiodal granuloma often with caseation necrosis.

Diagnosis :

a. Sputum, urine and pus should be examined by wet smear and culture (arthospores are formed in chain from alternate cells of septate hyphae).

b. On *biopsy* appearance of *mature spherule is diagnostic.*

c. Serological test are very helpful.

PARACOCCIDIODES BRASILLIENSIS

– Dimorphic fungi with septate hyphae + rare globose conidia and chlamydospores.
– Tissue form : Yeast with characteristic multiple budding.
– Causative agent of *'South American Blastomycosis'* in which *pulmonary infection spreads hematogenously to* mucosa of mouth, nose; lymph node; skin and other internal organs (eg. adrenal, git).
Ulcerative granuloma of buccal and nasal mucosa are prominent feature of disease.

Diagnosis : Culture of sputum, pus and mucosal lesion are often diagnostic.

Treatment :
- Mild disease - Itraconazole
- Advanced disease - Amphotericin B

SPOROTHORIX

Sporothrix schenckii is ***dimorphic fungi*** causing subcutaneous mycoses (not systemic like other dimorphic fungi).
Colonies are blackish (variation in pigmentation) and shiny but becomes wrinkled and fuzzy with age.

Source of Infection

Acquired from thorn pricks of rose, sphagnum moss etc into subcutaneous tissue through minor trauma.

Clinical feature

- Most cases occur in upper limb.
- Usual site of infection : extremity (facial lesion in case of children).
- Sporotrichosis is characterized by development on skin, subcutaneous tissue and in lymph nodes, of nodules which soften and break to form indolent ulcers.
- It is of following types :
  a. ***Plaque sporotrichosis*** : Non tender lesion confined to site of inoculation.
  b. ***Lymphangitis sporotrichosis*** : It is ***MC*** manifestation in which there is painless red papule at a primary site as well as along proximal lymphatic channels often with skip areas is quite distinctive. Nodules may ulcerate or exudate pus.
  c. **Extracutaneous sporotrichosis** : Portal is probably lung. Pulmonary sporotrichosis is usually present as single chronic cavitary upper lobe lesion.

Diagnosis

- ***Culture*** (most reliable) of pus, joint fluid, sputum or skin biopsy in which septate hyphae carrying flower like cluster of small conidia is seen.
  In tissue – Fungus is seen as 'cigar shaped yeast' yeast cell without mycelia.
- Sometimes 'Asteroid Bodies' can seen which is formed due to antigen-antibody reaction.

Treatment

- Cutaneous sporotrichosis – ***DOC*** Itraconazole
- Alternative potassium iodide
- Extracutaneous sporotrichosis – IV Amphotericin B ***DOC***
- Alternative Itraconazole.

QUESTIONS

1. All of the following are dimorphic fungi except :
a) Sporotricum **[AI 97]**
b) Blastomycetes
c) Histoplasma
d) Cryptococcus

2. What is true about Histoplasmosis : [AIIMS 08
a) In early stages it is indistinguishable from TB
b) Blood culure is not diagnostic
c) Hyphal forms are infectious form
d) Person to person spread occurs by droplet infection

3. A patient resident of Himachal Pradesh presented with a series of ulcers in a row, on his right leg. The biopsy from affected area is taken and cultured on sabauraud's dextrose agar What would be the most likely etiological agent :
a) Sporothrix schenckii **[AIIMS 03]**
b) Cladosporium sp
c) Pseudo allescheria boydii
d) Nocardia brasilensis

3. The following fungi are thermally dimorphic except : [AIIMS 03]
a) Sporothrix schenkii
b) Cryptococcus neoformains
c) Blastomycosis dermatidis
d) Histoplasma capsulatum

4. All are examples of dimorphic fungi except :
a) Histoplasma capsulatum **[AIIMS 97]**
b) Bastomycosis dermatitidis
c) Cryptococcus neoformans
d) Coccidiodes immitis

5. Dimorphic fungus are : [PGI 02]
a) Candida
b) Cryptococcus
c) Blastomycosis
d) Coccidiodimycosis
e) Sporotrichosis

Answer
1. d) Cryptococcus
2. a) In early stage ...
3. a) Sporothrix ...
4. b) Cryptococcus ...
5. c) Cryptococcus ...
6. c, d and e

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is d i.e. Cryptococcus *Ref. Jawtez 24/e, p 645, Chakraborty 2/e, p 611*

Dimorphic fungus

- Fungus which occur in two forms :
  - ***Yeast form -*** in host tissue and on culture at 37^0C.
  - ***Filamentous (mold) from -*** In soil and culture at 22 - 25^0C or sabroud's agar at room temperature.

Dimorphic fungus are :

– **S**porothrix schenekii	– Penicillium marneffi
– **B**lastomyces	– **H**istoplasma
– **C**occidiodomycosis	– **P**aracoccidiodomycosis
– **C**andida albicans (not other species of candida)	

Mnemonic : **SBH C**a **P**owerful **P**ersonal **C**omputer

2. Ans. is a i.e. In early stages it is indistinguishable from TB *Ref. Harrison 17/e, p 1244*

Clinical manifestation of Histoplasma

1. Majority of infections are asymptomatic or mild (acute primary pulmonary histoplasmosis).
   - Cough, fever, malaise, and chest X-ray finding of hilar adenopathy due to caseation necrosis or calcification (which mimics TB) with or without 1 or more areas of pneumonitis are typical features.
2. In small proportion of patient (who lack history of acute primary pulmonary disease) develop progressive disease in either form :
   - Chronic pulmonary histoplasmosis or chronic fibrocavitary pneumonia.
   - Disseminated disease : Among immunosuppresed and user of TNF α antagonist infliximab. It mimics disseminated TB.

Options options:

- Fungal culture is the gold standard diagnostic test for histoplasmosis.
- Mycelia are the naturally infectious forms.
- Infection occurs through aerosolization of bird or fat droping.

3. Ans. is a i.e. Sporothrix schenckii *Ref. Harrison 17/e, p 1265*

Important features of sporothrix

S. schenckii

– Dimorphic fungus lives as saprophyte on plants.
– Infection results from inoculation into subcutaneous tissue after minor trauma.
– Nursery worker, florist, gardeners acquire the illness from roses, and other plants.
– *Most common* manifestation is nearly painless red papule at the site of inoculation, over the next several weeks similar nodules forms along proximal lymphatic channels. The nodules may ulcerate. Thus series of ulcer may form.

Diagnosis : – In skin lesion the organism is hard to find .
– Culture of pus or a skin biopsy is preferred method of diagnosis.

Treatment : – Potassium iodide
– Itraconazole.

4. Ans. is b i.e. Cryptococcus neoformans *Ref. Chakraborty 2/e, p 611*

Don't get confuse with term thermally dimorphic as it is same as dimorphic fungi i.e. fungi that occur as yeast at body temperature and Mould in soil ambient temperature.

5. Ans. is c i.e. Cryptococcus neoformans *Ref. Chakraborty 2/e, p 611*

Already explained, refer answer no. 1

6. Ans. is c, d and e i.e. Blastomycosis; Coccidiodimycosis; and Sporotrichosis
Ref. Chakraborty 2/e, p 611; Jawetz 24/e, p 645

Remember : Candida as a whole is not dimorphic only candida albicans is dimorphic.

Fore more detail, refer answer no. 1

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Which among are dimorphic fungi :

a) Blastomycosis **[Jharkhand 05]**
b) Paracoccidioidomycosis
c) Histoplasmosis
d) otomycosis

[Ref. Ananthnarayan 7/e, p 611]

2. All of the following regarding histoplasmosis are true except : **[MP 06]**

a) Very rare in patients with AIDS
b) Bone marrow is involved
c) Gomori methamine silver stain used
d) Dimorphic fungus

[Ref. Harrison 17/e, p 1245; AA 7/e, p 592; Robbins 7/e, p 754 - 755]

Answer 1. a) Blastomycosis ... 2. a) Very rare in patients ...

NOTES

UNIT – IV PARASITOLOGY

1.	Basics of Parasitology	403 – 407
2.	Protozoa	408 – 431
3.	Helminths	432 – 450

1 Basics of Parasitology

HUMAN PARASITES

Protozoa				*Metazoa (Helminths)*		
Sarcosmastigophora	Apicomplexa (formaly known as sporozoa)	Microspora	Ciliophora	Trematodes	Cestodes	Nematodes
Amoebae, Flagellates			Balantidium coli			

AMOEBAE

Amoebae of alimentary canal	*Pathogenic free living amoebae (Brain parasite)*
• Entamoeba histolytica	• Naegleria fowleri
• Entamoeba coli	• Acanthamoeba

FLAGELLATES

Intestinal flagellates	*Hemoflagellates*
• Giardia lamblia	• Trypanosoma
• Trichomonas	• Leishmania

SPOROZOA

- Plasmodium
- Isospora belli
- Cyclospora
- Toxoplasma Gondii
- Cryptosporidium parvum
- Sarcocystis
- Babesia

TREMATODES (FLUKES)

Dioecious Blood flukes (Schistosomes) **[infection by cercarial penetration]**	***Hermaphrodites flukes*** **[infection by ingestion of cercaria]**
• S. hematobium/ bilharziasis hematobium [live in vesical and pelvic venous plexus]	• *Biliary tract (liver flukes)*
• S. Mansoni/ Intestinal bilharziasis [live in inferior mesenteric vein]	– Clonorchis sinensis
	– Fasciola hepatica
	– Opisthorchis species

Continue .....

- S. japonicum/ oriental shcistosomiasis/ Katyama disease [live in superior mesentric vein]
- Intestinal flukes
  - Small Intestine → Fasiolopsis buski etc
  - Large Intestine → Gastrodiscoides hominis
- Lung flukes (Paragonimus westermani)

CESTODES (TAPEWORMS)	
Operculated eggs, ciliated larvae	***Non-operculated eggs Non ciliated larvae (bladder worms)***
• *Fish tapeworm* (Diphyllobothrium latum) • *Sparganum*	• *Taenia* – T. saginata (Beef tapeworm) – T. solium (Pork taperworm) • *Echinococcus* – E. granulosus (Dog tapeworm) – E. multilocularis • *Hymenolepsis* – H. nana (dwarf tapeworm) – H. diminuta (rat tapeworm) • *Dipylidium caninum* (double pored dog tapeworm)

NEMATODES			
Intestinal Nematodes		**Tissue Nematodes**	
• *Small intestine*	– Ascaris/ roundworm	• *Lymphatic*	– Wuchereria
	– Hookworm/Ancyclostoma		– Brugia
	– Necator	• Subcutaneous	– Loa-loa
	– Strongyloides		– Onchocerca
	– Trichinella		– Dracunculus (Guinea worm / serpent worm)
• *Large intestine*	– Enterobius (Pinworm/ thread worm/ seat worm)	• *Mesentery*	– Mansonelia
	– Trichuris (Whipworm)	• *Conjunctiva*	– Loa-loa

NEMATODES CAN ALSO CLASSIFIED AS –

- **On the basis of Mode of infection**

1. *By ingestion*
   a. Eggs - **E**nterobius, **A**scaris, **T**richuris
      Mnemonic = **EAT**
   b. Larvae within intermediate host - Dracunculus
   c. Encysted larvae in muscle - Trichinella.

2. *By penetration of skin* - **A**ncylostoma, **N**ecator, **S**trongyloides
   Mnemonic = **ANS**

3. *By blood sucking insects* - Filariae
4. *By inhalation of Dust Containing eggs* - Ascaris, Enterobius.

- **Based on whether they lay eggs or larvae :**

1. *Oviparous* = *Laying eggs*
   a Unsegmented eggs : Ascaris, Trichuris
   b. **S**egmented eggs : **A**ncylostoma, **N**ecator
   Mnemonic = **ANS**
   c. ***E***ggs containing larvae : ***E***nterobius

2. *Viviparous = Producing larvae*
   – Trichinella – Wuchereria
   – Brugia – Dracunculus.

3. Ovoviviparous (laying eggs containing fully formed larvae which hatch out immediately)
   – Strongyloides

Two Intermediate host are seen in :

- Paragonimus Westerman (Lung fluke)
- Clonorchis sinesis (Chinese tapeworm)
- Diphyllobothrium latum (Fish tape worm)
- Metagonimus yokogawai.

Man is intermediate (Secondary) host in :

- Plasmodium
- Sarcocystis lindemanni
- Toxoplasma gondii
- T. solium (man also act as definitive host).
- Echinococcus granulo sus [dog tapeworm/ hydatid worm/ Taenia echinococcus]

Remember : In other parasitic infection, man act as definitive (primary) host.

Auto-Infection occur in :

- **H**. nana
- **E**. vermicularis
- **T**. solium
- **S**trongyloides stercoralis.

Mnemonic = **HETS**

Eggs float (eggs can be demonstrated) in concentrated saturated solution :

- E. granulosus
- All nematodes (but not unfertilized egg of Ascaris).
- H. nana

Charcot leyden crystal seen in :

- E. histolytica (amoebic dysentery)
- Ascaris pneumonia
- Whip worm dysentery
- Bronchial asthma.

Worms that crawl out :

- Enterobius vermicularis
- T. saginata.

Worms which does not multiply in host :

- Ancylostoma duodenale
- W. bancrofti.
- Enterobius vermicularis

Parasites associated with malignancy :

- Clonorchis
- Opisthorchis

} Bile duct carcinoma

- Schistosoma hematobium - bladder carcinoma.

Premunition (immunity to reinfection) seen in :

- Syphilis
- Cutaneous leishmaniasis.
- Hyper/Holoendemic malarial area

Cystic stage is absent in :

- Dientamoeba fragilis
- Entamoeba gingivalis
- Trichomonas vaginalis
- Trichomonas intestinalis.

Undulating membrane seen in :

- Trichomonas species
- Hemoflagellates

Only ***'Protozoan'*** parasite found in lumen of human small intestine - Giardia Lamblia

Only ***'Ciliate protozoan'*** Parasite of man - Balantidium coli

Parthenogenic worm (female is able to produce fertile eggs or larvae without meeting with males) : Strongyloides stercoralis

Largest protozoa : Balantidum coli

Smallest intestinal amoeba : Dientamoeba fragilis

Smallest and commonest tapeworm found in human intestine : H. nana

Largest helminth T. saginata (beef tapeworm)

Largest liver fluke F. hepatica

Largest trematode infecting man - Fasciolopsis buski

Largest Nematode - Ascaris (roundworm)

Smallest Nematode - Trichinella.

MC protozoan parasite - Toxoplasma gondii

Dogs are responsible for transmission of :

- Hydatid disease
- Toxocara canis
- L. donovani infantum.

Eggs needs development in soil :

- Ancylostoma duodenale
- Ascaris
- Trichuris (whip-worm)
- S. stercoralis.

Sputum examination done for :

- Rhabditiform larva of Ascaris
- Golden brown - eggs of paragonimus

- Filariform larva of Strongyloides, Ancylostoma
- Entamoeba histolytica (due to hepatobronchial fistula).

Cutaneous larva Migrans caused by :

- Necator americanus
- Gnathostomiasis
- Loa-loa and Dicrofilaria
- Fasciola and Paragonimus
- Sparganosis
- Hypoderma and Gastrophilus.
- Ancylostoma braziliense, A. caninum, A. duodenale
- Strongyloides stercoralis (larva currens/racing larvae).

Visceral Larva Migrans caused by :

- Dog ascarid Toxocara canis ***(MC)***
- Anisakis (Large ascarid)
- Cat ascarid T. cati
- Gnathostoma.

Worms Pass through lung during its life cycle :

- Schisto. hematobium (Lung act as 2nd filter)
- Echinococcus
- A. dudodenale
- Paragonimus
- Strong. sterocoralis
- Ascaris.

Intracellular Parasites :

- Leishmania (amastigote form)
- Plasmodium
- Sarcocystis.
- Babesia
- Toxoplasma gondii
- Trypanosoma cruzi (amastigote form)

NEUROPARASITES

Protozoa	Helminthes		
	Larvae of cestodes	Nematodes	Ecotopic ova of
• E. histolytica • Naegleria • Acarthamoeba • Trypanosoma • P. falciparum • T. gondii	• T.solium • E. granulosus • Multiceps sp.	• Visceral larva migrans • Ascaris lumbricoides • Strongyloides stercoralis • Gnathostoma spinigerum	• Schistosoma sp (hematobium) • F. hepatica • Heterophyes hyterophyes

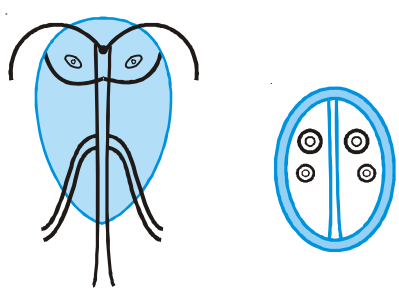
IMPORTANT POINTS ABOUT MALARIA

- Infective forms for human is sporozoites in saliva of mosquito
- Infective forms for mosquito is gametocytes in human blood. At least 12 gametocytes per cubic mm of blood must be present to infect mosquito.
  - Gametocytes are maximum in number during the early stages of infections (may exceed 1000 per cubic mm of blood).
  - Nonmotile zygote converted into motile ookinete in about 18 - 24 hours.
- Human reservoir is one who harbours the sexual forms (gametocytes) of the parasite.
- Only animal reservoir is chimpanzees.

2 Protozoa

QUESTIONS

1. An anxious mother brought her 4 old daughter to the pediatrician. The girl was passing loose bulky stools for the past 20 days. This was often associated with pain in abdomen. The pediatrician ordered the stool examination, which showed the following organism. Identify the organism :



a) Entamoeba histolytica **[AI 03]**
b) Giardia lamblia
c) Cryptosporidium
d) E. coli

2. A patient present with diarrhoea. Analysis of stool on wet mount shows mobile protozoa without RBCs and pus cells. the Diagnosis is : [AI 00]

a) Balantidium coli
b) Giardiasis
c) Trichomonas hominis
d) Entamoeba histolytica

3. All of the following statements about toxoplasmosis are true except : [AI 97]

a) Oocyst in freshly passed cat's faeces is not infective
b) May spread by organ transplantation
c) Maternal infection after 6 months has high risk of transmission
d) Arthalgia, sore throat and abdominal pain are the most common manifestation

4. Plasmodium falciparum infection of man is characterized by : [AI 97]

a) The erythrocytes are increased in size
b) All stages of erythrocytic schizogony are seen in peripheral blood
c) Multiple infection of erythrocytes are seen
d) Each erythrocytic cycle lasts 72 hours

5. Which of the following is true about malaria :

a) Size of RBC is enlarged in Vivax infection
b) Size of RBC is enlarged in Falciparum infection
c) Schuffner's dots are seen in Malariae infection
d) Relapse is seen in Falciparum infection **[AI 96]**

Answer

1. b) Giardia lamblia
2. b) Giardiasis
3. d) Arthalgia ...
4. c) Multiple ...
5. a) Size of RBC ...

6. Which of the following is true about P. falciparum
a) James dots are seen **[AI 96]**
b) Accole forms are seen
c) Relapse are frequent
d) Longest incubation period

7. Which of the following is true about. mature cysts of E. histolytica : [AI 96]
a) Endoplasm and ectoplasm are clearly defined
b) Eight chromatid bodies
c) Shows chromatid bodies and glycogen mass
d) Nuclear structure retains characteristic of trophozoite

8. Which of the following is true regarding the, Trophozoite of E. histolytica : [AI 96]
a) Has eccentric karyosomes
b) Presence of bacteria inside
c) Has four nuclei
d) Shows erythrophagocytosis

9. Acute primary amoebic meningoencephalitis true is ? [AIIMS 08]
a) Meningitis caused by acanthamoeba species is acute in nature
b) Diagnosed by trophozite in CSF
c) Caused by feco oral transmission
d) More common in tropical climate

10. Vector of Kala-azar is : [AIIMS 07]
a. Flea
b. Tsetse fly
c. Sand fly
d. Mite

11. A patient presents with lower gastrointestinal bleed. Sigmoidoscopy shows ulcers in the sigmoid. Biopsy from this area shows flask-shaped ulcers. Which of the following is the most appropriate treatment ? [AIIMS 05]
a) Intravenous ceftriaxone
b) Intravenous metronidazole
c) Intravenous steroids and sulphasalazine
d) Hydrocortisone enemas

12. A 30 year old patient treated with features of acute meningoencephalitis in casualty. His CSF on wet mount microscopy revealed motile unicellular microorganisms. The most likely organism is :
a) Naegleria fowleri **[AIIMS 05]**
b) Acanthamoeba castellani
c) Entamoeba histolytica
d) Trypanosoma cruzi

13. Reduvid bug is a vector for the transmission of :
a) Relapsing fever **[AIIMS 05]**
b) Lyme's disease
c) Scrub typhus
d) Chaga's disease

14. Which of the following infestations leads to malabsorption : [AI 06; AIIMS 04]
a) Giardia lamblia
b) Ascaris lumbricoides
c) Necator americana
d) Ancylostoma duodenale

15. Which one of the following is detected by the antigen detection test used for the diagnosis of P. falciparum malaria : [AIIMS 04]
a) Circum sporozoite protein
b) Merozoite surface antigen
c) Histidine rich protein I (HRPI)
d) Histidine rich protein II (HRP II)

16. Which of the following statement is false :
a) The presence of ingested erythrocytes is seen only in Entamoeba histolytica **[AIIMS 03]**
b) Young adult male of low socioenconomic status are most commonly affected by invasive amoebiasis
c) A low iron content in the diet predispose to invasive amoebiasis
d) The pathogenic and non pathogenic strains of E. histolytica can be differentiated by the electrophoretic study of zymodemes

17. Toxoplasmosis in the foetus can be best confirmed by : [AIIMS 02]
a) IgM antibodies against Toxoplasma in the mother
b) IgM antibodies against Toxoplasma in the foetus
c) IgG antibodies against Toxoplasma in the mother
d) IgG antibodies against Toxoplasma in the foetus

18. Invasive amoebiasis can be best diagnosed by :
a) ELISA **[AIIMS 01]**
b) Counter current immunoelectrophoresis
c) Indirect hemagglutination test
d) Complement fixation test

Answer

6. b) Accole ... 7. d) Nuclear ... 8. d) Shows ... 9. b) Diagnosed by... 10. c) Sand fly
11. b) Intravenous ... 12. a) Naegleria ... 13. d) Chaga's ... 14. a) Giardia lamblia 15. d) Histidine ...
16. c) A low ... 17. b) IgM antibodies ... 18. a) ELISA

19. True about toxoplasmosis is all except :
a) In adults toxoplasmosis is usually asymptomatic
b) IgG antibodies are diagnostic in congenital toxoplasmosis **[AIIMS 01]**
c) Is a anthroponotic disease
d) Encephalitis is uncommon (rare) in immunocompetent individuals

20. A 35 year old male suffering from sudden onset of high grade fever. On malarial slide examination all stages of parasites are seen with schizonts of 20 microns size with 14-20 merozoites per cell and yellow brown pigment. The diagnosis is : [AIIMS 01]
a) Plasmodium falciparum
b) Plasmodium vivax
c) Plasmodium malariae
d) Plasmodium ovale

21. Recurrent Giardiasis is associated with :
a) Severe combined immunodeficiency
b) Common variable immunodeficiency
c) Digeorge syndrome **[AIIMS 00; 97]**
d) C8 deficiency

22. Oocyst of toxoplasma is found in : [AIIMS 97]
a) Cat
b) Dog
c) Mosquito
d) Cow

23. Parasitic encephalitis is caused by : [PGI 05]
a) Ascaris
b) Naegleria
c) Acanthamoeba
d) Balamuthia
e) Entamoeba

24. Which of the following is true about Giardia lamblia:
a) Malabsorption commonly seen **[PGI 05]**
b) Trophozoite form is binucleate pear shaped
c) Diarrhea is seen
d) Jejunal wash fluid is diagnostic
e) Is a free living nematode

25. About microsporidia all of the following are false except : [PGI 05]
a) It is a fungus
b) It is a protozoa
c) It is a bacteria
d) It is trematoda
e) It is associated with diarrhoea in HIV patients

26. Stages seen in peripheral smear of falciparum malaria : [PGI 05]
a) Schizonts
b) Gametocytes
c) Accole trophozoite
d) Ring form

27. Parasite causing encephalitis is/are : [PGI 04]
a) Entamoeba histolytica
b) T. gondii
c) Angiostrongyloid cantonensis
d) T. cruzi

28. P. Falciparum causes : [PGI 05]
a) Thrombocytopenia
b) DIC
c) Hemolysis
d) Haematemesis

29. True about toxoplasmosis : [PGI 03]
a) Due to ingestion of sporocyst with meat
b) Due to ingestion of oocyst from cat's faeces
c) Spiramycin given in pregnancy
d) Due to bite of anopheles mosquito
e) Mostly symptomatic

30. True about Babesiosis : [PGI 03]
a) Caused by Babesis microti
b) Resides in RBC
c) Resides in WBC
d) Chloroquine is drug of choice
e) It is a filarial parasite

31. True about Cryptosporidium parvum : [PGI 03]
a) Affect only in immunocompromised patient
b) It is one of the common opportunistic infection in AIDS
c) Cyst size 12-15 mm
d) AFB +ve cyst
e) Treatment is metronidazole

32. True about amoebic colitis is : [PGI 02]
a) Caused by E. histolytica
b) Cyst contains 8 nuclei
c) Flask-shaped ulcers are present
d) Caecum is most commonly affected
e) Is premalignant

Answer

19. b) IgG anti ...	20. b) Plasmodium ...	21. b) Common ...	22. a) Cat	23. b, c and d
24. a, b, c and d	25. b ande	26. b, c and d	27. b, c and d	28. a, b, c and d
29. b and c	30. a and b	31. b and d	32. a, c and d	

33. Chronic complication of malaria : **[PGI 02]**
a) Splenomegaly
b) Nephrotic syndrome
c) Pneumonia
d) Hodgkin's disease

34. Visceral Leishmaniasis : **[PGI 00]**
a) Caused L. tropica
b) Post leishmaniasis dermatitis is common
c) Antimonial are useful drugs
d) Diagnosed by blood smear
e) Vector is phlebotomus sargenti

35. "Amastigote forms" are seen in : **[PGI 01]**
a) Leishmania donovani
b) Toxoplasma gondii
c) Leishmania major
d) Entamoeba

36. Eosinophilic meningocencephalitis is caused by:
a) Ganthostoma spiralis **[PGI 00]**
b) Naegleria
c) Toxocara canis
d) Angiostrongylus cantonensis

37. True of malaria diagnosis : **[PGI 00]**
a) Thick smear to identify parasite
b) ABER reveals positivity by 100
c) All have same incubation
d) Fluorescein Ab within 1 week

38. Stage of falciparum not seen in PBS is :
a) Schizont **[PGI 99]**
b) Gametocyte
c) Ring form
d) Double ring

39. Mucocutaneous leishmaniasis is caused by :
a) L-braziliensis **[PGI 97]**
b) L.Tropica
c) L-donovani
d) L.orientalis

40. Amoebae not found in human intestine :
a) E.histolytica **[PGI 97]**
b) E. coli
c) E.nana
d) E. gingivalis

41. Tachy-zoites are seen in : **[PGI 97]**
a) Toxoplasma
b) Toxocara
c) Pulm eosinophilia
d) Ascaris

42. In plasmodium falciparum following are seen in blood except : **[PGI 97]**
a) Schizonts
b) Mature trophozoite
c) Mature gametocytes
d) None

43. Cerebral malaria is caused by plasmodium :
a) Falciparum **[PGI 97]**
b) Ovale
c) Malaria
d) Vivax

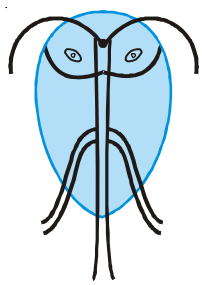
44. Which of the following is true about giardia :
a) CFT is diagnostic **[PGI 95]**
b) Trophozoites and cysts are seen in man
c) Lives in lower intestine
d) Invades normal mucosa

Answer
33. a and b
34. c and d
35. a and c
36. b and d
37. a) Thick ...
38. a) Schizont
39. a) L-braziliensis
40. d) E. gingivalis
41. a) Toxoplasma
42. a and b
43. a) Falciparum
44. b) Trophozoites ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is b i.e. Giardia lamblia *Ref. Paniker 6/e, p 37 - 38*

It is typical figure of ***trophozoite and cyst of Giardia lamblia*** which is the ***MC*** intestinal protozoan parasite.



Trophozoite	Cyst
• Pyriform / Heart/ Tennis or badminton racket shaped • Bilateral symmetrical and has large concave sucking disc; 2 axostyles; 2 parabasal or median bodies; 4 pairs of flagella; **2 nuclei** with prominent central karyosomes • Divides by longitudinal binary fission • Passed in stool but ***not infectious*** • Motility resemble *"falling leaf"*	• Encystation occur in colon • Ovoid with hyaline cyst wall • Mature cyst has ***4 nuclei (= infective stage)*** • Passed in stool and ***is infectious*** • Infective dose is as few as 10 cyst

2. Ans. is b i.e. Giardiasis *Ref. Paniker 6/e, p 36 - 39; Jawetz 24/e, p 660 - 661*

Let consider each option one by one.

a. Balantidium coli – Live in large intestine causing balantidiasis (zoonosis).

- Occurs in 2 stages; trophozoite (binucleated) and cyst (= infective form).
- Clinical disease results only when trophozoites burrow into mucosa causing ulcer and submucosal abscesses resembling lesion of amoebiasis so it 'resembles amoebiasis' causing diarrhoea or frank dysentery so stool may contains pus cells.
- Treatment : Tetracyline / Metronidazole / Nitroimidazole

b. Giardia lamblia – Intestinal flagellate, the only protozoan parasite found in the lumen of human small intestine (Duodenum and upper jejunum).

- Infection is acquired by ingestion of cysts in contaminated food and water.
- It does not invade tissue (so no RBC and pus cells in faeces) but remains attached to epithelial surface by sucking disc which may cause abnormalities of villous architecture and loss of brush border enzymic activities leading to self limited mucus diarrhoea; malabsorption like syndrome; weight loss; abdominal cramps. Occasionally cause biliary colic and jajundice. *... Paniker 6/e, p 38*
- **Diagnosis :** Detection of cysts (encystation occur in colon) as well as trophozoite (die outside so not infectious) in stool sample or in duodenal aspiration by enterotest if biliary symptoms predominate.
- Detection of antigen by ELISA or immunochromatographic strip test.
- Giardiasis is a cause of traveller's diarrhoea.

- **Treatment :** ***DOC*** – Metronidazole / Tinidazole
  Allternative – quinacrine hydrochloride and furazolidone.

c. Trichomonas vaginalis – Not cause diarrhoea.

d. Entamoeba histolytica – It cause amoebic dysentery so stool contain cellular exudate as well as RBC, charcot leyden crystals, amoeba etc.

3. Ans. is d i.e. Arthalgia, sore throat and abdominal pain are the most common manifestation

Ref. Paniker 6/e, p 97 - 100; Harrison 17/e, p 1307 - 1308

Toxoplasma gondii

- It is ***obligate intracellular*** sporozoan.
- It has three forms :
  1. *Trophozoites* -
     – It can invade any nucleated cell (i.e. not ***RBC***) and replicate by endodyogeny or internal budding. This rapidly multiplying trophozoite is known as tachyzoites. It can be seen extracellularly also.
     – Cell distended with crescentic parasites is formed called as pseudocyst or pseudocolony. It is differentiating from true tissue cyst by its staining property.
     – Stained by Giemsa.
     – It is *non infective.*
     – It is formed during acute phase.
  2. *Tissue cyst* -
     – It is formed during chronic phase in various organs but persist principally in central nervous system and muscles.
     – Cyst contain slowly multiplying rounded parasite called Bradyzoites.
     – It is stained by silver stains.
  3. *Oocyst* -
     – It develops *only* in intestine of definitive host.
     – It contains two sporocysts with sporozoites inside.

So,

- **Asexual** (schizogony) forms of parasite – Torphozoite and tissue cyst
- **Sexual** form (gametogony or sporogony) – Oocyst
- **Definitive** host – Domestic cat and other felines.
  – ***All three forms present.***
- ***Intermediate host*** – Man, mammals and birds; only asexual forms present.
- ***Infective stage*** for man – Oocyst with sporozoites and tissue cyst with bradyzoites.
- Freshly passed oocyst is not infectious (needs development in soil).
- Mature Oocyst containing 8 sporozoites is the infective form.
- Human infection is dead end for the parasite.
- **Mode of transmission :**
  – Usually by ingestion of either sporulated oocyst from contaminated soil, food, water or bradyzoites from undercooked meat (ingestion of single cyst is required for infection). Also transmit by blood transfusion and organ transplantation and transplacentally.

- **Clinical features :**
  - Human toxoplasmosis is zoonosis (ANTHROPO-ZOONOSES). It is of following types :
    a. *Toxoplasmosis in immunocompetent person* : Mostly asymptomatic.
       - ***MC*** manifestation : ***Cervical lymphadenopathy*** which is generalized in 20-30%.
       - Headache, fever, myalgia, splenomegaly often present.
       - Meningoencephalitis, mycocarditis, pneumonitis, chorioretinitis are rare.

    b. *Toxoplasmosis in immuno compromised person :*
       - ***MC*** site is **CNS** (usually brainstem).
       - ***MC*** symptom : Altered mental status.

    c. *Congenital toxoplasmosis*
       - Occurs only when mother gets primary toxoplasmosis infection whether clinical or asymptomatic during pregnancy or < 6months before conception (i.e. no risk if acquired > 6 months before conception).
       - As gestational age is increased, risk of transmission to fetus increased i.e. max. in 3rd trimester while severity of fetal damage is decreased i.e. infant is usually asymptomatic if infection transmit in 3rd trimester.
       - It causes :
         - hydrocephalous
         - diffuse cerebral calcification
         - hepatosplenomegaly
         - mental retardation
         - myocarditis
         - microencephaly
         - myocarditis
         - chorioretinitis
         - multiorgan failure
         - pneumonitis
         - lymphadenitis

4. Ans. is c i.e. Multiple infection of erythrocytes are seen

Ref. Harrison 17/e, p 1280; Paniker 6/e, p 75

Blood Smears of Plasmodium

Feature	P. falciparum	P. vivax	P. malariae	P. ovale
Features of red cells				
Size	All sizes / normal	Large (young), pale	Small (Old) / Normal	Large (Young)
Shape	Round may be crenated	Round or oval	Round	Round or pear-shaped, fimbriated
Stippling	Maurer's clefts; Large; red up to 20 Basophilic stippling ±	Schuffner's dots: numerous, small, red	None Occasionally, Zieman's stippling	Schuffner's dots, James dot
Features of Parasite				
Ring (early torphozoite)	Theradlike, multiple infections, double chromatin dots, accole form or appluque	Thicker	Compact	Compact
Mature / Late tropho zoites (amoeboid form)	Absent/occasionally seen	Ameboid, may fill cell	More regular, smaller; **Band form**	Less ameboid and **smaller** than those of P. vivax;
Schizonts	Absent/occasionally 8-24 merozoites in grape like pattern	12 to 24 merozoites grape like pattern	8 to 12 merozoites, often rosetted around pigment	8 to 12 merozoites irregularly arranged

Gametocytes	Sausage or crescentic / Banana shaped central chromatin (female) or diffuse (male)	Round, fills cell, pigment often central	Round, large coarse pigment	Smaller and oval, but similar to those of P. vivax
Diagnostic keys				
	Gametocyte, multiple rings, double chromatin dots, accole forms, heavy infection	Schizont, large RBCs; ameboid forms	Schizont, small RBCs; band forms	Schizont and large RBCs; pear-shaped, fimbirated RBCs

Characteristics of Plasmodium Species infecting Humans

Characteristic	P. falciparum	P. vivax	P. ovale	P. malariae
Incubation period	12 days (shortest)	14 days	14 days	30 days (Longest)
Number of merozoites released per infected hepatocyte	30,000	10,000	15,000	15,000
Duration of erythrocytic cycle (hours)	48 (Malignant tertian malaria)	48 (Benign tertian malaria)	50 (Ovale tertiar malaria)	72 (Quartan malaria)
Red cell preference	Younger cells (but can invade cells of all ages), > 2% of RBC	Red cells up to 14 days old, < 1% of RBC infect	Reticulocytes	Older cells
Morphology	Usually only ring forms; banana shaped gametocytes	Irregularly shaped large rings and trophozoites; enlarged erythrocytes; Schuffner's dots	Infected erythrocytes enlarged and oval with tufted ends; Schuffner's dots	Band or rectangular forms of trophozoites common
Pigment color	Black	Yellow-brown	Dark brown	Brown-black
Ability to cause relapses = Hypnozoites or exo erythrocytic schizogony	No	Yes	Yes	No

5. Ans. is a i.e. Size of RBC is enlarged in Vivax infection

Ref. Harrison 17/e, p 1280; Paniker 6/e, p 75

Schuffner dots are seen in P.vivax and P. ovale malaria.

For more details, refer answer no 4.

6. Ans. is b i.e. Accole forms are seen *Ref. Harrison 17/e, p 1280; Paniker 6/e, p 75*

Already explanation, refer answer no. 4

7. Ans. is d i.e. Nuclear structure retains characteristic of trophozoite

Ref. Paniker 6/e, p 17; Jawetz 24/e, p 671

Jawetz writes – *"**Nuclei of cyst resemble those of trophozoites.**"*

8. Ans. is d i.e. Shows erythrophagocytosis *Ref. Paniker 6/e, p 27*

Differential features of intestinal entamoebae

Features	E. histolytica	E. hartmanni	E.coli
Trophozoite			
Size (μ m)	12-60	4-12	20-50
Motility	Active	Active	Sluggish
Pseudopodia	Finger shaped, rapidly extruded	Finger shaped, rapidly extruded	Short, blunt, slowly extruded
Cytoplasm	*Clearly defined into* endoplasm & ectoplasm	Clearly defined into ectoplasm & endoplasm	Not defined
Inclusions	*Red blood cells present,* no bacteria	Bacteria and other particles, no red blood cells	Bacteria and other particles, no red blood cells
Nucleus	Not clearly visible in unstained films; It is *eccentric*	Not clearly visible in unstained films	Visible in unstained films
Karyosome	Small, *central*	Small, eccentric	Large, *eccentric*
Nuclear membrane	Delicate, with *fine chromatin dots*	Coarse chromatin granules	Thick, with coarse chromatin granules
Cyst			
Size (μm)	10-15	5-10	10-30
Nuclei in mature cyst	4, central karyosome	4	8, eccentric karyosome
Glycogen mass	Seen in uninucleate, but not in quadrinucleate stage	Seen in uninucleate, but not in quadrinucleate stage	Seen upto quadrinucleate stage
Chromatidial bars	1-4, with rounded ends	Often numerous, shape irregular	Splinter like with angular ends

9. Ans. is b i.e. Diagnosis by trophozite in CSF

Ref. Paniker 6/e, p 31 - 33; Harrison 17/e, p 1277, 1279, 1301

Pathogenic free living amoebae are :

i. *Naegleria fowleri* (Amoebaflagellates) – Causing acute primary amoebic meningoencephalitis (PAM).

ii. *Acanthamoeba spp.* – causing chronic granulomatous amoebic encephalitis (GAE), chronic amoebic keratitis (associated with use of contact lens).

NAEGLERI FOWLERI : It has 3 stage -

Amoeboid trophozoite form	
Pear shaped flagellated form ***(main infective stage)***	Dormant cyst form (Outside the body)

Route of Transmission :

Aspiration of water contaminated with trophozoites or cysts or inhalation of cyst leading to invasion of olfactory neuroepithelium, then into meninges and brain.

Clinical features :

- ***MC*** in ***other wise*** healthy children or young adults who often report recent swimming in lakes or heated swimming pools.
- Parosmia / anosmia, headache, high fever, nausea, vomiting, meningismus.
- Photophobia and palsies of 3rd, 4rh and 6th cranial nerves are common.
- Seizures, coma and most patient die within a week.

Diagnosis :

- Detection of motile trophozoites in wet mounts of fresh spinal fluid.
- Bacterial meningitis *without any bacteria on* Gram's staining/antigen detection assay and culture.

Treatment :

- Amphotericin
- Rifampicin may added.

Remember :

- Balamuthia mandrillaris / leptomyxid free-living ameba causing subactue meningoencephalitis in immunocompetent hosts. Multiple hypodense lesion with neutrophilic pleocytosis suggest its diagnosis.

10. Ans. is c i.e. Sand fly *Ref. Harrison 17/e, p 1299; Paniker 6/e, p 56 - 61*

Visceral Leishmaniasis / Kala-azar – Caused by L.donovani.

Beside the bite of Sand fly *(P. argentipes)*, it is also transmitted by blood transfusion, sexual contact, inoculation and congenitally.

Clinical features

- ***MC*** organ affected → **spleen.**
- Progressive emaciation, irregular fever sometimes hectic, hepatosplenomegaly, Bone marrow infiltration epistaxis, bleeding, cancrum oris, pneumonia may occur.
- Some develops post kala azar dermal leishmaniasis (PKDL) characterized by skin lesion mostly on face.
- PKDL may occur during therapy or post cure florid cutaneous resurgence within a few months or years later which occur in cutaenous lesions with abundant parasites.
- PKDL occur in 10-20% cases and it is seen mainly in India.
- Relapse of visceral lesion can also occur.

Diagnosis

- *Specimen* : Peripheral blood – *Best* to examine buffy coat.
  Bone marrow aspirate – ***MC*** diagnostic specimen collected.
  Spleen aspirates – Diagnostic yields is highest.

1. *Demonstration of parasites by* :
   - Microscopy [LD bodies i.e. amastigote seen within macrophages].
   - Culture in NNN or Tobie's medium shows only promastigote while in Schneiders's liquid tissue culture amasitgote form also seen.
   - Animal inoculation – Hamster is the animal employed.
2. *Demonstration of antibodies by* using specific (direct agglutination test, CFT etc) or non specific (WKK) antigen.
3. *Non specific serum test* (Napier's aldehyde or Formol gel test and Chopra's antimony test) ***based on increased globulin content*** of serum.

4. *Absence of hypersensitivity to* leishmanial Antigen i.e. Montenegro (leishmanin) skin test is negative in kala-azar.
5. *Others* – Anemia, leucopenia, neutropenia, thrombocytopenia with hypergammaglobulinaemia and reversal of albuminglobulin ratio.

Treatment :
- – First line therapy
  - Pentavalent antimony
  - Amphotericin B lipid formulation
- – Alternative
  - Amphotericin B (deoxy cholate), paromomycin sulfate, pentamidine isethionate, Miltefosine.

11. Ans. is b i.e. Intravenous metronidazole *Ref. Harrison 17/e, p 1278*

It is case of intestinal amoebiasis in the form of amoebic dysentry.

Drug Therapy for Amebiasis

Asymptomatic carrier (Luminal agents)	Acute colitis	Amebic liver abscess
• Iodoquinol • Paromomycin	• Metronidazole plus Luminal agent	• Metronidazole or Tinidazole or tinidazole or ornidazole plus Luminal agent

12. Ans. is a i.e. Naegleria fowleri *Ref. Paniker 6/e, p 31 - 33; Harrison 17/e, p 1277, 1301*

It is a typical presentation of meningitis cause by Naegleria fowleri.

Let's consider other options:

ACANTHAMOEBA SPP

- No flagellated stage
- Trophozoite ⇌ Cyst (Formed in tissue) ***(infective stage)***
- Encephalitis occurs typically in chronically ill or debilitated patient (lymphoproliferative disorder, chemotherapy etc) and features of CNS lesion often mimics space occupying lesion.
- Infection reaches the CNS hematogenously from primary focus in the sinuses, skin nodules / ulcers and lungs.

Diagnosis :

- Demonstration of trophozoites and cyst on wet mount of CSF.
- Culture on non-nutrient agar plates seeded with E.coli.

ENTAMOEBA HISTOLYTICA

Brain may occasionally involve (<0.1%), result from hematogenous spread from amoebic lesions of colon.

... Harrison 17/e, p 1277

TRYPANOSOMA CRUZI

Neurologic sign are not common but meningoencephalitis have been reported. *... Harrison 17/e, p 1301*

So, from above description it is clear that patient of 30 year (young adult with no chronic disease and no GI symptoms) with meningoencephalitis and motile unicellular (all protozoan are unicellular) microorganism on wet mount; is a typical case of PAM of Naegleri fowleri.

13. Ans. is d i.e. Chagas disease *Ref. Paniker 6/e, p 42 - 43*

Hemoflagellate	Vector	Disease	Infective stage for man
Trypanosomes			
i. *T. brucei gambiense and T. brucei rhodesiense*	Tse-Tse fly	African trypanosomiasis (sleeping sickness)	Metacyclic trypomastigote by inoculative route of fly
ii. *T. cruzi* (Intracellular)	Reduvid bug	Chagas disease (South American trypanosomiasis)	Metacylic trypomastigote by rubbing faces into wound made by bite of bug (Stercorarian transmission)
Leishmania – In man, amastigote form present in macrophage forming LD (leishamania donovani) body			
i. *L. donovani*	Female Sandfly (P. argentipes)	Visceral leishmaniasis (=kala azar)	Promastigote form by bite of fly
ii. *L. Tropica*	P. sargenti and P. papatasi	Cutaneous leish-maniasis (=oriental sore)	Promastigote form by bite of fly
iii. *L. braziliensis*	Sandfly	Mucocutaneous leishmaniasis	Promastigote form by bite of fly

14. Ans. is a i.e. Giardia lamblia *Ref. Ghai 6/e, p 252; Harrison 17/e, p 1320 - 1321*

Remember :
- Ascaris lumbricoides in small intestine usually cause no symptoms. In children it may cause pain and intestinal obstruction sometimes complicated by perforation, intussusception or volvulus.
- Migration to aberrant site can cause biliary colic, cholecystitis, cholangitis, pancreatitis or rarely intrahepatic abscess.
- Intestinal phase of A.duodenale cause epigastric pain, inflammatory diarrhea and iron deficiency anemia.

For more detail, refer answer no. 2

15. Ans. is d i.e. Histidine rich protein II (HRPII) *Ref. Harrison 17/e, p 1287 - 1288; Park 19/e, p 215*

Diagnosis of Malaria

a. Demonstration of parasite (= Asexual forms)

- ***Thin film*** *is fixed and stained :*
  - *Giemsa (Romanowsky stains) at p H 7.2 is preferred.*
  - RBC is examined in tail region for identification of species/type of malaria.
- Rapid, simple, sensitive and specific antibody based diagnostic dip stick (antigen capture assay) or card test that detect P. falciparum specific (pf HRP-2) histidine rich protein 2 or lactate dehydrogenase antigen in finger prick blood sample is done.
  - Pf HRP-2 is antibody based test remains positive for several weeks after acute infection so it has disadvantage in high transmission areas.
  - ***Advantage of HRP-2 Antibody based test :*** In cases of severe malaria who have taken antimalarial drugs and cleared parasitemia, Pf HRP-2 remains strongly positive.

Remember : In severe malaria, poor prognosis is indicated by predominance of more mature P. falciparum parasites (>20% of parasites with visible pigment) in peripheral blood film or presence of phagocytosed malarial pigment in >5% of neutrophils.

- ***Thick blood film*** is stained without fixing for searching of *parasites.*

b. *Malarial fluorescent antibody test is usually becomes positive 2 weeks or more after primary infection so positive test is not necessarily an indication of current infection. It is of greatest value in epidemiological studies and in determining whether a person has had malaria in the past.*

16. Ans. is c i.e. A low iron content in the diet predispose to invasive amoebiasis

Ref. Park 19/e p 200-201; Paniker 6/e, p 23 - 28

Option "a' : Trophozoites from acute dysenteric stool, often contain phagocytosed erythrocytes This features is diagnostic for E. histolytica as phagycytosed red cells are not found in the minuta form or in other commensal intestinal amoebae. *...Paniker 6/e, p 23*

Option "b" : Amoebiasis is more related to poor sanitation and socioeconomic status than to climate. *....Park 19/e, 201*

More common in adults than in children and in males than in females. *...Paniker 6/e, p 28*

Option "c" : Iron in diet is not related to invasive amoebiasis since it spreads by contaminated food and water containing quadrinucleate mature cyst passed in feces of convalescent and carriers.

Option "d" : Enzyme electrophoretic mobility analysis have so far identified 7 potentially pathogenic and 11 non pathogenic zymodemes. *...Park 19/e, p 200*

Remember : Ordinary residual chlorination of water may not destroy cyst (but kill trophozoites) though super chlorination does. ***Tetraglycine hydroperiodide*** (Iodination) is *best* disinfectant.

17. Ans. is b i.e. IgM antibodies against Toxoplasma in the foetus *Ref. Harrison 17/e, p 1309 - 1310*

Diagnosis of Toxoplasmosis

i. Tissue and body fluids : Demonstration of tachyzoites in lymphnodes establishes the diagnosis of acute toxoplasmosis.

ii. Serology

- Commonest method of laboratory diagnosis.
- Diagnosis of acute infection can be established by detection of simultaneous presence of IgG (by Sabin Feldman dye test, indirect fluorescent antibody test and ELISA) and IgM (by double sandwitch IgM ELISA and IgM immunosorbent assay).
- Presence of IgA also favours diagnosis of acute infection. IgA ELISA is more sensitive than IgM ELISA for detecting congenital infection.

iii. Molecular diagnosis

- Real time PCR for either the B_1 gene or the 529-bp sequence.

Immunocompetent Adult or child

Patient with lymphadenopathy only, a positive IgM titre is an indication of acute infection and indication of therapy.

Immunocompromised host

i. Person should be tested for IgG antibody to T. gondii soon after diagnosis of HIV infection.

ii. IgM serum antibody is usually not detectable.

Congenital infection

i. Antibodies in neonate may be either due to congenital infection (IgG, IgM) or due to passive transfer of antibodies from mother (IgG only).

So detection of IgM specific antibody in fetus is helpful in diagnosing congenital toxoplasmosis since it does not cross placenta.

Harrison writes : ***"Persistence of IgG antibody or positive IgM titer after first week of life – diagnosis of congenital Toxoplasmosis."***

ii. PCR of amniotic fluid to detect B1 gene of the parasite has replaced fetal blood sampling.

Ocular toxoplasmosis

i. Positive IgG titer with typical eye lesions.

ii. Antibody production is expressed in terms of Goldmann-Witmer coefficient.

18. Ans. is a i.e. ELISA *Ref. Harrison 17/e, p 1277 - 1278; Jawetz 24/e, p 670 - 671; Paniker 6/e, p 19, 23*

DIAGNOSIS OF AMOEBIASIS

Specimen :

- Fluid feces for examination of trophozoite.
- Formed feces for cysts.
- Scrapings and biopsies – ***most commonly*** by colonoscopy.
- Liver abscess aspirate for trophozoites *(as cyst are absent in tissues)* from edge of abscess, not the necrotic center.
- Blood for serologic test and cell counts.

i. ***Fecal findings suggestive of amoebic colitis -*** positive test for heme, paucity of neutrophils, ***amoebic cyst or hematophagous trophozoite*** *(definitive)*. Examine at least 3 fresh stool specimen.

ii. ***Culture -*** Dobells diphasic, Cleveland - Collier and Robinson's media are used.

iii. ***Trophozoites in biopsy*** specimen from colonic mass confirm the diagnosis of amoeboma.

iv. ***Serology :***

- Is primarily for extra-intestinal amoebiasis when stools are often negative.
- *Most commonly* done by indirect hemagglutination assay (IHA) but it can't distinguish recent from past infection since it remains positive for as long as 10 year.
- ELISA and agar gel diffusion assay are positive in more than 90% of patients with colitis, amoebomas or liver abscess.

So, ***best test*** for invasive amoebiasis - ***ELISA***

MC test done for invasive amoebiasis - ***IHA***

- Antamoebic antibodies occur only with E. histolytica not with other entamoeba.
- Enzymeba test is based on finding of histolysain (major cysteine protease of virulent form) in the intestine (stool) plus circulating antibodies to histolysain after tissue invasion.
- Enzymeba and ELISA helps to distinguish pathogenic from non pathogenic strain (E. dispar) in a stool specimen.

iv. ***Radiation methods –*** Hepatic abscess usually shows elevation of right dome of diaphragm by US, CT, MRI etc.

v. ***Liver enzyme*** are normal or minimally elevated (alkaline phosphatase most often elevated) even with large liver abscess.

19. Ans. is b i.e. IgG antibodies are diagnostic in congenital toxoplasmosis

Ref. Harrison 17/e, p 1309 - 1310

Already explained, refer answer no. 3 and 17

20. Ans. is b i.e. Plasmodium vivax *Ref. Harrison 17/e, p 1280*

Catch clue of answer from question. In this question clue is 'colour of pigment' which are :

- **Black pigment** = P. falciparum
- **Brown black** = P. malariae
- **Dark brown** = P. ovale
- **Yellow brown** = P. vivax

Mnemonic : *Learn dark shade to light shade (black to yellow), so species arranged alphabetically.*

21. Ans. is b i.e. Common variable immunodeficiency *Ref. Robbin's 7/e, p 240*

Giardiasis is common in **b**lood group A; **a**chlorhydria; **c**annabis users; **c**hronic pancreatitis; **m**alnutrition; **i**mmune defects such a selective IgA deficiency, hypogammaglobulinemia, combined variable immunodeficiency, X-linked and autosomal recessive agammaglobulinemia, and AIDS *...Harrison, 17/e p 2056*

Infectious agents in different type of Immune deficiencies.

Pathogen Type	T-Cell Defect	B-Cell Defect	Granulocyte Defect	Complement Defect
Bacteria	Bacterial sepsis	Streptococci, staphylococci, Haemophilus	Staphylococci Pseudomonas	Neisserial infections, other pyogenic bacterial infections
Viruses	CMV, EBV, Varicella, chronicinfections with respiratory and intestinal viruses	Enteroviral encephalitis		
Fungi and parasites	Candida, Pneumocystis carinii	Severe intestinal giardiasis	Candida, Nocardia Aspergillus	

22. Ans. is a i.e. Cat *Ref. Paniker 6/e, p 97 - 100; Harrison 17/e, p 1307 - 1308*

Already explained, refer answer no. 3

23. Ans. is b, c and d i.e. Naegleria; Acanthamoeba; and Balamuthia *Ref. Harrison 17/e, p 2632*

ENCEPHALITIS
(Infection of brain parenchyma)

Viral	Bacterial	Fungal	Parasitic
– HSV1 ***(MC)***	– Listeria	– Cryptococcus	– Naegleria
– VZV	– Mycoplasma	– Mucor	– Acanthamoeba
– Enterovirus	– Leptospira		– Balamuthia
			– Baylisascaris procyonis
			– Toxoplasma

24. Ans. is a, b, c and d i.e. Malabsorption commonly seen; Trophozoite form is binucleate pear shaped; Diarrhea is seen; and Jejunal wash fluid is diagnostic

Ref. Paniker 6/e, p 36 - 39; Jawetz 24/e, p 660 - 661

Already explained, refer answer no. 2

25. Ans. is b and e i.e. It is a protozoa; and It is associated with diarrhoea in HIV patients

Ref. Harrison 17/e, p 1314

- **Microsporadia** are gram positive, obligate intracellular, spore forming protozoa that cause disease in humans especially as opportunistic pathogens in **AIDS.**
- In **AIDS** patient microsporidium cause diarrhoea.
- Diagnosis is made by demonstration of spore in smear of faeces or duodenal aspirate by modified trichome or chromotrope 2R based staining or Uveitx 2B or calcofluor fluoroscent staining.

26. Ans. is b, c and d i.e. Gametocytes; Accole trophozoite; and Ring form

Ref. Harrison 17/e, p 1280; 15/e p 1191

Already explained, refer answer no. 4

27. Ans. is b, c and d i.e. T. gondii; Angostrongyloid cantonensis; and T. cruzi

Ref. Harrison 17/e, p 2632; 16/e, p 1239, 1245

Parasities causing encephalitis are :

i. Toxoplasma gondii (rarely)
ii. Trypanosoma cruzi (occasionally)
iii. Angiostrongylyd cantonensis (eosinophilic meningoencephalitis)
iv. Acanthamoeba (Granulomatous amoebic encephalitis)
v. Naegleria fowleri (Primary amoebic meningoencephalitis)
vi. Balamuthia.

28. Ans. is a, b, c and d i.e. Thrombocytopenia; DIC; Hemolysis; and Haematemesis

Ref. Harrison 17/e, p 1284

Manifestation of severe falciparum malaria :

i. ***Cerebral malaria / unarousable coma :***
   - Coma is characteristic and omnious feature of falciparum malaria.
   - Manifest as diffuse symmetric encephalopathy, focal neurologic signs are unusual.
ii. ***Hypoglycemia –*** associated with poor prognosis.
iii. ***Lactic acidosis –*** Plasma conc of HCO^{3-} & Lactate are *best* biochemical prognosticators in severe malaria.
iv. ***Non cardiogenic pulmonary edema.***
v. ***Renal impairment.***
vi. ***Hematologic abnormalities :***
   - Anemia due to ↑ RBC destruction, removal by spleen and ineffective erythropoiesis
   - Mild thrombocytopenia
   - Bleeding with DIC
   - Hematemesis due to stress ulceration or acute gastric erosion.
vii. ***Liver dysfunction –*** Associated with poor prognosis.
viii. ***Convulsion, chest infection, catheter induced UTI, septicemia, salmonella bacteremia.***

29. Ans. is b and c i.e. Due to ingestion of oocyst from cat's faeces; and Spiramycin given in pregnancy

Ref. Harrison 17/e, p 1310; Jawetz 24/e, p 684

Treatment of Toxoplasmosis

i. ***Congenital infection :*** – Pyrimethamine and sulfadiazine
– Spiramycin + prednisone

ii. ***Infection in immunocompetent :***
– If only lymphadenopathy : No treatment unless have severe persistent symptoms.
– If ocular toxoplasmosis : Pyrimethamine + sulfadiazine or clindamycin.

iii. ***Infection in pregnancy*** : Spiramycin (rovamycine) is ***DOC.***

iv. ***Infection in Immunocompromised :***
– Prophylaxis for AIDS who are seropositive for T. gondii and have CD4 T cell <100/µl - Trimethoprim + sulfamethoxazole / Dapsone + Pyrimethamine.
- Pyrimethamine + Sulfadiazine (preferred but not widely available).

Remember : Sporocyst, sporoblast, sporozoites are formed during sporulation of Oocyst in soil not in tissues.

30. Ans. is a and b i.e. Caused by Babesis microti; and Resides in RBC

Ref. Harrison 17/e, p 1295; Jawetz 24/e, p 680; Paniker 6/e, p 108

- Babesia (protozoan) is intraerythrocytic (blood) Parasite causing piroplasmosis/Texas fever/Acute hemolytic disease/Babesiosis incidentally in human.
- ***Most*** human infection are caused by B. microti and B. divergens.
- ***Vector*** Ixodid ticks (I. dammini or I. scapularis, I. Ricinus).
- ***Mode of transmission*** – Tick bite and blood transfusion.
- **Clinical features :**
  – Mostly asymptomatic.
  – Characterized by malaise, fever, sweat, depression, myalgia, arthralgia which resembles malaria and rickettsiosis.
  – Most severe illness is seen in immunosuppressed; splenectomized (usually infected by B. divergens – may develop Jaundice, renal insufficiency) and elderly persons.
  – Rash is absent.
- **Diagnosis :**
  – Giemsa stained thick and thin film shows small intraerythrocytic parasites resembling malaria but ***it does not form pigment, schizonts, or gametocytes*** and seen as tetrad forms infrequently.
  – ***'Maltese cross'*** form in RBC *without pigment or gametocyte is diagnostic.*
- **Treatment :**

Organisms	Adult / child
B.microti (mild)	Atovaquone + azithromycin
B. divergens and Others	Quinine + Clindamycin + exchange transfusion

31. Ans. is b and d i.e. It is one of the common opportunistic infection in AIDS; and AFB +ve cyst

Ref. Harrison 17/e, p 1313; Jawetz 24/e, p 682; Paniker 6/e, p 105 - 107

Cryptosporidium

- Cryposporidium is a Acid fast coccidian intracellular but extracytoplasmic parasite.
- Completes its life cycle in one host (monoxenous).
- **Most human** infection is caused by C. parvum.
- **Infective stage :** Oocyst (contain 4 sporozoites) in feces which is *infective immediately* without further developement so person to person transmission can occur.
- **Mode of infection :** Acquired from infected animal or human feces or from feces contaminated food or water.
- **Principal site of infection :** Surface of villi of lower small bowel.
- **Clinical features**

In immunocompetent	In immunosuppressed AIDS patient
• Self limited watery non bloody diarrhoea • Traveller's diarrhoea can occur	• Chronic, persistent and profuse diarrhoea • Due to involvement of biliary tract papillary stenosis, sclerosing cholangitis or cholecystitis can occur

- **Diagnosis**
  - Fecal examination for small oocyst of 4-5 μm in diameter.
  - Modified acid fast and Direct immunofluorescent stains and enzyme immunoassay (for fecal antigen).
  - Biopsy may show cryptosporidium at apical surfaces of intestinal epithelium.
- **Treatment :**
  - No chemotherapy is effective
  - Paromomycin - partially effective in HIV patient
  - Nitrazoxanide - in children
  - Spiramycin or combination therapy with azithromycin is also effective.

32. Ans. is a, c and d i.e. Caused by E. histolytica; Flask-shaped ulcers are present; and Caecum is most commonly affected *Ref. Paniker 6/e, p 17; Jawetz 24/e, p 669 - 671*

E. histolytica – It has 3 stages :

a. Trophozoite or Vegetative or Amoeboid form
- It is the only form present in tissue.
- It can't initiate infection.

b. Pre-cystic stage
- Encystment occur in intestinal lumen not in feces or not in tissues.
- Not contain RBC and other ingested food particles.

c. Cystic stage
- Mature Quadrinucleate cyst : *Infective stage*
- It is present *only in lumen* of colon and in mushy or formed feces.
- When stained with iodine, nuclear chromatin and karyosome appears bright yellow while chromidial bars are unstained.

Pathogenesis

8 small trophozoites (=amoebulae or metacystic trophozoites) are released per infective cyst causing :

Primary amoebiasis	Secondary intestinal lesion	Chronic infection	Invasive amoebiasis
• ***MC*** site *caecum*	• ***MC*** in cecum, appendix or nearby ascending colon	• Occurs when organism travel to ileocaecal valve and terminal ileum	• Extraintestinal infection is metastatic through portal circulation
• Lesion with Pinhead sized center and raised edges	• It occurs due to extension from primary lesion	• Sigmoid colon and rectum are favoured site • Amoeboma may form	• ***MC*** form is amebic hepatitis or liver abscess
• *Flask shaped ulcers* with narrow neck and broad base			
• Mucosa surface between ulcer is normal			
• Ulcer is *not premalignant*			

- Intestinal amoebiasis present usually as amoebic dysentery.
- Contents of amoebic abscess is called as *anchovy paste.*
- ***MC*** complication of amoeba liver abscess is *Pleuropulmonary involvement.*

33. Ans. is a and b i.e. Splenomegaly; and Nephrotic syndrome *Ref. Harrison 17/e, p 1285 - 1286*

Chronic complication of malaria are :

i. *Tropical splenomegaly (Hyperreactive Malarial Splenomegaly).*
- Produce hypergammaglobulinemia.
- Normocytic normochromic anemia and splenomegaly.
- Hepatomegaly with marked elevation of IgM, malarial antibody, hepatic sinusoidal lymphocytosis, peripheral B cell lymphocytosis, formation of cryoglobulins (IgM aggregates and immune complexes), cytotoxic antibodes to suppressor CD-8 cells and increased vulnerability to respiratory and skin infection.

ii. Quartan malarial nephropathy of P. malariae causing neprotic syndrome, focal or segmental glomerulonephritis.

iii. Burkitt's lymphoma and EBV infection. Due to malaria related immunosuppression.

34. Ans. is c and d i.e. Antimonial are useful drugs; and Diagnosed by blood smear
Ref. Harrison 17/e, p 1299; Paniker 6/e, p 56 - 61

Already explained, refer answer no. 10

35. Ans. is a and c i.e. Leishmania donovani; Leishmania major *Ref. Harrison 17/e, p 1296*

Leshmania exist in 2 forms :

a. **Amastigote form** : Non flagellated, occur in macrophage of man as leishmania donovani (LD) bodies.

b. **Promastigote form** : Flagellated, occur in gut of sandfly and artificial culture.

36. Ans. is b and d i.e. Naegleria; and Angiostrongylus cantonensis *Ref. Jawetz 23/e, p 688*

Already explained, refer answer no. 27

37. Ans. is a i.e. Thick smear to identify parasite *Ref. Park 19/e p 215; Paniker 6/e, p 76, 90 - 92*

- Annual blood examination rate, **ABER** = $\frac{\text{No of slides examined}}{\text{population}}$ x 100
- Incubation period of different malaria is different.

38. Ans. is a i.e. Schizont *Ref. Harrison 15/e p 1191*

Already explained, refer answer no. 4

39. Ans. is a i.e. L-brazillensis *Ref. Paniker 6/e, p 42 - 43*

Already explained, refer answer no. 13

40. Ans. is d i.e. E. gingivalis *Ref. Paniker 6/e, p 14, 30*

- Entamoeba gingivalis is present in the mouth, being found in large numbers when oral hygiene is poor.
- It has no cystic stage so transmit by kissing, airborne droplet and by fomites.

Remember :
- *Cystic stage is absent in :*
  - Dientamoeba fragilis
  - Trichomonas vaginalis
  - T. intestinalis.
- Entamoeba histolytica, entamoeba coli and Endolimax nana inhabit human intestine.

41. Ans. is a i.e. Toxoplasma *Ref. Paniker 6/e, p 97 - 100; Harrison 17/e, p 1307 - 1308*

Already explained, refer answer no. 3

42. Ans. is a and b i.e. Schizonts; and Mature trophozoite *Ref. Harrison 15/e, p 1191*

Already explained, refer answer no. 4

43. Ans. is a i.e. Falciparum *Ref. Harrison 17/e, p 1284*

Already explained, refer answer no. 28

44. Ans. is b i.e. Trophozoites and cysts are seen in man
Ref. Paniker 6/e, p 36 - 39; Jawetz 24/e, p 660 - 661

Already explained, refer answer no. 2

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Vector fot T. cruzi is : **[JIPMER 90]**

a) Reduvid bug
b) Tse Tse fly
c) Sand fly
d) Hard tick

[Ref. Paniker 6/e, p 49]

2. Band shaped torphozoites are seen in : **[AI 90]**

a) P. ovale
b) P. vivax
c) P. falciparum
d) P. malariae

[Ref. Paniker 6/e, p 75]

3. Which of the following is most severly affected in Kala-azar : **[BIHAR 90]**

a) Spleen
b) Liver
c) Adrenal gland
d) Bone marrow

[Ref. Paniker 6/e, p 57]

4. The following are true of kala-azar except :

a) Persistent hypergammaglo-bulinemia **[TN 90]**
b) Pancytopenia
c) Cancrum oris can occur
d) Full treatment prevents post kala-azar dermal leishmaniasis

[Ref. Paniker 6/e, p 56-60]

5. Diagnostic test for amoebic hepatitis is : **[AI 90]**

a) Indirect hemagglutination test
b) Isolation from pus
c) Isolation from wall of cavity
d) Cyst in stools

[Ref. Harrison 17/e, p 1277]

6. The normal habitat of giardia is : **[AIIMS 90]**

a) Duodenum and jejunum
b) Stomach
c) Caecum
d) Ileum

[Ref. Paniker 6/e, p 38]

7. Amoebic liver abscess can be diagnosed by demonstrating : **[AI 91]**

a) Cysts in the sterile pus
b) Trophozoites in the pus
c) Cysts in the intestine
d) Trophozoites in the faces

[Ref. Paniker 6/e, p 27]

8. The main reservoir for entamoeba histolytica is :

a) Man **[AI 91]**
b) Dirty water
c) Soil
d) Ponds

[Ref. Park 19/e, p 201]

9. All are true about Entamoeba Histolytica except :

a) Cyst are 8 nucleated **[AI 91]**
b) Cyst are 4 nucleated
c) Trophozoites colonise in the colon
d) The chromatid bodies are our stained by iodides

[Ref. Paniker 6/e, p 17]

10. The following is true of Giardiasis except :

a) Complement fixation test is diagnostic **[AI 92]**
b) Stools contain only cysts
c) Habitat is colon
d) Trophozoite and cysts are found in duredenum

[Ref. Paniker 6/e, p 38-39]

11. The cystic form of all are seen in man except :

a) E. histolytica **[AI 92]**
b) Girdia
c) Trichomonas
d) Toxoplasma *[Ref. Paniker 6/e, p 40]*

Answer

1. a) Reduvid bug
2. d) P. malariae
3. a) Spleen
4. d) Full treatment ...
5. a) Indirect ...
6. a) Duodenum ...
7. b) Trophozoites ...
8. a) Man
9. a) Cyst are 8 ...
10. a) Complement ...
11. c) Trichomonas

12. Prolonged parasitism in malaria is due to :
a) Antigenic variation **[JIPMER 92]**
b) Intracellularity of parasite
c) Immunosupression
d) Sequestration
[Ref. Robbin's 7/e, p 401-402]

13. Which is true of malaria : **[AI 93]**
a) Rods forms are seen in P. Malariae
b) RBC size is more in P. Vivax
c) Relapse seen in P. falciparum
d) Male and Female mosquito transmit disease
[Ref. Harrison 15/e, p 1191]

14. Commonest site of extraintestinal amoebiasis is :
a) Brain **[Delhi 93]**
b) Liver
c) Spleen
d) Lungs
[Ref. Paniker 6/e]

15. Which is true of torphozoites of E. histolytica :
a) Has eccentric Karyosome **[AI 93]**
b) Nuclear membrane with out chromatin
c) Shows erythrophagocytosis
d) Presence of bacteria inside cell
[Ref. Paniker 6/e, p 27]

16. Which of the following organism is biggest :
a) Balantidium Coli **[JIPMER 93]**
b) Entamoeba coli
c) Escherichia coli
d) Entamoeba Histolytica
[Ref. Paniker 6/e, p 111]

17. All are seen in cyst of E. histolytica except :
a) Glycogen mass **[Kerala 94]**
b) Chromatidial bars
c) Eccenteric nucleus
d) Refractile nucleus
[Ref. Paniker 6/e, p 27]

18. Which is true about post infusion malaria :
a) Caused by plasmodium malaria **[Bihar 94]**
b) Radical chemotherapy is required
c) Transmitted by needles
d) Caused by P. ovale
[Ref. Paniker 6/e, p 87; Harrison 17/e, p 1285]

19. The infective form of toxoplasma gondii is :
a) Oocyst **[Karn. 94]**
b) Bradycyst
c) Tachyzoite
d) All of the above
[Ref. Paniker 4/e, p 94]

20. Plasmodium falciparum affects all organs except
a) Lung **[Kerala 95]**
b) Liver
c) Kidney
d) Heart
[Ref. Harrison 17/e, p 1285; Robbin's 7/e, p 402, 403]

21. The mature cyst of Entamoeaba histolytica differs from Entamoeba coli, in the following except :
a) Size is 6 to 15 microns **[Karnat 96]**
b) Nuclei are 1 to 4 in number
c) Karyosome is central in position
d) Chromatioid bars seen
[Ref. Paniker 6/e, p 27]

22. Fulminant Amoeba meningoencephalitis caused by : **[AP 96]**
a) Acanthamoeba
b) N. folwleri
c) E. histolytica
d) E. coli
[Ref. Paniker 6/e, p 31]

23. Kala-azar in India is caused by : **[AP 96]**
a) P. papatasi
b) P. serpenti
c) P. argentipes
d) Oncocercus
[Ref. Paniker 6/e, p 56]

24. Mucocutaneous leishmaniasis is caused by :
a) L. tropica **[PGI 97, Kerala 97]**
b) L. Brasilliensis
c) L. mexicana
d) None of the above
[Ref. Paniker 6/e, p 63]

25. The most distinctive feature of pathogenic Entamoeba histolytica on fresh stool examination is :
a) Presence of active pseudopodia **[UP 97]**
b) Erythrophagocytosis
c) Presence of intracytoplasmic vacuoles
d) Presence of two nucleoli
[Ref. Paniker 6/e, p 23]

Answer

12. b) Intracellularity ...	13. b) RBC size is ...	14. b) Liver	15. c) Shows ...	16. a) Balantidium ...
17. d) Refractile ...	18. a, c and d	19. a) Oocyst	20. d) Heart	21. None
22. a) Acanthamoeba	23. c) P. argentipes	24. b) L. Brasilliensis	25. b) Erythrophago ...	

26. All of the following are seen in cerebral malaria except : [UPSC 97]

a) Hyperglycaemia
b) Thrombocytopania
c) Acute respiratory distress synsrome
d) Heavy parasitemia

[Ref. Harrison 17/e, p 1284]

27. Amastigote form is seen in : [UP 98]

a) Macrophages
b) RES
c) Lymphocytes
d) RBC

[Ref. Paniker 6/e, p 53]

28. Reidel-Walker co-efficient is related with :

a) Disinfecting power **[Orrisa 98]**
b) Parasitic clearance
c) Dietary requirement
d) Statistical correlation

[Ref. KDT 5/e, p 805]

29. Drugs of choice in Giardiasis is : [UP 99]

a) Metronidazole/Tinidazole
b) Albendazole
c) Thiabendazole
d) Diloxanide furoate

[Ref. Paniker 6/e, p 39]

30. Primary amoebic meningoencephalitis is caused by : [Kar 00]

a) Nagleria fowleri
b) Entamoeba hystolitica
c) Endolimax nana
d) Dientamoeba fragilis

[Ref. Paniker 6/e, p 31]

31. Malarial parasites are easily detected if blood films are taken and examined : [Kar 01]

a) When the patient is febrile
b) When the patient is having chills
c) One hour after the height of the paroxysm
d) When the patient is afebrile

[Ref. Nelson, p 1050]

32. Spot the incorrect statement regarding entamoeba histolytica : [Kolkata 02]

a) Cysts are necessary for the transmission of infection from one host to another
b) Cysts are necessary for the tranmission of infection from one host to anotehr
c) A cyst may be transferred into a trophozoite to cause invasion in the same
d) Cysts are found in the submucosa of the lower intestinal wall

[Ref. Paniker 6/e, p 17-21]

33. The most important reservoir of Leishmaniasis in India is : [JIPMER 02]

a) Dogs
b) Rodents
c) Acute visceral leishmaniasis
d) Case of postkalazar dermal leishmaniasis

[Ref. Park 19/e, p 256]

34. The infective form of malarial parasite in the vertebrate host is : [Kar 03]

a) Sporozoite
b) Merozoite
c) Schizont
d) Gametocyte

[Ref. Paniker 6/e, p 69]

35. In malaria the shuffner's dots are due to :

a) The disintegrated parts of the parasite
b) The intracellular space not occupied by the parasite **[SGPGI 03]**
c) The pigment released from breakdown of hemoglobin
d) The gametocytes

[Ref. Paniker 6/e, p 71]

36. In falaciparum malaria all of the following are seen except : [SGPGI 03]

a) Crescent shaped gametes
b) Maurer's dots
c) Schizont
d) Merozoites

[Ref. Harrison 15/e, 1191]

37. Babesoisis is transmitted : [Kar 04]

a) Tick
b) Mites
c) Flea
d) Mosquito

[Ref. Paniker 6/e, p 108]

38. Complication in malaria are commonly with :

a) Plasmodium ovale **[Kar 04]**
b) Plasmodium vivax
c) Plasmodium falciparum
d) Plasmodium malariae

[Ref. Harrison 17/e, p 1283-1285]

Answer

26. a) Hyperglycaemia 27. b) RES 28. a) Disinfecting ... 29. a) Metronidazole ... 30. a) Nagleria ...
31. c) One hour ... 32. c) A cyst may ... 33. c) Acute ... 34. a) Sporozoite 35. c) The pigment ...
36. c) Schizont 37. a) Tick 38. c) Plasmodium ...

39. Which of the following parasite passes through three hosts : **[Kolkata 04]**

a) Fasciola hepatica
b) Fasciola buski
c) Schistosoma haematobolium
d) Clonorchis sinensis

[Ref. Paniker 6/e, p 127]

40. P. vivax attacks with : **[Jharkhand 04]**

a) Reticulocytes
b) Young RBC
c) Old RBC
d) Dead RBC

[Ref. Ananthnarayan 6/e, p 75]

41. Entamoeba which is not found in gut : **[MP 04]**

a) E. coli
b) E. histolytica
c) E. gingivalis
d) E. nana

[Ref. Paniker 6/e, p 14]

42. Largest intestinal protozoa is : **[DNB 04]**

a) Entamoeba coli
b) Balantidium coli
c) Giardia lamblia
d) Toxoplasma gondii

[Ref. Panikar 6/e, p 111]

43. Route of transmission of toxoplasma :

a) Blood **[DNB 04]**
b) Faeces
c) Urine
d) None

[Ref. Harrison 17/e, p 1306]

44. Most fatal amoebic encephalitis is caused by :

a) Entamoeba histolytica **[Bihar 05]**
b) Naegleria
c) Entamoeba dispar
d) Acanthamoea

[Ref. Harrison 17/e, p 1279]

45. Nephrotic syndrome is casued by :

a) P. falciparum **[Bihar 05]**
b) P.ovale
c) P. vivax
d) P. malariae

[Ref. ww.pubmedcentral.nih.]

46. In malaria reservoir, parasite remains as :

a) Merozoite **[Bihar 06]**
b) Sporozoite
c) Trophozoite
d) None

[Ref. Chaterjee Parasitology, p 113; Ghai 6/e, p 241]

Answer

39. d) Clonorchis ...
40. b) Young RBC
41. c) E. gingivalis
42. b) Balantidium ...
43. a) Blood
44. b and d
45. d) P. malariae
46. d) None

3 Helminths

QUESTIONS

1. All of the following causes biliary obstruction except : **[AI 08]**
a) Clonorchis
b) Ascaris
c) Ankylostoma duodenale
d) Fasciola

2. Which of the following is not a neuroparasite :
a) Taenia solium **[AI 05; PGI 05]**
b) Acanthamoeba
c) Naegleria
d) Trichinella spiralis

3. The organism most commonly causing genital filariasis in most parts of Bihar and Easter U.P. is
a) Wuchereria bancrofti **[AI 03]**
b) Brugia malayi
c) Onchocerca volvulus
d) Dirofilaria

4. In which stage of filariasis are microfilaria seen in peripheral blood : **[AI 01]**
a) Tropical eosinophilia
b) Early adenolymphangitis stage
c) Late adenolymphangitis stage
d) Elephantiasis

5. Pancreatic Ca is caused by : **[AI 01]**
a) Fasciola
b) Clonorchis
c) Paragonimus
d) None

6. Consumption of uncooked pork is likely to cause which of the following helminthic disease :
a) Taenia saginata **[AI 01]**
b) Taenia solium
c) Hydatid cyst
d) Trichuris trichura

7. A child from Bihar comes with fever. Blood examination shows sheathed microfilaria with nuclei up to tail tip. The diagnosis is : **[AI 00]**
a) B. malayi
b) W. bancrofti
c) Loa loa
d) Oncicerca volvulus

8. Autoinfection is a mode of transmission in :
a) Trichinella **[AI 00]**
b) Cysticercosis
c) Ancylostoma
d) Ascaris

9. Pigs are resevoir for : **[AI 00]**
a) T.solium
b) T.saginata
c) Trichinella spiralis
d) Ancyclostoma

Answer

1. c) Ankylostoma ... 2. d) Trichinella ... 3. a) Wuchereria ... 4. b) Early adeno ... 5. d) None
6. b) Taenia ... 7. a) B. malayi 8. b) Cysticercosis 9. a andc

10. Commonest parasite of CNS in India is : [AI 99]
a) Schistosomiasis
b) Cysticercosis
c) Trichenella spiralis
d) Hydatid cyst

11. Sputum examination is not useful in diagnosis of: [AI 98; AIIMS 96]
a) Trichuriasis trichura
b) Ancylostoma duodenale
c) Paragonimus
d) Strongyloides

12. Most common presenting symptom of thread worm infection amongst the following is :
a) Abdominal pain **[AI 97]**
b) Rectal prolapse
c) Urticaria
d) Vaginitis

13. Which one of the following does not pass through the lungs : [AI 96]
a) Hookworm
b) Ascaris
c) Strongyloidis
d) Enterobius Vermicularis

14. Which of the following disease is transmitted by egg ingestion : [AI 95]
a) Taeniasis
b) Trichinosis
c) Hydatidosis
d) Strongyloidosis

15. All the following are True about Brugia malayi except : [AI 95]
a) The intermediate hosts in the India are Mansoni
b) The tail tip is free from nuclei
c) Nuclei are blurred, so counting is difficult
d) Adult worm is found in the lymphaitc system

16. Which of the following is the most common location of intracranial neurocysticerosis ?
a) Brain parenchyma **[AIIMS 05]**
b) Subarachnoid space
c) Spinal cord
d) Orbit

17. Kalu, 30 year old man, presented with subacutaneous itchy nodules over left iliac crest. On examination they are firm, non-tender, and mobile Skin scrappings contain microfilaria and adult worms of : [AIIMS May 01]
a) Loa-loa
b) Onchocerca volvulus
c) Brugia malayi
d) Mansonella persetans

18. Autoinfection is seen with : [AIIMS 01]
a) Ankylostoma
b) Enterobius
c) Echinococcus
d) Ascariasis

19. On microscopic examination eggs are seen, but on saturation with salt solution no eggs are seen, The eggs are likely to be of : [AIIMS 99]
a) Trichuris trichura
b) Taenia solium
c) Ascaris lumbricoides
d) Ancylostoma duodenale

20. Larva found in muscle is : [AIIMS 98]
a) Trichinella spiralis
b) Ankylostoma duodenale
c) Trichuris trichura
d) Enterobius vermicularis

21. Which of the following parasite does not enter into the body by skin penetration : [AIIMS 97]
a) Dracunculus
b) Necatar americana
c) Ancylostoma duodenale
d) Strongyloides

22. Liver is the target organ for : [AIIMS 97]
a) Fasciola buski
b) Paragonimus westermani
c) Clonorchis sinenses
d) Schistosoma Hematobium

23. All are true regarding filariasis except :
a) Man is an intermediate host **[AIIMS 97]**
b) Caused by Wuchereria bancrofti
c) Involves lymphatic system
d) DEC is used in treatment

24. Megaloblastic anaemia is caused by : [AIIMS 95]
a) Diphyllobothrium latum
b) Schistosoma hematobium
c) Echinococcus granulosus
d) Taenia solium

Answer

10.	b) Cysticercosis	11.	a) Trichuriasis ...	12.	a) Abdominal ...	13.	d) Enterobius ...	14.	c) Hydatidosis
15.	b) The tail ...	16.	a) Brain ...	17.	b) Onchocerca ...	18.	b) Enterobius	19.	b) Taenia ...
20.	a) Trichinella ...	21.	a) Dracunculus	22.	c) Clonorchis ...	23.	a) Man is ...	24.	a) Diphyllob ...

25. All float in a saturated salt solution except :
a) Clonorchis sinensis **[AIIMS 95]**
b) Fertilised eggs of ascaris
c) Larva of strongyloidis
d) Trichuris trichura

26. Nematodes are differentiated from other worms by : [PGI 05]
a) Absent fragmentation
b) Flat or fleshy leaf like worms
c) Separate sexes
d) Cylindrical body
e) GIT is formed completely

27. Fish acts as intermediate host in : [PGI 04]
a) D.Latum
b) Clonorchis Sinensis
c) H.Diminuta
d) H.Nana

28. Parasites causing lung infestation are : [PGI 03]
a) H.nana
b) Paragonimus westermani
c) Taenia saginata
d) E.granulosus
e) E.multiocularis

29. Cholangiocarcinoma is caused by : [PGI 02]
a) Fasciola infestation
b) Clonorchis infestation
c) Paragonimus infestation
d) Ascaris infestation
e) None of these

30. Hydatid disease of liver is caused : [PGI 01]
a) Srongyloides
b) Echinococcus granulosus
c) Taenia solium
d) Trichinella spiralis
e) Echinococcus multilocularis

31. Larval form in stool is found in : [PGI 01]
a) Strongyloides
b) Ancylostoma duodenale
c) Ascaris lumbricoides
d) Necator americanas
e) Trichuria

32. Parasites penetrating through skin for entry into the body are : [PGI 99; 01]
a) Ankylostoma duodenale
b) Srongyloides
c) Round worm
d) Trichuris trichura

33. Cysticercosis is caused by larva of : [PGI 99]
a) Taenia solium
b) T.saginata
c) Echinococcus
d) Ascaris

34. Neurocysticerosis, following are true except :
a) Not acquired by eating contaminated vegetables
b) Caused by regurgitation of larva **[PGI 98]**
c) Acquired by orofaecal route
d) Acquired by eating pork

Answer
25. a) Clonorchis ... 26. a, c,d and e 27. a and b 28. b, d and e 29. b) Clonorchis ...
30. b and e 31. a, b and d 32. a and b 33. a) Taenia ... 34. a) Not acquired ...

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is c i.e. Ankylostoma *Ref. Harrison 7/e p 1334, 1335, 2000*

Hepatobiliary Parasitism

– Common in Southern China

– Biliary tract is infestated by adult helminths or their ova

– *Causes*: Trematodes (Liver or biliary flukes) *MC*
  - Clonorchis sinensis
  - Opisthorchis viverrini or O. felineus
  - Fasciola hepatica

  Nematode (Ascaris lumbricoides by intraductal migration of adult worm)

  Cestodes (Echinococcus spp by intrabiliary rupture of hydatid cyst)

– *Clinical Features*:
  - Chronic/recurrent pyogenic cholangitis ± multiple hepatic abscess
  - Ductal stones
  - Biliary obstruction

– *Diagnosis*: • Cholangiography
  • Characteristic ova on stool examination

– *Treatment*: If obstruction is present, TOC is laparotomy under antibiotic coverage with common duct exploration and biliary drainage procedure.

Helminths causing obstructive jaundice are : *Ascaris, Clonorchis, Fasziola, Echinococcus.*

2. Ans. is d i.e. Trichinella spiralis

Brain parasites

Protozoa	Helminthes		
↓	Larvae of cestodes	Nematodes	Ecotopic ova
– E. histolytica – Naegleria – Acanthamoeba – Trypanosoma – P. falciparum – Toxoplasma gondii	– Cysticercus cellulosae (T. solium) – Hydatid cyst (E. granulosus) – Multiceps sp	– Visceral larva migrans – Ascaris lumbricoides – Strongyloides stercoralis – Gnathosoma spinigerum	– F. hepatica – Heterophyes hyterophyes – Schitosoma (hematobium)

3. Ans. is a i.e. Wuchereria Bancrofti *Ref. Paniker 6/e, p 196; Harrison 17/e, p 1324 - 1326*

Filariasis

- *Definitive host* - man.
- *Intermediate host* - insects

Parasite	Location in body		Characteristics of Microfilaria	Principal vector	Clinical Features	DOC
	Adult	Microfilaria				
I. *Lymphatic Filariasis*						
Wuchereria bancrofiti	Lymphatic	Blood	Nuclear column discrete, Sheathed, pointed tail tip free of nuclei	Culex quinque fasciatus (culex fatigans)	Asymptomatic or subclinical microflaremia; hydrocele; acute adenolymphangitis (high fever, lymphatic inflammation, local edema);	DEC
Burgia malayi	Lymphatic	Blood	Sheathed, blunt tail tip with two terminal nuclei, nuclear column blurred	Mansonia spp	Chronic lymphatic disease (elephantiasis); funiculitis; scrotal pain and tenderness	
Burgia timori	Lymphatic	Blood	Sheathed, longer than Mf malayi	Anopheles barbirostris (Not in India) Mansonia		
II. *Subcutaneous filariasis*						
Loa loa	Connective tissue, conjunctiva	Blood	Sheathed, nuclei extending up to pointed tail	Chyrsops spp	Recurrent transients subcutaneous swelling is fugitive or calabar swellings, ocular manifestation	DEC
Onchocerca volvulus= Convulated = binding filaria	Subcutaneous nodules,	Skin, eyes	Unsheathed, blunt tail tip free of nuclei	Simulium spp.	Pruritus, and rash (MC); Iverm palpable subcutaneous ectin nodules; lymphadenopathy; visual impairment (River blindness)	
Mansonella streptocerca	Subcutaneous	Skin	Unsheathed; blunt tail tip with nuclei	Culicoides	Pruritus, papular rash, Ivermpigmentation; inguinal ectin, adenopathy DEC	
III. *Serous cavity filariasis*						
Mansonella ozzardi	Peritoneum and pleura	Blood	Unsheathed pointed tail tip without nuclei	Culicoides	Headache articular Ivermpain,fever, pulmonary ectin symptoms, adenopathy, hepatomegaly, pruritus, eosinophilia	
Mansonella perstans	Peritoneum; and pleura, mesentery, peri-renal tissue	Blood	Unsheathed, pointed tail tip with nuclei	Culicoides	Asymptomatic mostly; DEC transient angioedema; pruritus of arm, face; fever; headache; arthralgia; right upper quadrant pain	

- ***Genital filariasis*** is type or manifestation of Lymphatic filariasis.
- Lymphatic filariasis is caused by Brugia and Wuchereria bancrofti so ***"c"*** and ***"d"*** ***choices are ruled out.***
- Lymphadenits and Lymphangitis involve both upper and lower extremities in both bancroftian and brugian filarisis but involvement of genital lymphatics occur almost exclusively with W. bancrofti and brugian rarely involved genitalia.

4. Ans. is b i.e. Early adeno-lymphangitis stage

Ref. Park 19/e, 222; Paniker 6/e, p 200 - 204; Chatterjee 12/e, p 195 - 197

Clinical manifestations

Lymphatic filariasis	
i. *Asymptomatic amicrofilaraemia*	– No microfilarae and no clinical manifestation.
ii. *Asymptomatic microfilaremia*	– Positive for Mf without any symptoms.
iii. *Stage of acute manifestation*	– Recurrent episodes of acute inflammation in lymph glands and vessels characterized by lymphadenitis, lymphangitis, filarial fever, lymphangiovarix and lymphorrhagia. It is caused by adult worm but blood ***may reveals microfilarae in early phase.***
iv. *Stage of chronic obstructive lesions*	– Caused by adult worm blocking lymph nodes and vessels either mechanically or are commonly due to allergic inflammatory reactions to worm antigens and secretions. Granuloma may form. – Main features are Hydrocele, elephantiasis (***MC*** site is leg), Lymphadema ***(non pitting or brawny edema).*** – Microfilaria in blood are absent either due to death or their failure to reach the systemic circulation due to lymphatic obstruction.
Occult filariasis	
Meyers Kouwenaar syndrome	– It is due to hypersenstivity reactions to filarial antigens It ***includes Tropical pulmonary eosinophilia*** characterized by Nocturnal paroxysmal cough, wheeze and blood eosinophil count is above 3000 per cmm. – ***Microfilariae*** are ***not usually*** detectable in blood but lung biopsies may show microfilariae – Antifilarial antibody titres are characteristically elevated

5. Ans. is d i.e. None *Ref. Paniker 6/e, p 7*

Name of Parasite	Carcinoma
• Clonorchis sinensis	– Chloangiocarcinoma
• Opisthorchis viverrini	– Cholangiocarcinoma
• Schistosoma hematobium	– Bladder cancer

6. Ans. is b i.e. Taenia solium *Ref. Paniker 6/e, p 144 - 145*

Taenia Solium – Causative agent of CYSTICERCOSIS.

- ***Definitive host*** = Adult worm lives in jejunum of man.

  Infective stage for man :

  – Pork's flesh containing cysticercus cellulosae larvae or bladder worm.

  – Also by eggs either by ingestion in water/vegetables; Autoinfection by fingers contaminated with eggs from perianal skin or feces and retrograde peristalsis.

- ***Intermediate host*** = Pig

  Infected stage for pig = Eggs containing hexacanth larvae so eggs are infective for both man & pig.

Remember :
- Larvae is found in both man and pig.
- But in man it is Dead end Infection.
- Infection occur in both vegetarian and non vegetarian.

Taenia saginata – Causative agent of CYSTICERCOSIS BOVIS.

- ***Definitive host*** = Adult worm lives in jejunum of man.
  Infected stage for man – Undercooked beef containing cysticercus bovis larvae in striated muscle.
- ***Intermediate host*** = Cow/bufflao = harbours larval stage.
  Infective stage of intermediate host = Eggs containing oncosphere during grazing.

Remember :
- Larva is absent in man.
- Eggs not infect man.
- Infection not occur in vegetarians.
- MC site involved in man is striated muscles particularly muscles of tongue, neck, shoulder, ham and myocardium.

Trichuris – Trichura = Whipworm

- Life cycle in ***one host only*** (monoxenous).
- Adult worm lives in caecum and appendix ***(Large intestine).***
- ***Mode of infection :***
  Feco-oral when mature embryonated eggs containing infective rhabditiform larva are swallowed in food or water.

Remember : All nematodes are monoxenous (one host) except T. spiralis, Filaria, Guinea worm.

Echinococcus Granulosus = Dog or Hydatid tape worm – Causative agent of cystic or unilocular hydatid disease.

- ***Definitive host*** – Dog and other canine carnivora.
  Infective stage – Fertile hydatid contaning fully developed scolex.
- ***Intermediate host*** – Sheep and man (***Dead end*** in man).
  Infective stage – Egg during grazing or ingestion of Eggs passed by infectetd dogs.

Remember : Alveolar or multilocular hydatid disease is caused by E.multilocularis.

7. Ans. is a i.e. B Malayi *Ref. Paniker 6/e, p 208; Park 19/e, 220*

- Heavily infected areas of lymphatic filariasis is found in Uttar Pradesh, Bihar, Jharkand, Andhra Pradesh, Orissa, Tamil Nadu, Kerala and Gujarat. So, it is case of lymphatic filariasis.
- ***Sheathed microfilaria are*** :

Low L – Loa-loa
Birth B – Burgia. Malayi
Weight W – W. bancrofti

Tail tip has nuclei but loa-loa cause subcutaneous filariasis of Africa not lymphatic filariasis of Bihar.
Tail tip free of nuclei.

Features	Mf bancrofti	Mf. malayi
Length	250-300μm (longer)	175-300μm
Appearance	Graceful sweeping curves	Kinky, with secondary curves
Cephalic space	Length and breadth equal	Almost twice as long as broad
Stylet at anterior end	Single	Double
Excretory pore	Not prominent	Prominent
Nuclear column	Discrete nuclei	Blurred/smudged
Tail tip	Pointed, free of nuclei	Kinkled and 2 distinct nuclei one at tip, the other subterminal
Sheath	Faintly stained	Well stained

8. Ans. is b i.e. Cysticercosis *Ref. Paniker 6/e, p 149*

Autoinfection is seen in :

H = **H**ymenolepis Nana
E = **E**nterobius vermicularis
T = **T**aenia solium (cysticercosis)
S = **S**trongyloides sterocoralis

- Autoinfection in cysticercosis occur by finger contamination with the eggs from the perineal skin or faeces and by gravid segments reaching the stomach by retrograde peristalsis from jejunum.

9. Ans. is a and c i.e. T. solium; and Trichinella spiralis *Ref. Paniker 6/e, p 149, 163*

TAENIA SOLIUM

- Also known as ***pork taperworm.***
- Intermediate host is pig.

TRICHINELLA SPIRALIS

- ***Primary host*** = Man – Mucosal epithelium of small intestine.
- ***Infective form*** is the encysted larvae found in the muscles of pig and other animals (larvae is tissue parasite).
- ***Intermediate host*** = Pig
- ***Mode of Infection*** – Uncooked pork meat containing encysted larvae.
- Female worm is viviparous (eggs are absent).
- Human infection is dead end infection.

In this condition, you can only pray that you get only one correct option in every question.

10. Ans. is b i.e. Cysticercosis *Ref. Harrison 17/e, p 1336; 16/e, p 2487*

"Neurocysticercosis is the most common parasitic disease of CNS worldwide."

NEUROCYSTICERCOSIS = CYSTICERCOSIS OF CNS

Mode of transmission in T.solium

Ingestion of cysticercus cellulosae or bladder worm (larvae) in pork meat	Ingestion of eggs in water or vegetables which develops in to larvae than into ↓
	Adult worm
Autoinfection by finger contamination with eggs from perianal skin or feces.	***Autoinfection*** by gravid segments reaching the stomach by retrograde peristalsis from jejunum when they are digested and thousands of eggs released.

- So man is ***both*** definitive and intermediate host for T. solium but in man it is Dead end infection.

Clinical features :

- ***MC*** manifestation is new-onset partial seizures with or withour secondary generalization.

Site	Symptoms
• Brain parenchyma ***(MC)***	• Seizures or focal neurological defects
• Subarachnoid or ventricular space	• Increased intra-cranial tension
• Spinal cyst	• Mimic intraspinal tumour

Diagnosis :
- By non contrast CT.
- ***MC*** finding on neuroimaging is parenchymal brain calcification.

Treatment : Antiepileptic therapy + Albendazole or praziquantel.

Remember : Site of cysticercosis – CNS > Subcutaneous tissue > globe of eye.

11. Ans. is a i.e. Trichuris trichura *Ref. Paniker 6/e, p 192*

- Any parasite which pass through lungs at some or other stage during their life cycle, sputum examination can be done for them.
- **These parasites are :**
  - Rhabditiform larva of Ascaris
  - Golden brown eggs of Paragonimus Westermani (Lung fluke)
  - Filariform larvae of Strongyloides, Ancylostoma
  - Entamamoeba histolytica - Chocolate brown sputum due to hepatobronchial fistula.

12. Ans. is a i.e. Abdominal Pain *Ref. Paniker 6/e, p 183 - 187; Harrison 17/e, p 1320*

Enterobius vermicularis = Pinworm = thread worm = seat worm

- Life cycle in ***one host only (man).***
- *No* intermediate host.
- Adult worm live in caecum, appendix and adjacent part of ascending colon (i.e. in large intestine).
- *Mode of infection* – By ingestion of egg containing infective larvae (=autoinfection) and retroinfection.
- **Clinical features :**
  - Mostly asymptomatic.
  - *Cardinal symptoms :* Perianal pruritus (It is nocturnal and cause excoriation + bacterial superinfection).
  - Abdominal pain and weight loss.
  - Vulvovaginitis and pelvic or peritoneal granuloma.
- **Diagnosis :**
  - Fecel examination is not useful.
  - Apply clear cellulose acetate tape to perianal region in the morning and see characteristic ***planoconvex, non bile stained*** pin worm *eggs* (containing tadpole shaped coiled embryo) on microscopy.
  - Sampling can also done by NIH swab, scotch tape, glass pestle swab.
- **Treatment :**
  - Mebendazole / Albendazole / Pyrantel pamoate.

13. Ans. is d i.e. Enterobius vermicularis *Ref. Paniker 6/e, p 184*

Already explained, refer answer no. 11

14. Ans. is c i.e. Hydatidosis *Ref. Paniker 6/e, p 159*

Following parasitic infection occur by ingestion of eggs :

- **E**chnicoccus granulosus
- **H**ymenolepis Nana

- **A**scaris — ***Mnemonic*** - **I**sha **HATE T**ushar
- **T**richuris
- **E**nterobius
- **T**aenia solium *(but mainly transmit by ingestion of undercooked pork meat containing cysticercus cellulose).*

15. Ans. is b i.e. The tail tip is free from nuclei *Ref. Paniker 6/e, p 196*

Microfilaria tail free of nuclei
- W.**B**ancrofti
- **O**.Volvulus — ***Mnemonic :*** **BOO**
- M.**O**zzardi

16. Ans. is a i.e. Brain parenchyma *Ref. Harrison 17/e, p 1336; 16/e, p 2487*

Already explained, refer answer no. 10

17. Ans. is b i.e. Onchocerca volvulus *Ref. Pniker 6/e, p 208 - 211*

- *It is a case of subcutaneous filariasis* so causes of lymphatic filariasis (Brugia) and serous cavity filariasis (M.perstans) are ruled out. So we left with only 2 options :

LOA LOA = EYE WORM : CAUSE LOIASIS / FUGITIVE SWELLINGS OR CALABAR SWELLINGS

- ***Definitive host*** = Man (in subcutaneous tissue)
- ***Intermediate host*** = Vector – day biting flies Chyrysops
- ***Mode of trnsmission :*** Bite of infected Chyrysops
- ***Microfilariae :*** Are sheathed and show diurnal periodicity and appear in blood only during day and taken by chyrysops in which Mf develop into infective third stage larvae.
- **Clinical features :** Is due to migration of adult worms causing fugitive swellings (which disappear in few days only to reappear elsewhere); Ocular manifestations.
- **Diagnosis :** Demonstration of adult worm from scraping of skin or conjunctiva.
- **Treatment :** Surgery to remove worms; DEC; corticosteroids

ONCHOCERCA VOLVULUS :

- Convulated or blinding filaria causing ***onchocerciasis or river blindness.***
- It is 2nd major cause of blindness in the world.
- **Vector :** Day biting female black flies (are pool feeders) Simulium which breed in fast flowing rivers.
- ***Microfilariae :*** Unsheathed; non periodic; found in skin, subctaneous lymphatics, conjunctiva and rarely in blood.
- **Clinical features *:*** Subcutaneous nodule or onchocercoma which is circumscirbed, firm, non-tender tumor tend to occur over anatomical sites where bones are superficial such as scalp, scapula, ribs, elbow, iliac crest, sacrum, knees.

  Lesions in skin (pruritus, pigmentation, atrophy, fibrosis) and eyes (photophobia to blindness, glaucoma, punctate or sclerosing keratitis, iridocyclitis, glaucoma) also seen.
- **Diagnosis :** Demonstrating microfilariae by slicing off a silver of skin; aspirating subcutaneous nodules, conjunctival biopsies.
- **Treatment :** *Ivermectin; Enucleation of nodules; DEC (cause Mazotti reaction) and Suramin.*

18. Ans. is b i.e. Enterobius *Ref. Paniker 6/e, p 149*

Already explained, refer answer no. 8

19. Ans. is b i.e. Taenia solium

- **Eggs float** in or can be demonstrated in case of :
  i. Cestodes : a. Echinococcus
  b. Hymenolepis nana.
  ii. All nematodes *except* unfertilized eggs of Ascaris.
- In this question all choices are nematodes except Taenia solium is cestode.
- So guys, learn by heart 'classification of parasites, given in our book in Section *Basics of Parasitology.*

20. Ans. is a i.e. Trichinella spiralis *Ref. Paniker 6/e, p 159*

Classification of Nematodes on the basis of Mode of infection.

Ingestion	Penetration of skin	By blood sucking insect	Inhalation of dust containing eggs
a. *Eggs* - Ascaris – Enterobius – Trichuris	• **A**ncylostoma • **N**ecator • **S**trongyloides	• Filariae	• Ascaris • Enterobius
b. *Larvae within Intermediate host* or drinking water containing cyclops – Dracunculus	***Mnemonics :* ANS**		
c. *Encysted larvae in muscle* : Trichinella	i.e. Autonomic Nervous system		

For more details, refer answer no. 9

21. Ans. is a i.e. Dracunculus *Ref. Paniker 6/e, p 159*

Already explained, refer answer no. 20

22. Ans. is c i.e. Clonorchis sinensis *Ref. Paniker 6/e, p 117*

- All are trematodes *(also known as **flukes**).*
- Man is definitive and snails are intermediate host usually.
- They are classified as :

FLUKES	HABITAT	INTERMEDIATE *HOST*	MODE OF TRANS.MISSION
a. Blood flukes			
i. *Schistosoma (Bilharzia) hematobium*	Vesical and pelvic vein plexuses	Snail which is infected by miracidium	– Water borne disease – Man is infected by bathing in contaminated
ii. *S.mansoni*	Inferior mesentric vein (Intestinal bilharziasis) or Schistosomal dysentry		water when cercaria penetrates unbroken skin
iii. *S.japonicum or oriental schistosomiasis*	Superior mesentric vein (katayama disease)		
b. Liver Flukes			
i. *Clonorchis sinensis (=Chinese liver flukes)*	Biliary tract (associate with Cholangio carci-noma)	1st intermediate host : snail 2nd intermediate host : fish	Fish containing metacercariae are eaten raw or inadequately processed
ii. *Fasciola hepatica (=sheep liver fluke)*	Biliary tract	Primary host : man/sheep Intermediate host : snails	Ingestion of watercress or other water vegetation containing metacercaria
c. Intestinal flukes			
i. *Fasciolopsis buski (Giant intestinal fluke)*	Duodenum or jejunum	Molluscum Snails	Ingestion of roots of lotus, bulb of water chesnut and other acquatic vegetations
ii. *Heterophyes*	Small intestine	Molluscum Snails	Ingestion of fishes since cercriae encyst on fishes
iii. *Metagonimus Yokogawai*	Small intestine	1st intermediate host : fresh water snail; 2nd interme diate host : fish	Ingestion of raw fish
v. *Gastrodiscoides hominis (only fluke inhabiting human large intestine)*	Large intestine	Molluscum	Ingestion of water plants
d. Lung Fluke			
Paragonimus Westermani = *Oriental lung fluke*	Cystic space of lung	1st intermediate host : snail 2nd intermediate host : fresh water cray fish or crab fish	Inadequately cooked crabs, cray fish

23. Ans. is a i.e. Man is an intermediate host

Already explained, refer answer no. 3

24. Ans. is a i.e. Diphyllobothrium latum *Ref. Paniker 6/e, p 139 - 143; Harrison 17/e, p 1340*

Diphyllobothrum (Fish Tapeworm = Broad Tapeworm)

- ***Definitive host*** – Adult worm lives in small intestine *(usually in the ileum)* of man, cat, dog and other fish eating mammals.

  Infective stage for man – Plerocercoid larva / sparganum.
- ***Intermediate host***

  First – Cyclops infected by coracidium larva.

  Second – Freshwater fish infected by procercoid larvae.
- ***Eggs*** – Operculated, shed in feces but are not infective to man.
- ***Mode of infection*** – Ingestion of imperfectly cooked infected fish containing plerocercoid larva.
- **Clinical features :**
  - Mechanical obstruction
  - Abdominal discomfort
  - Diarrhoea
  - Nausea
  - Anaemia (pernicious type called as ***Bothriocephalus Anaemia***) which is due to vitamin B_{12} deficiency.
- **Diagnosis :** Demonstration of eggs in feces.
- **Treatment :** Praziquantel / Niclosamide

25. Ans. is a i.e. Clonorchis sinensis

Already explained, refer answer no. 19

26. Ans. is a, c, d and e i.e. Absent fragmentation; Separate sexes; Cylindrical body; and GIT is formed completely *Ref. Paniker 6/e, p 113 - 114*

Features	Nematodes	Trematodes	Cestodes
Shape	Cylindrical/thread	Flat or fleshy leaf like or flukes	Tape worms
Segmentation	Unsegmented	Unsegmented	Segmented
GIT	Complete	Incomplete	Absent
Suckers	Absent	Present	Present
Hooks	Absent	Absent	May present
Sex	Separate (Dioecious)	Monoecious except Schistosomes	Monoecious
Number of host	Monoxenous except Trichnella, filarial, Dracunculus medinesis	Digenetic	Digenetic except H.nana
Body cavity	Present	Absent	Absent

Remember : Nematodes may be viviparous or oviparous or Ovo-viviparous but other worms are oviparous.

27. Ans. is a and b i.e. D. Latum; and Clonorchis Sinensis *Ref. See below*

Two intermediate host with fish as one of them are seen in :

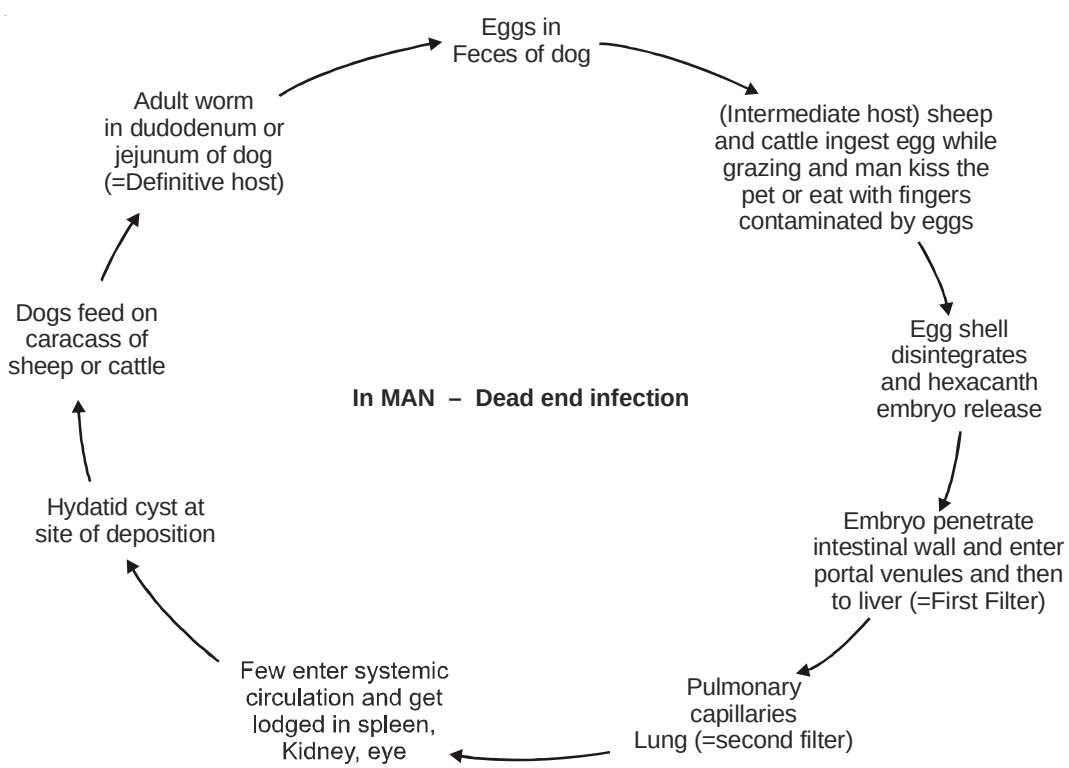
Parasite	Ist intermediate ost	IInd intermediate host
i. *Paragonimus westermani* (Trematode)	Snail	Fresh water cray fish or crab
ii. *Clonorchis sinensis* (Trematode)	Snail	Fish
iii. *Metagonimus Yokgawai* (trematode)	Fresh water snail	Fish
iv. *Diphyllobothrium latum* (cestode)	Cyclops	Fresh water fish

Remember :
- All cestodes are digenetic (require 2 host) except H. nana.
- Intermediate host for H. diminuta is Rat flea.

28. Ans. is b, d and e i.e. Paragonimus westermani; E. granulosus; and E. multiocularis
Ref. Paniker 6/e, 150 - 1555

- Taenia saginata and H. nana are intestinal cestodes.
- Paragonimus is lung fluke so there is no doubt about this.

LIFE CYCLE OF E. GRANULOSUS



Clinical features

- ***MC*** site of Hydatid cyst (E. granulosus typically develops unilocular cyst) : ***Liver***; mostly in right lobe presenting as Hepatomegaly, pain, obstructive jaundice.
- ***Next common*** site is ***lung*** usually in the lower lobe of right lung – cough, hemoptysis, chest pain, dyspnea.
- Hypersensitivity, fatal anaphylaxis if cyst ruptures.
- Kidney - pain, hematuria.
- Osseus hydatid.

E. MULTILOCULARIS : Cause alveolar or multilocular hydatid disease in man.

- ***Definitive host*** : Foxes, dogs, cats
- ***Intermediate host*** : Rodents (main), man
- Man infected by eating fruits or vegetables contaminated with feces.
- ***Clinical features :***
  - ***MC*** site liver : Multilocular infiltrating lesion mistaken for malignant tumor.
  - Also metastasize to lungs and brain.
- ***Treatment :*** Resection is ***TOC.***

29. Ans. is b i.e. Clonorchis infestation *Ref. Paniker 6/e, p 7*

Already explained, refer answer no. 5

30. Ans. is b and e i.e. Echinococcus granulosus; and Echinococcus multilocularis
Ref. Paniker 6/e, 150 - 155

Already explained, refer answer no. 28

31. Ans. is a, b and d i.e. Strongyloides; Ancylostoma duodenale; and Necator americanas
Ref. See below

Nematodes	Fecal examination
i. *Trichinella spiralis*	Adult worm
ii. *Trichuris trichuria*	Eggs (barrel shaped)
iii. *Strongyloides*	Rhabditiform larvae
iv. *Ancylostoma duodenale and Necator anericanas*	Egg which may hatched, so rhabditiform larvae can also seen
v. *Enterobius vermicularis*	Usually not useful
vi. *Ascaris lumbricoides*	Eggs and adult worm (*Larvae in sputum or gastric washings)
vii. *Filariasis*	No role
viii. *Dracunculus medinensis*	No role (* tip of worm projects from base of ulcer)

32. Ans. is a and b i.e. Ankylostoma duodenale; and Strongyloides *Ref. Paniker 6/e, p 159*

Already explained, refer answer no. 20

33. Ans. is a i.e. Taenia solium *Ref. Harrison 17/e, p 1336; 16/e, p 2487*

Already explained, refer answer no. 10

34. Ans. is a i.e. Not acquired by eating contaminated vegetables *Ref. Paniker 6/e, p 149*

Already explained, refer answer no. 10

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. Which is false about Wuchereria bancrofti :
a) Causes filariasis **[AI 90]**
b) Body is long and slender
c) Terminal nuclei absent
d) Man and anopheles are host
[Ref. Paniker 6/e, p 196, 208]

2. Schistosoma Japonicum resides in : **[AI 92]**
a) Vesical Plexus
b) Splenic Vein
c) Systemic Circulation
d) Gall bladder
[Ref. Paniker 6/e, p 117]

3. Definitive host for Guinea worm is : **[AIIMS 93]**
a) Man
b) Cyclops
c) Snail
d) Cyclops and man
[Ref. Paniker 6/e, p 214]

4. Ankylostoma enters by human body by :
a) Ingestion **[Kerala 94]**
b) Inhalation
c) Penetration of skin
d) Inoculation
[Ref. Paniker 6/e, p 159]

5. Cysticerocosis Cellulose is caused by :
a) T. Solium **[Karn. 94]**
b) Echinococcus granulosus
c) T. saginata-C. bovis
d) H. nana
[Ref. Paniker 6/e, p 149]

6. Habitat of hookworm is : **[Kerala 94]**
a) Jejunum
b) Ileum
c) Colon
d) Duodenum
[Ref. Paniker 6/e, p 175]

7. Visceral larva migrans is caused by : **[PGI 94]**
a) Toxocara canis
b) Anchylostoma brazilliensis
c) A. duodenale
d) Necator americanus
[Ref. Paniker 6/e, p 219]

8. Spinal cord compression may be caused by :
a) Cysticercosis **[Kerala 94]**
b) Ankylostoiasis
c) Echinococcus Granulosus
d) Visceral larva migrans
[Ref. Schwartz's 7/e, p 1903]

9. Terminal spined eggs seen in : **[Kerala 95]**
a) Schistosoma haematobium
b) Sch. mansoni
c) Sch. japonicum
d) Chlonorchis sinesis
[Ref. Paniker 6/e, p 123]

10. Dracunculosis infection occur through :
a) Ingestion of water containing cyclops
b) Ingestion of water containing the parasite
c) Ingestion of fish **[Delhi 96]**
d) Penetration of skin
[Ref. Paniker 6/e, p 214]

11. Least common site of calcified hydatid cyst is :
a) Lung **[Kerla 96]**
b) Mediastinum
c) Extraperitoneal site
d) Liver
[Ref. Sutton 7/e, p 152]

12. Painless terminal hematuria is seen as one of the manifestations in the infection caused by :
a) Schistosoma Japonicum **[Karn. 96]**
b) Schistosoma mansoni
c) Schistosoma haematobium
d) Plasmodium falciparum
[Ref. Paniker 6/e, p 121]

Answer

1. d) Man and ...	2. b) Splenic ...	3. a) Man	4. c) Penetration ...	5. a) T. Solium
6. a) Jejunum	7. a) Toxocara ...	8. c) Echinococcus ...	9. a) Schistosoma ...	10. a) Ingestion of ...
11. a) Lung	12. c) Schistosoma ...			

13. HIghest incidence of anemia in the tropics is due to : **[AI 97]**
a) Hookworm
b) Thread Worm
c) Ascaris
d) Guinea worm

[Ref. Paniker 6/e, p 181]

14. The most common manifesation of Thread worm infestation is : **[AI 97]**
a) Urticaria
b) Rectal prolapse
c) Abdominal pains
d) Vaginitis

[Ref. Harrison 17/e, p 1322]

15. Auto infection is seen with : **[AP 97]**
a) Trichuris trichura
b) Ankylostoma duodenale
c) Ascaris
d) Enterobius

[Ref. Paniker 6/e, p 186]

16. The cause of larva currents : **[TN 98]**
a) Stronghyloides stercoralis
b) Necator americansus
c) Ankylostoma duodonale
d) H. nana

[Ref. Paniker 6/e, p 219]

17. Man is both intermediate and definitive host for :
a) T. solium **[Mahe 98]**
b) T. saginata
c) D. latum
d) Dicroftis hominis

[Ref. Paniker 6/e, p 148]

18. Autoinfection occur in : **[UP 00]**
a) Strongyloides
b) Trichuris trichura
c) Ankylostoma-duodenale
d) Necator-americana

[Ref. Paniker 6/e, p 171]

19. One of the following microfilaria does not possess nuclei upto the tail tip : **[Kar 0]**
a) Wuchereria bancrofti
b) Loa loa
c) Acanthochelonemia perstans
d) Brugia malayi

[Ref. Paniker 6/e, p 196]

20. The following eggs have hexacanth embryos except : **[Kar 00]**
a) Taenia solium
b) Taenia saginata
c) Chlonorchis nana
d) Hymenolepsis nana

21. The larval form of taenia is referred to as :
a) Cysticercus **[Kar 01]**
b) Cysticercoid
c) Echinococcus
d) Conerus

[Ref. Paniker 6/e, p 148]

22. Which worm is longest : **[HPU 01]**
a) T. solium
b) T. saginata
c) Hookworm
d) A. lumbricoides

[Ref. Paniker 6/e, p 144]

23. Drug of choice in cerebral cysticercosis is :
a) Piperazine **[JIPMER 01]**
b) Pyrvinium
c) Thiabendazole
d) Mebendazole

[Ref. CMDT 08, p 1316]

24. Katayama fever is caused by : **[UP 01]**
a) F. hepatica
b) Chlonorchis-sinesus
c) S. hematobium
d) C. Japonicum

[Ref. Paniker 6/e, p 121]

25. The following infection resembles malignancy :
a) Echinococcus granulosum **[JIPMER 02]**
b) E. multilocularis
c) E. vogeli
d) E. oligarthus

[Ref. Paniker 6/e, p 155]

26. Which of the following parasites is infectious as it is passes from stool : **[UP 02]**
a) Ancyclostoma duodenale
b) Enterobius vermicularis
c) T. solium
d) Ascaris

[Ref. Paniker 6/e, p 184]

Answer

13. a) Hookworm
14. c) Abdominal ...
15. d) Enterobius
16. a) Stronghyloides ...
17. a) T. solium
18. a) Strongyloides
19. a) Wuchereria ...
20. c) Chlonorchis ...
21. a) Cysticercus
22. b) T. saginata
23. None
24. c) S. hematobium
25. b) E. multilocularis
26. b) Enterobius ...

27. All are true about Brugia-malayi except :
a) Nucelated tail tip **[Delhi 02]**
b) Enveloped sheath
c) Nocturnal periodicity
d) Smooth curved in stain preparation
[Ref. Paniker 6/e, p 196, 208]

28. Which of the following resides in caecum :
a) Trichuris trichuria **[UP 02]**
b) A. lumbricoides
c) Strongyloides
d) Ancylostoma
[Ref. Paniker 6/e, p 165]

29. Which of the following is not a cestode ?
a) D. latum **[Kar 03]**
b) T. saginata
c) Schistosoma mansonia
d) E. granulosus
[Ref. Paniker 6/e, p 139]

30. Dracunculus medinensis is transmitted by :
a) Cyclops **[Bihar 03]**
b) House fly
c) Tick
d) Flea
[Ref. Ananthnarayan 7/e, p 213]

31. Cysticercus cellulose seen in : [Kolkata 04]
a) T.saginata
b) T.solium
c) D.latum
d) S.haemato
[Ref. Paniker 6/e, p 149]

32. Diphylobothrium latum is causative organism of
a) Megaloblastic anemia **[SGPGI 04]**
b) Iron deficiency anemia
c) Peptic ulcer
d) None
[Ref. Paniker 6/e, p 142]

33. Hydatid cyst occurs most commonly in :
a) Liver **[DNB 04]**
b) Lungs
c) Brain
d) Spleen
[Ref. Paniker 6/e, p 153]

34. One of the following transmitted through skin :
a) Ascaris lumbricoides **[UP 04]**
b) Trichuris-trichura
c) Necator americana
d) Strongyloides
[Ref. Paniker 6/e, p 159]

35. Which of the following is viviparous :
a) Strongyloidis stercoralis **[SPGPGI 05]**
b) Trichinella spiralis
c) Enterobious
d) Ascaris
[Ref. Paniker 6/e, p 159]

36. Visceral larva migrains is due to : [DNB 05]
a) Ascariasis
b) Toxocaracanis
c) Schistosomiasis
d) Clonorchis Buski
e) Loa Loa
[Ref. Paniker 6/e, p 219]

37. The intermediate host for T. Saginata is :
a) Man **[DNB 05]**
b) Cow
c) Dog
d) Pig
[Ref. Paniker 6/e, p 145]

38. Neurocysticerosis is caused by :
a) T. solium **[Jharkhand 05]**
b) T. saginata
c) D. latum
d) Ascaris lumbricodis
[Ref. CMDT 08 p 1316]

Answer
27. d) Smooth ... 28. a) Trichuris ... 29. c) Schistosoma ... 30. a) Cyclops 31. b) T.solium
32. a) Megaloblastic ... 33. a) Liver 34. c and d 35. b) Trichinella ... 36. b) Toxocaracanis
37. b) Cow 38. a) T. solium

UNIT – V IMMUNOLOGY

1. Basics of Immune System 453– 457
2. Antigen & Antibody 458 – 463
3. Hypersensitivity 464 – 494

1 Basics of Immune System

CLASSIFICATION

LYMPHORETICULAR SYSTEM

Lymphoid system

Lymphoid cells
- Lymphocyte
- Plasma cells

Lymphoid organs

Central (Primary) Lymphoid organ
Organs in which precursor Lymphocyte proliferate, develop and mature
- Thymus
- Bone marrow

Peripheral (Secondary) Lymphoid organ
- Lymphnodes
- Spleen **(largest lymphoid organ)**
- Mucosa associated lymphoid tissue (MALT)

Reticular system
- Consist of phagocytic cells that are concerned with scavenger function

CELLS OF LYMPHORETICULAR SYSTEM

- **Lymphocyte**
  - ***1. T.lymphocyte***
  - ***2. B.lymphocyte***
- **3. Null cell OR LGL**
- **4. Phagocytic cells**
  - ***Macrophages***
  - ***Microphages***
- **5. Dendritic cells**

Lymphocyte - Human body contain 10^{12} lymphocyte out of which 10^{9} are renewed daily.
Mature B and T cells before they encounter antigen are called **naive cells.**

1. T. lymphocyte

- Thymus derived lymphocyte, constitute 60-70% of peripheral lymphocyte.
- Found in ***paracortical*** area of lymphnodes and periarteriolar sheaths of **spleen.**
- Antigen binds to TCR [T cell receptor] which is responsible for signal 1.
- Demonstration of TCR gene by southern blot analysis is a molecular *marker of T lineage cell.*
- All T-lymphocyte contain **CD-3 molecule** which are involved in transduction of signal 1.
- Other surface molecules or co-receptors include CD 2, CD 4 or CD 8, CD 11a, ***CD 28 (Binds to B 7-1 and B 7-2 of antigen presenting cells and provide signal 2)***, CD 40.
- ***CD 4*** is expressed on 60% of T cells, while ***30% expressed CD 8.***

T Cells

CD4 (60%)
Also called Helper T cell/Inducer cells/TH - 0 cells
Binds MHC Class II

TH_1
- *Secrete **IL-2, IFNγ***
- ***Facilitates delayed hypersensitivity, macrophage activation, synthesis of IgG2b antibodies***

TH_2
- *Secrete **IL_4, IL_5***
- ***Facilitates synthesis of all antibody except IgG2b***

CD8 (30%) cytotoxic T Cells
Also called cytotoxic/ suppressor cells
Binds MHC Class I
- *Secrete **IL-2, IFNγ***
- ***Facilitates type II hypersensitivity***

2. B. Lymphocyte

- 10 - 20% of peripheral lymphocyte.
- Responsible for *humoral immunity.*
- Present in Bone Marrow, peripheral lymphoid tissue eg. lymph node (superficial cortex), spleen (white pulp), tonsils and extralymphatic organs eg. GIT.
- In spleen and lymph node it *form lymphoid follicles.*
- Unlike T cell, it responds to *free Ag.*
- B cell act as *Antigen presenting* cells.
- Antigenic binding component of B cell receptor is *surface IgM.* Thus presence of rearranged Ig genes in lymphoid cell is used as molecular marker of B cell lineage.
- Other molecules are complement receptor, Fc receptors, *CD 21 (receptor of EBV),* CD 40 (essential for interaction of T and B cell which cause B cell *maturation* so mutation in ***CD 40*** ligand cause immunodeficiency called *X-linked hyper - IgM syndrome*).

Differentiation of T and B cells

	T cells	***B cells***
a. ***Ag binding site***	Ag receptor (= TCR with CD. 3)	Surface Ig
b. ***Fc receptor***	Absent	Present
c. ***Complement receptor***	Absent	Present
d. ***EAC rosette (C 3 receptor CR 2; EBV receptor)***	Absent	Present
e. ***E/SRBC rosette (CD 2; measles receptor)***	+	–

Continue .....

f. ***Microvilli on surface***	–	+
g. ***Thymus specific Ag***	+	–
h. ***Blast transformation***	Occurs by anti CD-3, Phytohemagglutinin Concanavalin	Occurs by anti Ig Endotoxin S. aureus (cowan I strain) EBV

3. Null Cell/Large Granular Lymphocyte (LGL)

- ***Do not bear*** TCR or surface Ig and are non adherent, non-phagocytic.
- They together with macrophage *form innate immunity* in comparison ***of adaptive*** immunity *by lymphocytes.*
- Constitute 5 - 10% of peripheral lymphocytes
- They are classified as :
  - i. ***ADCC*** lymphocyte
  - ii. ***NK cell*** { LAK - lymphokine activated killer cell / NK/T Cell
- LGL express :
  - Receptor for Fc portion of IgG (CD-16) which is used for ADCC **(antibody dependent cell mediated cytotoxicity)**.
  - Receptor for NCAM-I (CD 56).
- Many LGL express some T lineage markers particularly CD-8, CD-2.
- Usually CD-3 negative but subset of NK cell are ***CD-3 positive*** called NK/T cell.
- Some NK proliferate in the presence of ***IL-2*** called as LAK cells.
- LGL can arise ***in both*** bone marrow and thymic microenvironment.
- Target cell killing by NK cell is :
  - Inversely related to target cell expression of MHC class I molecule.
  - So, it kills the cell that express little or no HLA class I molecule (provide immunosurveillance) such as ***virus infected cells, certain tumour cells and allogenic cells.***
  - Non-immune i.e. without previous sensitization, MHC unrestricted and non-antibody mediated.
  - It kill host cell infected with intracellular bacteria eg. Mycobacteria, TB, listeria monocytogens.
  - Not kill cells which express class I MHC (all normal nucleated cell express it).
- **Receptors**
  - NK has two receptors - Killer cell inhibitory receptors (KIRs) which recognized classic MHC-I and -CD 94/ NKG- 2 receptor which recognized MHCIb or HLA - E.
- **NK cell secrete**
  - TNF α, GMCSF, IFN - γ, Cytolytic factors (perforin).
  - Also secrete IL-4 to recruit TH.2 T cell; IgG1, IgE.

Remember :
- IFNγ favours differentiation of T_H 1 cell so NK cell can influence CD4 and B cell.
- NK cell is abnormal in HIV disease and hyporesponsive in Chediak - Higashi syndrome.

4. Phagocytic cells

It is of two types :

i. ***Mononuclear Macrophages of blood and tissues :***

- Blood macrophages (monocytes) are ***largest*** of lymphoid cells.
- Tissue macrophages (histiocytes) are :
  - Microglia in CNS
  - Kupffer in liver
  - Alveolar macrophage in lung
  - Osteoclast in bone
  - Sinus histiocyte - spleen, lymph node.
- Half life of *blood monocyte* is about *1d* while life span of ***tissue macrophage*** is ***several months.***
- Have role in chronic inflammation in the form of activated macrophages, fusion giant cell and epitheloid cell of granulomatous lesion.
- It is obligatory for induction of Cell mediated immunity since it is required *to process and present antigen* to immuno competent T cell.
- Like other Ag presenting / processing cell, it has both class of MHC I and *II (more).*
- Also important for effector phase of humoral immunity.

ii. ***Microphages*** which are polymorphonuclear leucocytes of blood-neutrophil, eosinophil and basophil. They do not have any role in specific immune processes.

5. Dendritic Cells

- These are ***Antigen presenting cells*** to T cell during primary immune response.
- They are *bone marrow derived cells* of lineage different from macrophages and T or B cell.
- They possess MHC I and *II (more).*
- They have little or no phagocytic activity.
- It is of following types -
  a. ***Interdigitating dendritic (= Dendritic) cells -*** Found in lymphoid tissue and interstitium of non-lymphoid organs eg. heart and lung. Possess costimulatory molecules like B 7-1 and B 7-2.

     Most potent antigen presenting cell for naive T cell (ideally CD - 4).

  b. ***Langerhans cell -*** They process and present antigens which reach the dermis.

  c. ***Follicular dendritic cells -*** Bear Fc receptor for IgG. Hence can trap antigen bound to antibodies. They are present in germinal centers of lymphoid follicles in spleen and lymph nodes.

MAJOR HISTOCOMPATIBILITY COMPLEX (MHC)

- Located on short arm of chromosome six which codes for Histocompatibility (transplantation) antigen.
- Main function of Histocompatibility (MHC) molecule is to bind peptide fragments of foreign protein for presentation to appropriate antigen specific T cells.
- MHC gene products are classified as :

a. Class I antigens

- Are glycoprotein expressed on all nucleated cells and platelets.
- Cells with class I antigen presents antigen to CD - 8.
- It is the principal antigen involved in graft rejection and cell mediated cytolysis.
- Locus of class I gene - A, B, C.

b. Class II antigen

- Glycoprotein, restricted to antigen presenting cells (macrophage, dendritic cell, B cell) to CD - 4.
- Locus - D region.
- Responsible for graft versus host response and mixed leucocyte reaction (MLR).

c. Class III

- Soluble protein of complement system; (C_2 and C_4 of classical pathway; properdin factor B of alternative pathway); heat shock protein; TNF alpha and beta.

COMPLEMENT SYSTEM

Consist of heat labile factor called alexine or complement (Serum proteins).

Fixation of Complement is not influenced by nature of antigens but only by class of Ig.

- IgM > IgG_3 > IgG_1 > IgG_2 – Classic pathway activators
- IgA_1, IgA_2, IgD, IgG_4 – Alternate pathway activators
- ***Classic C3 convertase*** ***Classic C5 convertase***
  - C4b2b – C4b2b3b
- ***Alternate C3 convertase*** ***Alternate C5 convertase***
  - C3bBb – C3bBb3b
- Role of complement derived factors in inflammation :
  i. C3b and C3bi - act as opsonin so cause phagocytosis.
  ii. C3a + C5a [= Anaphylatoxin] - ↑ vascular permeability, vasodilation.
  iii. C5a - activate lipoxygenase pathway, chemotaxis, activation and adhesion.
  iv. C5b-9 (= Membrane attack complex) - Lysis of cell.

2 Antigen & Antibody

ANTIGENS

Haptens – Non immunogenic but has immunological reactivity i.e. incapable of inducing antibody formation but can react with antibodies.

They become immunogenic on combining with larger molecule carrier.

Hapten is of two types :

i. Simple haptens are non-precipitating.

ii. Complex haptens are precipitating, since they have two or more antibody combining sites.

Epitope or antigenic determinant

- It is smallest unit of antigenicity (small area on the antigen) which is capable of sensitising an immunocyte and of reacting with its complementary site on specific antibody or T cell receptor.
- ***T*** cell identify ***linear or sequential*** epitope, while ***B*** cell identify ***conformational*** epitope.

Paratope

- It is combining area of the antibody molecule, corresponding to the epitope.
- Epitope and paratope determine **specificity** which is hallmark of immunological reaction.
- Bacteria/virus may contain antigen mosaic (different epitopes) while same epitope on different antigen may present causing antigenic cross reaction.
- Specific antigen determinants on paratope are called IDIOTOPES.

Determinants of Antigenicity

– Molecular size (<5000 are non-antigenic)
– Chemical nature (usually protein and polysaccharide)
– Susceptibility to tissue enzymes
– Foreignness
– Antigen specificity
– Species specificity
– Isospecificity
– Autospecificity (except lens protein and sperm)
– Organ specificity
– Heterogenetic / heterophile specificity (Forssman antigen; Weil felix reaction in typhus fever, Paul Bunnel test in infectious mononucleosis; Cold agglutinin test in primary atypical pneumonia).

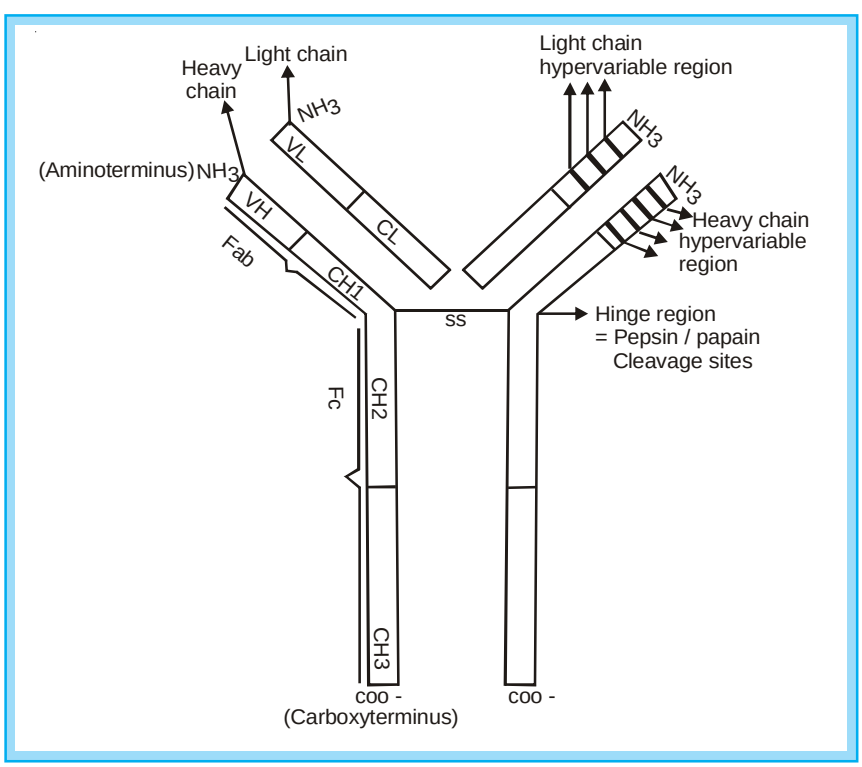
ANTIBODIES

Fractionation of serum proteins by NH_4SO_4		
Soluble albumins	***Insoluble globulin***	
	Water soluble (pseudoglobulins)	Insouble (Euglobulin)

- ***Most*** of the antibody is euglobulin and are usually gamma globulin (but equine antitoxin is beta or alpha globulins).
- All antibodies are Ig but all Ig may not be antibodies because Ig not only involves antibody globulins but also involve abnormal proteins of myeloma macroglobulinemia, cryoglobulinemia and naturally occuring subunits of Ig.
- Ig constitute 20-25% of total serum proteins.

Structure of Ig

- **VL** = Variable domain of light chain.
- **CL** = Constant domain of light chain.
- **VH** = Variable domain of heavy chain.
- **CH** = Constant domain of heavy chain.
- **S-S** = Disulphide bond.



- ***Constant region*** = Carboxyterminus = Fc = [contains only heavy chain] which determines Ig biological properties.
- ***Variable region*** = Aminoterminus = Fab = Antigen binding region [=contains both Heavy and Light chains] which determines immunological specificity of antibody molecule.
- Ig (glycoprotein) consist of two pairs of polypeptide chains **(2H and 2L).**
- H = heavy chain has molecular weight 50,000.

  - H chain are structurally and antigenically distinct for each class and are designated by Greek letter γ, α, μ, δ, ε corresponding to Ig class IgG, IgA, IgM, IgD, IgE. respectively.
  - H chain consist of 1 variable (V_H) and three domains in constant region (CH_1, CH_2, CH_3).
- L = Light chain with molecular weight of 25,000.
  - L chain is similar in all classes of Ig.
  - 2 types of L chain are Kappa (K) and lambda (λ).
  - 1 molecule of Ig may have either kappa or lambda chains but never both.
  - Kappa and Lambda occur in ratio of about K : λ = 2 : 1.
  - L chain consist of 1 variable (V_L) and 1 constant domain (C_L).
- Highly variable zones (3 in L and 4 in H chain) are known as *Hypervariable regions* or *Hot spots.* They are involved in the formation of antigen-binding sites. Sites on the hypervariable regions which make actual contact with the epitope are called *complementarity determining regions* or *CDR's.*
- Fd piece - is portion of H chain present in Fab fragment.

Immunoglobulin classes

It has following properties :

- *Sedimentation coefficient* - ***max***. IgM
- *Molecular weight* - ***max***. IgM, ***min*** - IgG
- *Serum concentration, Half life in days, Daily production (mg/kg)* – G > A > M > D > E
- *Intravascular distribution (%)* - ***max*** IgM, ***min*** - IgA
- *Carbohydrate (%)* - ***max*** IgE *..... Harrison 16/e, p 1922*
- *Complement fixation* : Classical - IgM > IgG
  Alternative - IgA, IgD, IgG
- *Placental transport* - only IgG
- *Present in milk* - IgG and IgA
- *Selective secretion by seromucinous gland* - IgA
- *Heat labile :* **only** IgE
- J chain - IgA and IgM

i. **IgG**
  - General purpose antibody, enhances phagocytosis by opsonization.
  - It has four subclasses $G_1 > G_2 > G_3 > G_4$
  - IgG decrease from birth to reach minimum levels by 3rd month.

ii. **IgA**
  - Occur in two forms - Serum IgA (monomer) and secretory IgA i.e. SIgA (dimer joined by J chain present on respiratory/intestinal mucosa and in secretions).
  - J chain is also produced by plasma cells but secretory piece/secretory component of SIgA is not produced by lymphoid cells but by mucosal or glandular epithelial cells.

iii. **IgM**
  - Effective valency is five.
  - Earliest Ig to be synthesized by fetus (begin at 20 week of age) is IgM.
  - At 20th weeks Peyer's patches and lymphoid cells in spleen, and lymph nodes are developed so fetus has IgM, IgD, IgG (transplacentally) but not IgA and IgE.
  - IgM detection is useful in diagnosis of congenital infection.
  - Monomeric IgM is major antibody receptor on surface of B lymphocytes for antigen recognition.

iv. **IgD** – Resemble IgG structurally and also serve as recognition receptor for antigen.

v. **IgE** – Mostly extravascular and exhibits Homocytotrophism.

– Chiefly produced in the lining of intestinal and respiratory tract.
– It mediates Reaginic hypersensitivity and Prausnitz kustner (PK) reaction.

Remember : *IgG protect body fluids, IgA body surfaces and IgM the blood stream.*

Types of Antibody in various conditions :

IgM
– Biological false positive Ab in syphilis
– Rheumatoid factor
– Ab against ABO
– Ab to typhoid O Ag (endotoxin).

IgG
– Ab against Rh factor (Anti Rh D)
– (LATS) long acting thyroid stimulator Ab in Grave's
– AutoAb in SLE, GB Syndrome
– Reagin Ab in syphilis (LA, aCL).

..... Harrison 16/e, p 1923

Abnormal Ig

i. ***Bence Jones Protein (BJP)***
– Monoclonal Ig consist of light chain found typically in multiple myeloma.
– Identified in urine by its characteristic property of coagulation when heated to 50^0C but redissolving at 70^0C.

ii. ***Myeloma (M) protein***
– Monoclonal Ab seen in multiple myeloma (IgG, IgA, IgD, IgE) and waldenstrom's macroglobulinemia (IgM).

iii. ***F_c parts of Ig heavy chain***
– ↑ in Heavy chain disease.

iv. ***Cryo globulinemia***
– Formation of gel or precipitate on cooling the serum, which redissolves on warming.
– Most cryoglobulin consist of either IgG, IgM or mixed precipitates.

ANTIGEN – ANTIBODY REACTIONS

Ag-Ab reaction is reversible, occur ***at surface*** and there is no denaturation of Ag or Ab during reaction. Reactions occur in three stages :

i. ***Primary stage :***
Ag-Ab combined by weaker intermolecular forces such as Van-der waal's, ionic bond and H_2 binding rather than by firmer covalent bonding; without any visible effects.

ii. ***Secondary stage :***
Usually present but not always. It leads to demonstrable events such as precipitation, agglutination, lysis of cells etc.

iii. ***Tertiary stage (reaction) :***
Leads to tissue damage e.g. allergy and other immunological diseases.

Serological reactions

- *Comparative efficiency of Ig in different serological reactions :*

Reaction	IgG	IgM	IgA
• *Neutralization (N)*	More effective	Less effective	Variable
• *Precipitation (P)*	Strong	Weak	Variable
• *Classical complement fixation (C)*	Strong	Strongest	Negative
• *Immunohemolysis (I)* and *Bactericidal (opsonization) (O)*	Less effective	More effective	Moderate
• *Agglutination (A)*	Weak	Strong	Moderate
• *Lysis (L)*	Weak	Strong	Negative

..... Harrison 16/e, p 1992

Mnemonic for strong reaction in IgG = ***G***-N-P (Neutralization, Precipitation).

Mnemonic for strong reaction in IgM = CO-***M***-ALI (Classical Complement fixation, Opsonization, Agglutination, lysis, Immunohemolysis).

i. Precipitation Reaction

When ***soluble antigen*** combines with its antibody in presence of electrolytes, it forms *insoluble precipitates/ floccules.*

- This reaction show "zone phenomenon" ***(also in agglutination)*** either in the form of prozone (***antibody*** excess) or postzone (***antigen*** excess).
- It occur in zone of equivalence due to lattice formation ***(also in agglutination)***.
- It is very ***sensitive*** in antigen detection (but relatively less sensitive for antibody detection).
- It is of following types :
  a. ***Ring test*** – Simplest type eg. Ascoli's thermoprecipitin test and streptococcal lancefield grouping.
  b. ***Slide test*** – VDRL test of syphilis
  c. ***Tube test*** – Kahn test of syphilis
  d. ***Immunodiffusion (ppt in gel)*** – Eg. Elek test for toxigenicity in diphtheria (double diffusion).
  e. ***Electro immunodiffusion*** – Eg. rocket electrophoresis for quantitative estimation of antigen.

ii. Agglutination Reaction

It is more sensitive than precipitation for antibody detection. Occur in presence of electrolytes.

- *Incomplete or monovalent antibodies* (usually Ab are bivalent) do not cause agglutination, though they combine with the antigen. They also *act as blocking Ab* since they inhibits agglutination by complete Ab. Agglutination is of following types :
  a. ***Slide agglutination*** – used for blood grouping and cross matching.
  b. ***Tube agglutination*** – Eg. Widal test, Brucellosis, Weil-Felix reaction, Paul Bunnel test, cold agglutination and Streptococcus MG test.
  c. ***Antiglobulin (Coombs) test*** – used for detecting incomplete Ab of brucellosis; anti-Rh Ab.
  d. ***Passive agglutination test*** – used to detect Ab by adsorbing soluble Ag on carrier particles so precipitation reaction converts into agglutination test which are *more convenient* and *more sensitive.* Eg. Rose waller test, test detecting RA factor by using amboceptor.

e. ***Latex agglutination test (latex fixation test)*** – for detection of ASO, CRP, RA factor, HCG; Streptozyme test.

f. ***Reversed passive agglutination*** - Estimation of antigen by adsorbing antibody to carrier particles.

iii. Complement Fixation Test (CFT)

- Antigen may be soluble or particulate.
- Source of complement is guinea pig serum Eg. Wassermann reaction; coaglutinating complement adsorption test using horse complement; immuno adherence of V.cholera and T. pallidum; Immobilization test of T. pallidum; Cytolytic or cytocidal test.

iv. Neutralisation Tests

Includes virus neutralisation test ***(plaque inhibition test),*** Toxin neutralisation ***(Schick, antistreptolysin O)*** test.

v. Radio - Immunoassay (RIA)

- ***MC*** labels used are radio-isotopes and enzymes.
- It measures analytes upto picogram (10^{-12}g) quantities.
- Used for quantitation of hormones, drugs, tumour markers, IgE and viral antigen.

vi. Enzyme Immunoassay (EIA)

- Measures enzyme labelled antigen, hapten or antibody.
- It may be homogenous or heterogenous.
- Major type of heterogenous EIA is ELISA which involves the use of immunosorbent - an absorbing material specific for one of components of reaction, the antigen or antibody. Eg ELISA for detection of ***Rotavirus in feces or HIV antibody in serum.***

3 Hypersensitivity [HSN]

Hypersensitivity is defined as immunologic tissue injury in response of subsequent exposure with the allergen (shocking or challenge dose). It is following types :

Type	Mechanism and Effects	Examples
1. *Type I (Immediate or reaginic HSN)* Systemic acute anaphylaxis Local anaphylaxis = atopy	• **Ab** - IgE (cytotropic) • **Cells** - IgE B cell, mast cells, basophils, Eosinophil • **Pivotol role** - by T_H2 cell • Most important ***vasoactive amine*** : Histamine • Slow reacting substance of anaphylaxis ***(SRS-A)*** = Leukotrienes ***(LT B_4, C_4, D_4, E_4)***	• Urticaria; angioedema; hay fever and some forms of asthma; eczema • Anaphylactic shock • Casoni's test, • Theobald smith phenomenon • Schultz dale phenomenon • Prausnitz kustner (PK) reaction
2. *Type II [cytotoxic or cytolytic] HSN* a. Complement dependent	• **Ab :** IgG or IgM • Lysis or phagocytosis by opsonisation • Most commonly involves blood cells (II HSN involve blood : b is second alphabet → ***Mnemonic***)	• Transfusion reactions • Erythoblastosis fetalis (Hemolytic disease of neotates) • AI hemolytic anemia or agraulocytosis or thrombocytopenia; • Pemphigus syndrome • Bullous pemphigoid • Pernicious anemia • Thrombotic phenomenon • Acute rheumatic fever • Some forms of vasculitides and certain drug reactions.
b) Type VI HSN = Antibody dependent cell mediated cytotoxicity (ADCC)	• **Ab -** usually IgG sometimes IgE • Cell lysis without phagocytosis by monocytes, neutrophil, eosinophils and NK cells	• Phagocytosis of tumour cells or parasite • Some role in graft rejection
c) Type V HSN = Antibody mediated cellular dysfunction.	Antireceptor Antibody • Stimulation • Inhibition	• Thyrotoxicosis / Grave's disesas • Myasthenia gravis

Continue .....

3. Type III [Immune complex] HSN Local immure complex disease [= Arthus reaction] Systemic immune complex [Serum sickness]	• **Ab -** IgG or IgM • Ag-Ab complex activate complement → attack neutrophil → release of lysosomal enzymes • **Ab -** No antibody • Initiated by specifically sensitized T lymphocytes	• SLE • Certain forms of acute glomerulonephritis • Rheumatoid arthritis • Hyperacute graft rejection • Hypersensitivity preumonitis • Infective endocarditis • PAN • Henoch schonlein purpura • Schick test • Type 2 lepra reaction (ENL)
4. Type IV [Cell mediated] HSN a. Delayed type by CD4 T_H1 - Induration is its characteristic b. Cell mediated cytotoxicity by CD - 8 T cells		a. • Tuberculin test • Lepromin test • Fairleys (Schistosomiasis) test • Frie's (LGV) test • Granulomatous inflammation • Contact dermatitis • Defence against intracellular pathogen • Type I lepra reaction b. • Graft rejection • Resistance to virus infection • Tumour immunity

QUESTIONS

1. The serum concentration of which of the following human IgG subclass is maximum : [AI 05]
a) IgG1
b) IgG2
c) IgG3
d) IgG4

2. Adenosine deaminase deficiency is seen in the following : [AI 05, 01]
a) Common variable immunodeficiency
b) Severe combined immunodeficiency
c) Chronic granulomatous disease
d) Nezelof syndrome

3. A woman with infertility receives an ovary transplant from her sister who is an identical twin. What type of graft it is ? [AI 05]
a) Xenograft
b) Autograft
c) Allograft
d) Isograft

4. Which of the following statements is true about hapten ? [AI 04]
a) It induces brisk immune response
b) It needs carrier to induce immune response
c) It is a T-independent antigen
d) It has no association with MHC

5. The earliest immunoglobulin to be synthesized by the fetus is : [AI 03]
a) IgA
b) IgG
c) IgE
d) IgM

6. Neonatal thymectomy leads to : [AI 02]
a) Decreased size of germinal center
b) Decreased size of paracortical areas
c) Increased antibody marrow production by B cells
d) Increased bone marrow production of lymphocytes

7. IL-I produces : [AI 02]
a) T lymphocyte activation
b) Delayed wound healing
c) Increased pain perception
d) Decreased PMN release from bone marrow

8. Regarding NK cells, false statement is : [AI 01]
a) It is activated by IL-2
b) Expresses CD3 receptor
c) It is a variant of large lymphocyte
d) There is antibody induced proliferation of NK cells

9. Type of graft, best suited for renal transplantation: [AI 99]
a) Allograft
b) Autograft
c) Xenograft
d) Isograft

10. Haptane is : [AI 98]
a) Same as epitope
b) Small molecular weight protein
c) Requires carrier for specific antibody production
d) Simple haptens are precipitating

11. All of the following forces are involoved in Antigen antibody reaction except :
a) Vander Waal's forces [AI 98, AIIMS 96]
b) Electrostatic bond
c) Hydrogen bond
d) Covalent bond

12. Examples of type I hypersensitivity is : [AI 98]
a) Lepromin test
b) Tuberculin
c) Casoni's test
d) Arthus reaction

13. IL-2 is produced by : [AI 97; 00; AIIMS 97]
a) T cells
b) B cells
c) Monocytes
d) Neutrophils

14. All of the following are glycoproteins except :
a) Blood antigen [AI 97; 94]
b) Albumin
c) Immunoglobin
d) HCG

15. Which of the following statements concerning immunoglobins is wrong : [AI 97]
a) IgM does not cross placenta
b) IgE is ↑ ed in parasitic infection
c) IgM increased in primary response
d) Fetal infection is characterized by increase in IgG

Answer

1. a) IgG1	2. b) Severe ...	3. d) Isograft	4. b) It needs ...	5. d) IgM
6. b) Decreased ...	7. a) T lymph ...	8. d) There is ...	9. d) Isograft	10. c) Requires ...
11. d) Covalent ...	12. c) Casoni's ...	13. a) T cells	14. b) Albumin	15. d) Fetal

16. Which of the following is an example of Type IV hypersensitivity : **[AI 97]**
a) Arthrus reaction
b) Serum sickness
c) Schwartzmann reaction
d) Granulomatous reaction

17. Diagnosis of ABO incompatability can be from all of the following except : **[AI 97]**
a) Sweat
b) Saliva
c) Semen
d) CSF

18. Helper cells belong to : **[AI 96]**
a) T cells
b) Macrophages
c) B cells
d) Monocytes

19. The type of receptors present on T cells are :
a) IgG **[AI 96]**
b) IgD
c) CD3
d) Prostaglandins

20. What enhances multiplication of T cells in culture
a) Phytohemagglutinin **[AI 96]**
b) Chemotactic factor
c) Leukotrienes
d) Prostaglandins

21. Which of the following is an example of type IV hypersensitivity : **[AI 96]**
a) Granulomatous reaction
b) Schwartzman reaction
c) Arthus reaction
d) Serum sickness

22. Which precipitates at 50^0C-60^0C but disappears on heating : **[AI 96]**
a) Heavy chain
b) Light chain
c) Both
d) None of the above

23. Bence Jones protein are best described as :
a) μ chains **[AI 96]**
b) γ chains
c) Kappa and Lambda chains
d) Fibrin split products

24. Prozone phenomenon is due to : **[AI 96, PGI 03]**
a) Antigen excess
b) Antibody excess
c) False +ve reaction
d) False -ve reaction

25. A single immunoglobulin molecule contains :
a) 1 light chain, 1 heavy chain **[AI 95]**
b) 2 heavy chains, 1 light
c) 2 light chains, 2 heavy
d) 2 light chains, 1 heavy chains

26. Which of the following is false : **[AI 95]**
a) Theobald-Smith phenomenon is a type I hypersensitivity reaction
b) Serum sickness is a type II hypersensitivity reaction
c) Allograft rejection is a type IV hypersensitivity reaction
d) Transfusion reaction is a type II hypersensitivity reaction

27. NK cells kill the viral infected cells due to :
a) Increased expression of MHC class I molecules
b) Decreased expression of MHC class I molecules **[AIIMS 06]**
c) Increased expression of MHC class II molecules
d) Decreased expression of MHC class II molecules

28. The following methods of diagnosis utilize labeled antibodies except : **[AIIMS 05]**
a) ELISA
b) Haemagglutination inhibition test
c) Radio immuno assay
d) Immun-ofluorescence

29. All of the following are part of innate immunity except : **[AIIMS 05]**
a) Complement
b) NK cells
c) Macrophages
d) T cells

30. Which of the following is class specific antigenic determinants of an Ig : **[AIIMS 04]**
a) L-chain
b) H-chain
c) J-chain
d) Variable region

Answer

16. d) Granulo ... 17. d) C S F 18. a) T cells 19. c) CD3 20. a) Phytohem ...
21. a) Granul ... 22. b) Light ... 23. c) Kappa ... 24. b and d 25. c) 2 light ...
26. b) Serum ... 27. a) Increased ... 28. b) Haem .... 29. d) T cells 30. b) H-chain

31. Which of the following best denotes classical complement pathway activation in immuno inflammatory condition : [AIIMS 04]
a) C2, C4 and C3 decreased
b) C2 and C4 normal, C3 is decreased
c) C3 normal and C2 C4 decreased
d) C2, C4, C3 all are elevated

32. The most avidly complement fixing antibody is : [AIIMS 02]
a) IgA
b) IgG
c) IgM
d) IgE

33. Which is not a Macrophage : [AIIMS 97]
a) Monocyte
b) Microgila
c) Kupffer cells
d) Lymphocytes

34. True about immunoglobulins is : [AIIMS 97]
a) IgE fixes complements
b) IgM fixes complements
c) IgG is found in minimum concentration
d) IgG is elevated in primary immune response

35. Which of the following is true : [AIIMS 96]
a) Paul Bunnel test is used to diagnose measles
b) Rose Waller test is a complement fixation test
c) Indirect hemagglutination test is less sensitive than gel diffusion test
d) Antigen, Antibody reaction cannot occur in absence of electrolytes

36. In Respiratory and GIT infection, which is the most affected immunoglobulin : [AIIMS 96]
a) IgA
b) IgG
c) IgM
d) IgD

37. The reaction between antibody and soluble antigen is demonstrated by : [AIIMS 96]
a) Agglutination
b) Precipitation
c) Complement fixation
d) Hemagglutination test

38. C-reactive protein is : [AIIMS 96]
a) An antibody as a result of pneumococcal infection
b) Derived from pneumococci
c) Detected by precipitation reaction
d) Increased in pneumococcal infection

39. Common between B and T cells : [PGI June 07]
a) Origin from same cell lineage
b) Site differentiation
c) Antigenic marker
d) Both humoral and cellular immunity
e) Further differentiation seen

40. Haemolytic disease of newborn is which type of hypersensitivity reaction : [PGI June 07]
a) Type - I
b) Type - II
c) Type - III
d) Type IV
e) Type V

41. Skin test is used for which hypersensitivity reaction :
a) I **[PGI June 07]**
b) II
c) III
d) IV

42. Antibody diversity is due to : [PGI Dec. 07]
a) Gene re-arrangement
b) Gene translocation
c) Antigenic variation
d) CD_{40} molecules
e) Mutation

43. MHC class III genes encode : [PGI 06]
a) Complement component C3
b) Tumor necrosis factor - alpha
c) Tumor necrosis factor - beta
d) Interleukin 2
e) Beta 2 microglobulin

44. Skin test based on neutralization reaction is/are:
a) Casoni test **[PGI 04]**
b) Lepromin test
c) Tuberculin test
d) Schick test

45. Acute phase reactants (APR) in acute inflammation are : [PGI 03]
a) Albumin
b) Fibrinogen
c) Haptoglobulin
d) Gammaglobulin

46. Antigen binding site on antibody is : [PGI 02]
a) Hinge region
b) Constant region
c) Variable region
d) Hypervariable region
e) Idiotype region

Answer

31. a) C2, C4	32. c) IgM	33. d) Lymphocytes	34. b) IgM fixes ...	35. d) Antigen, ...
36. a) IgA	37. b) Precipitation	38. d) Increased ...	39. a and e	40. b) Type - II
41. a, c and d	42. c) Antigenic ...	43. b and c	44. d) Schick ...	45. b and c
46. d and e				

47. Apart from B cells, and T cells, there is a 3rd distinct type of lymphocyte. This is : [PGI 02]
a) MHC cell
b) NK cell
c) Macrophage
d) Neutrophil
e) Microglia

48. IgE is secreted by : [PGI 02]
a) Mast cell
b) Basophils
c) Eosinophils
d) Plasma cells
e) Neutrophils

49. All of these are antigen presenting cells except :
a) T cells [PGI 02]
b) B cells
c) Fibroblasts
d) Dendritic cells
e) Langerhans cells

50. Classic complement is activated by : [PGI 02]
a) IgG
b) IgA
c) IgM
d) IgE
e) IgD

51. Perforins are produced by : [PGI 02]
a) Cytotoxic T cells
b) Suppressor T cells
c) Memory helper T cells
d) Plasma cells
e) NK cells

52. The secretory component of molecule is :
a) Formed by epithelial cell of lining mucosa
b) Formed by plasma cell [PGI 01]
c) Formed by epithelial cell and plasma cell
d) Secreted by bone marrow

53. True of the following is/are : [PGI 01]
a) IgA crosses placenta
b) Half life of IgG is 23 days
c) IgD is heat stable
d) IgE has highest carbohydrate content
e) IgG induces leukotrienes release during inflammation

54. Which of the following immunoglobulins can cross placenta : [PGI 01]
a) IgA
b) IgM
c) IgG
d) IgD

55. C.reactive proteins are : [PGI 00]
a) Alpha-globulin
b) Beta-1 globulin
c) Alpha-2 globulin
d) Non-specific inflammatory protien

56. IL-I is produced by : [PGI 00]
a) Macrophage
b) Helper T lymphocytes
c) B cells
d) Cytotoxic T-cells

57. Type-1 hypersensitivity includes all of the following except : [PGI 00]
a) Autoimmune hemolytic anemia
b) Anaphylaxis
c) Extrinsic Asthma
d) Hay Fever

58. True about anaphylaxis : [PGI 00]
a) Type-1 reaction
b) Large amount of histamine released
c) Cytokines like IL4, IL5, and IL6 and GMCSF are released
d) Mediated through allergen specific IgE

59. Which is not heterophile agglutination test :
a) Weil-Felix test [PGI 99]
b) Widal test
c) Paul-Bunnel test
d) Streptoccus MG

60. True about secondary immune response is:
a) Long latent period [PGI 98, 96]
b) Usually of low titre
c) Antibodies appear in short time
d) Persist for long

61. True about interferon is : [PGI 98]
a) It is a synthetic antiviral agent
b) Inhibits viral replicatiion in cells
c) Is specific for particular virus
d) None

62. Which of the following is very difficult to induce antibody : [PGI 97]
a) Polysaccharide
b) Protein
c) Antigens
d) Repeated infection

Answer
47. b) NK cell 48. d) Plasma .. 49. a and c 50. a and c 51. a) Cytotoxic ...
52. c) Formed ... 53. b, c and d 54. c) IgG 55. b and d 56. a) Macrophage
57. a) Autoimmune ... 58. a, b, c and d 59. b) Widal test 60. c and d 61. b) Inhibits ...
62. a) Polysaccharide

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is a i.e. IgG1 *Ref. Jawetz 24/e, p 131; Ananthnarayan 7/e, p 88*

- *Molecular formula of IgG* - H_2L_2 since two heavy and two light chain.
- *IgG is divalent.*
- IgG has subclasses IgG1 to IgG4 based on antigenic difference in the H chain (gamma chain) and on the number and location of disulfide bonds.
- They are distributed as G1 > G2 > G3 > G4.
- *IgG2* is directed against polysaccharide antigen so it is important in defence against encapsulated bacteria.
- IgG is produced in secondary response of immunity.

Remember :
- Most abundant Ig in new borns – IgG.
- Only immunoglobulin which crosses placenta – IgG
- Basic structure of all Ig is 2 pairs of polypeptide chains (2H and 2L).

2. Ans. is b i.e. Severe combined immunodeficiency

Ref. Ananthnarayan 7/e, p 153, Harrison 17/e, p 2056-2059

Immunodeficiency { Primary immunodeficiency syndrome - genetically determined; Secondary immunodieficiency syndrome eg. AIDS.

Classification of important Immunodeficiency syndrome

	Name of syndrome	*Defect*
i.	**Humoral immunodeficiency (B cell defects)**	
	a. X lilnked agammaglobulinemia :	Mutation in bruton tyrosine kinase
		Pre/pro B cell $\xrightarrow{\times}$ B cell
	b. Common variable immunodeficiency :	B cell $\xrightarrow{\times}$ Plasma cells
	c. Immunodeficiency with hyper IgM :	Mutation in CD40 ligand gene
ii.	**Cellular immunodeficiency (T cell defect)**	
	a. Thymic hypoplasia ***(Digeorges syndrome)*** :	Failure of development of 3rd and 4th pharyngeal pouch (hypoplasia of thyroid and parathyroid also).
iii.	**Combined immunodeficiencies (B and T cell defect)**	
	a. Cellular immunodeficiency with abnormal Ig synthesis ***(Nezlof syndrome)*** :	Abnormal T cell maturation in thymus with normal, ↓ or ↑ Ig
	b. Ataxia telengiectasia :	DNA repair defect
	c. ***Wiskott Aldrich syndrome :***	WASP gene mutation (secondary ↓ of T lymphocytes)
	d. Severe combined immunodeficiency :	Adenosine deaminase deficiency

3. Ans. is d i.e. Isograft *Ref. Ananthnarayan 7/e, 176 - 177*

Types of Graft

- *Autograft* : Graft from same individual (self).
- *Isograft (isologous/ syngeneic/ syngraft)* – Graft from different individual, genetically identical with recipient eg twins.
- *Allograft (Homograft)* : Graft from genetically unrelated member of same species.
- *Xenograft (Heterograft)* : From different species.
- *Orthotopic graft* : Graft applied in anatomically normal site eg skin graft.
- *Heterotopic graft* : Graft applied in anatomicaly abnormal site eg thyroid tissues transplanted in subcutaneous pocket.

4. Ans. is b i.e. It needs carrier to induce immune response *Ref. Ananthnarayan 7/e, p 80*

Antigen can be of two types :

Complete antigens	Hapten
They are immunogenic as well as immulogical reactive	They are non-immunogenic (incapable of inducing antibody formation) but has immunological reactivity (combine with Antibody). *They are of 2 types :* – Complex hapten (Precipitate with specific antibody) – Simple hapten (non precipitating)

- Hapten become imunogenic only on combining with a larger molecule called carrier.

5. Ans. is d i.e. IgM *Ref. Ananthnarayan 7/e, p 89*

- **IgM**, a millionare molecule composed of five H_2L_2 and 1 J chain and is heaviest immunoglobulin.
- It has valency of 10 (effective valency - 5).
- Its presence in the serum indicates recent infection (primary response).
- It has ***highest avidity*** among all Ig.
- *By 20th week, fetus produce IgM, IgD and receives maternal IgG so IgA and IgE are not present.*

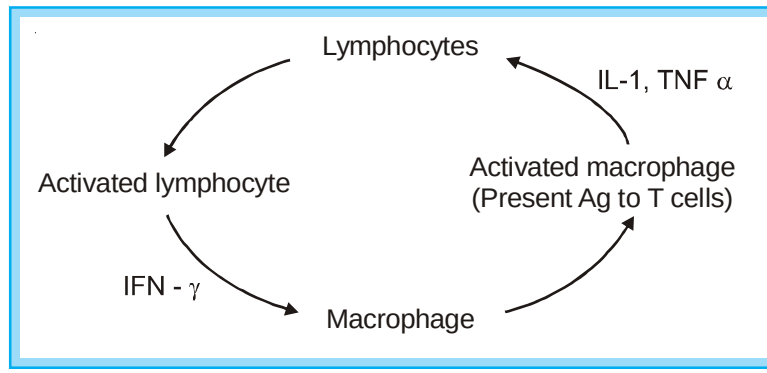
6. Ans. is b i.e. Decreased size of paracortical areas *Ref. Ananthnarayan 7/e, p 119 - 120*

- Neonatal thymectomy leads to depletion of thymus dependent areas.
- *Peripheral lymphoid tissue is of two types :*

Features	Thymus dependent (contain T lymphocytes)	Bone marrow dependent (contain B lymphocytes)
Spleen	Periaterial lymphoid collecion known as malpighian Corpuscles in white pulp.	Perifollicular Germinal centre Mantle layer
Lymph node	Paracortical areas between cortical follicles and medullary cords.	Corticle follicles with germinal centre Medullary cords

- B cells also found in tonsils, extralymphoid organs such as GIT.

7. Ans. is a i.e. T lymphocyte activation *Ref. Ananthnarayan 7/e, p 144; Robbin's 7/e, p 82*



Interleukins	Main source	Major function
IL-1 (α+β)	Macrophage	Proliferation and differentiation of T,B cells; pyrogenic; ↑ acute phase reactants; BM cell proliferation.
IL-2	TH1 cells	Growth and differentiation of T and B cells; cytotoxicity of T and NK cells.
IL-3	T cells	Stimulation of hematopoietic progenitors.
IL-4	TH2 cells	Proliferation of B and cytotoxic T cells; ↑ IgG1 and IgE production; ↑ MHC class II and IgE receptor.
IL-5	TH2 cells	Proliferation of eosinophil; ↑ IgA and IgM production.
IL-6	TH1, macrophages,	Promote B cell differentiation, IgA production, Acute phase proteins.
IL-7	Spleen, BM stromal cells	B and T cell growth factor.

8. Ans. is d i.e. There is antibody induced proliferation of NK cells *Ref. Harrison 17/e, p 2028*

NK cell activity is non-immune; MHC unrestricted; non-antibody mediated killer of target cells which are usually malignant cells types, transplanted foreign cells or virus infected cells.

9. Ans. is d i.e. Isograft *Ref. Ananthnarayan 7/e, p 177*

Already explained, refer answer no. 3

10. Ans. is c i.e. Requires carrier for specific antibody production *Ref. Ananthnarayan 7/e, p 80*

Already explained, refer answer no. 4

11. Ans. is d i.e. Covalent bonds *Ref. Ananthnarayan 7/e, p 93*

Combination between Ag and Ab is reversible, effected by the weaker intermolecular forces such as Vander Wal's forces, Ionic bonds and hydrogen bonding, not by the firmer covalent bonds.

12. Ans. is c i.e. Casoni's test *Ref. Taylor 3/e, p 107*

Type I HSN (IgE mediated)	Type II HSN (IgG and IgM mediated)
• Eczema • Hay fever • ***Asthma*** (atopy) • Urticaira • Anaphylactic shock • Acute dermatitis • **Theobald smith phenomenon** • PK ***(Prusnitz Kunster)*** reaction • Casoni's skin test • ***Schultz*** Dale phebnomenon	• ***Blood transfusion reactions*** • Erythroblastosis fetalis • ***AI Hemolytic anemia*** or agranulocytosis or thrombocytopenia • Pemphigus vulgaris • ***Good pasture*** syndrome • Bullous pemphigoid • Pernicious anemia • ***Acute rheumatic*** fever • Diabetes mellitus • ***Graves disease*** • Myasthenia gravis
Type III HSN (IgM or IgG mediated)	**Type IV HSN (cell mediated)**
• Local - ***arthus*** reaction • **Systemic - serum sickness** • Schick skin test • PAN • ***Rheumatoid*** arthritis • SLE • Acute viral hepatitis • Penicillamine toxicity • ***Hyperacute graft rejection*** • Type 2 lepra reaction (ENL) • Hypersensitivity pneumonitis	• Tuberculin skin test • Lepromin skin test • Contact dermatitis • Jones Mote reaction ***(cutaneous basophilic HSN)*** • ***TB*** • Sarcoidosis • Temporal arteritis • Patch test • ***Granulomatous inflammation*** • Type I lepra reaction

13. Ans. is a i.e. T-cells *Ref. Ananthnarayan 7/e, p 144*

Already explained, refer answer no. 7

14. Ans. is b i.e. Albumin *Ref. Harper 25/e, p 675; Lipincott 2/e, p 157*

Glycoprotein are proteins to which usually 2 - 10 oligosaccharides are covalently attached eg.

• **Ig** • Mucin • Lectin • **Globular proteins except albumin** • HCG, TSH • HLA class I, II • Transferrin, ceruloplasmin	• Glycophorin • **Blood group antigen** • Selectin • Secreted enzymes and proteins • Collagen • Alkaline phosphatase • IFN β and γ

15. Ans. is d i.e. Fetal infection is characterized by ↑in IgG *Ref. Ananthnarayan 7/e, p 87-89*

IgM	• Antigen receptor on B cells • Useful for diagnosing congenital infections • ***Earliest Ig*** to be synthesized by fetus

Continue .....

	• Increased in ***primary*** response • ***Max*** sedementation cofficient, max molecular weight and max intravascular distribution. • Exhibits strong classical complement fixation, opsonization, agglutination, lysis, immunohemolysis.
IgG	• Max serum conc and half life • Ig increase in ***secondary*** immune response and is opsonising antibody. • Only Ig which ***cross placenta*** so its presence in fetus indicates immunity not infection. • Exhibits strong precipitation and neutrallization reaction.
IgE	• Ig increase in parasitic infection, allergic response • Only ***heat labile*** Ig • Max carbohydrate conc. *..... Harrison, p 1922*
IgA	• Only Ig which is secreted by seromucinous gland such as saliva, tears, colostrum, respiratory and gastrointestinal secretions.

Remember :
- Ig present in milk : IgA and IgG
- Complement fixation : *Classical IgG* (except IgG4), IgM; *Alternate IgA,* IgD, IgG4.
- Polymeric form contain J chain : IgA, IgM.

16. Ans. is d i.e. Granulomatous reaction *Ref. Ananthnarayan 7/e, p 167*

Schwartzman reaction is ***not an immune reaction*** but alteration in factors (eg massive activation of complement) affecting intravascular coagulation eg. Purpuric rashes of meningcoccoal septicemia; Water house Friderichsen syndrome.

For more detail, refer answer no. 12

17. Ans is d i.e. CSF *Ref. Reddy 5/e, p 378*

ABO group specific substances are found in high concentration in saliva, semen, vaginal secretion and gastric juice and while in low concentration in sweat, tears and urine, so it is possible to determine blood group from an examination of these secretions

Thus, they are present in all tissues except CSF.

18. Ans. is a i.e. T cells *Ref. Ananthnarayan 7/e, p 128*

Extra thymic (Mature) T cells	
• Helper / Inducer CD4 cells	• Cytotoxic killer/ suppressor CD-8 cells

19. Ans. is c i.e. CD3 *Ref. Ananthnarayan 7/e, p 125*

Surface markers	**T cells**	**B cells**
CD-3 receptor	+	–
Surface Ig	–	+
Thymus specific Ag	+	–
Ag receptor	+	–
Fc receptor	–	+
Complement receptor	–	+
Rosettes	SRBC or E rosette (CD-2; measles receptor)	EAC rosette (C3 receptor; CR-2; EBV receptor)
Numerous microvilli	–	+

20. Ans. is a i.e. Phytohemagglutinin *Ref. Ananthnarayan 7/e, p 123*

Blast transformation or proliferation stimulus are :

Stimulus	T cell	B cell
Anti CD-3	+	–
Anti Ig.	–	+
PHA (Phytohemagglutinin)	+	–
Concanavalin A	+	–
Endotoxins	–	+
S-aureus (cowan strain)	–	+
EB virus	–	+

+ *Means* proliferation occurs
– *Means* no proliferation

21. Ans. is a i.e. Granulomatous reaction *Ref. Ananthnarayan 7/e, p 166*

Already explained, refer answer no.12

22. Ans. is b i.e. Light chain *Ref. Ananthnarayan 7/e, p 90*

- **BJP** are identified in urine by its characteristic property of coagulation when heated at 50^0C and dissolved at 70^0C.
- BJP (abnormal Ig) are light chain of Ig found typically in multiple myeloma.
- Light chain consist of either Kappa or lambda, never both.

23. Ans. is c i.e. Kappa and Lambda chains *Ref. Ananthnarayan 7/e, p 90*

Already explained, refer answer no. 22

24. Ans. is b and d i.e. Antibody excess; and False negative *Ref. Ananthnarayan 7/e, p 94*

Zone phenomenon (seen in agglutination and precipitation) consist of 3 parts :

i. **Prozone** = Ab excess = weak or absent precipitation reaction = False –ve
ii. **Zone of equivalence** = peak amount of precipitation.
iii. **Post zone = Ag excess** = weak or absent precipitation reaction.

25. Ans. is c i.e. 2 light chain and 2 heavy chain *Ref. Ananthnarayan 7/e, p 85*

Already explained, refer answer no. 1

26. Ans. is b i.e. Serum sickness is type II HSN *Ref. Taylor 3/e, p 119*

Type of Rejection	Type of HSN	Target sites in Transplantation
• *Hyperactue rejection (preformed Ab against donor transplantation Ag)*	Type II cytotoxic Type III HSN	Small blood vessels in donor tissues
• *Acute rejection*	Type II cytotoxic Type III HSN	Parenchymal cells Small blood vessels
• *Chronic rejection*	Type III HSN Type IV HSN	Small blood vessels

For more detail, refer answer no. 12

27. Ans. is a i.e. Increased expression of MHC class I molecules

Target cell killing by NK cell is :

- Inversely related to target cell expression of MHC class I molecule.
  So, it kills the cell that express little or no HLA class I molecule (provide immunosurveillance) such as ***virus infected cells, certain tumour cells and allogenic cells.***
- Non-immune i.e. without previous sensitization, MHC unrestricted and non-antibody mediated.
- It kill host cell infected with intracellular bacteria eg. Mycobacteria, TB, listeria monocytogens.
- Not kill cells which express class I MHC (all normal nucleated cell express it).

28. Ans. is b i.e. Haemagglutination inhibition test *Ref. Ananthnarayan 7/e, p 104, 108, 503 - 504*

Following serological test use labelled antibodies :

A. IMMUNOFLUORESCENCE (IF) = FLOURESCENT ANTIBODY TECHNIQUE

- **Principle :** Labels (fluorescent dyes) conjugated with Antibodies of serum = labelled antibodies which is used to locate and identify *antigens* in tissues.
- Fluorescent dyes commonly used are ***fluorescein Isothiocynate and lissamine - rhodamine***

Immunofluorescence may be	
Direct IF test	**Indirect IF test**
• Antigen + labelled antibodies ↓ Antigen - Antibody complex is fluorescent • Eg. detection of *rabies virus* antigen in brain smears • **Disadvantage** - Separate fluoresent conjugates have to be prepared against each antigen to be tested	• Antigen + Antibody ↓ • Antigen - Antibody complex + fluorescent conjugated antiglobulin serum ↓ • Final product is fluorescent • Eg fluorescent *treponemal antibody* test for syphilis • **Advantage -** A single antihuman globulin fluorescent conjugate can be used for detecting human antibody to any antigen

- Fluorescent dyes can also conjugated with *complement.*

- Labelled complement can be used for detection of antigen or antibody.
- Antibody is detected by Sandwich technique.
- **Major disadvantage** of immuno fluorescence is frequent occurence of non specific flurescence in tissues and other materials.

B. RADIOIMMUNOASSAY (RIA) = BINDER LIGAND ASSAYS

Principle **:** Labels ***(MC radioisotopes and enzymes)*** conjugated to antigen / antibody = labelled reactants which ***measure*** antigen ***and*** antibodies.

- The substance (antigen) whose concentration is to be determined is termed the analyte or ligand.
- Binding protein (usually antibody) which bind to ligand is called the binder.
- RIA measure analytes upto picogram 10^{-12}g quantities.
- RIA has application in quantitation of hormones, drugs, tumour markers, IgE and viral antigens.
- Fixed amount of antibody reacts with radiolabelled antigen as well as varying known amount of unlabelled (test) antigen competitively.
- Concentration of test antigen is calculated from standard dose response or calibrating curve.

C. ENZYME IMMUNOASSAYS (EIA)

- It is the most widely used procedure in clinical serology.
- It uses enzyme labelled antigen and antibodies as serological reagents, for the assay of antibodies and antigens.
- It is of two types :
  - i. **Homogenous EIA (one step test) -**
    - Used only for assay of haptens such as drugs (opiates, cocaine etc)
  - ii. **Heterogenous EIA (multistep test)** -
    - Major type of heterogenous EIA is **ELISA** which involves the use of immunosorbent specific for one of the component of reaction, the antigen or antibody.
    - Immunosorbent may be particulate or solid phase
    - ELISA is usually done on 96 well microtitre plates

      Eg. – *Non competitive sand witch ELISA*
      - ***Detection of rotavirus antigen in feces.***
      - Anti HIV antibody test.

      – *Competitive ELISA*

      – *IgM specific ELISA*

      – *Capture ELISA*

      – *Immunometric ELISA*

      – *Card and dipstick methods*

      – *Cylinder or* Casette *ELISA* for the detection of HIV type 1 and 2 antibodies. It is rapid.

D. CHEMILUMINESCENCE IMMUNOASSAY (CLIA)

Uses chemiluminescent compounds (such as luminol or acridinium esters) as the label to provide signal during antigen- antibody reaction.

E. IMMUNOELECTROBLOT TECHNIQUES

Eg. western blot test.

F. IMMUNOCHROMATOGRAPHIC TESTS

Test system is a small cassette contaning membrane impregnated with anti HbsAg antibody - colloidal gold dye conjugate ***Eg. HBsAg detection.***

G. IMMUNOFERRITIN TEST

Antibody conjugate with ferritin.

H. IMMUNOENZYME TEST

Stable enzyme like peroxidase conjugated with antibodies.

Remember :

Hemagglutination inhibition test - convenient method for detection and quantitation of antibody to the virus.

29. Ans. is d i.e. T cells *Ref. Harrison 17/e, p 2021, 2031*

Components of the Adaptive Immune System

Cellular	Thymus-derived (T) lymphocytes - T cell precursors in the thymus; naive mature T lymphocytes before antigen exposure; memory T lymphocytes after antigen contact; helper T lymphocytes for B and T cell responses; cytotoxic T lymphocytes that kill pathogen- infected target cells.
Humoral	Bone-marrow-derived (B) lymphocytes - B cell precursors in bone marrow; naive B cells prior to antigen recognition; memory B cells after antigen contact; plasma cells that secrete specific antibody.
Cytokines	Soluble proteins that direct focus and regulate specific T versus B lymphocyte immune responses.

Major Components of the Innate Immune System

• *Pattern recognition receptors (PRR)*	C type lectins, leucine-rich proteins, scavenger receptors, pentraxins, lipid transferases; integrins.
• *Antimicrobial peptides*	α-Defensins, β-defensins, cathelin, protegrin, granulsyin, histatin, secretory leukoprotease inhibitor, and probiotics.
• *Cells*	Macrophages, dendritic cells, NK cells, NK-T cells, neutrophils, eosinophils, mast cells, basophils, and epithelial cells.
• *Complement components*	Classic and alternative complement pathway, and proteins that bind complement components.
• *Cytokines*	Autocrine, paracrine, endocrine cytokines that mediate host defense and inflammation, as well as recruit, direct, and regulate adaptive immune responses.

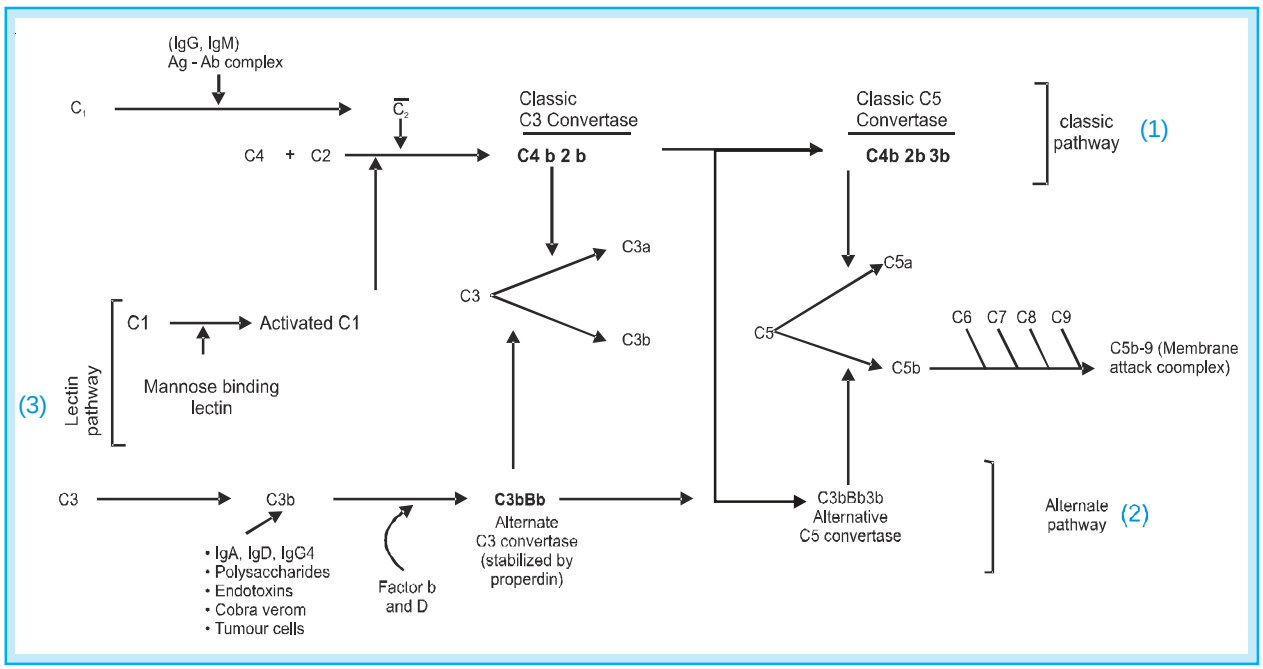
30. Ans. is b i.e. H chain *Ref. Ananthnarayan 7/e, p 86*

It is the class of heavy chain (H) which determines class of Ig. eg. gamma (γ), alpha (α), mu (μ), delta (δ), epsilon (ε) are H chain of IgG, IgA, IgM, IgD, IgE, respectively.

31. Ans. is a i.e. C2, C4, C3 decreased

Ref. Jawetz 23/e, p 136, Harrison 17/e, p 2030; Robbins 7/e, p 66

Complements are activated by 3 pathways.



- *So, in Classic pathway* level of C1 to C9 *decrease while in Alternate pathway* **all complement level decrease** except C1, C2, C4.

32. Ans. is c i.e. IgM *Ref. Harrison 17/e, p 2036*

Already explained, refer answer no. 15

33. Ans. is d i.e. Lymphocytes *Ref. Ananthnaryan 7/e, p 126*

Macrophages	
Activation into	***Differentiation into***
• Activated macrophages • Epitheloid cells • Giant cells (fusion type)	Microglia (CNS) Kupffer (liver) cells Alveolar macrophages (lung) Osteoclast (bone) Sinus histiocytes (spleen and lymph node)

34. Ans. b i.e. IgM fixes complements *Ref. Ananthnaryan 7/e, p 87*

Already explained, refer answer no. 15

35. Ans. is d i.e. Ag-Ab reaction can't occur in absence of electrolytes *Ref. Ananthnaryan 7/e, p 98*

General features of Ag-Ab reaction :

- Reaction is specific, though specificity is not absolute.

- Entire molecule not fragments combine in the presence of electrolytes at specific pH and temperature.
- Combination occur at the ***surface.***
- It is firm but ***reversible.***
- ***Ab*** are generally bivalent while Ag may have valency upto hundred.

Remember these test :

Serological test	Type	Used to diagnose
i. AscolisThermoprecipitin test	Ring precipitation	Anthrax
ii. Lancefield test	Ring precipitation	Grouping of streptococci
iii. Kahn flocculation test	Tube precipitation	Syphilis
iv. VDRL test	Slide precipitation	Syphilis
v. Paul Bunnel test	Tube agglutination	Infectious mononucleosis
vi. Rose waller test	Passive hemagglutination	Rheumatoid arthritis
vii. Widal test	Tube agglutination	Typhoid
viii.Weil Felix test	Heterophile tube agglutintion	Rickettsiae
ix. Wasserman reaction	Complement fixation test	Syphilis

- *Agglutination* (eg. indirect HA) is *more sensitive* than precipitation (eg. gel diffusion test) *for antibody* detection.

36. Ans. is a i.e. IgA *Ref. Ananthnarayan 7/e, p 87*

Already explained, refer answer no. 15

37. Ans. is b i.e. Precipitation *Ref. Ananthnarayan 7/e, p 94 - 101*

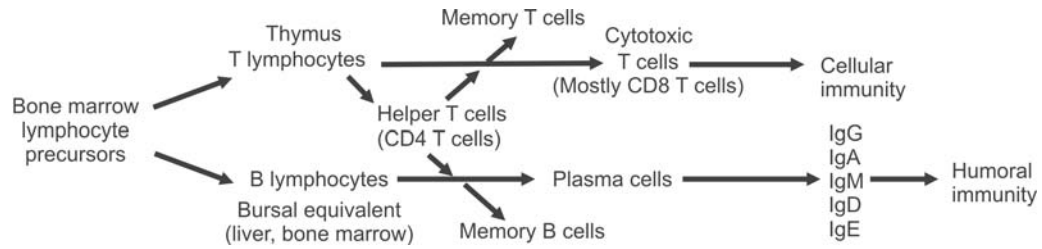
Precipitation	Agglutination	Complement fixation
• Soluble antigen • Antibody • Electrolyte	• Particulate antigen • Antibody • Electrolyte • Hemagglutination is type of agglutination	• Ag (particulate or soluble) • Antibody • Source of complement is guinea Pig serum

38. Ans. is d i.e. Increased in pneumococcal infection *Ref. Ananthnarayan 7/e, p 218*

- **CRP** (beta1 globulin, not antibody) is acute phase reactant (produced in hepatocytes) which is produced in bacterial infections, malignancies, tissue inflammation, rheumatic fever etc (i.e., non specific inflammatory protein).
- CRP is detected by passive agglutinatoin using latex particles.

39. Ans. is a and e i.e. Origin from same cell lineage; further differentiation seen

Ref. Ganong 22/e, p 525



40. Ans. is b i.e. Type - II *Ref. Taylor 3/e, p 107*

Already eplained, refer answer no. 12

41. Ans. is a, c and d I, III and IV *Ref. Taylor 3/e, p 107; Jawetz 24/e, p 142-143*

Already eplained, refer answer no. 12

42. Ans. is c i.e. Antigenic variation *Ref. Harrison 17/e, p 2035*

Learn it

43. Ans. is b and c i.e. Tumor necrosis factor - alpha; and Tumor necrosis factor - beta

"MHC Class genes is classified as Class I, Class II, Class III."

Class III include :

- Soluble protein of complement system
- Properdin factor B of alternative pathway
- TNF alpha and Beta.
- C_2 and C_4 of classical pathway
- Heat shock protein

44. Ans. is d i.e. Schick test *Ref. Ananthnarayan 7/e, p 103*

Neutralization test	
Virus	**Bacteria**
Eg. plaque inhibition test	In vivo eg. Schick test; In vitro ASO test

- Bacterial exotoxin can be neutralized (eg. diptheria, tetanus) while endotoxins can't be neutralized by antitoxin.

45. Ans. is b and c i.e. Fibrinogen; and Haptoglobin *Ref. Ananthnarayan 7/e, p 75; Meharban Singh, p 216*

Acute phase reactants are produced during acute inflammation or certain types of tissues damage. It consist of :

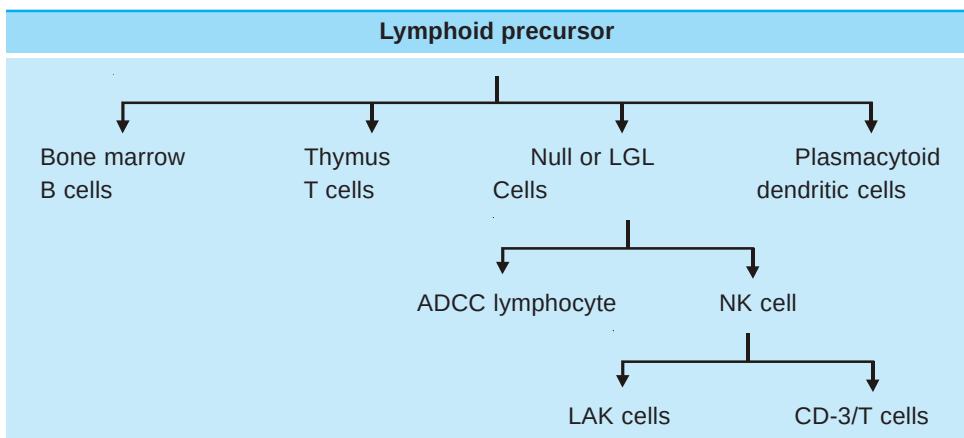
i. C-reactive protein (B_1 globulin)]
ii. α 1 Antitrypsin |
iii. Haptoglobin (α_2 glycoprotein) } ↑ with inflammation
iv. α1 acid glycoprotein (orosomucoid) |
v. Fibrinogen]

vi. Pre-albumin
vii. Transferrin
} Decreased with inflammation

46. Ans. is d and e i.e. Hypervariable region; and Idiotype region *Ref. Harper 24/e, p 746, AN, p 86*

- Each H and L chain of Ig consist of variable (V) region/domain and constant (C) region/domain.
- H has 1 VH and 3(CH1, CH2, CH3) constant region.
- L has 1 V_L and 1C_L region.
- V_H and V_L domain (formed by amino terminal portion) is specific antigen binding region (=Fab) not antibody binding region as given in *Harrison, p 1922*
- V_L and V_H region have hypervariable regions (hot spots=extreme sequence variability) that constitute Ag binding 'Site' (not region) unique to each Ig molecule (at tip).
- L chain has 3 (in V_L) and H chain has 4 (in VH) Hypervariable regions. Also called as complementarity determinig regions (CDRs).
- Idiotype is specific region of Fab portion to which antigen binds.
- CH2 of IgG binds C1q in classical component, CH3 domain mediates adherence to monocyte surface.
- The area of H chain in C region between CH1 and CH2 is hinge region which cleaves by papain to form 1Fc and 2 Fab fragments.

47. Ans. is b i.e. NK cell *Ref. Ananthnarayan 7/e, p 125; Harrison 17/e, p 2024*



48. Ans. is d i.e. Plasma cells *Ref. Ananthnarayan 7/e, p 125*

- **IgE** is antibody and all antibodies are produced by plasma cells which are oval, twice the size of small lymphocyte with eccentric nucleus containing large blocks of chromatin peripherally (cart wheel appearance). They are formed from B cells.
- *Don't Get Confused with Eosinophils* because eosinophils are activated by IgE not produced it.

49. Ans. is a and c i.e. T cells; and Fibroblast *Ref. Robbin's 7/e, p 204*

Antigen presenting cells are :
- Macrophages
- Dendritic cells ***(most potent)***
- Bcells
- Activated T cells.

50. Ans. is a and c i.e. IgG; IgM *Ref. Harrison 17/e, p 2036*

- Classic complement pathway is not activated by IgG4 subtype.
- Alternate complement pathway is activated by IgA, IgD, IgG4.

51. Ans. is a i.e. Cytotoxic T cells *Ref. Robbin's 7/e, p 218*

- CD-8 cytotoxic killer cells secrete soluble mediators like granzymes and perforins (role in Type IV HSN).
- Peforins cause drilling holes in the target cells through which water enter cells, causing osmotic lysis.
- Pores also allow granzymes to enter target cells which activate apoptosis of target cells.

52. Ans. is c i.e. Formed by epithelial cell and plasma cell *Ref. Ananthnarayan 7/e, p 88*

IgA is of two types	**Serum Iga** - ***Monomeric***, synthesized by plasma cells **Secretory IgA** (SIgA) – 2 monomers joined by J chain

- ***J chain*** is synthesized by plasma cells near mucosal or glandular epithelium while secretory component/ secretory piece (glycine rich polypeptide) of SIgA is synthesized by mucosal or glandular epithelial cells not by lymphoid cells.

53. Ans. is b, c and d i.e. Half life of IgG is 23 days; IgD is heat stable; and IgE has highest carbohydrate content *Ref. Ananthnarayan 7/e, p 87*

"IgD has highest percent of carbohydrate but according to Harrison – it is IgE."

Half life of Ig : IgG 23d > IgA 6d > IgM 5d > IgD > IgE.

54. Ans. is c i.e. IgG *Ref. Ananthnarayan 7/e, p 87*

Already explained, refer answer no. 1

55. Ans. is b and d i.e. Beta - 1 globulin; and Non specific inflammatory protein
Ref. Ananthnarayan 7/e, p 218

Already explained, refer answer no. 45

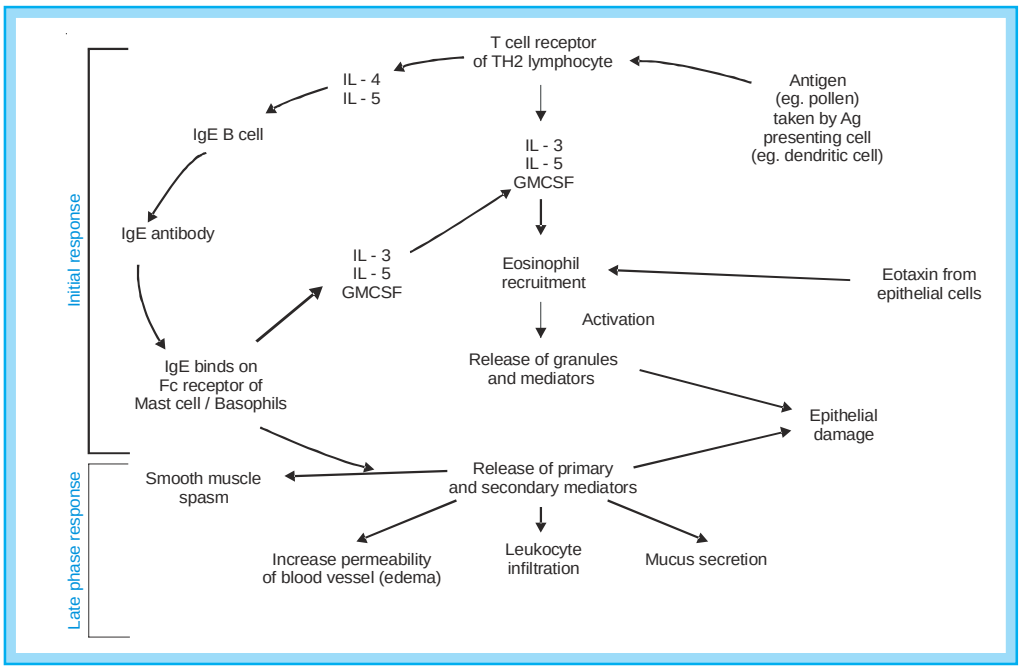
56. Ans. is a i.e. Macrophages *Ref. Ananthnarayan 7/e, p 144; Robbin's 7/e, p 82*

Already explained, refer answer no. 7

57. Ans. is a i.e. Autoimmune hemolytic anemia

HSN involving blood components are usually Type II HSN. [It is not the rule, it is just for remembering]

58. Ans. is a, b, c and d i.e. Type I reaction; Large amount of histamine released; Cytokines like IL-4, IL-5, IL-6, GMCSF are released; and Mediated through allergen specific IgE *Ref. Robbin's 7/e, p 207*



59. Ans. is b i.e. Widal Test *Ref. Ananthnarayan 7/e, p 82*

The same or closely related antigen may sometimes occurs in different biological species / classes etc. It is called ***heterogenetic or heterophile antigen.*** Eg.

- Forssman antigen for pneumococcus, salmonella.
- Paul Bunnel test in infectious mononucleosis.
- Streptococcus MG agglutination.
- Weil felix reaction (between proteus and Rickettsia).
- Cold agglutination test in primary atypical pneumonia.
- Antigen between E. coli & human RBC of b/g B.

Remember : Widal test is tube agglutination test.

60. Ans. is c and d i.e. Antibodies appear in short time; and Persist for long
Ref. Ananthnarayan 7/e, p 134 - 135

Secondary immune response is characterized by :

- Prompt, ***powerful,*** prolonged *response.*
- Much higher level of antibodies that last for *long periods.*
- ***Short,*** negligible *lag* phase.
- Ab is predominantly *IgG.*

61. Ans. is b i.e. inhibits viral replication in cells *Ref. Ananthnarayan 7/e, p 45; Harrison 17/e, p 2025-26*

- **Interferon (host coded protein)** has no direct action on viruses but inhibit viral replication by selectively inhibiting translation of viral m-RNA without affecting cellular m-RNA.
- IFN are not virus specific but species specific.
- It is of 3 types :

	Type	Cell source	Cell Target	Biological activity
•	*IFN α (protein) or leucocyte IFN*	All cells	All cells	Antiviral activity; stimulates T cell, macrophages and NK cell activity
•	*IFN β (glycoprotein) or Fibroblast IFN*	All cells	All cells	Direct antitumour effects Upregulates MHC class I antigen expression Used therepeutically in viral and autoimmune disease
•	*IFNγ (glycoprotein) or immune IFN*	Tcells NK cells	All cells	Regulate macrophage and NK cells activation Stimulates Ig secretion by B cells Induction of class II Histocompatibility antigens TH1 T cell differentiation

62. Ans. is a i.e. Polysaccharide *Ref. Ananthnarayan 7/e, p 81*

- *Most* naturally Ag are ***proteins*** and ***polysaccharides.***
- Protein are better Ag than polysaccharides.
- All proteins *except* ***gelatin*** is antigenic.
- Lipids and nucleic acids are also less antgenic so their antigenicity is increased by combining with proteins.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. The use of monoclonal antibodies is : [PGI 90]

a) Immunotherapy
b) Immunological identification of cells and tissues
c) Radioimmunoimaging
d) All of the above

[Ref. Ananthnarayan 7/e, p 105 - 106; Harrison 17/e, p 2043]

2. Most sensitive test for antigen detection is :

a) RIA **[PGI 90]**
b) ELISA
c) Immunoflurescence
d) Passive hemaglutination

[Ref. Ananthnarayan 7/e, p 105]

3. Function of T-lymphocyte is/are :

a) Production of interferon **[TN 90]**
b) Lymphokine production
c) Rosette formation
d) All of the above

[Ref. Ananthnarayan 7/e, p 124, 143]

4. Binary (Secondary) exposure to an antigen results in sudden increase in : [TN 90]

a) IgA
b) IgD
c) IgG
d) IgM

[Ref. Park 19/e, p 95]

5. Reaction of Soluble antigen with antibody is known is : [AI 90]

a) Agglutination
b) Precipitation
c) Flocculation
d) Complement fixation

[Ref. Ananthnarayan 7/e, p 94]

6. Monoclonal antibodies are associated with name of : [Orrisa 91]

a) Medwar
b) Oven
c) Burner
d) Pasteur

[Ref. Ananthnarayan 7/e, p 150]

7. NK cells are : [DNB 91]

a) Activated macrophages
b) Antibody-activated T cells
c) Null cells activated by complement
d) Derived from plasma cells
e) Independent of antibody

[Ref. Ananthnarayan 7/e, p 126]

8. T-cell mature in : [Kerala 91]

a) Peyers patch
b) Lymph node
c) Thymus
d) Bursa of fabricius

[Ref. Ananthnarayan 7/e, p 128]

9. The prototype of type -II hypersensitivity reaction is : [Kerala-91]

a) Arthus reaction
b) SLE
c) Auto immune hemolytic anemia
d) Contact dermatitis

[Ref. Robbin's 7/e, p 210]

10. T4/T8 ratio reversal is seen in : [JIPMER 91]

a) T-cell lymphoma
b) Hairy cell leukemia
c) AIDS
d) Infectious mononucleosis

[Ref. Ananthnarayan 7/e, p 588]

Answer

1. d) All of the ... 2. a) RIA 3. d) All of the ... 4. d) IgM 5. b) Precipitation
6. c) Burner 7. d) Derived ... 8. c) Thymus 9. c) Auto immune ... 10. c) AIDS

11. Leukotrienes are secreted by all except :
a) Macrophages **[JIPMER-91]**
b) T4 cells
c) T8 cells
d) Platelets
[Ref. Ananthnarayan 7/e, p 163]

12. An example of type-I hypersensitivity reaction is :
a) Schicks test **[AI 92]**
b) Mantoux test
c) Lepromin test
d) Casoni's test *[Ref. Paniker 6/e, p 154]*

13. HLA typing is useful in : [JIPMER 92]
a) Blood gruoping
b) Assesing prognosis of disease
c) Cancer therapy
d) Cases of paternal dispute
[Ref. Ananthnarayan 7/e, p 132]

14. T-cell functions are assesed by : [AIIMS 92]
a) Phagocytic index
b) T-cell count
c) Migration inhibition test
d) Immunoglobulin index
[Ref. Park 18/e, p 258]

15. N.K. cell and cytotoxic cells are differentiated by :
a) Interferons reduce N.K. cell activity
b) Antibody specificity **[JIPMER 92]**
c) Receptor for IgG
d) Presence in spleen
[Ref. Robbin's 7/e, p 198-202]

16. The main aim of an adjuvant is to increase :
a) Distribution **[JIPMER 92]**
b) Absorption
c) Antigenicity
d) Metabolism
[Ref. Ananthnarayan 7/e, p 140]

17. Delayed hypersensitivity involves : [AIIMS 92]
a) Neutrophils
b) Monocyts
c) Eosinophils
d) Lymphocytes *[Ref. Robbin's 7/e, p 206]*

18. Which is an example of type-III hypersenstivity :
a) Contact dermatitis **[Karn. 92]**
b) Hemolytic anemia
c) Serum sickness
d) Good pasture's syndrome
[Ref. Robbin's 7/e, p 211-212]

19. Interferon : [PGI 93]
a) Is species specific
b) Reacts directly with virus particles to inactivate them
c) Reacts with cells, and the affected cell then become resistant to a number of different viruses
d) To constitutively produced at high levels in cells but requires an inducer for activity
[Ref. Ananthnarayan 7/e, p 454, 455]

20. Rossette formation with sheep RBC's indicate functioning of : [Delhi 93]
a) T-cells
b) B-cells
c) Neutorphils
d) Monocytes
[Ref. Ananthnarayan 7/e, p 123]

21. Secretory piece of IgA is synthesised in :
a) T-cells **[PGI 93]**
b) B-cells
c) Lymph nodes
d) Mucosal epithelium
[Ref. Ananthnarayan 7/e, p 88]

22. Life long immunity is seen in all of the following except : [PGI 93, Bihar 93]
a) Pertusis
b) Mumps
c) Rubella
d) Plague
[Ref. Park 19/e, p 245]

23. Prozone phenomenon is due to : [AI 93]
a) Disproprotionate antigen-antibody levels
b) Excess antigen
c) Excess antibody
d) Hyper immune reaction
[Ref. Ananthnarayan 7/e, p 94]

24. N.K. cells provides immunity agianst :
a) Virus **[Jipmer 93]**
b) Bacteria
c) Fungus
d) Chlamydia
[Ref. Harrison 17/e, p 2028]

25. Anti-Rh antibodies belong predominantly to :
a) IgG1 **[JIPMER 93]**
b) IgG2
c) IgG3
d) IgG4
[Ref. Under consideration]

Answer

11. d) Platelets	12. d) Casoni's ...	13. d) Cases of ...	14. c) Migration ...	15. d) Presence ...
16. c) Antigenicity	17. d) Lymphocytes	18. c) Serum ...	19. a and c	20. a) T-cells
21. d) Mucosal ...	22. d) Plague	23. c) Excess ...	24. a) Virus	25. a) IgG1

26. T-cell multiplication is stimulated by : [AI 93]
a) Macrolin
b) Heat
c) Bovine serum
d) Phytohemagglutin
[Ref. Ananthnarayan 7/e, p 123]

27. Type of Receptor present on T-cells are : [AI 93]
a) IgA
b) IgG
c) Prostaglandins
d) CD4
[Ref. Robbin's 7/e, p 197]

28. Helper Cells belong to : [AI 93]
a) Macrophages
b) T-cells
c) B-cells
d) Monocytes
[Ref. Ananthnarayan 7/e, p 124]

29. T-cell are identified by : [Kerala 94]
a) Rosette formation with sheep RBC
b) Immunoglobulins on their surface
c) EAC Rossette with sheep erythrocytes
d) Have filamentous projections on their surface
[Ref. Ananthnarayan 7/e, p 123]

30. Contact dermatitis is : [Kerala 94]
a) Type-I hypersensitivity
b) Type-II hypersensitivity
c) Type-III hypersensitivity
d) Type-IV hypersensitivity
[Ref. Robbin's 7/e, p 217]

31. Humoral graft rejection is characterised by :
a) Intense mononuclear infiltration **[Kerala 94]**
b) Neovascularisation of grafted tissue
c) Thrombosis of the blood vessels and ischemic necrosis
d) Monocytic infiltration
[Ref. Robbin's 7/e, p 220]

32. Insitu hypridisation is used for : [Kerla 94]
a) Diagnosis of specific genetic disease
b) Diagnosis of enzyme dificiency disease
c) Treatment of genetic diseases
d) All of the above
[Ref. Harrison 17/e, p 408]

33. Active immunity is not acquired by : [Kerla 94]
a) Infection
b) Vaccination
c) Immunoglobulin transfer
d) Sub-clinical infection
[Ref. Ananthnarayan 7/e, p 77]

34. Opsonisation is by : [Kerala 94]
a) IgA
b) IgE
c) IgG
d) IgM
[Ref. Ananthnarayan 7/e, p 89]

35. Lysozyme is present in the following secretions of the body except : [Karnat 94]
a) Lacrimal secretions
b) CSF
c) Saliva
d) Respiratory tract secretions
[Ref. Ananthnarayan 7/e, p 73]

36. Most common infections after splenectomy are :
a) Capsulated bacteria **[JIPMER 95]**
b) Uncapsulated bacteria
c) Gram positive sepsis
d) Gram Negative bacteria
[Ref. Harrison 17/e, p 375]

37. VDRL is a : [TN 95]
a) Slide fiocculation test
b) Tube flocculation test
c) Gel precipitation
d) Indirect haemaglutination test
[Ref. Ananthnarayan 7/e, p 95]

38. The process increasing the ability for phagocytosis of foreign bodies by body is called :
a) Cross reactivity **[JIPMER 95]**
b) Opsonisation
c) Immune Tolerance
d) Immune Surveiliance
[Ref. Robbin's 7/e, p 59]

39. Hep-2 cells are a type of : [Karn 95]
a) Primary cell culture
b) Diploid cell lines
c) Continous cell lines
d) Explant culture
[Ref. Ananthnarayan 7/e, p 441]

40. M band is absent in : [PGI 95]
a) IgG myeloma
b) IgM myeloma
c) IgA myeloma
d) Light chain disease
[Ref. Ananthnarayan 7/e, p 90]

Answer
26. d) Phytohemagglutin 27. d) CD4 28. b) T-cells 29. a) Rosette ... 30. d) Type-IV ...
31. c) Thrombosis ... 32. a) Diagnosis ... 33. c) Immunoglo ... 34. c) IgG 35. b) CSF
36. a) Capsulated ... 37. a) Slide ... 38. b) Opsonisation 39. c) Continous ... 40. d) Light chain ...

41. Secondary response is mediated by : [UP 95]
a) IgG
b) IgM
c) IgE
d) IgA

[Ref. Park 19/e, p 95]

42. Virus infected cell is killed by : [Kerala 96]
a) Interferons
b) Macrophages
c) Neutrophils
d) Autolysis
e) None of the above

[Ref. Ananthnarayan 7/e, p 454, 455]

43. Phagocytosis enhanced by coating the surface of antigen is called : [Kerala 96]
a) Opsonisation
b) Chemotaxis
c) De coding
d) CFT

[Ref. Ananthnarayan 7/e, p 59]

44. The following are true for T lymphocytes except :
a) Consitute 70 to 80% of circulating pool of lymphocytes **[Karnat 96]**
b) Release macrophage inhibition factor
c) Secrete specific antibodies
d) Release lymphotoxin

[Ref. Ananthnarayan 7/e, p 119]

45. The reagnic antibody is : [Karnat 96]
a) IgA
b) IgD
c) IgE
d) IgG

[Ref. Ananthnarayan 7/e, p 90]

46. The commonest IgG with maximum individual variation is : [PGI 96]
a) IgG 1
b) IgG 2
c) IgG3
d) IgG 4

[Ref. NMS Immunology]

47. Blood tranfusion mismatch in erythroblastosis foetalis is a type of : [NIMS 96]
a) Atopic hypersensitivity
b) Cytotoxic type
c) Arthus phenomenon
d) Delaled hypersensistivity

[Ref. Robbins's 7/e, p 210]

48. Antigen recoginition on the surface of antigen processing cells is by : [Delhi 96, PGI 90]
a) T- cell recognition antigen
b) Fc protion of immunoglobulin
c) Fab protion of immunoglobulin
d) Cell recognition antigen

[Ref. Robbin's 7/e, p 200]

49. Immune granulomas are not seen in :
a) Tuberculosis **[Kerala 97]**
b) Syphilis
c) Silicosis
d) Berryliosis

[Ref. Robbin's 7/e, p 82 - 83]

50. Animal used to demonstrate anaphylaxis in the lab is : [JIPMER 98]
a) Rabbit
b) Adult mice
c) Monkey
d) Guinea pig

[Ref. Ananthnarayan 7/e, p 161]

51. Opsonins are : [MP 98]
a) C_3a
b) C_3b
c) C_5a
d) C_5-C_9 complex

[Ref. Robbin's 7/e, p 59]

52. Which of the following cytokinin is secreted by T helper cells except : [UP 98]
a) IL_1
b) IL_2
c) IL_4
d) IL_5

[Ref. Ananthnarayan 7/e, p 144]

53. Agglutination test is : [UP 98]
a) ABO incompatibility
b) VDRL
c) Weil Felix
d) FTA-AB

[Ref. Ananthnarayan 7/e, p 99]

54. IgA secretion is seen in : [UP 98]
a) Tears and saliva
b) CSF
c) Hairs
d) Vaginal fluid

[Ref. Ananthnarayan 7/e, p 88]

Answer

41. a) IgG	42. a) Interferons	43. b) Chemotaxis	44. b and c	45. c) IgE
46. b) IgG 2	47. b) Cytotoxic ...	48. b) Fc protion ...	49. c) Silicosis	50. d) Guinea pig
51. b) C_3b	52. a) IL_1	53. c) Weil Felix	54. a) Tears and ...	

55. All of the following are immune complex disease except : [GUPGEE 99]

a) Serum sickness
b) Farmer's lungs
c) SLE
d) Graft rejection

[Ref. Robbin's 7/e, p 211, 212]

56. When an antigen is administered for the first time to animal or a human being who has never been exposed to it, the first antibody to develop : [DNB 99]

a) IgG type
b) IgM type
c) IgA type
d) IgE type

[Ref. Park 19/e, p 95]

57. Antigen combining site of the antibody is : [TN 99]

a) Idiotype
b) Paratope
c) Epitope
d) Hapten

[Ref. Ananthnarayan 7/e, p 81]

58. Most important inflammatory mediator : [UP 99]

a) TNF
b) IL2
c) Interferon
d) PAF

[Ref. Robbin's 7/e, p 71]

59. Pentameric structure : [JIPMER 99]

a) IgM
b) IgG
c) IgA
d) IgD

[Ref. Ananthnarayan 7/e, p 89]

60. Interleukin - 7 produced by which one of the following : [Kerla 00]

a) Macrophages
b) B cells
c) T cells
d) Dendritic cells
e) Stromal cells

[Ref. Ananthnarayan 7/e, 144]

61. Group B cell lymphocyte belongs to : [UP 00]

a) CD-19
b) CD-69
c) CD-59
d) CD-68

[Ref. Ananthnarayan 7/e, p 124]

62. Defference between natural killer and cytotoxic cells is : [UP 00]

a) Interferons decreased natural killer actvity
b) NK has CD4
c) Cytotoxic cell lyse IgG coated target cells
d) NK contain azurophilic cytoplasmic granulocyte

[Ref. Ananthnarayan 7/e, p 126]

63. The exact part of the antigen that reacts with the immune system is called as : [Karnat 01]

a) Clone
b) Epitope
c) Idiotope
d) Effector

[Ref. Ananthnarayan 7/e, p 82]

64. Which of the following cells is known as large granular lymphocyte (LGL) : [Karnat 01]

a) Plasma cells
b) NK cells
c) T cells
d) K cells

[Ref. Ananthnarayan 7/e, p 126]

65. Which leukotriene is the adhesion factor for the neutorphill on the cell surface to attach to endothelium : [Kerala 01]

a) B4
b) C4
c) D4
d) E4

[Ref. Robbin's 7/e, p 69 Table (2.4)]

66. Rapid serological diagnostic test include all except : [UP 01]

a) Latex agglutination
b) Spectrophotometry
c) Gel electrophoresis
d) Radiommunpassay

[Ref. Under consideration]

67. Immunoglobulin found in B lymphocyte : [UP 01]

a) IgA
b) IgE
c) IgG
d) IgD

[Ref. Ananthnarayan 7/e, p 124]

68. Delayed tuberculin test response is due to : [TN 01]

a) B lymphocytes
b) T lymphocytes
c) Monocytes
d) Histocytes

[Ref. Robbin's 7/e, p 217]

Answer

55. d) Graft rejection
56. b) IgM type
57. b) Paratope
58. a) TNF
59. a) IgM
60. e) Stromal cells
61. a) CD-19
62. d) NK contain ...
63. b) Epitope
64. b) NK cells
65. a) B4
66. b) Spectrophoto ...
67. d) IgD
68. b) T lymphocytes

69. Variable protion of antibody molecule is :
a) C-terminal **[UP 01]**
b) N-terminal
c) Intermediate region
d) Carbohydrate moiety
[Ref. Ananthnarayan 7/e, p 86]

70. Phagocytic cells elaborate : **[JIPMER 01]**
a) Prostaglandins
b) Thromboxane
c) Leukotrienes
d) All of the above
[Ref. Robbin's 7/e, p 68]

71. Portion of immunoglobulin molecule with molecular weight of 50,000 : **[JIPMER 01]**
a) Secretory Piece
b) H chain
c) L chain
d) J peice
[Ref. Ananthnarayan 7/e, p 85]

72. Function of IgA is : **[Kerla 01]**
a) Acts as a mucosa barrier for infection
b) Circulating antibody
c) Kills virus infected cells
d) Activates macrophages
e) Cause delayed hyper sensitivity reaction
[Ref. Ananthnarayan 7/e, p 88, 89]

73. Runt disease is : **[TN 02]**
a) Graft rejection
b) Graft versus host treaction
c) Deficient T cell function
d) Complement dificiency
[Ref. Ananthnarayan 7/e, p 118]

74. The following constitutes approximately 75% of total immunoglobin in hymans : **[Karnat 02]**
a) IgG
b) IgM
c) IgE
d) IgA
[Ref. Ananthnarayan 7/e, p 87]

75. Virus infected cells are killed by : **[MP 02]**
a) Macrophages
b) Complement system
c) MHC II related cells
d) NK cells
[Ref. Ananthnarayan 7/e, p 126]

76. The immunoglobin that can cross the placenta :
a) IgG [SGPGI 03]
b) IgA
c) IgE
d) IgM
[Ref. Ananthnarayan 7/e, p 88]

77. HLA III gene codes in graft rejection : **[MP 03]**
a) Immunological raection in graft rejection
b) Complement
c) Graft virsus host reaction
d) Immunoglobulins
[Ref. Ananthnarayan 7/e, p 129]

78. Structure of antibodies is composed of : **[UP 03]**
a) Single peptide chain
b) Two peptide chain
c) Non sulphur amino acid
d) 2 long and 2 short peptide chain
[Ref. Ananthnarayan 7/e, p 85]

79. IL-2 is produced by : **[SGPGI 04]**
a) T cells (CD4 cells)
b) B cells
c) Monocytes
d) Neutrophils
[Ref. Ananthnarayan 7/e, p 144]

80. Dieorge syndrome is characterized by all except :
a) Congenital thymic hypoplasia **[SGPGI 04]**
b) Abnormal developmental of third and fourth pouches
c) Hypothyroidism
d) Hypocalcemic tetany
[Ref. Ananthnarayan 7/e, p 155]

81. CD4 are associated with : **[UP 04]**
a) Helper T cell
b) Sypressor T cells
c) NK cells
d) T cells antigen receptor complex
[Ref. Ananthnarayan 7/e, p 129]

82. All the following types of hypersensitivity reactions can be demonstrated by skin test except :
a) Type I **[UP 04]**
b) Type II
c) Type III
d) Type IV
[Ref. Robbin's 7/e, p 206 Table (6.2)]

Answer

69. b) N-terminal	70. a and c	71. b) H chain	72. a) Acts as a ...	73. c) Deficient T ...
74. a) IgG	75. d) NK cells	76. a) IgG	77. b) Complement	78. d) 2 long and ...
79. a) T cells ...	80. c) Hypothyroi...	81. a) Helper T ...	82. b) Type II	

83. Isoantigens are : **[UP 05]**
a) Found in some but all members of species
b) Found in some but not all members of species
c) Occurs in different biological species, class and kingdoms
d) All individuals in a particular species
[Ref. Ananthnarayan 7/e, p 82]

84. Paul Bunnal antibodies are reactive in all except :
a) OX **[SGPGI 05]**
b) Sheep
c) Dog
d) Horse
[Ref. Ananthnarayan 7/e, p 484]

85. Antibodies are most responsive to : **[SGPGI 05]**
a) Recipients tissue
b) Donor tissue
c) Isografts
d) Allograft
[Ref. Ananthnarayan 7/e, p 84]

86. First immunoglobin to appear following infections:
a) IgG **[SGPGI 05]**
b) IgM
c) IgA
d) IgE
[Ref. Park 19/e, p 95]

87. Phagocytic function is assessed by : **[MP 06]**
a) Proliferative response to mitogen
b) Reduction of NBT (Nitroblue tetrazolium test)
c) Serum Immunoglobulin assay
d) Skin test with purified protein derivative
[Ref. Harrison 17/e, p 381]

88. The exact part of the antigen that reacts with immune system is called as : **[Kar 01]**
a) Clone
b) Epitope
c) Idiotype
d. Effector
[Ref. Ananthnaranay 7/e, p 80]

89. Which of the following cells is knows as large grnaular lymphocyte ? **[Kar 01]**
a) Plasma cells
b) NK cells
c) K cells
d) T cells
[Ref. Ananthnarayan 7/e, p 126]

90. Which of the following is a flocculation test :
a) Widal test **[Kar 01]**
b) Weil-felix test
c) VDRL
d) Paul-Bunnell test
[Ref. Ananthnarayan 7/e, p 381]

91. Transplantation of the hosts own tissue is known as : **[Kar 01]**
a) Isograft
b) Allograft
c) Xenograft
d) Autograft *[Ref. Learn it]*

92. Pro-inflammatory cytokines include all except :
a) Interlukin 1 **[Kar 01]**
b) Interleukin 2
c) Interleutkin 6
d) TNF-alfa *[Ref. Harrison 17/e, p 1156]*

93. Delayed hypersensitivity reaction is mediated b the following : **[Kar 02]**
a) B lymphocytes
b) NK cells
c) Mast cells
d) T lymphocytes
[Ref. Ananthnarayan 7/e, p 166]

94. The following constitutes approximately 75% of total immunogobulin in humans : **[Kar 02]**
a) IgG
b) IgM
c) IgE
d) IgA
[Ref. Ananthnarayan 7/e, p 87]

95. Which immunoglobulin is least important in human beings: **[Kolkata 03]**
a) IgE
b) IgD
c) IgG
d) IgA
[Ref. Ananthnarayan 7/e, p 90]

96. Chemoattractant is : **[Jharkhand 03]**
a) C5a
b) C1
c) C3
d) C2 *[Ref. Robbin's 7/e, p 56]*

97. Complement C5-C9 predispose to which infection
a) Menigococi **[Jharkhand 03]**
b) Pneumococcal
c) Pseudomonas
d) All
[Ref. Harrison 17/e, p 911]

Answer

83. b) Found in...	84. a) OX	85. b) Donor	86. b) IgM	87. b) Reduction ...
88. b) Epitope	89. b) NK cells	90. c) VDRL	91. d) Autograft	92. b) Interleukin 2
93. d) T lymphocytes	94. a) IgG	95. b) IgD	96. a) C5a	97. a) Meningococci

98. Opsonization occurs due to : **[Bihar 04]**
a) Endotoxin
b) Complement
c) IgM
d) IgG
[Ref. Aanthnarayan 7/e, p 104]

99. Primary immune response is mediated by :
a) IgE **[Jharkhand 04]**
b) IgM
c) IgA
d) IgD
[Ref. Park 19/e, p 95]

100. Which is not pyrogenic IL : **[Kolkata 05]**
a) IL – 1
b) TNF-
c) IL – 4
d) IL – 6
[Ref. Harrison 17/e, p 119]

101. First antibody response is mediated by :
a) IgD **[Jharkhand 05]**
b) TgM
c) IgA
d) IgE
[Ref. Park 19/e, p 95]

102. Tuberculin test is reaction of : **[UP 06]**
a) Anaphyxis mediated
b) Cell mediated
c) Antibody mediated
d) Immuno complex mediated
[Ref. Ananthnarayan 7/e, p 166]

103. Antibody transfer mother to fetus is :
a) IgG **[Bihar 06]**
b) IgM
c) IgD
d) IgA
[Ref. Ananthnarayan 7/e, p 87]

104. Atopy is mediated by : **[Jharkhand 06]**
a) IgE
b) IgD
c) IgM
d) IgA
[Ref. Anantharayan 7/e, p 164]

105. All are type-II hypersensitivity reaction except :
a) Hemorrhagic disease of newborn
b) Grave's disease **[Jharkhand 06]**
c) Autoimmune diseases
d) Hemolytic anemia
[Ref. Anantharayan 7/e, p 161]

106. Humoral antibody arises from :
a) T cell **[Jharkhand 06]**
b) B cell
c) Null cell
d) K cell
[Ref. Anantharayan 7/e, p 133]

Answer 98. b) Complement 99. b) IgM 100. a, b and c 101. b) TgM 102. c) Antibody ...
103. None 104. a) IgE 105. a) Hemorrhagic ... 106. b) B cell

NOTES

MISCELLANEOUS

Miscellaneous

QUESTIONS

1. Which of the following is not transmitted by soil ?

a) Coccidiodomycosis **[AI 08]**
b) Tetanus
c) Brucella
d) Anthrax

2. Isolation is not useful for all except : **[AI 08]**

a) Mumps
b) Measles
c) Hepatitis A
d) Pneumonic plague

3. Congenital infection affecting fetus with minimal teratogenic risk is : **[AI 08]**

a) HIV
b) Rubella
c) Varicella
d) CMV

4. Which of the following congenital infection leads to maximum CNS damage in the fetus : **[AI 08]**

a) Rubella and CMV
b) Rubella and toxoplasmosis
c) CMV and toxoplasmosis
d) HIV and CMV

5. With reference to Bacteroides fragilis the following statements are true except :

a) B. fragilis is the most frequent anaerobe isolated from clinical samples **[AI 07; AIIMS 06]**
b) B. fragilis is not uniformly sensitive to metronidazole
c) The lipopolysaccharide formed by B.fragilis is structurally and functionally different from the conventional endotoxin
d) Shock and disseminated intravascular coagulation are common in Bacteroides bacteremia

6. Which of the following is least likely to cause infective endocarditis : **[AI 06]**

a) Staphylococcus albus
b) Streptococcus faecalis
c) Salmonella typhi
d) Pseudomonas aeruginosa

7. A 40 years old woman presented to the gyencologist with complaint of profuse vaginal discharge. There was no discharge from the cervical os on the the speculum examination. The diagnosis of bacterial vaginosis was made based upon all of the following findings on microscopy except : **[AI 06]**

a) Abundance of gram variable coccobacilli
b) Absence of Lactobacilli
c) Abundance of polymorphs
d) Presence of clue cells

8. Apart from Escherichia coli, the other most common organism implicated in acute suppurative bacterial peritonitis is : **[AI 06]**

a) Bacteroides
b) Klebsiella
c) Peptostreptococcus
d) Pseudomonas

Answer

1. c) Brucella
2. d) Pneumonic ..
3. a) HIV
4. c) CMV and....
5. d) Shock and ...
6. c) Salmonella ...
7. c) Abundance ...
8. b) Klebsiella

9. Virus mediated transfer of host DNA from one cell to another is known is : [AI 05]

a) Transduction
b) Transformation
c) Transcription
d) Integration

10. All of the following organisms are known to survive intracellularly except : [AI 05]

a) Neisseria meningitides
b) Salmonella typhi
c) Streptococcus pyogenes
d) Legionella pneumophilia

11. Virus can be isolated from clinical samples by cultivation in the following except : [AI 05]

a) Tissue culture
b) Embryonated eggs
c) Animals
d) Chemically defined media

12. It is true regarding the normal microbial flora present on the skin and mucous membranes that:

a) It cannot be eradicated by by antimicrobial agents
b) It is absent in the stomach due to acidic pH
c) It establishes in the body only after the neonatal period **[AI 05]**
d) The flora in the small bronchi is similar to that of the trachea

13. The most common pathogens responsible for nosocomial pneumonia in the ICU : [AI 05]

a) Gram positive organism
b) Gram -ve organism
c) Mycoplasma
d) Virus infections

14. Which of the following toxins acts by inhibiting protein synthesis : [AI 04]

a) Cholera toxin
b) Shiga toxin
c) Pertusis toxin
d) LT of Enterotoxigenic E. coli

15. Toxins are implicated the major pathogenic mechanism in all of the following bacterial diarrheas except : [AI 04]

a) Vibrio cholerae
b) Shigella sp.
c) Vibrio parahaemolyticus
d) Staphylococcus aureus

16. All of the following infections are often associated with acute intravascular hemolysis except : [AI 03; AIIMS 03]

a) Clostridium tetani
b) Bartonella bacilliformis
c) Plasmodium falciprum
d) Babesia microti

17. Bacteria may acquire characteristics by all of the following except : [AI 02]

a) Taking up soluble DNA fragments across their cell wall from other species
b) Incorporating part of host DNA
c) Through bacteriophages
d) Through conjugation

18. Heat stable enterotoxin causing food poisoning is caused by all the following except : [AI 02]

a) Bacillus cereus
b) Yersinia enterocolitica
c) Staphylococcus
d) Clostridium perfringens

19. All of the following are sexually transmitted except : [AI 02]

a) Candida albicans
b) Echinococcus
c) Molluscum contagiosum
d) Group B streptococcus

20. All of the following infections may be transmitted via blood transfusion except : [AI 02]

a) Parvo B-19
b) Dengue virus
c) CMV
d) Hepatitis G virus

21. The following diagnostic tests are useful for corresponding purpose except : [AI 02]

a) Zeihl Nelson staining - Detection of mycobacteria
b) Immunoflorescence - Detection of Influenza virus
c) Specific IgM antibodies - Immunity against Rubella
d) Specific IgM antibodies - Detection of acute infection

22. Cystine lactose enzyme deficient medium CLED is preferred over McConkey agar in UTI because:

a) Former prevents swarming of proteus **[AI 01]**
b) Is a selective medium
c) Promotes growth of pseudomonas
d) Promotes growth of Candida and Staphylococcus

Answer

9. a) Transduction ... 10. c) Streptococcus ... 11. d) Chemically ... 12. c) It establishes ... 13. b) Gram -...
14. b) Shiga ... 15. c) Vibrio ... 16. a) Clostridium ... 17. b) Incorporating ... 18. d) Clostridium ...
19. b) Echinococcus 20. b) Dengue virus 21. c) Specific ... 22. d) Promotes ...

23. All of the following bacteria test "Urease positive" except : [AI 98]
a) E. coli
b) Proteus
c) Kleibsella
d) Staphylococcus

24. Plaque formation in virus is done for : [AI 98]
a) Isolation and typing of viurses
b) Cloning separation of specific viruses
c) Determining infectivity of virus
d) Assessing multiplication of virus

25. Bacterial genome has been completely recognised for which one of the following agents:
a) H. pylori [AI 98]
b) Yersinia enterocolitis
c) Campylobacter jejuni
d) Streptococcus

26. Most common agents responsible, for human, bite infections are : [AI 98]
a) Gram -ve bacilli
b) Gram +ve bacilli
c) Spirochaete
d) Anaerobic streptococci

27. Which bacteria acts by inhibiting protein synthesis : [AI 98]
a) Pseudomonas
b) Staphylococcus
c) Streptococcus
d) Kleibsiella

28. Prokaryotes are characterised by : [AI 97]
a) Absence of nuclear membrane
b) Presence of microvilli on its surface
c) Presence of smooth endoplasmic reticulum
d) All of the above

29. A substance, when added to a culture causes inhibition of multiplication but on removal causes enhanced growth. This substance is called :
a) Bacteriostatic [AI 96]
b) Bactericidal
c) Sterilization
d) Bacteriophage

30. Reactive arthritis is caused by : [AIIMS 08]
a) Staphylococcus
b) H. influenzae
c) N. gonorrhoe
d) Chlamydia trachomatus

31. HACEK group includes all of the following except:
a) Hemophilus arophilus [AIIMS 08]
b) Acinetobacter baumanni
c) Eikenella corrodens
d) Cardiobacterium hominis

32. Cy Bromide green dye is used for : [AIIMS 06]
a) HLPR
b) PCR
c) ELISA
d) Immunofluroscence

33. The single most common cause of pyrexia of unknown origin is : [AIIMS 06, 03]
a) Mycobacterium tuberculosis
b) Salmonella typhi
c) Brucella sp.
d) Salmonella paratyphi A

34. In the gut, anaerobic bacteria outnumber the aerobes by a ratio of : [AIIMS 06]
a) 10 : 1
b) 100 : 1
c) 1000 : 1
d) 10,000 : 1

35. In all of the following diseases chronic carriers are found except : [AIIMS 06]
a) Measles
b) Typhoid
c) Hepatitis B
d) Gonorrhoea

36. A 30 year old male present with urethritis. All of the following can be causative agent except :
a) N. gonorrhoeae [AIIMS 04]
b) Chalmydia trachomatis
c) Trichomonas vaginalis
d) Hemophilus ducreyi

37. Humoral immunodeficiency is suspected in patient and he is under investigation. Which of the following infections would be consistent with the diagnosis : [AIIMS 04]
a) Giardiasis
b) Pneumocystics carinii pneumonia
c) Recurrent sinusitis
d) Recurrent subcutaneous abscess

Answer

23.	a) E. coli	24.	c) Determining ...	25.	a) H. pylori	26.	d) Anaerobic ...	27.	a) Pseudomonas
28.	a) Absence ...	29.	a) Bacteriostatic	30.	d) Chlamydia ...	31.	b) Aconetobacter .	32.	b) PCR
33.	a) Mycobacteri ...	34.	c) 1000 : 1	35.	a) Mealses	36.	d) Hemophilus ...	37.	b) Pneumocyst ...

38. All the following are most common nosocomial infection except : [AIIMS 03]

a) Staph. aureus
b) P. aeroginosa
c) Enterobacteriaceae
d) Mycobacterium

39. The following phenomenon is responsible for antibiotic resistance in bacteria due to slime production : [AIIMS 03]

a) Co-aggregation
b) Biofilm formation
c) Mutation involving an altered target site for antibiotics
d) Mutation involving a target bypass mechanism

40. With reference to Bacterioides fragilis all of the following statement are true except : [AIIMS 03]

a) It is the most frequent anaerobe isolated from clinical sample
b) It is not uniformly sensitive to metronidazole
c) The lipopolysaccharide formed by B. fragilis is structurally and functionally different from conventional endotoxin
d) Shock and DIC are common in bacteremia due to B. fragilis

41. A patient present with frontal abscess. Foul smelling. pus is aspirated. Pus shows red. Fluorenscence on ultraviolet examination. The most, likely organism causing the frontal abscess is :

a) Bacteriodes [AIIMS 02]
b) Peptostreptococcus
c) Pseudomonas
d) Acanthamoeba

42. In a patient with UTI, CLED (Cysteine lactose electrolyte deficient) Media is preferred over MacConkey's media because : [AIIMS 01]

a) It is a differential medium
b) It inhibits swarming of proteus
c) Promotes growth of pseudomonas
d) Promotes growth of S. aureus and Candida

43. Preformed toxin is important in food poisoning due to all except : [AIIMS 01]

a) S. aureus
b) Clostridium botulism
c) ETEC
d) B. cereus

44. Endotoxin from gram negative organism is :

a) Polysaccharide [AIIMS 00]
b) Glycoprotein
c) Lipoprotein
d) Lipo-polysaccharide

45. Most common tumour caused by virus is :

a) Warts [AIIMS 97]
b) Carcinoma cervix
c) Nasopharyngeal carcinoma
d) Lymphoma

46. Which is not an oncogenic virus : [AIIMS 97]

a) HTLV-1
b) Herpessimplex
c) Papilloma virus
d) HBV

47. Viral plaque is made in lab for : [AIIMS 96]

a) Quantitative assay of infectivity of virus
b) Diagnosis of virus
c) Qualitative assay of infectivity of virus
d) Type of virus

48. Exotoxins are : [AIIMS 95]

a) Lipopolysaccharide in nature
b) Produced by gram -ve bacilli
c) Highly antigenic
d) Very stable and resistant to chemical agents

49. The term "viable not cultivable" (VNC) is used for:

a) M. leprae [PGI Dec. 07]
b) M. Tuberculosis
c) Trepenoma pallidum
d) Salmonella
e) Staph.

50. Micro-organisms invading the GIT causing gastroenteritis : [PGI Dec. 07]

a) EHEC
b) Shigella
c) Vibrio parahaemolyticus
d) Campylobacter
e) Salmonella

51. Which of the following can cause rhabdomyo-lysis? [PGI June 07]

a) Clostridium Perfringes
b) Streptococcus
c) Clostridium difficle
d) Cl. tetani

Answer

38. d) Mycobacterium
39. b) Biofilm ...
40. d) Shock ...
41. a) Bacteriodes
42. d) Promotes ...
43. c) ETEC
44. d) Lipo-...
45. a) Warts
46. b) Herpessimplex
47. a) Quantitative ...
48. c) Highly ...
49. a and c
50. b, c, d and e
51. a, b and d

52. Genital elephantiasis is seen in : **[PGI 06]**
a) Donovanosis
b) Lymphogranuloma venerum
c) Congenital syphilis
d) Herpes simplex

53. Rhinosporidiosis is caused by : **[PGI 06]**
a) Fungus
b) Bucteria
c) Virus
d) Protozoan
e) Parasite

54. Which human infection spreads through urine :
a) Leptospira **[PGI 06]**
b) Legionella
c) Plague
d) Diphtheria

55. Urease test is positive in : **[PGI 05]**
a) H.pylori
b) S.aureus
c) Klebsiella
d) Bacillus cereus
e) Pseudomonas

56. Resolution provided by light microscope is :
a) 200 nm **[PGI 05]**
b) 20 nm
c) 0.2 nm
d) 2.0 nm
e) 120 nm

57. Pus cell in diarrhoea seen in : **[PGI 05]**
a) Vibrio cholera
b) EPEC
c) Rotavirus
d) Shigella
e) Campylobacter

58. C.M.I is seen in : **[PGI 05]**
a) Histoplasmosis
b) Leprosy
c) Tetanus
d) Measles

59. Which of the following has malignant potential :
a) HSV - 1 **[PGI 05]**
b) EBV
c) CMV
d) Varicella

60. Man is intermediate host in : **[PGI 05]**
a) Taenia saginata
b) Trichenella spiralis
c) Strongyloidis
d) P. falciparum

61. Capsulated organism : **[PGI 03]**
a) Candida
b) Klebsiella
c) Proteus
d) Cryptococcus
e) Histoplasma

62. Which of the following are transfusion transmitted viruses : **[PGI 03]**
a) Hepatitis B
b) CMV
c) HTLV - 1
d) Rubella
e) HHV - 8

63. Enteropathogenic organisms are : **[PGI 02]**
a) Cryptococcus
b) B. Coli
c) Microsporidium species
d) E. dispar
e) Giardia intestinalis

64. Which of the following is a bacteria taxonomically:
a) Chlamydia **[PGI 01]**
b) Rickettsia
c) Mycoplasma
d) Prion
e) Bacteriophage

65. Which of the following is transmitted by blood:
a) Toxoplasma **[PGI 01]**
b) Syphilis
c) CMV
d) Hepatitis B and C
e) Hepatitis E

66. Stool examination is required for diagnosis of infection with : **[PGI 01]**
a) Staph. food poisoning
b) Clostridia
c) Shigella
d) Campylobacter
e) E. vermicularis

Answer

52. a) Donovanosis	53. a) Fungus	54. a) Leptospira	55. a, b and c	56. a) 200 nm
57. d and e	58. a, b and d	59. b) EBV	60. d) P. falciparum	61. b and d
62. a, b and c	63. b, c, d and e	64. a, b and c	65. a, b and c	66. a, b, c, d and e

67. True about bacteria : **[PGI 00]**
a) Mitochondria always absent
b) Sterols always present in cell wall
c) Divide by binary fission
d) Can be seen only under electron microscope

68. Which of the following are intracellular :
a) Viruses **[PGI 00]**
b) Chlamydia
c) Mycoplasma
d) Rickettsia

69. Treatment of partner is required in all infection except : **[PGI 00]**
a) Candida
b) Herpes
c) Trichomonas
d) Gardnerella

70. MC commensal gut flora in adult : **[PGI 00]**
a) Lactobacillus
b) Bacteroides
c) E, coli
d) Klebsiella

71. Obligatory anaerobes are all except : **[PGI 99]**
a) Clostridia botulinum
b) Eikenella corrodens
c) Bacteriodes
d) H. pylori

72. The difference between gram +ve and gram -ve organism is the gram-ve organism contains :
a) Teichoic acid **[PGI 98]**
b) Muramic acid
c) N- acetyl neuraminic acid
d) Aromatic amino acids

73. Maternal viremia most commonly spreading to fetus in utero : **[PGI 98]**
a) CMV
b) Rubella
c) HIV
d) Herpes

74. The following transmit drug resistance except :
a) RTF **[PGI 98]**
b) Plasmids
c) Hfr
d) Chromosome

75. One virus particles prevents multiplication of 2nd virus. This phenomena is : **[PGI 97, 96]**
a) Viral interference
b) Mutation
c) Supervision
d) Permutation

76. DNA covering material in a virus is called as:
a) Capsomere **[PGI 96]**
b) Capsid
c) Nucleocapsid
d) Envelope

Answer
67. a and c
68. a, b and d
69. d) Gardnerella
70. a and b
71. b and d
72. d) Aromatic ...
73. a) CMV
74. c) Hfr
75. a) Viral ...
76. b) Capsid

EXPLANATIONS AND REFERENCES WITH ILLUSTRATIVE ANSWERS

1. Ans. is c i.e. Brucella *Ref. Park 19/e, p 242*

Modes of transmission of Brucella :

- *Contact infection (MC)*: Through direct contact with infected tissue, blood, urine vaginal discharge. Mostly occupational.
- *Food borne infection*: Through ingestion of raw milk, dairy products.
- *Air borne infection*: In the environment of slaughter house.

Infection transmitted through soil :

- Man-soil-man- All the disease transmitted fecorally eg. typhoid, hepatitis A.
- Soil as storehouse of spores - Tetanus, mycosis, botulism.

2. Ans. is d i.e. Pneumonic plage *Ref. Park 19/e, p 103*

Periods of isolation recommended

Disease	Duration of isolation
Chickenpox	Until all lesions crusted; usually about 6 days after onset of rash
Measles	From the onset of catarrhal stage through 3rd day of rash
German measles	None, except that women in the first trimester or sexually active, non-immune women in child–bearing years not using contraceptive measures should not be exposed
Cholera, Diphtheria	3 days after tetracyclines started, until 48 hours of antibiotics (or negative cultures after treatment)
Shigellosis Salmonellosis	Until 3 consecutive negative stool cultures
Hepatitis A	3 weeks
Influenza	3 days after onset
Polio	2 weeks adult, 6 weeks paediatric
Tuberculosis (sputum +)	Until 3 weeks of effective chemotherapy
Herpes zoster	6 days after onset of rash
Mumps	Until swelling subsides
Pertussis	4 weeks or until paroxysms cease
Meningococcal meningitis Streptococcal pharyngitis	Until the first 6 hours of effective antibiotic therapy are completed

3. Ans. is a i.e. HIV *Ref. Dutta 6/e, p 301*

HIV has got no teratogenic effect on fetus.

Viral infection in pergnancy :

Infection	Fetal effect
Rubella	Sensoneural deafness Septal defect, PDA, cataract, retinopathy
Varicella	Hypoplasia of limbs, limb deformity, choroidoretinal scarring, cataract, microcephaly
CMV	IUGR, microcephaly, Intracranial calcification, Mental retardation, choriodoretinitis, deafness
PARVO virus	Aplastric crisic, CHF, hydrops
Mumps	No ill effect on fetus

4. Ans. is c i.e. Rubella and toxoplasmosis *Ref. Dutta 6/e, p 296, 299*

- Among Rubella and CMV, rubella is mainly associated with cardiac anomalies while CMV is associated with CNS anomalies.
- Toxoplasmosis leads to hydrocephalus, choriodoretinitis, cerebral calicfication, microcephaly and mental retardation.

5. Ans. is d i.e. Shock and disseminated intravascular coagulation are common in Bacteroides bacteremia

Ref. Ananthnarayan 7/e, p 267 - 268

Anaerobic Gram negative bacilli.

Includes Bacteroides, Fusobacterium, Leptotrichia, Prophyromonas, Prevatella.

Bacteroides are MC anaerobes isolated from clinical specimen.

- They are N. sporing, N. motile, strict anaerobes and capsulated (Virulence factor).
- They are classified on ***the basis of colonial, biochemical features (Sacchrolytic effects) and on characteristics of short chain fatty acid patterns in gas liquid chromatography.***
- ***MC*** isolate of Bacteroides is **B. fragilis.**
- B. fragilis (also Prevotella melaninogenic) possess ***lipopolysaccharides (endotoxin)*** that are **less *biologically potent than endotoxins associated with aerobic gram negative bacteria.*** Due to this relative biologic inactivity, infection caused by bacteriodes less frequently ***produce the clinical signs of sepsis.***
- ***First line therapy*** for anaerobes includes Metronidazole, Ticarcillin/ Clavulanic acid, Piperacillin/tazobactan, Imipenem.
- Resistance to metronidazole is seen in <2% cases i.e. not uniformly sensitive.

... Harrison 17/e, p 1005, Tab. 157-2

6. Ans. is c i.e. Salmonella typhi

Ref. Jawetz 24/e, p 740; Mandell's Principal & Practice of Infectious Disease 6/e, p 998; Braunwald's Heart Disease 7/e, p 1637

Though both salmonella and pseudomonas cause endocarditis, pseudomonas is a more common etiologic agent than salmonella.

Organism causing endocarditis are :

- Streptococci (***MC***) (60 - 80%) : – S. viridans (30 - 40%) – Enterococci (5 - 18%)
  – Other streptococci (15 - 25%)
- Staphylococci (20 - 35%) : – Coagulase positive (10 - 27%) – CoNS (1 - 3%)
- Gram negative bacilli (1.5 - 13%) : – Enterobacteriaceae – Pseudomonas
- HACEK Group of Organisms
- Fungi : – Candida – Cryptococcus

Remember :
- Among streptococci ***MC*** cause are S.sanguis, S.bovis, S.mutans, S.mitior.
- Among enterobacteraciae ***MC*** cause – Salmonella.
- P.aeroginosa is ***MC*** gram negative bacilli causing endocarditis.

7. Ans. is c i.e. Abundance of polymorphs *Ref. Shaw's 13/e, p 129; COGDT 10/e, p 670*

Bacterial Vaginosis

Defined as Alteration in normal vaginal flora rather than true infection	
Causative organism :	– G. vaginalis – H. vaginalis – Mobiluncus

Microscopy of vaginal secretions in ***bacterial vaginosis*** shows :
- Characteristic clue cells
- Decreased or absent lactobacillus
- Decreased leucocytes.

Clinical criteria for diagnosis :
- Homogenous white non inflammatory discharge with fishy odour.
- Microscopic presence of >20% clue cells.
- Vaginal discharge with pH>4.5
- Fishy odour with or without addition of 10% KOH.

Treatment : Metronidazole for both pregnant and non pregnant women.

Remember :
- Clue cells represent epithelial cells adherant to G.vaginalis.
- Bacterial vaginosis is most prevalent vaginal infection.

8. Ans. is b i.e. Klebsiella *Ref. CSDT 12/e, p 494*

Causative organism of acute bacterial peritonitis.

Aerobic (30%)	Anaerobic (10%)
– E.coli ***(MC)***	– Bacteroides
– Klebsiella	– Peptostreptococci
– Enterococci	

So, Klebsiella comes after E.coli.

Remember : In 60% of cases mixed anaerobic and aerobic infection is found.

9. Ans. is a i.e. Transduction *Ref. Ananthnarayan 7/e, p 55 - 57*

Transmission of genetic material = gene transfer = acquistion of characteristic occur by four process.

a. **Transformation** = Transfer of genetic information (about 10-50 genes) through the free DNA.
   - Seen mainly in pneumococci; bacillus species and Hemophilus influenza.
   - Any characteristic may be transferred by transformation.

b. **Transduction** = Transfer of portion of DNA from one to other bacteria by agency of bacteriophage (acts only as vehicle).
   - It may be generalised (when it involves any segment of donor DNA) or restricted (when specific bacteriophage transduces only a particular genetic trait).
   - It is most widespread mechanism of gene transfer among prokaryotes.
   - Episomes and plasmids (Eg plasmid determining Pn resistance in staphylococci) may also transduced.
   - It is used in *genetic engineering* in the treatment of some inborn errors of metabolism.

c. **Conjugation** (Bacterial equivalent of sexual mating) – Described by Leder berg and Tatum in strain of E. coli (K12) eg. Transfer of episomes and plasmids of drug resistance.

d. **Lysogenic conversion** – Phage DNA becomes integrated with bacterial chromosome as the prophage which codes for new characteristic eg. toxin production in C. diptheriae.

10. Ans is c i.e. Streptococcus pyogenes

See below

Intracellular organisms are :

a. ***Bacteria***	*b.* ***Parasites***	*c.* ***Viruses*** *are obligate intracellular parasite*	*d.* ***Fungi***
• **L**isteria monocytogens • **L**egionella • **R**ickettsia • **M**ycobacteria TB & mycobacteria Leprae • **C**halamydia • **N**eisseria meningococci and Gonococci • **Y**ersinia pestis • **B**ordetella • **S**almonella • **D**. granulomatosis • **S**higella • **B**rucella • **P**neumococci	• Babesia • Plasmodium • Cryptosporidium parvum • Microsporidia sp. • *Toxoplasma*		• Histoplasma capsulatum

Mnemonic : **LLRM Medical College Ne Yaha Bulakar, SDS ko Bahut Pareshaan kiya.**

Remember : ***Cell Mediated Immunity play vital role against these organisms.***

11. Ans. is d i.e. Chemically defined media *Ref. Ananthnarayan 7/e, p 457*

Isolation of virus

Method of isolation consist of :

"Inoculation into animals, eggs or tissue culture after the specimen is processed to remove bacterial contaminants." *..... Ananthnarayan 7/e, p 457*

As many viruses (adenoviruses, enteroviruses) are frequently found in normal individuals so only recovery of viral agent from patient doesn't proved that it is the causative agent of the patient illness.

Organism not grown in **artificial cultural media are :**

- M. Leprae
- Rickettsia
- Viruses.
- Pathogenic treponemes
- Chlamydia

12. Ans. is c i.e. It establishes in the body only after the neonatal period *Ref. Jawetz 24/e, p 197-200*

Term "normal microbial flora" denotes the population of microorganisms that inhabit the skin and mucous membranes of healthy normal persons. They are not essential to life.

MC resident organisms of upper respiratory tract is streptococci of viridans group.

MC resident bacteria of large intestine is bacteroides species.

Lines from *Jawetz* clears all choice to you -

"***Mucous membranes of mouth and pharynx are often sterile at birth Within 4-12 hrs after birth, viridans streptococci become establish as most prominent member of resident flora and remain so for life."***

"In the pharynx and trachea, similar flora establish itself whereas few bacteria are found in normal bronchi. Small bronchi and alveoli are normally sterile."

"Stomach acidity keep the number of micro-organisms at a minimum (10^3 - 10^5) unless obstruction at the pylorus favours the proliferation of gram positive cocci and bacilli."

"Antimicrobials drugs taken orally can, in humans, temporilly suppress the drug susceptible components of the fecal flora."

13. Ans. is b i.e. Gram –ve organisms *Ref. Jawetz 24/e, p 739; Harrison 16/e, p 1539*

Guys, this is a twisted question, understand the choice clearly.

– ***MC*** cause of nosocomial pneumonia in **ICU** now is S.aureus (Gram +ve). *..... Harrison 16/e, p 1539*

– After this comes enterobacteriacea followed by pseudomonas aeruginesa (Gram –ve).

- But if we take enterobacteriacea and P. aeruginosa (Gram –ve organism) together they can over number S. aureus (Gram +ve organism).

So, the answer will be ***Gram –ve organism.***

Now word nosocomial has been replaced by hospital acquired pneumonia.

14. Ans. is b i.e. Shiga toxin *Ref. Ananthnarayan 7/e, p 286; Harrison 17/e, p 963*

Shiga toxin, a protein encoded by the iron regulated chromosomal gene. It composed of two peptide subunits-

A subunit is N-glycosidase that hydrolyzes adenine from specific sites of ribosomal RNA of mammalian 60s-ribosomal subunit, irreversibly inhibiting protein synthesis.

B subunit recognizes the receptor glycolipid Gp3 on host cells.

Toxin acts by inhibiting protein synthesis are :

– Diptheria toxin
– Verocytotoxin or Shiga like toxin of E. coli 0157
– Pseudomonas toxin
– Shiga toxin of Sh dysenteriae I.

15. Ans. is c i.e. Vibrio parahemolyticus *Ref. Harrison 17/e, p 814*

Non - inflammatory (Enterotoxin) mediated acute diarrheas are :

- Vibrio cholera
- Clostridium perfringens
- S. aureus
- Plesiomonas shigelloides
- Rota virus
- Enteric adenoviruses
- Cyclospora sp
- ETEC (LT or ST)
- Bacillus cereus
- Aeromonas hydrophila
- Norwalk like viruses
- Girdia lamblia
- Cryptosporidium
- Microsporidia

Vibrio parahemolyticus produce no enterotoxin, it cause enteritis by invasion of intestinal epithelium.

.....Ananthnarayan 7/e, p 317

16. Ans. is a i.e. Clostridium tetani *See below*

Infection associated with severe hemolysis are :

- **B**artonella
- **B**abesiosis
- **B**acteremia with pneumococci, staphylococi, escherichia coli.
- **M**alaria (Plasmodium falciprum)
- **C**lostridium welchii

17. Ans. is b i.e. Incorporating part of host DNA *Ref. Ananthnarayan 7/e, p 55 - 57*

Already explained, please see answer no. 10

18. Ans. is d i.e. Clostridium perfringes *Ref. Ananthnarayan 7/e, p 252; Harrison 17/e, p 986*

Heat stable enterotoxin :

1. Staph aureus enterotoxin.
2. Enterotoxin of K. pneumoniae.
3. Emetic type toxin of B. cereus (Diarrhoeal type is LabileToxin).
4. ST of ETEC (LT is same as toxin of V-cholera).
5. Yersinia enterocolitis (by some strains).
6. Clostridium botulism toxin (Relatively stable).

19. Ans. is b i.e. Echinococcus granulosus *Ref. Harrison 17/e, p 822*

Bacteria	Viruses	Other
TRANSMITTED IN ADULTS PREDOMINANTLY BY SEXUAL INTERCOURSE		
Neisseria gonorrhoeae	HIV (types 1 and 2)	*Trichomonas vaginalis*
Chlamydia trachomatis	Human T-cell lymphotropic virus type I	*Phthirus pubis*
Treponema pallidum	Herpes simplex virus type 2	
Haemophilus ducreyi	Human papillomavirus	
Calymmatobacterium granulomatis	Hepatitis B virus	
Ureaplasma urealyticum	Molluscum contagiosum virus	

SEXUAL TRANSMISSION REPEATEDLY DESCRIBED BUT NOT WELL DEFINED OR NOT THE PREDOMIANT MODE		
Mycoplasma hominis	*Cytomegalovirus*	*Candida albicans*
Mycoplasma genitalium	HTLV - II	*Sarcoptes scabiei*
Gardnerella vaginalis and other	Hepatitis C, D viruses	
Vaginal bacteria	Herpes simplex virus type 1	
Group b *Streptococcus*	Epstein-Barr virus	
Mobiluncus spp.	Transfusion-transmitted virus	
Helicobacter cinaedi		
Sporothrix fennelliae		

E. granulosus spread by feco-oral route when eggs in dog's feces are ingested either by direct contact with infected dogs or by taking vegetable contaminated with dog's feces.

20. Ans. is b i.e. Dengue virus *Ref. Harrison 17/e, p 712*

Infectious complications of blood transfusion

Viral infection	– Hepatitis C virus	– Hepatitis B virus
	– Hepatitis G virus	– Hepatitis A virus (rarely)
	– TTV and SENV virus	– HIV
	– Cytomegalovirus	– HTLV type I
	– Parovirus B-09	– West nile virus
	– Varian Creutzfeild jakob disease	
Bacterial infection	– Syphilis	– Yersinia
	– Pseudomonas	– Gram +ve cocci including coagulase negative staphylococci .
	– Lyme disease	
Parasites	– Malaria	– Babesia
	– Trypanosoma cruzi	– Toxoplasmosis *.....Harrison 17/e, p 1305*

21. Ans. is c i.e. Specific IgM antibodies - Immunity against Rubella *Ref. Ananthnarayan 7/e, p 507*

- **Zeihl Nelson** (Acid fast staining) is used for Mycobacteria detection.
- Rapid diagnosis of Influenza is made by demonstration of virus antigen on the surface of nasopharyngeal cells by immunofluorescence.
- IgM antibodies are antibodies of primary response (IgG is antibody of secondary response) so IgM indicates acute or recent infection. Its production signify that immune response of individual is proper but doesn't mean that person has immunity against that infection (eg. Rubella).

22. Ans. is d i.e. Promotes growth of Candida and Staphylococcus

Ref. MM 13/e, p 453; Scot Microbiology 9/e, p 81; Ananthnarayan 7/e, p 283

CLED = Cystine Lactose Electrolyte deficient agar

- It is primarily is used for isolation and enumeration of bacteria in urine.
- It inhibits swarming of proteus like McConkey agar.
- It is selective and differential media like McConkey agar.
- Both show greenish colour, matt surface and rough periphery of pseudomonas colonies.
- It has advantage in supporting growth of certain staphylococcus, Streptococci and Candida strain.

23. Ans. is a i.e. E. coli *See below*

Urease test is positive in urease producing bacteria which includes :

i. **P**roteus	ii. **S**. aureus	iii. **M**organella
iv. **K**lebsella	v. **Y**ersinia	vi. **C**ryptococcus
vii. **D**iptheroids	viii. **M**ycobacterium except MAC	ix. **H**. Pylori

Mnemonic : **PSM KY CD M**eri **H**ai

24. Ans. is c i.e. Determining infectivity of virus *Ref. Ananthnarayan 7/e, p 441 - 442*

Viral assay

Total virus Particles

By *Electron microscopy*

By *Hemagglutination inhibition*

Infectivity assay

Quantal assay

- Indicates presence or absence of infectious viruses.
- Titre is usually expressed as '50 percent infections dose" (ID5O) per ml calculated by statistical methods eg. Reed and Muench

Quantitative Infectivity assay of virus

Measure actual number of infectious particle in inoculum

Plaque assay or or monolayer cell culture

Transformation assay
For oncogenic viral Viruses

Pockassay on **choronic allan-toic membrane (CAM)**
Eg. variola, vaccina
Herpes virus
Monkey pox, cow pox

Plaque Assay : Each infectious particle give rise to a localiszed focus of infected cells that can be seen with naked eye. Such foci are knows as plaque and each plaque indicates an infectious virus.

25. Ans. is a i.e. H. pylori *Ref. Harrison 17/e, p 946*

Remember : H. influenzae is the first free living organism whose complete genome has been sequenced.

26. Ans. is d i.e. Anaerobic streptococci *Ref. CMDT-08, p 114*

Human bites

- Human bites are usually inflicted by children; in adults bites are associated with alcohol use and closed fist injury.
- Bites inflicted by children rarely get infected and bites by adults become infected in 15-30% of cases.

- Bacteriology of bite infection:
  - Human bites are mixture of aerobes and anaerobes (54%) or due to aerobes only (44%).
  - Streptococcus, staphylococcus and Eikenella corrodens are most common aerobes.
  - Prevotella and fusobacterium are the most common anaerobe

Remember :

- Cat bites are most likely to become infected (30-50%)
- Dog bite become infected only in 5% of cases.
- Pasturella species are the single most common isolate in dog and cat bites.

About the question

This question is of 1998, at that time Harrison 15/e was running. In 15/e, Anaerobes (including pepto streptococcus) were given as more common, So, was the answer.

27. Ans. is a i.e. Pseudomonas *Ref. Ananthnarayan 7/e, p 321*

Already explained, refer answer no. 14

28. Ans. is a i.e. Absence of nuclear membrane *Ref. Ananthnarayan 7/e, p 7*

Differences between prokaryotic and eukaryotic cells

Character	Prokaryotes	Eukaryotes
Nucleus (Main basis of classification)		
• Nuclear membrane	Absent	Present
• Nucleolus	Absent	Present
• Deoxyribonucleoprotein	Absent	Present
• Chromosome	One (Circular)	More than one (linear)
• Mitotic division	Absent	Present
Cytoplasm		
• Cytoplasmic streaming	Absent	Present
• Pinocytosis	Absent	Present
• Mitochondria	Absent	Present
• Lysosomes	Absent	Present
• Golgi apparatus	Absent	Present
• Ribosomes	70s	80s
Chemical composition		
• Sterols	Absent	Present
• Muramic acid	Present	Absent
• Amoeboid movement	+	±
• Flagella and Pilli	+	±
• Phosphrylation site	Plasma membrane (Mesosomes)	Ribosomes (Mitochondria)

29. Ans. is a i.e. Bacteriostatic *Ref. Jawetz 24/e, p 57*

Bacteriostatic – Chemical or substance inhibiting growth without killing.

Bactericidal – Chemical or substance killing organism.

Sterilization – The process by which article or medium is freed of all living microorganism either in the vegetative or spore state.

Bacteriophage – Virus infecting bacteria.

30. Ans. is d i.e. C. trachomalus *Ref. CMDT 08, p 749*

- Reactive arthritis is the clinical tetrad of uretheritis, conjunctivitis (or uveitis), mucocutaneous lesions and aseptic arthritis.
- Most cases develop within days weeks after either a dysenteric infection or urogential infection.
- Associated infection

GI	Urogenital
• Shigella • Salmonella • Yersina • Compylobacter	• Chlamydia trachomatus • Ureoplasma Urealyticum

31. Ans. is b i.e. Acineto bacter *Ref. Harrison 17/e, p 926*

HACEK organism are a group of fastidious, slow growing, Gram negative bacteria whose growth requires an atmosphere of CO_2. Species belonging to this group include :

- Haemophilus species
- Actinobacillus actinomycetemcomitans
- Cardiobacterium hominus
- Eikenella corrodens
- Kingella kingae

Endocarditis is the *most common* disease caused by them.

32. Ans. is b i.e. PCR **See below**

Cy Bromide green dye is a dye that binds to minor groove of double stranded DNA and generates fluorescence.

Uses :

– To determine presence of amplified DNA product.
– For optimizing PCR reaction.

33. Ans. is a i.e. Mycobacterium tuberculosis *Ref. Harrison 16/e, p 117*

Fever of unknown origin

Causes				
Infections (33%)	**Neoplasm (17%)**	**Non infectious inflammatory disease (21%)**	**Miscellaneous (15%)**	**Undiagnosed (14%)**
– Mycobacterium TB – Abdominal abscess – Endocarditis – UTI – Viral infections : - CMV - EBV – Kala azar – Brucellosis	– Lymphoma – Leukemia – Solid tumours			

34. Ans. is c i.e. 1000 : 1 *Ref. Jawetz 24/e, p 200*

Anaerobes outnumber facultative organism by 1000 fold.

Normal flora of intestinal tract

- At ***birth*** the intestine is sterile, but organism are soon introduced after birth.
- In breast feed children lactic acid streptococci and lactobacilli seen.
- Micro-organism are ***minimum*** (10^3 - 10^5g/ of contents) in stomach.
- In ***upper intestine*** lactobacilli and enterococci predominate.
- In ***colon*** bacteriodes fragilis is the *most common* organism found.
- Intestinal bacteria are important in synthesis of vitamin K.

35. Ans. is a i.e. Measles *Ref. Park 18/e, p 89; 19/e, p 90*

In measles and whooping cough only cases are found with no carriers.

Chronic carriers seen in :

- Typhoid
- Hepatitis B
- Malaria
- Dysentery
- Cerebrospinal meningitis
- Gonorrhea

36. Ans. is d i.e. Hemophilus ducreyi *Ref. Ananthnarayan 7/e, 228*

Causes of urethritis are :

- *Neisseria gonorrhoea (**MC**)*
- *Ureoplasma urealyticun*
- *Herpes virus*
- *Gardenella vaginalis*
- *Candida albicans*
- *Chlamydia trachomatis*
- *Mycoplasma hominis*
- *Cytomegalovirus*
- *Acinetobactor woffi, Ac calcoaceticus*
- *Trichomonas vaginalis*

37. Ans. is b i.e. Pneumocystis carinii pneumonia *See below*

Infection in patients with defects in humoral immunity :

- Recurrent or chronic sinopulmonary infection otitis media, meningitis and bacteremia; ***MC*** by pyogenic bacteria such as H. influenzae; Strep pneumoniae; Staphylococci

- Response to viral infection is good except increased risk of :
  - HBV
  - Polio
  - Echoviruses
  - Adenoviruses
- **Parasitic** – Giardial diarrhea
- Less frequent – Bacterial infection of skin and urinary tract.

Infection in patient with deficient CMI :

- Disseminates virus infection of Herpes simplex, Varicella zoster, and CMV
- Mucocutaneous candidiasis – Almost invariably
- Pneumonia caused by P. carinii
- Severe Enteritis caused by cryptosporidium
- *T cell deficiency is always accompanied by some abnormality of antibody response so patient with T cell defect are also subject to overwhelming bacterial infection.*

38. Ans. is d i.e. Mycobacterium *Ref. Ananthnarayan 7/e, p 635; Harrison 17/e, p 835-838*

- **Most important group of hospital pathogens are :**
  i. Enteric gram negative bacilli :
     - E. coli
     - Kliebsiella
     - Enterobacter
     - Proteus
     - Serratia
  ii. S. aureus
  iii. Pseudomonas aeruginosa and other pseudomonas
  iv. Tetanus spores
  v. Yeast (Candida albicans), moulds (Aspergillus mucor)
  vi. Protozoa (E. histolytica, Plasmodia, P. carinii, T. gondii)

Nosocomial infection	*Most common* causative organism
• Urinary tract infection (***MC* Nosocomial infection)**	E. coli; Candida
• *Early onset pneumonia* (within 4 days)	Strept pneumoniae
• *Late onset pneumonia*	S. aureus, P. aeruginosa
• *Surgical wound infections*	**S.aureus,** coagulase negative staphylococcus
• *Infections related to vascular acess*	**Coagulase negative Staph**, S. aureus

Remember :

- ***Candida is now the MC pathogen in nosocomial UTI in ICU patients.*** *..... Harrison 17/e, p 837*
- Examples of some emerging and potential, epidemic problems in Hospitals are : Chickenpox TB, Group A streptococci, Aspergillus, Legionella

39. Ans. is b i.e. Biofilm formulation *Ref. Jawetz 24/e, p 158*

- Slime is generally polysaccharide (Eg. pneumococcus) or polypeptide (eg. anthrax)
- A **biofilm** is an aggregate of interactive bacteria attached to solid or to each other and encased in an exopolysaccharide matrix of slime. It form slimy coat on solid surface and occur through out nature.

- A single species or more than one species of bacteria coaggregate to form a biofilm. Fungi including yeasts are occasionally involved
- ***Biofilms make infections persistant and difficult to treat*** eg. S. epidermidis and S. aureus infection of central venous catheters and with pseudomonas airway infection in cystic fibrosis patients.

40. Ans. is d i.e. Shock and DIC are common in bacteremia due to B. fragilis

Ref. Ananthnarayan 7/e, p 268; Jawetz 24/e, p 307

Already explained, refer answer no. 5

41. Ans. is a i.e. Bacteroides *Ref. Ananthnarayan 7/e, p 268; Jawetz 24/e, p 307*

Provotella is anaerobic gram negative bacilli.

MC isolate is **P. melaninogenicus** (Previously called Bacteroides melaningenicus)

- P. melaninogenica forms black or brown **colour** colonies
- Colony colour is not due to melanin but due to a hemin derivative
- ***Cultures of*** P. melaninogenica and even dressings from wounds infected with the bacillus give **characteristic red fluorescence when** exposed to ultraviolet light.

Remember : Anaerobes causing brain absecess – B. fragilis, Peptostreptococcus, Prevotella etc.

42. Ans. is d i.e. Promotes growth of S. arueus and Candida

Ref. MM 13/e, p 453; Scot Microbiology 9/e, p 81; Ananthnarayan 7/e, p 283

Already explained, refer answer no. 22

43. Ans. is c i.e. ETEC *Ref. Ananthnarayan 7/e, p 196, 247, 264*

Preformed toxins have role in :

- Staphylococcal food poisoning (enterotoxin)
- Botulism food poisoning
- Emetic type of food poisoning of B. cereus (resemble staph enterotoxin)

In case of **preformed toxin, incubation period is 'short'** in comparison to when organism has to produce toxin in the intestine.

44. Ans. is d i.e. Lipo-polysaccharide *Ref. Ananthnarayan 7/e, p 67, Table (9.1)*

Distinguishing features of exotoxins and endotoxins

Exotoxins	Endotoxins
• Proteins	Lipopolysaccharides
• Heat labile	Heat stable
• Actively secreted by cells; diffuse into surrounding medium	Form part of cell wall; do not diffuse into surrounding medium
• Readily separable from cultures by physical means such as filtration	Obtained only by cell lysis
• Action often enzymic	No enzymic action

• Specific pharmacological effects for each exotoxin	Effect nonspecific; action common to all endotoxins
• Specific tissue affinities	No specific tissue affinity
• Active in very minute doses	Active only in very large doses
• Highly antigenic	Weakly antigenic
• Action specifically neutralised by antibody	Neutralisatioh by antibody ineffective
• Can be toxoided	Can't toxoided
• Generally formed by gram positive incuding some gram negative shigella, vibrio cholera, ETEC, V parahemolyticus, Aeromonas Y. enterocolitica, Ps. aeroginosa	Generally formed by gram negative bacteria

45. Ans. is a i.e. Warts *Ref. Harrison 17/e, p 1117-1118*

Remember :

Disease	Associated Human papilloma viruses
Common warts (Verruca vulgaris)	***1, 2, 4***, 26, 27, 29, 41, 57, 65, 77
Condyloma accuminatum (Anogenital warts)	***6, 11, 30***, 42, 43, 44, 45 51, 54
Cervical carcinoma	***16, 18, 31, 33,*** 35, 39, 45
Laryngeal papillomas	***6, 11***
Low grade intraepithelial neoplasias	***6, 11, 16, 18***

46. Ans. is b i.e. Herpes simplex *Ref. Jawetz 24/e, p 586, Table (43.1)*

Association of viruses with human cancers.

Virus family	Virus	Human cancer
Papillomaviridae	Human papillomaviruses	Genital tumors, squamous cell carcinoma Oropharyngeal carcinoma
Herpesviridae	EB virus	Nasophryngeal carcinoma, African Burkitt's lymphoma, B cell lymphoma
Hepadna viridae	Hepatitis B virus	Hepatocellular carcinoma
Retroviridae	HTL virus HIV	Adult T cell leukemia AIDS - related malignancies
Flaviviridae	Hepatitis C virus	Hepatocellular carcinoma

47. Ans. is a i.e. Quantitative assay of infectivitiy of virus *Ref. Ananthnarayan 7/e, p 441 - 442*

Already explained, refer answer no. 27

48. Ans. is c i.e. Highly antigenic *Ref. Ananthnarayan 7/e, p 67, Table (9.1)*

Already explained, refer answer no. 44

49. Ans. is a and c. Leprae, Treponema pallidum *Ref. Ananthnarayan 7/e, p 457*

Already explained, refer answer no. 11

50. Ans. is b, c, d and e i.e. Shigella, Vibrio parahaemolyticus, Campylobacter and Salmonella

Invasive Diarrhoea		
Minimal inflammation	***Variable inflammation***	***Severe***
• Rotavirus • Norwalk agent	• Salmonella • Campylobacter • Aeromonas • Vibrio parahaemolyticus • Yersinia	• Shigella • EIEC • Entamoeba histolytica

51. Ans. is a, b, d i.e. Clostridium perfringes, Streptococcus and Cl. tetani

Rhabdomyolysis

Viral causes	Bacterial causes		Fungal causes
• Influenzae types A and B (most common) • HIV • Ebstein-Barr virus • Echovirus • Cytomegalovirus • Adenovirus • Herpes simplex virus • Parainfluenza virus • Varicella-zoster virus • Coxsackievirus	• Francisella tularensis • Streptococcus pneumoniae • Group B streptococci • Streptococcus pyogenes • Staphylococcus epidermidis • Escherichia coli • Borrelia burgdorferi • Clostridium tetani • Viridans streptococci	• Rickettsia species • Salmonella species • Listeria species • Legionella species • Mycoplasma species • Vibrio species • Brucella species • Bacillus species • Leptospira species	• Candida • Aspergillus

52. Ans. is a and b i.e. Donovanosis; and Lymphogranuloma venerum

Ref. Ananthnaraya 7/e, p 404

Genital elephantiasis is seen in Donovanosis which is caused by Calymmatobacterium granulomatosis or Granuloma iguinale / venerum.

Donovanosis

- Chronic progressive bacterial infection of the genital region that is generally sexually transmitted.
- **Causative organism :**
  - Calymmatobacterium granulomatis (Gram negative encapsulated bacterium).
  - Morphologicaly and antigenically related to Klebsiella.
  - Grow on egg yolk or modified levinthal agar.
- I.P. – 1 - 4 weeks.
- **Clinical features :** – Disease begin as one or more subcutaneous nodules that erode through the skin to produce clean granulomatous, sharply defined usually painless lesion.
  - Genitalia are involved in 90% of cases.

– Genital swelling particularly of labia is common and may progress to pseudo-elephantiasis.
– Complications include phimosis and paraphimosis.

- **Diagnosis :** – Diagnosis is made by demonstration of typical intracellular Donovan bodies (safety pin appearance) in Wright Giemsa stain.
- **Treatment :** – Azithromycin - ***DOC.***
  – Doxycycline - Second ***DOC.***
- **Remember :** – Genital elephantiasis is also seen in lymphatic filariasis. *... Harrison 16/e, p 1260*
  – Vulval elephantiasis or esthiomene is seen in lymphogranuloma venerum. *..... Ananthnarayan 7/e, p 428*

53. Ans. is a i.e. Fungus *Ref. Ananthnarayan 7/e, p 620; Dhingra 3/e, p 197*

- Rhinosporidiosis is a chronic granulomatous disease characterized by development of friable polyp usually confined to the nose, mouth or eye.
- Polyp is highly vascular which bleeds easily on touch. Its surface is studded with white dots which represents the sporangia of fungus.

- **Causative agent** – Rhinosporidium seeberi. The fungus has not been cultivated in media.
  – The infection is supposed to originate from stagnant water or aquatic life.
- **Diagnosis :** – Biopsy shows round or oval sporangia filled with spores which may burst through chitinous wall.
- **Treatment :** – Complete excision with diathermy knife and cauterization of its based.
  – Dapsone and Amphotericin B are also effective.

54. Ans. is a i.e. Leptospira *Ref. See below*

Disease	Mode of infection
Leptospira	Water contaminated by the urine of carrier animals enter the body through cut or abrasions on the skin or through intact mucosa of mouth, nose or conjunctiva.
Legionella	Inhalation of aerosols produced by AC, cooling towers.
Plague	Bite of rat flea, droplet infection
Diptheria	Droplet infection

55. Ans. is a, b, c i.e. H.pylori; S.aureus; and Klebsiella *Ref. See below*

Already explained, refer answer no. 23

56. Ans. is a i.e. 200 nm *Ref.See below*

Resolving power are :

Light microscope – 0.25 µm – 0.3 µm = 200 - 300 nm
Electron microscope – 2 - 10 A^0 = 0.2 - 1 nm

57. Ans. is d and e i.e. Shigella; and Campylobacter

GASTROINTESTINAL PATHOGENS CAUSING ACUTE DIARRHEA

Mechanism	Location	Illness	Stool findings	Examples of pathogens involved
Noninflammatory *(enterotoxin)*	Proximal small bowel	Watery diarrhea	No fecal leukocytes; mild or no increase in fecal lactoferrin	Vibrio cholerae, enterotoxigenic *Escherichia coli* (LT and /or ST), *Clostridium perfringens, Bacillus cereus,S. aureus, shigelloides, rotavirus,* Norwalk-like viruses, enteric adenoviruses, Giardia lamblia, Cryptosporidium spp., microsporidia
Inflammatory *(invasion or cytotoxin)*	Colon or distal small bowel	Dysentery or inflammatory diarrhea	Fecal Polymorphonuclear leukocytes; substantial increase *in fecal* lactoferrin	*Shigella spp., Salmonella* spp., *Campylobacter jejuni, enterohemorrhagic E. coli, enteroinv*asive E. coli, *Yersinia enterocolitica, Vibrio parahaemolyparahaemolyticus, Clostridium difficile, Entamoeba histolytica*
Penetrating	Distal small bowel	Enteric fever	Fecal mononuclear leukocytes	*Salmonella typhi, Y. enterocolitica, Campylobacter fetus*

58. Ans. is a, b and d i.e. Histoplasmosis; Leprosy; and Measles

Already explained, refer answer no. 10

59. Ans. is b i.e. EBV *Ref. Jawetz 24/e, p 586*

Already explained, refer answer no. 46

60. Ans. is d i.e. P. falciparum

Man is intermediate host (Secondary) in :

- Plasmodium
- Toxoplasma gondii
- Echinococcus granulosus [dog tapeworm/ hydatid worm/ Taenia echinococcus]
- Sarcocystis lindemanni
- T. solium (man also act as definitive host).

61. Ans. is b and d i.e. Kleibsella; and Cryptococcus

Capsulated bacterias are :

- **Pn**eumonococcus
- ***Kl***eibsella
- ***Ye***rsinia
- N. ***Me***ningococci
- ***Vi***brio parahemolyticus
- Bacillus ***an***thrax
- H. ***in***fluenza
- ***Bo***rdetella
- ***Cl.*** Perfringes and butyricum

Mnemonic : **PAKIYB - M.C.V**

Remember : *Capsulated fungi is Cryptococcus neofomans not Histoplasma capsulatum.*

62. Ans. is a, b and c i.e. Hepatitis B; CMV; and HTLV - 1 *Ref. Harrison 17/e, p 712*

Already explained, refer answer no. 20

63. Ans. is b, c, d and e i.e. B. Coli; Microsporidium species; E. dispar; and Giardia intestinalis

Let consider each options.

a. ***Cyptococcus*** is **fungus** causing pulmonary, cutaneous and cryptococcal meningitis. *... AA 7/e, p 620*

b. ***Balantidum coli*** – **only ciliate** protozoan parasite of man. Its trophozoite lives in ***large intestine.***
... Paniker 4/e, p 108

c. ***Microsporidium sp.*** – It ***is intracellular parasites.***
- Transmission is chiefly by ingestion of spores in food or water.
- Transplacental transmission is common.
- Also cause infection in AIDS patient *....Jawetz 24/e, p 684*

d. ***E. dispar***
- It is protozoa (amoeba)
- In case of intestinal amoebiasis, parasite remains luminal and trophozoite multiply as a bacteria feeding colony, ultimately encyst and pass out in feces. These are presumed to be due to E. dispar.

It is lumen dwelling non pathogenic commensal.

It is distinguished from E. histolytica only by isoenzyme electrophoresis and DNA analysis.
... Jawetz 24/e, p 672

e. ***Giardia lamblia*** is intestinal **flagellates.** *... Paniker 4/e, p 34*

64. Ans. is a, b and c i.e. Chlamydia; Rickettsia; and Mycoplasma
Ref. See index of any Microbiology Book

Prion is proteinacoeus infectious particle, without nucleic acid, cause slow virus disease.
Bacteriophage is the virus that infects bacteria.

65. Ans. is a, b and c i.e. Toxoplasma; Syphilis; and CMV *Ref. Harrison 17/e, p 712*

Already explained, refer answer no. 20

66. Ans. is a, b, c, d and e i.e. All are correct options
Ref. Jawetz 24/e, p 717-718; Harrison 17/e, p 814 Tab. (113-1)

Following infections required stool examination for diagnosis :

i. Toxins (of staphylococcus, Clostridia, Vibrios, Toxigenic E.coli)
ii. Shigella
iii. Salmonella
iv. Campylobacters
v. Yersinia enterocolitica
vi. Vibrios

vii. Enteric bacteria

viii. Enteroviruses

ix. Intestinal parasites (Giardia, E. histolytica, B. coli, Cryptosporidium, Fasciola hepatica, E. vermicularis etc).

67. Ans. is a and c i.e. Mitochondria always absent; and Divide by binary fission

Ref. Ananthnarayan 7/e, p 8, table (2.1), p 395

- Only bacteria having sterol in its cell membrane : **Mycoplasma**
- **Bacteria can be seen by :**
  - Optical or light microscopy
  - Phage contrast microscopy
  - Dark field or dark ground microscopy
  - Electron microscopy.

68. Ans. is a, b and d i.e. Viruses; Chlamydia; and Rickettsia *Ref. Ananthnarayan 7/e, p 55 - 57*

Already explained, refer answer no. 10

69. Ans. is d i.e. Gardenella *Ref. Harrison 17/e, p 827; Shaws 12/e, p 98 - 100*

"Treatment of male partners with metronidazoe does not prevent recurrence of bacterial vaginosis / gardenella associated with vaginal discharge."

Treatment of sexual partners is required in :
- Candidiasis
- Herpes genitalis
- Trichomoniases.

70. Ans. is a and b i.e. Lactobacillus; and Bacteroides

Ref. Ananthnarayan 7/e, p 601; Jawetz 24/e, p 199

Normal flora of intestinal tract :

- At birth intestine is sterile but organism are soon introduced with food.
- **Stomach's acidity** keep the number of microorganism at a minimum **(10^3-10^5** g of iontents) **level,as** the pH of intestinal contents becomes alkaline, resident flora gradually increases.
- ***In the upper intestine,*** *lactobacilli* and *enterococci* predominate but in lower ileum and caecum, flora is fecal.
- ***In normal adult colon,*** 96-99% of resident bacterial flora consist of *anaerobes* - *bacteriodes* sp. especially B. fragilis, fusobacterium sp; anaerobic lactobacilli eg bifidobacterium; clostridium (C. perfringes) and *anaerobic gram positive cocci* (peptostreptococcus).
  - Only 1-4% are facultative aerobes (gram negative coliform bacteria, enterococci, pseudomonas etc.)

71. Ans. is b and d i.e. Eikenella corrodens; and H. pylori *Ref. Ananthnarayan 7/e, p 266*

ANAEROBES BACTERIA

Cocci		
A. Gram positive a. Peptostretptococcus b. Peptococcus	*B. Gram negative* Veillonella	
Bacilli		
1. *Endospore forming* A. Clostiridia	2. *Nonsporing* A. Gram positive : a. Eubacterium c. Lactobacillus e. Bifidobacterium B. Gram negative : a. Bacteriodes c. Porphyromonas e. Leptotrichia	b. Propionibacterium d. Mobiluncus f. Actinomyces b. Prevotella d. Fusobacterium
Spirochetes		
A. Treponema	B. Borrelia	

72. Ans. is d i.e. Aromatic amino acid *Ref. Ananthnarayan 7/e, p 12, Table (2.2)*

Cell Wall

Features	Gram positive	Gram negative bacteria
Plasmolysis	Late	Early
Thickness (Peptidoglycan)	Thicker	Thinner
Variety of aminoacids	Few	Several
Aromatic and sulphur containing aminoacids	Absent	Present
Lipids	Absent or scant	Present
Teichoic acid	Present	Absent

73. Ans. is a i.e. CMV *Ref. Nelson 17/e, p 568, 623, 626, 631*

Transplacental transmission occurs in :

Viruses :	– Rubella – Varicella zoster virus – HIV – HBV and HCV	– CMV – Parvo B - 19 – West nile virus – Measles	– HSV – Coxasackie viruses – Enteroviruses
Bacteria :	– Syphilis	– *TB*	– Brucella
Parasite :	– Plasmodium – Toxoplasma	– T. cruzi	– Microsporidia

74. Ans. is c i.e. HFR *Ref. Anathnarayan 7/e, p 57 - 59*

Genetic basis of drug resistance

Mutation in gene = *Chromosomal mutation*

Gene transfer

Transformation	Transduction	Conjugation
• Significance in nature is not known	• Penicillin resistance in staphylococci • Chromosomal DNA, plasmid and episomes all can be transduced • Most widespred method of gene transfer	• ***It is most important method of drug resistance.*** • Occurs by plasmid called R factor. • It can promote chromosomal transfer from diverse bacteria including pseudomonas species

Remember :

- Transfer of drug resistance by conjugation of whole plasmid (RTF+r deteminants = R factor) is known as ***transferable or episomal or infectious drug resistance.***
- Enterotoxin and hemolysin production in some enteropathogenic E. coli are also transmitted by RTF (resistance transfer factor).
- Plasmid are genetic elements most frequently transferred by conjugation.

75. Ans. is a i.e. Viral interference *Ref. Ananthnarayan 7/e, p 445*

Viral interference

"Interference in which infection of a cell by one virus inhibits simultaneous or subsequent infection by another virus."

– ***Most important*** *mediator* of interference is *interferon.*

– Interference produced by destruction of cell receptors is seen *with myxoviruses and enterovirus.*

It is *applied* in the field in *controlling poliomyelitis* outbreaks by introducing into the population, the live attenuated poliovirus vaccine.

Remember : Interference is *Nongenetic interaction.*

76. Ans. is b i.e. Capsid *Ref. Ananthnarayan 7/e, p 431*

"Capsid is the protein coat which surrounds nucleic acid (RNA or DNA) of virus."

- Capsid + enclosed nucleic acid is known as nucelocapsid.
- ***Function of capsid is :***
  1. To *protect the* nucleic acid from inactivation by nucleases and other deleterious agents in the environment.
  2. To *introduce viral genome into host cells* by adsorbing readily to cell surfaces.
- Virions may be enveloped (Outer lipoprotein covering) or non enveloped.

Chapter Review

- This section includes questions of Various Other PGMEES from 1990 – 2007.
- Questions are arranged in decreasing order of yearwiz. This is done to make referral system easier and uncomplicated to save the precious time of PGMEE Aspirant.

1. DNA virus is : **[Delhi 89; 90]**
a) Polio type I
b) Polio type II
c) Echovirus
d) Adenovirus
[Ref. Ananthnarayan 7/e, p 446]

2. All are oncogenic except : **[AI 90]**
a) EB virus
b) Papilloma virus
c) Herpes simplex virus
d) Varicella zooster virus
[Ref. Ananthnarayan 7/e, Table (61.2]]

3. Which of the following does not infect the CNS :
a) Hepatitis B **[JIPMER 90]**
b) HTLV-III
c) H. Simplex-I
d) H. Simplex-II
[Ref. Harrison 17/e, p 2627]

4. Which is true of pus : **[AI 90]**
a) Fecal smelling pus in E. coli
b) Thick and clean coloured in staph aureus
c) Reddish in pseudomanas
d) Sulphur granules in candida
[Ref. Under consideration]

5. Septicemia is : **[TN 91]**
a) Bacteria in blood
b) Toxin in blood
c) Pus in blood
d) Multiplication of bacteria and toxins in blood
[Ref. Ananthnarayan 7/e, p 70]

6. Niacin is required by growth of : **[Kerala 91]**
a) M. tuberculosis
b) M. kanasasi
c) M. Scrofuloderma
d) M. Avium
[Ref. Ananthnarayan 7/e, p 353]

7. Herd immunity is not seen in : **[Kerala 91]**
a) Polio
b) Tetanus
c) T.B.
d) Leprosy
[Ref. Park 19/e, p 96]

8. Undulant fever is caused by : **[JIPMER 91]**
a) Bartonella
b) Brucella Melitensis
c) Bordetella
d) Borelia recurentis
[Ref. Ananthnarayan 7/e, p 345]

9. Toxic Shock syndrome is caused by :
a) Staph albus **[JIPMER 91]**
b) Staph aureus
c) Strep viridans
d) Strep Pyogenes
[Ref. Ananthnarayan 7/e, p 196, 208]

10. Human immune deficiency virus is a virus :
a) Rheo **[TN 91]**
b) Retro
c) Rhado
d) Flavi *[Ref. Ananthnarayan 7/e, p 582]*

11. Tuberculous infection most common in AIDS :
a) M. Avium Intracellulare **[JIPMER 91]**
b) M. Scrofulaceum
c) M. Ulcerans
d) M. Tuberculosis
[Ref. Harrison 16/e, p 1108, 1107 Fig (173-28)]

12. Segmented RNA is seen in : **[AI 91]**
a) Rabies virus
b) Coxsackie B virus
c) Influenza virus
d) Rabies virus
[Ref. Ananthnarayan 7/e, Table (55.1)]

13. Which of the following is a single stranded DNA :
a) Herpes simplex **[AI 91]**
b) Parvo virus
c) Papavo virus
d) Rabies virus
[Ref. Ananthnarayan 7/e, p 447]

14. Louis pasteur is not associated with :
a) Introduction of Complex media **[JIPMER 91]**
b) Discovery of Rabies Vaccine
c) Discovery of M.Tuberculosis
d) Disproved spontaneous regression theory
[Ref. Ananthnarayan 7/e, p 2]

Answer

1. d) Adenovirus	2. d) Varicella ...	3. a) Hepatitis B	4. b) Thick & clean ...	5. d) Multiplication ...
6. a) M. tuberculosis	7. b) Tetanus	8. b) Brucella ...	9. b and c	10. b) Retro
11. a) M. Avium ...	12. c) Influenza ...	13. b) Parvo virus	14. c) Discovery ...	

15. Oncogenic RNA virus : **[Kerala 91]**
a) Avian leuco virus
b) Herpes virus
c) Adenovirus
d) Toga virus
[Ref. Ananthnarayan 7/e, Table (61.2]

16. All are common organisms causing UTI except :
a) Streptococcus fecalis **[AIIMS 92]**
b) Escherichia coli
c) Proteus Mirabilis
d) Hemophilus influenzae
[Ref. Harrison 17/e, p 1820]

17. Which of the following "oncogenic viruses" is so far not shown to be oncogenic in man : **[DNB 92]**
a) Hepatitis B virus
b) Epstein - Barr virus
c) Herpes simplex virus
d) Adenovirus
e) Human T cell lymphotrophic virus (HTLVI)
[Ref. Ananthnarayan 7/e, p 576]

18. ELISA test when compared to western blot technique is : **[AI 93]**
a) Less sensitive, less Specific
b) More Sensitive, more specific
c) Less sensitive, more specific
d) More Sensitive, less specific
[Ref. Park 19/e, p 293]

19. Sero conversiion in HIV infection takes places in:
a) 22 weeks **[JIPMER 93]**
b) 14 weeks
c) 9 weeks
d) 12 weeks
[Ref. Harrison 17/e, p 1165]

20. F factor integrates to form : **[JIPMER 93]**
a) HFr
b) RTF+r
c) F (-)
d) RTF
[Ref. Ananthnarayan 7/e, p 54]

21. Double straded RNA is seen in : **[JIPMER 93]**
a) Reo virus
b) Rhabdo virus
c) Parvo virus
d) Retro virus
[Ref. Ananthnarayan 7/e, p 448]

22. All are oncogenic viruses except : **[UP 03]**
a) EB virus
b) Reo virus
c) Retrovirus
d) Human papilloma virus
[Ref. Ananthnarayan 7/e, p Table (61.2)]

23. The causative organism of traveller's diarrohea is: **[AIIMS 94]**
a) Shigella
b) E. coli
c) Salmonella
d) Viral
[Ref. Ananthnarayan 7/e, p 278]

24. What is true about Bordetella pertusis : **[PGI 95]**
a) Adhere to normal mucosa
b) Destroys cilia
c) Local tissue destruction
d) All of the above
[Ref. Ananthnarayan 7/e, p 278]

25. Smallest DNA virus is : **[Kerala 94]**
a) Herpes virus
b) Adeno virus
c) Parvo virus
d) Pox virus
[Ref. Ananthnarayan 7/e, p 447, 431]

26. The discovery of "gene transformation" came from the study of one of the following bacteria :
a) Bacillus subtilis **[Kar. 95]**
b) Streptococcus pyogenes
c) Streptoccus pneumoniae
d) Escherichia coli
[Ref. Ananthnarayan 7/e, p 55]

27. "Stalactite" growth is a feature of : **[TN 89, 95]**
a) Hemphilus
b) Pasteurella
c) Cornybacterium
d) Mycoplasma
[Ref. Ananthnarayan 7/e, p 325]

28. Prokaryotes are : **[Kerala 96]**
a) Have nucleus
b) Contain DNA and RNA
c) Does not contain cell wall
d) Unicellular
e) None *[Ref. Ananthnarayan 7/e, p 7]*

29. Ebola virus is a : **[Delhi 96]**
a) Reovirus
b) Filovirus
c) Arbovirus
d) Arena virus
[Ref. Ananthnarayan 7/e, p 448]

Answer

15. a) Avian leuco ...	16. d) Hemophilus ...	17. d) Adenovirus	18. d) More Sensitive...	19. c) 9 weeks
20. a) HFr	21. a) Reo virus	22. b) Reo virus	23. b) E. coli	24. d) All of ...
25. c) Parvo virus	26. c) Streptoccus ...	27. b) Pasteurella	28. a and d	29. b) Filovirus

30. Single stranded DNA virus is : **[Kerala 96]**

a) Parvo virus
b) Polio virus
c) Adeno virus
d) Rabies virus
e) None of the above

[Ref. Ananthnarayan 7/e, p 447]

31. All are capsulated bacteria except : **[M.P. 96]**

a) Step. Pneumonia
b) Kleb. Pneumonia
c) Vibrio cholera
d) H. Influenza

[Ref. Learn list of our book]

32. Which of the following does not posses both DNA and RNA : **[Kerala 96]**

a) Bacteria
b) Fungus
c) Virus
d) Spirochete

[Ref. Ananthnarayan 7/e, p 430]

33. The mechanism of genetic transfer where a phage serves as a vehicle is : **[Delhi 96]**

a) Transformation
b) Translation
c) Conjugation
d) Lysogeny

[Ref. Ananthnarayan 7/e, p 56]

34. Most of the drug resistance occurs due to :

a) Transduction **[Kerala 96]**
b) Translation
c) Mutation
d) Conjugation

[Ref. Ananthnarayan 7/e, p 57]

35. The mechanism by which specific information encoded in a nucleic acid chain in a virus transferred to mRNA known as : **[Karanat 96]**

a) Transcription
b) Translation
c) Transformation
d) Transduction

36. Property of acquiring antibiotic resistance from viral colony is by : **[SGPGI 96]**

a) Transferance
b) Conjugation
c) Transduction
d) Mutation

[Ref. Ananthnarayan 7/e, p 56]

37. Infection not transmitted transplacetally is :

a) Herpes **[DNB 05]**
b) EB virus
c) CMV
d) Polio

38. In a splenectomized patient there is increase of infection by all the organism except :

a) Pneumococci **[SGPGI 05]**
b) Klebsiclla
c) H. influenzae
d) Staph. aurcus

[Ref. Ananthnarayan 7/e, p 197

39. Nocardia resemble actinomyces morphological but : **[ICS 2K]**

a) Are anaerobic
b) Are faculative anaerobic
c) Are aerobic
d) Require Co_2 for growth

[Ref. Ananthnarayan 7/e, p 401]

40. Polysaccharide capsule resistance to phagocytosis is seen in : **[Nimhans 01]**

a) N. meningitis
b) K. pneumonia
c) Streptococcus pneumonia
d) Yeast

[Ref. Ananthnarayan 7/e, p 219]

41. Which is not oncogenic out of the following viruses:

a) Varicella **[UP 96]**
b) EBV
c) HTLV
d) All of the above

[Ref. Ananthnarayan 7/e, Table (61.2)]

42. Which of the following is not cultured :

a) Sporothrix - schenckii **[UP 07, 05]**
b) Rhinosporidium seeberi
c) Candida-albicans
d) Aspergillus fumigatus

[Ref. Ananthnarayan 7/e, p 620]

43. The important organism causing meningitis in immunocompromised patient is :

a) Histoplasma **[AI 91; Jipmer 91]**
b) Cryptococcosis
c) Coccidiomycosis
d) Candida albicans

[Ref. Harrison 17/e, p 2642]

Answer

30. a) Parvo virus 31. c) Vibrio ... 32. c) Virus 33. d) Lysogeny 34. d) Conjugation
35. a) Transcription 36. None 37. d) Polio 38. b) Klebsiclla 39. c) Are aerobic
40. c) Streptococcus ... 41. a) Varicella 42. b) Rhinosporidium ... 43. b) Cryptoco...

44. The following viruses has been associated with oncogenesis except: [UP 97]
a) Human papiloma viruses
b) Epstein papiloma virus
c) Human T cell leukamia virus
d) Varicella zoster virus
[Ref. Ananthnarayan 7/e, Table (61.2)]

45. Most Probable cause of food poisoning in a child who has eaten Ice Cream 16-18 hrs. earlier is :
a) Staph aureus **[AIIMS 92]**
b) Clostridum perfringens
c) Clostridium botulinum
d) Salmonella typhimurium
[Ref. Ananthnarayan 7/e, p 303]

46. Type of human papiloma virus associated with carcinoma cervix : [JIPMER 98]
a) Types 6, 12, 18
b) Types 16, 18, 31
c) Types 6, 8, 11
d) Types 3, 10, 19
[Ref. Ananthnarayan 7/e, p 575]

47. DNA melting refers to : [Delhi 98]
a) Splitting of DNA into single strands
b) Breaking *DNA* into fragments
c) Breaking DNA down to bases
d) Fusion of DNA
[Ref. Learn it given in Harper]

48. Plasmid : [JIPMER 98]
a) Involved in multidrug resistace transfer
b) Involved in conjugation
c) Imparts capsule formation
d) Imparts pili formation
[Ref. Ananthnarayan 7/e, p 53, 56]

49. Drug resistance is not transmitted by : [Delhi 98]
a) HFr
b) Transposons
c) Plasmids
d) Chromosomes
[Ref. Ananthnarayan 7/e, p 57]

50. Which of the following organism required tryptophan for growth : [DNB 98]
a) H. influenza
b) Vibrio
c) Gonococci
d) Salmonella typhi
[Ref. Ananthnarayan 7/e, p 290]

51. Which is a live attenuated vaccine : [PGI 93]
a) Rabies
b) BCG
c) Hepatitis B
d) Cholera
[Ref. Park 19/e, p 97]

52. Conjugation does not involve : [UPG 99]
a) Bacteriophages
b) HFr-
c) Fr
d) Plasmids
[Ref. Ananthnarayan 7/e, p 56]

53. Bacteria belongs to : [UP 99]
a) Plantae
b) Protista
c) Monera
d) Fungi
[Ref. N.C.E.R.T]

54. Which virus can cause hemorrhage :
a) Parvo virus **[JIPMER 93]**
b) Adeno virus
c) HPV
d) Corona virus
[Ref. Ananthnarayan 7/e, p 488]

55. Fungal infection is diagnosed with : [UP 00]
a) Giemastain
b) KOH
c) Foot and pad culture
d) Albert strain
[Ref. Ananthnarayan 7/e, p 611]

56. The fungi which do not have sexual reproduction belong to which of the following groups :
a) Phycomycetes **[Kerala 00]**
b) Fungi imperfecti
c) Basidomycetes
d) Asomycetes
e) None of the above
[Ref. Ananthnarayan 7/e, p 611]

57. Teichoic acids : [Kar 00]
a) Are found in the walls of many gram-positive bacteria
b) Make up the outer wall of bacteria
c) Provide receptors for phages
d) Influence the permeability of membrane
[Ref. Jawetz 24/e, p 22]

58. Which of the following is a non culturable fungus:
a) Rhinosporidium **[MAHE 01; UP 05]**
b) Candida
c) Sporothrix
d) Penicillium
[Ref. Ananthnarayan 7/e, p 620]

Answer
44. b) Epstein ... 45. d) Salmonella 46. b) Types ... 47. a) Splitting ... 48. a and b
49. a) HFr 50. d) Salmonella ... 51. b) BCG 52. a) Bacteriop ... 53. c) Monera
54. b) Adeno... 55. b) KOH 56. b) Fungi ... 57. a) Are found ... 58. a) Rhino...

59. All the true about bacterial nucleus except :
a) No nuclear membrane **[Kolkata 02]**
b) Divides by binary fission
c) The bacterial chromosome is diplid
d) No single molecule of double stranded DNA
[Ref. Ananthnarayan 7/e, p 14]

60. Louis pasteur is assoicated with : [Kolkata 02]
a) Discovery of the bacillus of tuberculosis
b) The cellular concept of immunity
c) Introduction of anthrax vaccine
d) Discovery of penicillin
[Ref. Ananthnarayan 7/e, p 2]

61. Nanometer equals : [Kolkata 02]
a) 10_{-5} mm
b) 10_{-3} mm
c) 10_{-4} mm
d) 10_{-6} mm

62. The role of plasmids in conjugation was first described by Lederberg and Tatum in : [Kar. 02]
a) Salmonella
b) Staph aureus
c) V. cholerae
d) Shigella dysenteriae
[Ref. Ananthnarayan 7/e, p 197, 466]

63. The following microorganisms constitutes the normal flora of the oral cavity : [Kar 2002]
a) E.coli
b) Staphylococcus epidermidis
c) Branhamella caterrhalis
d) Picorna virus
[Ref. Jawetz 24/e, p 199]

64. Phage typing is useful as an epidemiological tool in all except : [JIPMER 02]
a) H. influenzae
b) Corynebacterium
c) Pseudomonas
d) Esch. Coli
[Ref. Ananthnarayan 7/e, p 56]

65. Most common mode of transmission of nosocomial infections : [JIPMER 95]
a) Nasal droplets
b) Catheters
c) Contact with hospital personel
d) Contaminated needles
[Ref. Harrison 17/e, p 836]

66. All of the following diseases are mosquito borne except : [JIPMER 95]
a) Japanese encephalitis
b) Yellow fever
c) Dengue fever
d) Sleeping sickness
[Ref. Park 19/e, p 622]

67. Cell-Fraction derived vaccine is : [AP 97]
a) Hepatitis B
b) Measles
c) Mumps
d) Rubella
[Ref. Park 19/e, p 98]

68. Not transmitted to man by an insect vector :
a) Sleeping sickness **[Kerala 98]**
b) Q-fever
c) Malaria
d) Kala-azar
[Ref. Park 19/e, p 622]

69. Horizontal transmission of 'R' factor is by :
a) Trans dection **[JIPMER 03]**
b) Transformation
c) Conjugation
d) Fusion
[Ref. Ananthnarayan 7/e, p 56]

70. Which of the following isnot a killed vaccine ?
a) Yellow fever **[Kar 03]**
b) Salk (Polio)
c) Hepatitis B
d) Human diploid cell rabies vaccine
[Ref. Park 19/e, p 97]

71. Which of the following is not an obligate parasite?
a) Virus **[Bihar 03]**
b) Mycoplasma
c) Chlamydia
d) Rickettsia
[Ref. Ananthnarayan 7/e, p 395]

72. Mesosmes are : [Bihar 03]
a) Respiratory enzymes in bacteria
b) Cytoplasmic invagination
c) Destructive bodies
d) Protein forming bodies
[Ref. Anantharaya 7/e, p 13]

73. The following are motile organisms except :
a) Proteus **[DNB 04]**
b) Diphtherias
c) Clostridia
d) Anthrax
[Ref. Ananthnarayan 7/e, p 231]

Answer
59. c) The bacterial ... 60. c) Introduction ... 61. d) 10_{-6} mm 62. d) Shigella ... 63. c. Branhamella ...
64. b) Coryne ... 65. b) Catheters 66. d) Sleeping... 67. a) Hepatitis B 68. b) Q-fever
69. c) Conjugation 70. a) Yellow fever 71. b. Mycoplasma 72. a) Respiratory ... 73. b) Diphtherias

74. The biochemial composition of bacterial endotoxin is : **[MP 05]**
a) Peptidoglycan
b) Lipopolysaccharide
c) Glycopeptids
d) Lipoprotein
[Ref. Ananthnarayan 7/e, p 68]

75. Pigment producing colonies are seen in :
a) Pseudomonas **[Kar 04]**
b) Atypical mycobacteria
c) Serratia marcescens
d) All of the above
[Ref. Ananthnarayan 7/e, p 366, 282, 319]

76. Infective positive sense, nucleic acid genome are found in : **[UP 04; Kerala 01]**
a) Poliovirus
b) Papova-virus
c) Influenza virus
d) Picorna virus
[Ref. Ananthnarayan 7/e, p 437]

77. Brain abscess in immunodeficiant person is due to : **[Jharkhand 04]**
a) Cryptococus
b) Staphylococcus
c) Pnumococcus
d) E coli
[Ref. Harrison 17/e,p 2636]

78. Bacterial cell wall is composed of all except :
a) Muramic acid **[Bihar 04]**
b) Teichoic acid
c) Glucosamine
d) Mucopeptide
[Ref. Ananthnarayan 7/e, p 12]

79. Bacterial capsule is made up of :
a) Monosaccharide **[Bihar 04]**
b) Polysaccharide
c) Long chain fatty acid
d) Small chain fatty acid
[Ref. Jawetz 24/e, p 31]

80. Condyloma accuminatum caused by human papilloma virus (HPV) types of : **[UP 05]**
a) 18, 31
b) 17, 12
c) 6, 11
d) 16, 18
[Ref. Ananthnarayana 7/e, p 575]

81. Virus growth in cell cultures detected by cytopathic effect characteristic features of : **[UP 05]**
a) Syncytium formation
b) Budding formation
c) Flattening
d) All of the above
[Ref. Ananthnarayana 7/e, p 440]

82. Which among is not a fungus :
a) Rhinosporidiosis **[Jharkhand 05]**
b) Sporrotrichosis
c) Torulois
d) Candidosis
[Ref. Chakarborty 7/e, p 610]

83. Mesosomes in bacteria are functional unit for :
a) Lipid storage **[Bihar 05]**
b) Protein synthesis
c) Respiratory enzymes
d) None
[Ref. Ananthnarayan 7/e, p 13]

84. Most common organism causing lobar pneumonia: **[MP 06]**
a) Klebsiella pneumoniae
b) Streptococci pneumoniae
c) H. influenzae
d) Proteus
[Ref. Robbins 7/e, p 748; 6/e, p 719; AA 7/e, p 219]

85. Most common organism in gut is : **[MP 06]**
a) E. coli
b) Lactobacillus
c) Bacteroides
d) Klebsiella
[Ref. Jawetz 24/e, p 200]

86. Peptidoglycans are present in : **[UP 2006]**
a) Gram -ve bacteria
b) Gram +ve bacteria
c) Both a and b
d) Protozoa
[Ref. Chakraborty 2/e, p 18]

87. Cell wall structure is found in all except :
a) Staph aureus **[UP 06]**
b) Pseudomonas aeurogeinosa
c) Mycoplasma pleumoniae
d) Corynebacterium diphtheriae
[Ref. Ananthnarayan 7/e, p 395]

Answer
74. b) Lipopolysac ... 75. d. All of the ... 76. d) Picorna virus 77. a) Cryptococus 78. b) Teichoic acid
79. b) Polysac ... 80. c) 6, 11 81. a) Syncytium ... 82. c) Torulois 83. None
84. b) Streptococci ... 85. c) Bacteroides 86. b) Gram +ve ... 87. c) Mycoplasma ...

88. Vertically transmitted disease caused by all except: [UP 06]

a) Toxoplsma
b) Cytomegala
c) HIV
d) Treponema-pertenue

[Ref. Park 19/e, p 91]

89. All the disease caused by transfusion except : [UP 06]

a) HIV
b) Hepatitis-B
c) Hepatitis-C
d) Plague

[Ref. Harrison 17/e, p 712]

90. The cytoplasmic membrane bacteria is responsible for : [Kar 06]

a) Selective permeability
b) Motility
c) Cell division
d) Conjugation

91. In negative staining : [Kar 06]

a) The structure to be demonstrated is stained
b) The structure to be demonstrated is not stained
c) The background is not stained
d) The background and structure are stained

[Ref. Ananthnarayan 7/e, p 9]

Answer 88. d) Treponema ... 89. d) Plague 90. a) Selective ... 91. b) The structure ...

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