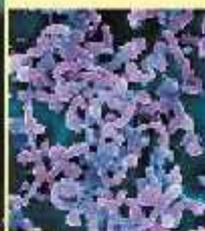
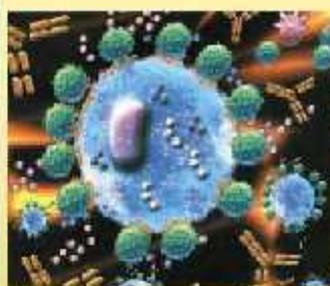


CLINICO - BASIC

MICROBIOLOGY

4th Revised Edition



Muhammad Shamim

Clinico-Basic MICROBIOLOGY

4th Revised Edition

Comprehensive & Quick Review for Undergraduates & Postgraduates

Based on Lectures, Demonstrations, Tutorials & Practicals of Most Medical Colleges & Universities of Pakistan, Bangladesh, China, Russia, Saudi Arabia, UAE, Sudan, Yemen, Egypt & Malaysia.

Author

Dr. Muhammad Shamim

MBBS, FCPS, FRCS, FACS, FICS, JMHP, PhD (h.c.)

- 1. Assistant Professor of Surgery, College of Medicine, Prince Sattam bin Abdulaziz University, Saudi Arabia*
- 2. Ex. Associate Professor, Dept. of Surgery, Baqai Medical University, Karachi.*
- 3. Supervisor & Chief Facilitator, College of Physicians & Surgeons Pakistan.*
- 4. Assistant Editor, Journal of Surgery Pakistan*

Editors

- **Dr. Syeda Ghazala Arfa** (BDS)
- **Dr. Shumaila Bano** (BDS)

6253 — Copy

All rights reserved. This publication cannot be reprinted, distributed or sold without prior written permission of the author.

ISBN 978-969-8691-16-5



Price ----- Rs. 150/= (Free online)

First Edition _____	December, 1992
Reprint _____	January, 1994
Second Edition _____	May, 1998
Second Revised Edition _____	March, 2000
Third Edition _____	January, 2003
Third Revised Edition _____	November, 2004
Fourth Edition _____	April, 2012
Fourth Revised Edition _____	April, 2017

Author

Dr. Muhammad Shamim

E-mail: surgeon.shamim@gmail.com

Web: <http://surgeonshamim.com/>

Editors

Dr. Syeda Ghazala Arfa

Dr. Shumaila Bano

Composer

M. Nadeem, Khurram & Brothers, Karachi

Printed At

Qureshi Art Press, Nazimabad No. 2, Karachi

Publisher

Khurram & Brothers, Karachi (ISBN 978-969-8691)

Dedicated with Regard
To
My Respectable Teachers of

KBV School (1979-1985)

DJ Science College (1985-1987)

Dow Medical College (1988-1993)

Civil Hospital Karachi (1990-2004)

Preface to the Fourth Edition

Microbes are integral part of our planet, sharing life with humans. They may have either beneficial roles in maintaining life, or undesirable roles in causing diseases. Also mutant strains are constantly arising that account for rapid evolutionary adaptation & emergence of diseases such as AIDS, & antibiotic-resistant tuberculosis. So, it becomes necessary to understand & employ the principles of microbiology & molecular mechanisms of pathogenesis, & newer developments in diagnostic aids & treatment, as this will make the physicians & medical scientists enable to control an increasing number of infectious diseases.

Clinico-basic Microbiology is effectively two books in one, encompassing comprehensive review of medically important microbes & parasites. The book is written at a level appropriate for medical students (undergraduates & postgraduates), physicians & infectious disease scientists. Informations are presented in a concept-making way, with emphasis on making it clear, & up to date.

- The book starts with chapters presenting the general concepts of bacterial microbiology.
- Following that, there are series of chapters on medically important bacterias. The chapters themselves are comprehensive yet free of unnecessary detail. An identical format is followed thru-out, designed according to the examination pattern in our country, & it consists of classification, morphology, culture, antigens, toxins, enzymes, habitat & transmission, pathogenesis & clinical findings, diagnostic laboratory tests, immunity, treatment, & prevention & control.
- **The whole microbiology section is extensively revised & updated..**
- **A new chapter on Helicobacter pylori is added.**
- Format of the chapters on parasites are modified according to the need, consisting of inclusion of life cycle, & exclusion of culture, antigens, enzymes, & toxins.
- A chapter on mycology provides basic brief review of medically important fungi.
- **The virology section is extended with 4 new chapters. Medically important viruses are described in some details along the same lines as that for bacteriology section.**
- Morphology is elaborated with the help of pictures of simple microscopy, or electron micrographs. Similarly life-cycles are elaborated in attractive diagrammatic form.
- Informative review boxes are given at appropriate places.
- Self-examination section is similarly extended with a new chapter according to the changing trends in examination pattern. One chapter comprises T/F type MCQs, & the other chapter comprises **single-best MCQs**.

In the end, I would like to say thanks to Dr. Ghazala Arfa, Dr. Shumaila Bano, Mr. Aamir Pervaiz, & Mr. M. Nadim for every sort of cooperation they have provided.

Any suggestion for the improvement of this book will be acknowledged with thanks.

Dr. Muhammad Shamjm
14th April 2012

Preface to the First Edition

Clinico-Basic Microbiology Plus Parasito is a book that provides comprehensive & concise knowledge about the medically important aspects of microbiology & parasitology. It is written with the aim to assist students in their preparation for theory & viva examinations.

- ❖ Informations are presented in a concept-making way, with emphasis on making it clear, & up to date.
- ❖ An identical format is followed thru-out this book, & this is designed according to the examination pattern in our country.
- ❖ Format for the description of microorganisms is:
 - (1) Classification → Sometime asked in viva.
 - (2) Morphology → May be asked in short questions, or in viva, or in MCQs.
 - (3) Culture → May be asked in MCQs. In viva, only media are usually asked.
 - (4) Antigens → Important for MCQs & viva
 - (5) Toxins → Important for MCQs & viva
 - (6) Enzyme → Important for MCQs & viva
 - (7) Habitat & Transmission → May be asked in MCQs, or in viva.
 - (8) Pathogenesis, & Clinical Findings → Important for short questions, viva & MCQs.
 - (9) Diagnostic Laboratory Tests → Important for short questions, viva, & may be asked in MCQs.
 - (10) Immunity → Sometime asked in viva, esp about immunization, & may be asked in MCQs.
 - (11) Treatment → Sometime asked in viva, & may be in MCQs.
 - (12) Prevention & Control → Usually not asked.
- ❖ Format for the description of parasites is essentially the same except for the following:
 - (1) Life cycle is included
Important for short questions, & may be asked in viva.
 - (2) Culture, antigens, enzyme, & toxins are eliminated (b/c of lack of their importance for examination).
- ❖ Description about viruses, is purposefully reduced to only the name of diseases, b/c only this is sometime asked in viva.
- ❖ Diagrams are given to make a clear idea about morphology. Similarly life-cycles are also given in diagrammatic form.
- ❖ In the last chapter, objective type questions & answers are given in the form of T/F type MCQs.
- ❖ In the end, I would like to say thanks to Lubna Fatima, Ashar Khan, Aamir Pervaiz, M. Firdaus, Ikraam, M.A. Qadir, Farah Yasmeen, Azhar Iqbal, Kamal Ahmed & Shahid Ahmed, for every sort of cooperation they have provided.
- ❖ Any suggestion for the improvement of this book will be acknowledged with thanks.

Muhammad Shamim
5th December, 1992

Contents

Section I

MICROBIOLOGY

1. General bacteriology _____	2
2. Culture media for bacteria _____	9
3. Medically important bacteria _____	13
4. Staphylococci _____	16
5. Streptococci _____	21
6. Streptococcus pneumonia _____	27
7. Corynebacterium diphtheria _____	31
8. Mycobacterium tuberculosis _____	34
9. Clostridium tetani _____	41
10. Clostridium botulinum _____	44
11. Clostridium perfringens _____	47
12. Neisseria gonorrhoeae _____	50
13. Neisseria meningitides _____	54
14. Escherichia coli _____	57
15. Klebsiella _____	62
16. Proteus _____	65
17. Salmonella _____	68
18. Shigella _____	72
19. Vibrio cholera _____	75
20. Helicobacter pylori _____	78
21. Pseudomonas aeruginosa _____	81
22. Chlamydiae _____	84
23. Rickettsiae _____	88
24. Treponema pallidum _____	92
25. Miscellaneous bacteria _____	96
26. Causative organisms of specific diseases _____	99
27. Mycology _____	102
28. General virology _____	108
29. DNA enveloped viruses _____	110
30. RNA enveloped viruses _____	118
31. Hepatitis viruses _____	131
32. Miscellaneous viruses _____	137

Section II

PARASITOLOGY

33. General parasitology _____	141
34. Entameba histolytica _____	143

35. Plasmodia	149
36. Giardia lamblia	154
37. Trichomonas vaginalis	157
38. Leishmania	159
39. Schistosoma	162
40. Diphyllbothrium latum	166
41. Tenia saginata	169
42. Tenia solium	172
43. Echinococcus granulosus	175
44. Hymenolepis nana	178
45. Ascaris lumbricoides	181
46. Ancylostoma duodenale	185
47. Enterobius vermicularis	188
48. Trichuris trichiura	191
49. Wuchereria bancrofti	194
50. X-borne diseases	197

Section III**SELF EXAMINATION**

51. Self-examination (true / false)	200
52. Self-examination (single best)	222

Khurram & Brothers Publications

A trusted name for comprehensive & quick review of undergraduate or postgraduate medical exams.

1. **Essential Human Anatomy (volume 1 & 2)**
By: M. Shamim
2. **Clinicobasic Pharmacology**
By: M. Shamim
3. **Clinicobasic Microbiology**
By: M. Shamim
4. **Essentials of Community Medicine**
By: M. Sarwar
5. **Essentials of Surgery**
By: M. Shamim
6. **Clinical Techniques in Surgery**
By: M. Shamim
7. **Essentials of Ophthalmology**
By: Naveed Akhtar
8. **Postgraduate MCQ (One-Best Type)**
By: M. S. Murad
9. **Anatomy & Physiology MCQ (T/F Type)**
By: M. S. Murad

COMING TITLES

10. **BCQs, MCQs & EMQs in Surgery**
By: M. Shamim
11. **Images, instruments & x-rays: OSCE/TOACS in surgery**
By: M. Shamim
12. **Essentials of Embryology**
By: M. S. Murad
13. **Essentials of Anatomy**
By: M. S. Murad
14. **Essential Human Anatomy (volume 3)**
By: M. Shamim
15. **Clinicobasic Physiology**
16. **Clinicobasic General Pathology**
17. **Clinicobasic Special Pathology**

Available Free Online

CLINICAL TECHNIQUES IN SURGERY

Muhammad Shamim

1. **A comprehensive guide on how to approach the patients in surgery.**
2. **A comprehensive guide to the art of history taking in surgery.**
3. **A comprehensive guide to the art of clinical examination in surgery, with the aid of photographs.**
4. **Demonstration of the examiners' favorite clinical signs.**
5. **A lot of colored clinical photographs.**
6. **Differential diagnosis.**
7. **Diagnostic investigations.**
8. **Quick memorizing tables & charts.**

Section "/"

Microbiology

Chapter 1

General Bacteriology

CLASSIFICATION OF MICROORGANISMS

- (I) Protists (Eukaryotes = Having complete nucleus)
 - (A) Algae
 - (B) Protozoa
 - (C) Fungi
 - (D) Slime molds
- (II) Prokaryotes (Having incomplete nucleus)
 - (A) Eubacteria
 - (B) Archebacteria
 - (C) Cyanobacteria
- (III) Viruses (either RNA or DNA + Capsid)
- (IV) Viroids (Circular RNA without capsid)
- (V) Prion (Proteinaceous infectious agents)

BACTERIAL CELL STRUCTURES

ESSENTIAL COMPONENTS

(A) Cell Wall

Outermost component present in all bacteria except *Mycoplasma* species. Composed of 2 layers; an inner peptidoglycan layer & an outer membrane which is different in Gram +ve & -ve bacteria.

(I) Peptidoglycan (inner layer)

- (a) Gives rigid support
- (b) Maintains shape of cell
- (c) Site of action of penicillins & cephalosporins
- (d) Degraded by lysozyme

- (e) Much thicker in gram +ve organisms being responsible for retaining of blue-dye complex, after alcohol washing.

(2) Outer membrane of Gram +ve organisms

(a) Teichoic & teichuronic acids

- (i) They encompass all wall, membrane, or capsular polymers containing glycerophosphate or ribitol phosphate residues.
- (ii) There are two types of teichoic acids: **wall teichoic acid (WTA)**, covalently linked to peptidoglycan, & **membrane teichoic acid**, covalently linked to membrane glycolipid. Because the latter are intimately associated with lipids, they have been called **lipoteichoic acids (LTA)**.
- (iii) **Teichuronic acids** are similar polymers, which are synthesized in place of teichoic acids when phosphate is limiting.

Functions

- (i) Teichoic acids are responsible for the negative charge of the cell surface, because of its negative charge.
- (ii) Together with peptidoglycan, WTA & LTA make up a polyanionic network or matrix that provides functions relating to the elasticity, porosity, tensile strength, & electrostatic properties of the envelope.

(iii) Teichoic acids constitute major surface antigens.

(b) Polysaccharides

Neutral sugars such as mannose, arabinose, rhamnose, glucosamine & acidic sugars such as glucuronic acid & mannuronic acid exist as subunits of polysaccharides in the cell wall.

(3) Outer membrane of Gram -ve organisms

(a) Outer membrane

It is a bilayered structure; its inner leaflet resembles in composition that of the cell membrane while its outer leaflet contains a distinctive component, a **lipopolysaccharide (LPS)**.

Functions

- (i) Its ability to exclude hydrophobic molecules, serves to protect the cell from deleterious substances such as bile salts.
- (ii) It has special channels, consisting of protein molecules called **porins**, which permit the passive diffusion of low-molecular-weight hydrophilic compounds like sugars, amino acids, & certain ions. Large antibiotic molecules penetrate relatively slowly, which accounts for the relatively high antibiotic resistance of gram -ve bacteria.
- (iii) Another protein, **LamB**, is an inducible porin that is also the receptor for lambda bacteriophage. It is responsible for transmembrane diffusion of maltose & maltodextrins.
- (iv) Similarly, **Tsx**, the receptor for T6 bacteriophage, is responsible for the transmembrane diffusion of nucleosides & some amino acids.
- (v) **OmpA** protein participates in the anchoring of outer membrane to the peptidoglycan layer; it is also the sex pilus receptor in F-mediated bacterial conjugation.
- (vi) Also contains proteins that are involved in the transport of specific molecules such as

vitamin B₁₂ & iron-siderophore complexes.

(vii) Additional minor proteins include enzymes, eg phospholipases & proteases.

(b) Lipopolysaccharide (LPS)

Consists of lipid A (complex glycolipid) & polysaccharide.

Functions

- (i) Polysaccharide forms the major surface antigen, the O antigen.
- (ii) Negatively charged LPS molecules are non-covalently cross-bridged by divalent cations (ie, Ca²⁺ & Mg²⁺); this stabilizes the membrane & provides a barrier to hydrophobic molecules.
- (iii) Lipid A portion form the **endotoxin** of gram -ve bacteria, which is released only when the cells are lysed.

Note: Outer membrane glycolipids of bacteria that colonize mucosal surfaces (eg, N meningitidis) have relatively short, branched glycans, called **lipooligosaccharides (LOS)**, which is an important virulence factor.

(c) Lipoprotein

Cross-link the outer membrane & peptidoglycan layers.

Functions

Stabilizes the outer membrane & anchor it to the peptidoglycan layer.

(B) Cytoplasmic Membrane

Lie just inside the peptidoglycan layer & is composed of protein (70%), phospholipid (30%) & small amounts of carbohydrates.

Functions

- (1) Active transport of molecules into the cell.
- (2) Energy generation by oxidative phosphorylation.
- (3) Synthesis of precursors of cell wall.
- (4) Secretion of enzymes & toxins.
- (5) Segregation of chromosomal & plasmid DNA into daughter cells.

(C) Periplasmic space

It is the space between cytoplasmic memb & cell wall, which contains the peptidoglycan layer & a solution of proteins.

Functions

- (i) The proteins include binding proteins for specific substrates (eg, amino acids, sugars, vitamins, & ions), hydrolytic enzymes (eg, alkaline phosphatase & 5'-nucleotidase), & detoxifying enzymes (eg, lactamase & aminoglycoside-phosphorylase).
- (ii) Also contains **membrane-derived oligosaccharides** which play a role in osmoregulation.

(D) Mesosome

Invagination of cytoplasmic memb.

Functions

Participates in cell division & secretion.

(E) Ribosomes

70 S in size, with 50 S & 30 S subunits.

Functions

- (1) Site of protein synthesis
- (2) Site of action of aminoglycosides, erythromycin, tetracyclines & chloramphenicol

(F) Nucleoid

Contains genetic information (DNA)

Long, hollow, helical filaments, usually several times the length of cell.

Types

- (1) Monotrichous → Single, at one pole
- (2) Amphitrichous → One each, at two poles.
- (3) Lophotrichous → Many, at one pole
- (4) Peritrichous → Many, distributed around the cell.

Functions

- (1) Motility.
- (2) High antigenicity (H antigens), which make identification of some bacterial species possible by using anti-flagellar antibodies.

(D) Spore

Highly resistant resting forms produced within the cells

Types

- (1) Central spore
- (2) Sub-terminal spore
- (3) Terminal spore
- (4) Racket-shaped or drum-stick spore
- (5) Oval equatorial spore
- (6) Polar germinative spore
- (7) Equatorial germinative spore

Functions

Provides resistance to dehydration, heat & chemicals

(E) Plasmid

Extrachromosomal, double-stranded circular DNA molecules

Functions

Contains a variety of genes for antibiotic resistance, enzymes & toxins.

(F) Granules

Storage site of food

(G) Glycocalyx (Slime layer)

Mediates adherence to surface

NON-ESSENTIAL COMPONENTS**(A) Capsule**

A gelatinous layer covering entire bacterium, composed of polysaccharides.

Functions

- (1) Act as a virulence factor by protecting against phagocytosis
- (2) Quelling reaction → In the presence of homologous antibody, it swell greatly.
- (3) Capable of eliciting protective antibodies, so used in certain vaccines.
- (4) Play role in adherence of bacteria to human tissues.

(B) Pilus (Fimbria)

Straight filaments, thinner & shorter than flagella, extending out from cell surface. Present mainly on Gram -ve organisms.

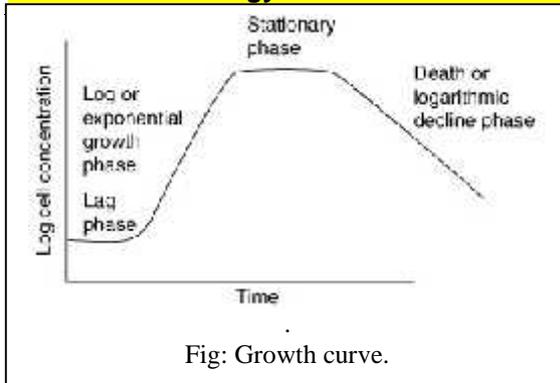
Functions

- (1) Mediate adherence to human cell surface
- (2) Mediate attachment between bacteria during conjugation (sexpilus).
- (3) Form one of the major surface antigens.

(C) Flagellum**BACTERIAL GROWTH****GROWTH CYCLE**

Bacteria undergo exponential (logarithmic) growth by binary fission.

Growth cycle of bacteria has 4 major phases. If a small number of bacteria are inoculated into a liquid



nutrient medium & bacteria are counted at frequent intervals, typical phases of a standard growth curve can be demonstrated (Fig).

Lag Phase

Vigorous metabolic activity occurs but cells do not divide. This can last for a few minutes up to many hours.

Log Phase

Cell mass or number increase in a logarithmic manner with a constant generation time. This can last for 20-30 min. upto 24 hours for very slow growing species.

Stationary Phase

Nutrient depletion or toxic products cause growth to slow until number of new cells produced balances the number of cells that die, resulting in a steady state. This can last for several hours.

Death Phase

Marked by a decline in number of viable bacteria. This can last for days.

GROWTH REQUIREMENTS

Nutrition

(1) Carbon source

Organic carbon source is needed, used both in biosynthetic processes as well as generation of energy.

(2) Nitrogen source

Organic nitrogen source is needed, for the assembly of nucleic acid, proteins & other cell constituents & for energy provision.

(3) Inorganic ions

- (a) Phosphate
- (b) Sulfate
- (c) Iron

- (d) Mg^{++}
- (e) K^{+}
- (f) Na^{+}
- (g) Ca^{++}

(4) Essential metabolites (Growth factors)

Many bacteria have lost the ability to synthesize one or more essential nutrients & so require it;

- (a) Amino acids
- (b) Vitamins
- (c) Hemin
- (d) NAD

Environmental Conditions

(1) Temperature

Different bacterial species vary widely in their optimal temperature ranges for growth.

(a) Psychrophiles

Grow best at low temperatures having an optimal range of 10 - 20 °C.

(b) Mesophiles

Include all of the pathogenic forms, having an optimal temp. range of 20 - 40 °C

(c) Thermophiles

Have an optimal temp. range of 50 - 60 °C.

(2) Hydrogen ion conc. (pH)

Different bacterial species vary in their optimal pH range for growth.

(a) Neutrophils

Include most of the medically important bacteria, grow best at a pH of 6.0-8.0

(b) Acidophils

Include lactobacillus acidophilus, having optimal pH 4.0

(c) Alkalophils

Include vibrio cholerae, grow best at a pH well above 8.0

(3) Oxygen

Different bacterial species vary widely in their oxygen requirements.

(a) Obligate aerobes

Require oxygen to grow because their ATP- generating system is dependent on O_2 as H^+ acceptor.

Example: Mycobacteria, pseudo-monas & some bacilli.

(b) Facultative anaerobes

Utilize O_2 to generate energy by respiration if it is present, but can use

fermentation pathway to synthesize ATP in absence of sufficient O₂.

Example: Enterics, staphylococcus

(c) *Obligate anaerobes*

Grow only in absence of O₂ but vary considerably in their sensitivity to it.

Example: Clostridia, anaerobic strepto- & staphylococci, spirochaetes listeria, fusobacterium, bacteroids.

(d) *Microaerophilics*

Grow in the presence of O₂ but can not use it as a final H⁺ acceptor & derive their energy solely from fermentative reactions.

Example: Most lactic acid bacteria & streptococci.

(e) *Capnophilics*

Refers to bacteria that require CO₂ for growth.

BACTERIAL STAINING

GRAM'S STAINING

Basis for Gram reaction

Treatment with crystal violet & Gram's iodine results in formation of large, insoluble blue-dye complexes inside the cell. During alcohol-washing step, cell memb. gets dissolved. However, blue-dye complex is retained in G +ve cells by thick peptidoglycan layer, whereas it is readily washed out thru very thin peptidoglycan layer remaining in G -ve cells after both memb. have been dissolved, So, G -ve cells take counter stain, carbol-fuchsin, (or safranin) & become pink in color.

Procedure

- (1) Cover the smear with crystal violet for 2-3 minutes, then wash it with water.
- (2) Apply Gram's iodine for 1-2 min, & again wash with water.
- (3) Wash the slide with alcohol or spirit, then immediately wash with water.
- (4) Cover the smear with 1/10 carbol- fuchsin or safranin for 1/2 to 1 min & again wash with water.
- (5) Dry the slide & observe it under oil emersion lens.

OTHER STAINING METHODS

- (1) Ziehl - Neelsen (Acid-Fast) Staining
- (2) Negative staining
- (3) Flagella staining
- (4) Capsule staining
- (5) Nucleus staining
- (6) Spore staining

DETERMINANTS OF BACTERIAL PATHOGENESIS

TRANSMISSION OF MICROORGANISMS

Most infections are acquired by transmission from external sources. There are 4 important portals of entry of microorganisms.

(A) *Respiratory tract*

(1) *Mechanism of transmission*

- (a) Dust - borne transmission
- (b) Droplet transmission
- (c) Direct transmission

(2) *Common pathogens*

- (a) Streptococcus pneumoniae
- (b) Neisseria meningitidis
- (c) Haemophilus influenza
- (d) Mycobacterium tuberculosis
- (e) Influenza virus
- (f) Rhinovirus
- (g) Epstein - Barr virus
- (h) Coccidioides immitis
- (i) Histoplasma capsulatum

(B) *Gastrointestinal tract*

(1) *Mechanism of transmission*

- (a) Food - borne transmission
- (b) Water - borne transmission
- (c) Direct transmission

(2) *Common pathogens*

- (a) Shigella dysenteriae
- (b) Salmonella typhi
- (c) Vibrio cholera
- (d) Hepatitis A virus
- (e) Polio virus
- (f) Trichinella spiralis

(C) *Skin*

(1) *Mechanism of transmission*

- (a) Simple contact
- (b) Wound infection
- (c) Injections
- (d) Insect biting

(2) Common pathogens

- (a) Clostridium tetani
- (b) Rickettsia rickettsii
- (c) Hepatitis B virus
- (d) Rabies virus
- (e) Trichophyton rubrum
- (f) Plasmodium vivax

(D) Genital Tract

(1) Mechanism of transmission

- (a) Venereal transmission
- (b) Non-venereal transmission

(2) Common pathogens

- (a) Neisseria gonorrhoeae
- (b) Treponema pallidum
- (c) Chlamydia trachomatis
- (d) Candida albicans

ADHERENCE TO CELL SURFACES

Specialized structures or substances present within some bacteria allow them to adhere to human cell surfaces, there- by enhancing their ability to cause disease.

Examples

- (1) Pili of Neisseria gonorrhoeae
- (2) Pili of Escherichia coli
- (3) Fimbriae of Streptococcus pyogenes
- (4) Vibrio cholerae

INVASIVENESS

Several enzymes secreted by the bacteria & several factors esp. antiphagocytics are responsible for invasiveness of bacteria.

(A) Enzymes

- (1) Collagenase
- (2) Hyaluronidase
- (3) Coagulase
- (4) IgA protease
- (5) Leukocidins
- (6) Streptokinase (fibrinolysin)

(B) Antiphagocytic factors

- (1) Capsule
- (2) M protein of group A streptococci

EXOTOXIN	ENDOTOXIN
<p>1) Source a) Produced by both G +ve & G -ve bacteria. b) Secreted by living cells.</p>	<p>1) Source a) Found only in G -ve bacteria. b) Integral part of cell wall, released on bacterial death & in part during growth.</p>
<p>2) Chemistry Polypeptide.</p>	<p>2) Chemistry Lipopolysaccharide.</p>
<p>3) Location of genes Plasmid or acterio-phage.</p>	<p>3) Location of genes Bacterial chromosome.</p>
<p>4) Toxicity Highly toxic, fatal dose on the order of 1 mg.</p>	<p>4) Toxicity Moderately toxic, fatal dose on the order of 100s of mg.</p>
<p>5) Antigenicity Induces high titer antibodies called antitoxins.</p>	<p>5) Antigenicity Poorly antigenic.</p>
<p>6) Stability Relatively unstable; toxicity often destroyed by heating at temp. above 60°C.</p>	<p>6) Stability Relatively stable; withstand heating at temp. above 60 oC for hours without loss of toxicity.</p>
<p>7) Vaccines Converted to antigenic, ontoxic toxoids by formalin, acid, heat etc. which are used as vaccines.</p>	<p>7) Vaccines Not converted to toxoids, so not used as vaccines.</p>
<p>8) Receptor binding Usually bind to specific receptors on cells.</p>	<p>8) Receptor binding Specific receptors not found on cells.</p>
<p>9) Fever production Usually do not produce fever in the host.</p>	<p>9) Fever production Usually produce fever by release of interleukin-1 & other mediators.</p>
<p>10) Typical disease Tetanus, botulism, diphtheria.</p>	<p>10) Typical disease Meningococemia, sepsis by G -ve rods.</p>

(3) Protein A of staphylococci

TOXIN PRODUCTION

Bacteria produce 2 groups of toxins, exotoxin & endotoxin.

Exotoxin producing organisms

(1) Gram-positive organisms

- (a) Corynebacterium diphtheriae
- (b) Clostridium tetani
- (c) Clostridium perfringens
- (d) Clostridium botulinum
- (e) Bacillus anthracis
- (f) Staphylococcus aureus
- (g) Streptococcus pyogenes

(2) Gram-negative organisms

- (a) Escherichia coli
- (b) Vibrio cholerae
- (c) Shigella
- (d) Bordetella pertussis

Endotoxin producing organisms

- (a) Brucella species
- (b) Enterobacteriaceae → E. coli, klebsiella pneumonia, salmonella, shigella, proteus, pseudomonas aeruginosa
- (c) Gonococci
- (d) Meningococci

- (c) Hydrogen peroxide
- (d) Formaldehyde & glutaraldehyde
- (e) Ethylene oxide
- (f) Strong acids & alkalies

(B) Physical agents

(1) Heat

(a) Dry heat

- (i) Incineration
- (ii) Flaming
- (iii) Hot air oven

(b) Moist heat

- (i) Pasteurization
- (ii) Boiling
- (iii) Steaming at 100 °C
- (iv) Sterilization in autoclave

(2) Radiation

- (a) Ultraviolet (UV) light
- (b) X-rays

(3) Filtration

Filters act by;

- (a) Physically trapping particles larger than pore-size
- (b) Retaining somewhat smaller particles owing to electrostatic attraction of particles to filters.

STERILIZATION & DISINFECTION

DEFINITION

Sterilization

It is the killing or removal of all microorganisms, including bacterial spores.

Disinfection

It is the killing of many, but not all, pathogenic microorganisms (some organisms & bacterial spores may survive).

METHODS

(A) Chemical agents

(1) Disruption of cell membrane

- (a) Alcohols, eg ethanol
- (b) Detergents
- (c) Phenols

(2) Modification of proteins

- (a) Halogens, eg chlorine & iodine
- (b) Heavy metals, eg mercury & silver

AUTOClave

It is a closed vessel in which super-heated steam is used at super-atmospheric pressure to sterilize surgical objects.

- (1) Pressure = 15 lb/in²
- (2) Temperature = 121°C
- (3) Time = 15-20 min.

Uses

- (1) To sterilize surgical dressing or theatre gown
- (2) To kill highly heat-resistant spores of clostridium botulinum

PASTEURIZATION

It consists of heating the milk to 62 °C for 30 minutes, followed by rapid cooling.

Uses

It kills vegetative cells of milk-borne pathogens, eg M. tuberculosis, salmonella, streptococci, brucella.

Chapter 2

Culture Media For Bacteria

DEFINITIONS

Medium

Any preparation that contains nutrients essential for bacterial growth, is called a media.

Culture medium

A medium that has been successfully inoculated with bacteria, is called culture medium

Inoculation of media

It means introduction of infected material to the medium for cultivation of organism present in the material.

Some enriched material like blood, serum or ascitic fluid is added to the medium, required for proper growth of some bacteria.

Example: Blood agar, chocolate aga.

(3) **Differential media**

Differentiate between two groups of bacteria.

Example: Blood agar, MacConkey's medium.

(4) **Selective media**

An inhibitory substance is added to the media which prevents growth of all organisms except the one for which it is designed.

Example: Lowenstein Jensen's medium.

(5) **Media for biochemical reaction**

Used to detect different biochemical reactions produced by different organisms.

Example: Simmon citrate medium.

CLASSIFICATION OF CULTURE MEDIA

According to physical state

(1) **Liquid media**

Fluid in nature, usually placed in test tubes

Example: Nutrient broth.

(2) **Solid media**

Prepared by adding solidifying agents like gelatin & agar to the liquid medium.

Example: Nutrient agar.

According to composition

(1) **Simple media**

Contains only basic substances such as nitrogen, carbon & minerals.

Example: Nutrient broth, nutrient agar, peptone water.

(2) **Enriched media**

IMPORTANT CULTURE MEDIA

NUTRIENT AGAR

Composition

(1) Solidified agar.

(2) Beef extract, Peptone water, NaCl.

Container

Petri dish.

Color

Whitish pale.

Consistency

Solid medium.

Microorganisms cultured

(1) Staph. albus → White colonies.

(2) Staph. aureus → Golden yellow colonies.

(3) Staph. citrus → Lemon yellow colonies.

- (4) Staph. roseus → Pink colonies.
- (5) Pseudomonas → Green colonies.
- (6) Proteus → Pale translucent colonies with fish smell.

BLOOD AGAR

Composition

- (1) Sterile defibrinated blood 5-10%.
- (2) Melted agar.
- (3) Beef extract, peptone water, NaCl.

Container

Petri dish.

Color

Opaque red.

Consistency

Solid medium.

Microorganisms cultured

To determine hemolytic properties:

- (1) Complete (beta) hemolysis, eg:
 - Streptococcus pyogenes.
- (2) Incomplete (alpha) hemolysis, eg:
 - (a) Streptococcus viridians.
 - (b) Streptococcus pneumoniae
- (3) No Hemolysis, eg:
 - (a) Staph. aureus.
 - (b) Staph. albus.
 - (c) Staph. citrus.
 - (d) Streptococcus fecalis.

CHOCOLATE AGAR

Composition

Same as blood agar. Blood agar plate is put in boiling water for about 1 hour until its color changes from red to chocolate brown. Heating converts hemoglobin into hematin.

Container

Petri dish.

Color

Opaque chocolate color.

Consistency

Solid medium.

Microorganisms cultured

- (1) Haemophilus influenza.
- (2) Neisseria gonorrhoeae.
- (3) Neisseria meningitides.
- (4) Streptococcus pneumoniae.

MacCONKEY'S MEDIUM

Composition

- (1) Nutrient agar.
- (2) Bile salt (Na taurocholate).
- (3) Lactose.
- (4) Neutral red (indicator).
- (5) Peptone water, NaCl.

Container

Petri dish.

Color

Transparent reddish brown or pink color.

Consistency

Solid medium.

Microorganisms cultured

For growth & isolation of enterobacteriaceae & to differentiate b/w lactose fermenters (LF), non-lactose fermenters (NLF) & late lactose fermenters (LLF):

- (1) Lactose fermenters (pink colonies), eg:
 - (a) E coli.
 - (b) Klebsiella species.
 - (c) Enterobacter species.
- (2) Non-lactose fermenters (pale colonies), eg:
 - (a) Shigella species except S sonnei.
 - (b) Salmonella species.
 - (c) Proteus species.
 - (d) Pseudomonas species.
- (3) Late lactose sermenters (pink colonies after 2-3 days), eg:
 - (a) Vibrio cholera.
 - (b) Serratia.
 - (c) Citrobacter.
 - (d) Shigella Sonnei.

LOWENSTEIN-JENSEN (LJ) MEDIUM

Composition

- (1) Penicillin or malachite green (Inhibit other bacteria).
- (2) Glycerol.
- (3) Egg yolk.
- (4) K₂ SO₄, MgSO₄, Mg citrate.
- (5) Water, Potato flour & asparagin.

Container

Screw capped bottle or test tube.

Color

Light green.

Consistency

Solid medium.

Microorganisms cultured

Mycobacterium tuberculosis.

LOEFFLER'S COAGULATED SERUM MEDIUM**Composition**

- (1) Ox, sheep or horse serum.
- (2) 1% glucose broth.

Container

Test tube.

Color

Milky white color.

Consistency

Solid medium.

Microorganism cultured

Corynebacterium diphtheriae.

ROBERTSON'S COOKED MEAT MEDIUM**Composition**

- (1) Pieces of meat.
- (2) NaOH (to neutralize lactic acid).
- (3) Broth.
- (4) Paraffin oil.

Container

Test tube.

Color

Light red color.

Consistency

Liquid medium with pieces of meat in it.

Microorganism cultured

To grow anaerobic bacteria, eg: Clostridium species.

TRIPPLE SUGAR IRON (TSI) MEDIUM**Composition**

- (1) Glucose (0.1%), Sucrose (1%), Lactose (1%).
- (2) Ferrous sulfate (for detection of H₂S).
- (3) Tissue extracts (proteins).
- (4) Phenol red (indicator).

Container

Test tube.

Color

- (1) Red before reaction (alkaline).

- (2) Yellow after reaction (acidic).

- (3) Black after H₂S production (FeS).

Consistency

Solid medium.

Uses

To differentiate salmonella & shigella from other enteric G-ve rods in stool culture:

- (1) Salmonella & shigella produce:
 - (a) Alkaline slant (red).
 - (b) Acidic but with no gas (Yellow without bubbles).
- (2) Other enteric G-ve rods produce:
 - (a) Acidic slant (Yellow)
 - (b) Acidic but with gas (Yellow with bubbles)

CHRISTENSEN'S UREA MEDIUM**Composition**

- (1) Monopotassium phosphate.
- (2) Agar.
- (3) Phenol red (indicator).
- (4) Peptone water, NaCl.

Container

Test tube.

Color

- (1) Pink before reaction.
- (2) Red after urea splitting.

Consistency

Liquid medium.

Uses

To demonstrate urease activity by:

- (1) Proteus species.
- (2) Morganella morganii.

SIMMON CITRATE MEDIUM**Composition**

- (1) Mineral salt solution (Bacto agar).
- (2) Bacto-bron thymol blue (indicator).

Container

Test tube.

Color

- (1) Green before reaction.
- (2) Blue after reaction.

Consistency

Liquid medium.

Uses

To demonstrate citrate utilization by:

- (1) Klebsiella.
- (2) Proteus.

PEPTONE WATER

Composition

- (1) Peptone.
- (2) H₂O.
- (3) NaCl.

Container

Test tube.

Color

Transparent light yellow color.

Consistency

Liquid medium.

Uses

- (1) Basis for fermentation tests
- (2) Indole production.
- (3) To study motility & chain formation of an organism.

NUTRIENT BROTH

Composition

- (1) Beef extract.
- (2) Peptone water, NaCl.

Container

Test tube.

Color

Light yellow.

Consistency

Liquid medium.

Uses

- (1) Bacterial growth.
- (2) Coagulase test.

SUGAR MEDIA

Composition

- (1) Nutrient broth.
- (2) Peptone water.
- (3) Bromocresol purple (indicator).
- (4) Sugar (eg: glucose, sucrose, lactose, maltose, xylose, mannitol).

Container

Test tube.

Color

- (1) Purple before reaction.

- (2) Yellow after reaction.

Consistency

Liquid medium.

Uses

To determine which sugar is utilized by bacteria. Type of sugar contained in test tube is known by the color of cotton plug of test tube, which are:

- (1) Glucose → Green (GG).
- (2) Sucrose → White (SW).
- (3) Lactose → Red (LR).
- (4) Maltose → Black (MB).
- (5) Xylose → Blue (XB).
- (6) Mannitol → Violet (MV).

Chapter 3

Medially Important Bacteria

CLASSIFICATION OF BACTERIA

Gram-positive bacteria that have cell wall

Aerobic & facultative bacteria

(1) **Cocci**

(a) **Catalase-positive**

Staphylococcus species.

(b) **Catalase-negative**

- (i) Beta-hemolytic streptococci.
- (ii) Enterococcus.
- (iii) Streptococcus viridians.
- (iv) Streptococcus pneumonia.

(2) **Bacilli**

(a) **Endospore-forming rods**

- (i) Bacillus anthracis
- (ii) Bacillus cereus

(b) **Regular, non-sporing**

- (i) Erysepeothrix rhusiopathiae
- (ii) Listeria monocytogenes

(c) **Irregular, non-sporing**

- (i) Corynebacterium species
- (ii) Mobiluncus

(d) **Acid-fast bacilli (AFB)**

- (i) Mycobacterium tuberculosis
- (ii) Mycobacterium bovis
- (iii) Mycobacterium ulcerans
- (iv) Atypical mycobacteria
- (v) Mycobacterium leprae

(e) **Actinomycetes**

- (i) Nocardia asteroides
- (ii) Streptomyces
- (iii) Rhodococcus equi

Anaerobic bacteria

(1) **Cocci**

Peptostreptococcus

(2) **Bacilli**

(a) **Endospore-forming rods**

- (i) Clostridium tetani
- (ii) Clostridium botulinum
- (iii) Clostridium difficile
- (iv) Clostridium perfringens
- (v) Clostridium septicum
- (vi) Clostridium histolyticum
- (vii) Clostridium novyi

(b) **Non-sporing**

- (i) Actinomyces species
- (ii) Bifidobacterium species
- (iii) Lactobacillus species
- (iv) Propionibacterium species

Gram-negative bacteria that have cell walls

Aerobic & facultative bacteria

(1) **Cocci**

- (a) Neisseria gonorrhoeae
- (b) Neisseria meningitides
- (c) Moraxella catarrhalis

(2) **Bacilli**

(a) **Enterobacteriaceae**

- (i) Escherichia coli & other coliforms
- (ii) Klebsiella species
- (iii) Proteus species
- (iv) Salmonella species
- (v) Shigella species
- (vi) Citrobacter species
- (vii) Edwardsiella species
- (viii) Enterobacter species
- (ix) Morganella morganii
- (x) Providencia species
- (xi) Serratia species
- (xii) Yersinia species

- (b) **Fermentative non-enterobacteriaceae**
- (i) *Vibrio cholera* & other vibrios
 - (ii) *Aeromonas* species
 - (iii) *Plesioiomonas shigelloides*
 - (iv) *Pasteurella multocida*
- (c) **Non-fermentative non-enterobacteriaceae**
- (i) *Pseudomonas* species
 - (ii) *Acinetobacter* species
 - (iii) *Alcaligenes* species
 - (iv) *Flavobacterium* species
 - (v) *Xanthomonas maltophilia*
- (3) **Coccobacilli**
- (a) *Actinobacillus*
 - (b) *Bartonella* species
 - (c) *Brucella* species
 - (d) *Bordetella* species
 - (e) *Francisella tularensis*
 - (f) *Haemophilus* species
 - (g) *Legionella* species
 - (h) *Coxiella burnetii*
 - (i) *Chlamydia* species
 - (j) *Rickettsia* species
- (4) **Motile helical/vibroid**
- (a) *Campylobacter* species
 - (b) *Helicobacter pylori*
 - (c) *Spirillum*
- (5) **Spiral forms (spirochetes)**
- (a) **Treponema**
- (i) *Treponema pallidum*
 - (ii) *Treponema carateum*
 - (iii) *Treponema vincentii*
- (b) **Borrelia**
- (i) *Borrelia recurrentis*
 - (ii) *Borrelia burgdorferi*
- (c) **Leptospira**
- (i) *Leptospira interrogans*
 - (ii) *Leptospira biflexa*

Anaerobic bacteria

- (1) **Cocci**
- Veillonella parvula*
- (2) **Bacilli**
- (a) *Bacteroides* species
 - (b) *Fusobacterium* species
 - (c) *Porphyromonas* species
 - (d) *Prevotella* species
 - (e) *Mobiluncus* species

Cell wall less eubacteria

Mycoplasmas

- (1) *Mycoplasma pneumoniae*
- (2) *Mycoplasma hominis*
- (3) *Mycoplasma genitalium*
- (4) *Mycoplasma orale*
- (5) *Mycoplasma salivarium*
- (6) *Ureaplasma*

Archaeobacteria

- (1) Methanogens.
- (2) Archaeal sulfate reducer.
- (3) Extremely halophilic archaeobacteria.
- (4) Cell wall less archaeobacteria.
- (5) Extremely thermophilic sulfur metabolizers.

NORMAL FLORA OF HUMAN BODY

NORMAL FLORA OF SKIN

- (1) *Staphylococcus epidermidis*
- (2) *Staphylococcus aureus*
- (3) *Corynebacterium diphtheria*
- (4) Group G streptococci
- (5) *Pseudomonas aeruginosa*
- (6) *Peptococcus*
- (7) *Candida albicans*

NORMAL FLORA OF RESPIRATORY TRACT

Nose

- (1) *Staphylococcus aureus*
- (2) *Staphylococcus epidermidis*
- (3) *Corynebacterium diphtheria*
- (4) Various streptococci

Throat (larynx & trachea)

- (1) *Viridans streptococci*
- (2) *Streptococcus pyogenes*
- (3) *Streptococcus pneumoniae*
- (4) *Neisseria* species
- (5) *Hemophilus influenzae*
- (6) *Staphylococcus epidermidis*

NORMAL FLORA OF ORAL CAVITY

Mouth

- (1) *Viridans streptococci*

(2) Various other streptococci

Dental plaque

Streptococcus mutans

Gingival crevices

- (1) Bacteriodes
- (2) Fusobacterium
- (3) Streptococci
- (4) Actinomyces

NORMAL FLORA OF INTESTINAL TRACT**Small intestine**

- (1) Enterococci
- (2) Lactobacilli
- (3) Staphylococci
- (4) Candida albicans

Colon

- (1) *Bacteriodes, esp, B fragilis*
- (2) *Escherichia coli*
- (3) Enterobacter
- (4) Serratia
- (5) Pseudomonas aeruginosa
- (6) Bifidobacterium
- (7) Fusobacterium
- (8) Lactobacillus
- (9) Enterococci, esp, E faecalis
- (10) Nonenterococci, esp, S bovis & S equinus
- (11) Streptococcus anginosus
- (12) Clostridium, esp, C perfringens

NORMAL FLORA OF GENITOURINARY TRACT**Vagina**

- (1) Lactobacillus
- (2) Streptococcus agalactiae
- (3) Streptococcus anginosus
- (4) Various G-ve rods
- (5) B fragilis
- (6) Corynebacterium
- (7) Candida albicans

Urethra

- (1) Staphylococcus epidermidis
- (2) Corynebacterium diphtheria
- (3) Various streptococci
- (4) Various G-ve rods
- (5) Mycoplasmas

(C) External Genitalia

Mycobacterium smegmatis

NORMAL FLORA OF EYE

- (1) Corynebacterium xerosis
- (2) Staphylococcus aureus
- (3) Staphylococcus epidermidis

Chapter 4

Staphylococci

CLASSIFICATION

Based on coagulase production

(1) Coagulase - positive

Staphylococcus aureus.

(2) Coagulase - negative

(a) Staphylococcus epidermidis (or S albus)

(b) Staphylococcus saprophyticus.

Based on pigment production

(1) S aureus → Golden yellow.

(2) S albus → White.

(3) S citreus → Yellow.

(4) S roseus → Pink colonies.

MORPHOLOGY

Shape

Individual organism is spherical in shape (cocci)

Arrangement

Cocci are arranged in grape-like irregular clusters. Single cocci, pairs, tetrads and chains are also seen in liquid culture media.

Capsule

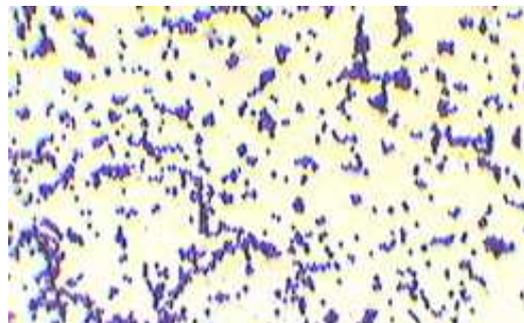
Some strains are capsulated.

Motility

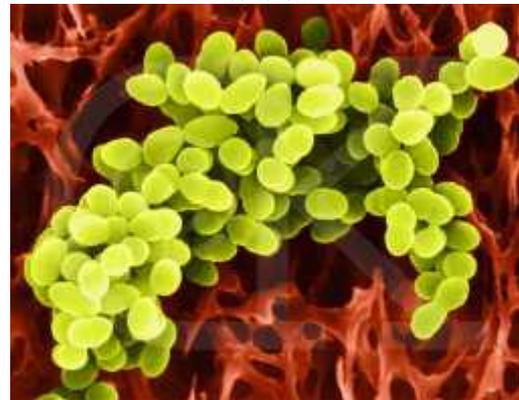
Non-motile.

Spore

Non-spore forming



Staphylococci: Gram stain appearance from broth culture.



Staphylococci: Electron micrograph.

STAINING

Gram's staining

(1) Young cocci stain strongly gram-positive (violet color).

- (2) On aging, many cells become gram-negative (pink color).

It means staphylococci are inhibited by a drug, but not killed by it. It is due to lack of activation of autocatalytic enzymes in cell wall.

CULTURE

Media

(1) Nutrient agar

Better pigment production.

(2) Blood agar

- (a) Better growth.
(b) *S aureus* shows beta hemolysis.

(3) Selective medium

Nutrient agar + 7-10% NaCl. It allows growth of *S aureus* only, and inhibits others.

Colonies

Round, raised, smooth and glistening.

- (1) *S aureus* → Golden yellow colonies on nutrient agar.
(2) *S albus* → White colonies on nutrient agar.
(3) *S citrus* → Yellow colonies on nutrient agar.

Growth characteristics

(1) O₂ requirement

Grow under aerobic or micro-aerophilic conditions.

(2) Energy source

Ferment many carbohydrates, produce lactic acid but no gas.

(3) Temperature

Grow rapidly at 37°C, but form pigment best at 20-25°C (room temp).

(4) Growth inhibited by

- (a) Dyes, eg. crystal violet.
(b) Chemicals, eg. hexachlorophene (3%).

(5) Resistance

- (a) Resistant to drying and heating (they withstand 50°C for 30 min).
(b) Resistant to 7-10% NaCl.
(c) Resistant to antimicrobial drugs due to:
(i) Beta-lactamase production → Most penicillins.
(ii) Lack or inaccessibility of penicillin-binding proteins (PBPs) → Nafcillin.
(iii) Plasmids → Tetracyclines, erythromycin & aminoglycosides.

(6) Tolerance

ANTIGENS

Peptidoglycan

Present in cell wall.

Functions

- (1) Elicits production of interleukin-1 (endogenous pyrogen)
(2) Elicits production of opsonic antibodies.
(3) Chemoattractant for polymorphs.
(4) Has endotoxin-like activity.
(5) Produce a localized Schwartzman phenomenon.
(6) Activate complement.

Teichoic acids

Present in cell wall linked to peptidoglycan.

Function

It is antigenic and causes production of antiteichoic antibodies in patients with active endocarditis due to *S aureus*.

Protein A

Present in cell wall.

Function

It binds to Fc portion of IgG antibodies. Fab portion of protein A-bound IgG is free to bind to other antigens. Thus, it causes "coagglutination" of bacteria.

Capsule

Only some strains of *S aureus* have outer capsule.

Function

Inhibits phagocytosis by polymorphonuclear leukocytes.

ENZYMES

Catalase

Converts H₂O₂ into water and oxygen (bubbles). This differentiates staphylococci from streptococci.

Coagulase (clumping factor)

Converts fibrinogen into fibrin. Therefore:

- (1) It clots citrated or oxalated plasma.
- (2) It deposits fibrin on surface of staphylococci, thus altering their ingestion or killing by phagocytotic cells.

OTHER ENZYMES**Staphylococcal hyaluronidase or spreading factor**

Splits hyaluronic acid in ground substance of connective tissue and helps spreading of staphylococci.

Staphylokinase

Activates plasminogen into plasmin (fibrinolysin) that splits fibrin.

Beta-lactamase

Splits beta-lactam ring and hydrolyses it to penicilloic acid (which has no antibacterial activity).

Proteinases

Splits protein.

Lipases

Splits fat.

TOXINS**Exotoxins (hemolysins)****Alpha toxin (hemolysin)**

- (1) Lyses RBCs and damages platelets and macrophages.
- (2) Degranulates polymorphonuclear leukocytes.

Beta toxin

- (1) Lyses RBCs, which require an initial incubation at 37°C followed by incubation at refrigerator temp, so it is also called hot-cold hemolysin.
- (2) Degrades sphingomyelin.

Gamma toxin

- (1) Antigenic.
- (2) Lyses RBCs.

Delta toxin

- (1) Antigenic.
- (2) Damages RBCs, polymorphs, macrophages, and platelets.

Leukocidin

Can kill WBCs. Antibodies to leukocidin play a role in resistance to recurrent staphylococcal infection.

Exfoliatin

Causes generalized desquamation in "Staphylococcal scalded skin syndrome" or "Bullous exfoliation". Specific antibodies protect against the exfoliative action of toxin.

Toxic shock syndrome toxin (TSST-1)

- (1) A superantigen, with potent inducer of interleukin-1 and cachectin (tumor necrosis factor).
- (2) Causes toxic shock syndrome within 5 days of onset of menses in young women who uses tampons.

Enterotoxins (A-F)

Superantigens that are heat stable and resistant to gut enzymes. Causes food poisoning.

HABITAT & TRANSMISSION**Habitat**

- (1) *S. epidermidis* (*S. albus*) → Members of normal flora of human skin, respiratory and gastrointestinal tracts.
- (2) *S. aureus* →
 - (a) Nasal carriage in 40-50% human beings.
 - (b) Found regularly on clothing, bed linens and other fomites of human environment.

Transmission

Contact spread via hands and fomites.

PATHOGENESIS & CLINICAL FINDINGS**Staphylococcus aureus****Localized infections**

- (1) Furuncle (hair follicle infection)
- (2) Carbuncle.
- (3) Acne and pimples.
- (4) Impetigo.

(5) Other localized abscesses.

Bacteremia & disseminated infections

Bacteremia occurs due to draining of organisms from a focal infection via lymphatics or capillaries to bloodstream. It causes disseminated infection in many parts of body, eg:

- (1) Pneumonia (esp. in pts with cystic fibrosis and those suffering from influenza virus infection).
- (2) Osteomyelitis.
- (3) Acute bacterial endocarditis.
- (4) Meningitis.
- (5) Empyema.
- (6) Pyelonephritis.

Scalded skin syndrome (bullous exfoliation or pemphigus)

Caused by exfoliatin toxin.

Clinical findings

Large vesicles (bullae) filled with clear fluid are formed on skin. These vesicles rupture causing exfoliation of skin.

Toxic shock syndrome

Caused by TSST-1. Occurs within 5 days of onset of menses in young women who uses tampons.

Clinical findings

Abrupt onset of high fever, vomiting, diarrhea, myalgias, scarlatiniform rash, hypotension with cardiac and renal failure.

Food poisoning

Caused by enterotoxins produced by *S aureus* in carbohydrate or protein foods.

Incubation period

1-8 hours (short, due to "preformed" toxins)

Clinical findings

Violent nausea, vomiting, diarrhea, rapid convalescence, no fever.

Other staphylococci

- (1) *S epidermidis* (albus) → Infection of orthopedic or cardiovascular prosthetic devices.
- (2) *S saprophyticus* → UTI in young women.

DIAGNOSTIC LABORATORY TESTS

Specimen

Surface swab, pus, blood, tracheal aspirate, CSF.

Microscopy

Gram stained smear of specimen is seen under microscope → Gram- positive cocci in grape-like clusters.

Culture

Specimens are cultured on nutrient agar, blood agar and on selective media (nutrient agar +7-10% NaCl) → Colonies develop in 18 hours at 37°C.

Catalase test

A drop of H₂O₂ is poured on culture → Bubbles (O₂) are produced → Positive test.

Coagulase test

Take two test tubes containing citrated rabbit or human plasma. To one test tube add "broth culture" and to other test tube add "sterile broth". Incubate at 37°C → Clot is formed in 1-4 hours → Positive test.

Serologic tests

- (1) Antiteichoic antibodies are found in staphylococcal endocarditis.
- (2) Antibiotic sensitivity test.
- (3) Phage typing.

Susceptibility testing

- (1) Broth microdilution or disk diffusion susceptibility testing.
- (2) Beta-lactamase test → Positive test indicate resistance to penicillin G.
- (3) Detection of 'mecA' gene by polymerase chain reaction → mecA gene is related to nafcillin resistance.
- (4) Culture on Mueller-Hinton agar containing 4% NaCl and 6 µg/mL of oxacillin → Shows mecA-positive staphylococcal growth.

IMMUNITY

Neither humoral nor cell-mediated immunity provide much protection against invasive staphylococcal disease, although antibodies to many cellular components and products of *S aureus* are found in normal human serum. However, antibodies to leukocidin may play a role in resistance to recurrent staphylococcal infection.

TREATMENT

Antimicrobial drugs

- (1) Penicillin G is the drug of choice for non-lactamase-producing *S aureus*.
- (2) Penicillin G-resistant strains are often susceptible to;
 - (a) Methicillin (penicillinase - resistant penicillin).
 - (b) Vancomycin (usually reserved for use with nafcillin-resistant staphylococci).
 - (c) Cephalosporins.
- (4) Tetracyclines (for acne)
- (3) Newer antimicrobial agents such as linezolid, daptomycin, & quinupristin/dalfopristin are reserved for serious staphylococcal or enterococcal infections that are resistant to traditional agents.

Surgical drainage

In addition to antimicrobial agents, surgical drainage & removal of necrotic tissues may be required in cases of;

- (1) Abscesses or other closed suppurating lesions.
- (2) Chronic & recurrent osteomyelitis.

PREVENTION & CONTROL

- (1) No effective immunization with toxoid or vaccines.
- (2) Cleanliness, eg. frequent hand washing.
- (3) Aseptic management of lesions.
- (4) Dissemination from nose or skin of carriers can be reduced by topical application of antimicrobial agents, eg chlorhexidine or bacitracin cream.

Chapter 5

Streptococci

CLASSIFICATION

Beta-hemolytic streptococci

They cause beta-hemolysis (complete hemolysis) on blood agar & have "Group-specific cell wall carbohydrate antigens" which give precipitin reaction with specific antisera. On the basis of precipitin reaction they are divided into "Lancefield groups A-H & K-U".

(1) Group A

eg, *S. Pyogenes*. They contain "M protein" of which there are more than 80 serotypes. So, "Group A" is divided into "Griffith types 1-80".

(2) Group B

eg, *S. agalactiae*.

(3) Groups C, F & G

eg, *S. anginosus*.

(4) Group E, H & K-U

Primarily occur in animals other than humans.

Non-beta-hemolytic streptococci

They show alpha-hemolysis (incomplete hemolysis) or no hemolysis.

(1) *Streptococcus pneumoniae*

See chapter 6.

(2) *Streptococcus viridians*

They are alpha-hemolytics, eg,

(a) *S. salivarius* (Group K)

(b) *S. sanguis* (Group H)

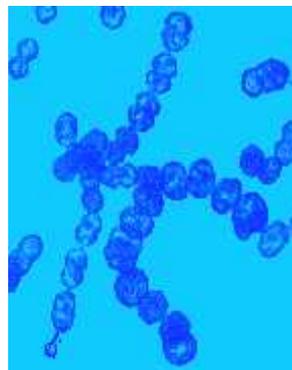
(c) *S. mutans*

(d) *S. mitis*

(3) Group D

(a) Enterococci, eg, *S. faecalis* & *S. faecium*.

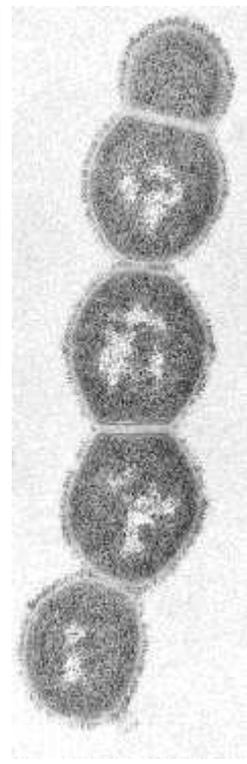
(b) Non-enterococci, eg, *S. bovis* & *S. equines*.



Staphylococci:

Above, electron micrograph.

Right, another electron micrograph of an ultra-thin section of group A streptococci. Cell surface fibrils, consisting of M protein are clearly evident. Bacterial cell wall is evident as light staining region b/w fibrils & dark staining cell interior. Cell division is also shown. (20,000 x)



(4) Group N streptococci

Also called lactic streptococci & are non-hemolytic.

(5) Peptostreptococci

They are anaerobic streptococci & causes variable hemolysis.

(6) Nutritionally variant streptococci

eg *S. defectives* & *S. adjacens*. They require pyridoxal or cysteine for growth on blood agar, & form part of normal flora.

MORPHOLOGY**Shape**

Individual organism is spherical in shape (cocci).

Arrangement

Arranged in chains or pairs.

Division

Cocci divide in a plane perpendicular to long axis of chains.

Capsule

Most group A, B & C strains are capsulated, composed of hyaluronic acid.

Motility

Non-motile.

Spore

Non-spore forming.

STAINING**Gram's staining**

Streptococci are gram-positive (appear violet colored).

CULTURE**Media**

- (1) Nutrient agar
- (2) Blood agar
- (3) MacConKey's medium (only E faecalis)

Colonies

Most strains produce discoid colonies (1-2 mm in diameter), while the strains with capsular material produce mucoid colonies.

- (1) On nutrient agar → Small translucent dew drop like colonies.
- (2) On blood agar → 2 types of hemolysis are seen:
 - (a) Beta (complete) hemolysis → A clear zone of hemolysis is formed around colonies due to rupture of RBCs with release of hemoglobin.

(b) Alpha (incomplete) hemolysis → A zone of greenish brown discoloration is formed around colonies that contains unlysed RBCs & a green, unidentified, reduced product of hemoglobin.

(3) On MacConKey's medium → "E faecalis" produces small pink colonies.

(4) Group A streptococci produce 2 types of colonies:

(a) Matt or mucoid colonies → Consist of streptococci that produce "much M proteins" → Virulent.

(b) Glossy colonies → Consist of streptococci that produce "little M proteins" → Non-virulent.

Growth characteristics**(1) O₂ requirements**

(a) Most streptococci are aerobes & facultative anaerobes (ie, can grow on aerobic & anaerobic media).

(b) Peptostreptococci are obligate anaerobes.

(2) Energy source

Ferment many sugars.

(3) Temperature

(a) Most streptococci grow at 37°C.

(b) Group D enterococci grow b/w 15°C & 45°C.

(4) Growth & hemolysis promoted by

10% CO₂.

ANTIGENS**Group-specific carbohydrate antigen**

Present in cell wall.

Functions

- (1) Gives precipitin reaction with specific anti-sera & forms basis for serologic grouping into "Lancefield groups A-H & K-U".
- (2) Serologic specificity of this antigen is determined by an "amino sugar".

M protein

Present in cell wall of organisms producing matt or mucoid colonies.

Functions

- (1) Associated with virulence of Group A streptococci.

- (2) Gives agglutination or precipitation reaction with "M protein type-specific antisera", & forms basis for serologic typing of group A into "Griffith types 1-80".
- (3) Interferes with ingestion of virulent streptococci by phagocytic cells.
- (4) Causes production of antibodies that acts as opsonins & protect against reinfection with this M type-specific group A streptococcus.

Other antigens

- (1) T substance.
- (2) R protein.
- (3) Nucleoproteins.
- (4) P substance.
- (5) Capsular polysaccharide (Some strains of groups A,B & C) → Impede phagocytosis.
- (6) Pili covered with lipoteichoic acid project thru capsule of group A → Help in attachment to epithelium.

ENZYMES

Streptokinase (fibrinolysin)

It is produced by many group A β -hemolytic streptococci. It transforms plasminogen into plasmin that digest fibrin, & is partially responsible for rapid spread of streptococcal infections by preventing formation of fibrin barrier around the infected site.

Clinical Uses

Given intravenously for:

- (1) Pulmonary emboli.
- (2) Venous thromboses.
- (3) Coronary artery thromboses.

Streptodornase (streptococcal DNase)

Depolymerises DNA, thus help to liquefy exudates & facilitate removal of pus & necrotic tissue.

Hyaluronidase (spreading factor)

Splits hyaluronic acid in ground substance of connective tissue, thus helps in spreading of infecting microorganisms.

Diphosphopyridine nucleotidase

Kills leukocytes.

Other enzymes

- (1) Proteinases.
- (2) Amylases.
- (3) NADase.
- (4) Peptidase → Cleaves C5a component of complement.

TOXINS

Hemolysins

Beta-hemolytic group A streptococci produce two hemolysins (streptolysins)

Streptolysin O

- (1) Causes hemolysis only in anaerobic conditions, b/c it is O₂ labile.
- (2) It bind to sterols in host's leukocyte memb. where it forms toxin oligomers resulting in large transmemb. pores → This causes release of lysosomal enzymes that results in degranulation & death of leukocytes as well as destruction of adjacent tissues.
- (3) Suppresses chemotaxis & leukocyte mobility.
- (4) It is antigenic & causes production of antistreptolysin O antibodies (ASO). An ASO serum titer more than 160-200 units suggests recent infection with streptococci.

Streptolysin S

- (1) Being O₂ stable, it is responsible for hemolytic zones around streptococcal colonies on blood agar plate.
- (2) It is not antigenic
- (3) Inhibits chemotaxis & phagocytosis.
- (4) Exert a cytotoxic effect on various eucaryotic cells by binding to phospholipid in target cell memb.

Erythrogenic toxin

- (1) Produced only by lysogenic streptococci
- (2) Possesses two functional parts
 - (a) Heat labile part → Induces fever & suppresses immune system.
 - (b) Heat stable part → Enhances pyrogenicity & produces rash in scarlet fever as a result of hypersensitivity reaction to this part.

HABITAT & TRANSMISSION**Habitat**

Widely distributed in nature. Some are members of normal human flora, while others are associated with important human diseases;

- (1) *S pyogenes* is the main human pathogen, found on skin & oropharynx in small numbers.
- (2) *S agalactiae* is the member of normal flora of female genital tract.
- (3) Group C, F & G occur in pharynx, colon & female genital tract.
- (4) Group D enterococci occur in colon.
- (5) Peptostreptococci occur in mouth, colon & female genital tract.
- (6) *Streptococcus viridans* occur in normal flora of upper respiratory tract & contribute to healthy state of mucosa. Also found in colon & female genital tract.
- (7) Nutritionally variant streptococci also form part of normal flora.

Transmission

Via respiratory droplets.

PATHOGENESIS & CLINICAL FINDINGS**Diseases due to invasion by beta-hemolytic group a streptococci*****Erysipelas***

Caused by invasion of skin.

Clinical findings

Massive brawny edema with a rapidly advancing margin of infection.

Cellulitis

This is an acute, rapidly spreading infection of the skin & subcutaneous tissues.

Clinical findings

Pain, tenderness, swelling, & erythema.

Necrotizing fasciitis (strep. gangrene)

There is extensive & very rapidly spreading necrosis of the skin & subcutaneous tissues. Causative group A streptococci is called "flesh-eating bacteria."

Puerperal fever (puerperal septicemia)

Caused by invasion of uterus after delivery. Streptococci enter blood via wound in uterus (endometritis).

Sepsis (surgical scarlet fever)

Caused by invasion of traumatic or surgical wound by streptococci.

Diseases due to local infection with beta-hemolytic group a streptococci***Streptococcal sore throat***

Caused by attachment of group A streptococci to pharyngeal epithelium by means of lipoteichoic acid covering surface pili.

Clinical findings in children

- (1) Subacute nasopharyngitis with thin serous discharge.
- (2) Little fever.
- (3) Enlarged cervical lymph nodes.

Clinical findings in adults

- (1) Acute & intense nasopharyngitis.
- (2) Tonsillitis.
- (3) Intense redness & edema of mucous memb.
- (4) Purulent discharge.
- (5) High fever.
- (6) Enlarged & tender cervical lymph nodes.

Other conditions associated with strep. sore throat

- (1) Scarlet Fever Rash → Due to production of erythrogenic toxin.
- (2) Quinsy (peritonsillar abscess).
- (3) Ludwig's angina → Characterized by blockage of air passages by massive swelling of floor of mouth.
- (4) Streptococcal toxic shock syndrome → Due to production of erythrogenic toxin.

Pneumonia

Occurs as a sequela of viral infections, eg influenza or measles, & is rapidly progressive & severe.

Streptococcal pyoderma (impetigo)

Caused by local infection of superficial layers of skin.

Clinical findings

Superficial blisters that break down & eroded areas are covered with pus or crust.

Infective endocarditis***Acute endocarditis***

In bacteremia, "beta-hemolytic streptococci" settle on normal or previously injured heart valves.

Clinical findings

Acute endocarditis, destruction of heart valves, cardiac failure.

Subacute endocarditis

It involves abnormal valves (congenital deformities, rheumatic or atherosclerotic lesions). Thrombi are formed on injured endothelium of valve leaflets. These thrombotic lesions are invaded by organisms of less virulence which accidentally reach bloodstream.

Causative organisms

- (1) Viridans streptococci → Reach bloodstream after dental extraction.
- (2) Gram negative rods of intestinal flora.
- (3) Enterococci of gut or urinary tract.

Clinical finding

Fever, anemia, weakness, heart murmur, emboli, enlarged spleen, renal lesions.

Fulminant group A streptococcal infections & streptococcal toxic shock syndrome

Fulminant, invasive *S. pyogenes* infections with streptococcal toxic shock syndrome are characterized by shock, bacteremia, respiratory failure, & multiorgan failure.

Pathogenesis

Group A streptococci with 'M' types 1 & 3 that produces pyrogenic exotoxin A or B & 'M' types 12 & 28, act as superantigens → Stimulate T cells → Activated T cells release cytokines that mediate shock & tissue injury.

Clinical finding

- (1) Infections tend to follow minor trauma in otherwise healthy persons, resulting in;
 - (a) Necrotizing fasciitis.
 - (b) Myositis.
 - (c) Infections at other soft tissue sites.
- (2) Bacteremia follows resulting in fulminant toxic shock syndrome, characterized by;
 - (a) Fever.
 - (b) Rapidly progressive shock with multiorgan failure.
 - (c) Erythema & desquamation may occur.

Post-streptococcal diseases

Occur 1-4 weeks following an acute group A streptococcal infection.

Acute glomerulonephritis

It develops 3 weeks after skin infection with group A streptococci (types 12, 4, 2 & 49). It is initiated by immune complexes formed by streptococcal antigen & antibodies directed against it. These immune complexes are deposited on glomerular basement memb. which is damaged by inflammatory reaction.

Clinical findings

Hematuria, proteinuria, edema, azotemia, hypocomplementemia, high blood pressure.

Rheumatic fever

It develops 1-4 weeks after sore throat with group A streptococci. It is due to cross-reaction b/w human heart antigen & antibodies directed against streptococcal M antigens. As a result, heart valves are damaged.

Clinical findings

- (1) **Heart:** Aschoff bodies are deposited in myocardium, wart like vegetations (verrucae) on heart valves, fish-mouth or buttonhole stentoid deformity of valves, MacCallum's plaques on atrial walls.
- (2) **Joints:** Migratory non-suppurative arthritis.
- (3) **Skin:** Subcutaneous nodules, erythema marginatum.
- (4) **Others:** Fever & malaise.

Other infections

(1) Group B (*S. agalactiae*)

- (a) **In women:** Bacteremia & meningitis occur in diabetics & in patients on immunosuppressive drugs.
- (b) **In Children born to infected mother:** Bacteremia, pneumonia, meningitis & sepsis.

(2) Groups C & G

Sinusitis, bacteremia & endocarditis.

(3) Group D

- (a) **Enterococci:** UTI, endocarditis, meningitis.
- (b) **Non-enterococci:** UTI, endocarditis.

(4) *S. pneumoniae*

Lobar pneumonia

(5) *Streptococcus viridans*

Subacute endocarditis.

(6) *Streptococcus mutans*

Dental caries.

(7) Group N streptococci

Coagulation (souring) of milk.

(8) *Peptostreptococci*

Mixed anaerobic infection in pelvis, abdomen, lung or brain.

(9) *Nutritionally variant streptococci*

Bacteremia, endocarditis, brain abscess.

DIAGNOSTIC LABORATORY TESTS

Specimens

Throat swab, pus, blood, urine, CSF.

Microscopy

Gram stained smear from pus seen under microscope → G +ve cocci in chains.

Culture

Specimens are cultured on nutrient agar, blood agar, MacConkey's medium (for *E faecalis*).

Schultz Charlton reaction

This is used to detect erythrogenic toxin. Antitoxin is injected subcutaneously → Person suffering from scarlet fever shows blanching at injection site due to neutralization of toxin by antitoxin.

Serologic tests

- (1) Group A streptococcal antigen from throat swab can be detected by commercial kits that use enzyme-linked immunosorbent assay (ELISA) or agglutination tests.
- (2) Rise in serum titers of antibodies to group A streptococcal antigens are detected by streptozyme test:
 - (a) Antistreptolysin 'O'.
 - (b) Antistreptokinase.
 - (c) Antistreptodornase.
 - (d) Antihyaluronidase.
 - (e) Anti-M type specific antibodies.

Bacitracin sensitivity test

Commercially available discs containing a calibrated amount of bacitracin, will inhibit the growth of group A streptococci but not other groups of streptococci b/c group A streptococci is more sensitive to antibiotic bacitracin.

IMMUNITY

- (1) Type-specific immunity to reinfection with streptococci, develops. It is due to anti-M type-specific antibodies.
- (2) Immunity also develops against erythrogenic toxin via production of antitoxin in blood. But this only protects against rash of scarlet fever, & has no effect on re-infection with streptococci.
- (3) Similarly, antistreptolysin O blocks hemolysis, but also has no effect on re-infection with streptococcus.

TREATMENT

- (1) Penicillin G.
- (2) Erythromycin.

PREVENTION & CONTROL

- (1) No specific immunization with toxoids or vaccines.
- (2) Prophylactic antibiotics in the course of surgical procedures on respiratory, GI & urinary tracts, & in patient with known heart valve deformity and to those with prosthetic valves or joints.
- (3) Detection & early antimicrobial therapy of respiratory & skin infections with group A streptococci.
- (4) Antistreptococcal chemoprophylaxis in persons who have suffered an attack of rheumatic fever.
- (5) Eradication of *S pyogenes* from carriers.
- (6) Pasteurization of milk.

Chapter 6

Streptococcus Pneumoniae

MORPHOLOGY

Shape

Individual organism is lancet- shaped.

Arrangement

In pairs (diplococci) or sometime in short chains.

Capsule

Encapsulated.

Motility

Non-motile.

Spore

Non-spore forming.

STAINING

Gram's staining

Strep pneumoniae are Gram-positive (appear violet colored).

CULTURE

Media

- (1) Blood agar.
- (2) Chocolate agar.

Colonies

(1) Appearance

Small round colonies, at first dome-shaped, later develop a central plateau with elevated rim.



Pneumococci: Gram stain appearance.

(2) Hemolysis

Alpha hemolysis on blood agar.

(3) Effect on capsular polysaccharide

Most of the pneumococci are polysaccharide-producing & give rise to smooth colonies; a few are unable to produce capsular polysaccharide & give rise to rough colonies.

(4) Transformation

When uncapsulated pneumococci are cultured in the presence of DNA extracted from a capsulated pneumococcus, encapsulated pneumococci of later type are formed. This is called transformation.

(5) Lysis

Pneumococcal colonies are sensitive to lysis by an autolytic enzyme, L-alanine-muramyl amidase, which cleaves bond linking L-alanine peptide to muramic acid of peptidoglycan wall. This enzyme is activated after the culture enters stationary phase of growth & will in time cause lysis of entire culture.

Growth characteristics

(1) O₂ requirements

Difference B/w Pneumococci & Strep. Viridans	
Pneumococci	Strep. Viridans
1) Capsulated.	1) Non-capsulated.
2) Lyse spontaneously in media.	2) Do not lyse spontaneously in media.
3) Lysed by ox bile (10%) or sodium deoxycholate (2%) (hence soluble in bile).	3) Not lysed by ox bile or sodium deoxycholate (hence insoluble in bile).
4) Growth inhibited around optochin disk.	4) Growth not inhibited around optochin disk.
5) Ferment inulin.	5) Do not ferment inulin.

Aerobic or facultative anaerobic.

(2) Energy source

Ferments glucose, produces lactic acid but not gas. Lactic acid limits the growth.

(3) Temperature

37°C.

(4) Growth promoted by

5-10 % CO₂ (candle jar).

ANTIGENS

Capsular polysaccharide

- (1) Distinct for each of more than 90 serologic types.
- (2) Virulence is due to capsule which protects it from phagocytosis.
- (3) Elicits B cell response, which provide type-specific immunity.

M protein

Characteristic for each type.

C carbohydrate

It is group specific, common to all pneumococci.

ENZYMES

IgA protease

It enhances organism's ability to colonize mucosa of upper respiratory tract.

TOXINS

Pneumolysin

- (1) Binds to cholesterol in host cell memb.
- (2) Inhibit antimicrobial properties of neutrophils & opsonic activity of serum.

HABITAT & TRANSMISSION

Habitat

Normal inhabitants of upper respiratory tract.

Transmission

Via respiratory droplets.

PATHOGENESIS & CLINICAL FINDINGS

Pneumococcal (lobar) pneumonia

Pathogenesis

(1) Bacterial factors

Pneumococci produce disease thru their ability to multiply in the tissues. Its virulence is determined by capsule, which prevents or delays ingestion by phagocytes.

(2) Host factors

Loss of natural resistance due to;

- (a) Viral & other respiratory tract infections that damage surface cells, & abnormal accumulations of mucus (eg, allergy), which protect pneumococci from phagocytosis.
- (b) Alcohol or drug intoxication, which depresses phagocytic activity & cough reflex.
- (c) Abnormal circulatory dynamics (eg, pulmonary congestion, heart failure).
- (d) Malnutrition, general debility, sickle cell anemia, hyposplenism, nephrosis, or complement deficiency.

Difference Between	
Lobar Pneumonia	Bronchopneumonia
1) Caused 90% by pneumococci, few cases by klebsiella pneumoniae, staph. aureus.	1) Caused by staphylococci, streptococci, H. influenzae, proteus & pseudomonas.
2) Occurs in otherwise healthy individuals b/w 30-50 years.	2) Occurs in infants, olds & those suffering chronic debilitating illness or immunosuppression.
3) Onset is sudden with high grade fever, shaking chills & bloody or rusty sputum.	3) Onset is insidious with low grade fever & cough productive of purulent sputum.
4) Consolidation of whole lobe.	4) Patchy pneumonic consolidation.
5) Complications: Bacteremia, meningitis, endocarditis, septic arthritis.	5) Complications: Fibrosis, bronchiectasis, lung abscess.

- (1) Meningitis.
- (2) Endocarditis.
- (3) Septic arthritis.

Other complications

Sinusitis, otitis media, pericarditis, empyema & septicemia.

Meningitis

Pneumococcus is the second common bacterial pathogen, that causes meningitis in adults.

Pathogenesis

- (1) It may arise as a complication of pneumonia, in which pneumococci reach the meninges by way of blood stream.
- (2) It may result from a skull fracture, permitting pneumococci from nasopharynx to enter the meninges.

Otitis media

Pneumococci is the etiologic agent of about 50% cases of otitis media in children.

Important sero-types

Types 6, 14, 19 & 23.

Pathology

It is characterized by exudation of fibrinous edema fluid into alveoli, followed by RBCs & leukocytes, with many pneumococci also present in alveoli. This causes consolidation of portions of lung. Later, mononuclear cells actively phagocytose the debris, & pneumococci, & this liquid phase is gradually reabsorbed.

Important sero-types

- (1) In adults, types 1-8.
- (2) In children, types 6, 14, 19, & 23.

Clinical findings

- (1) Sudden onset of high fever with violent, shaking chills.
- (2) Sharp pleural pain & friction rub.
- (3) Cough, at first dry or productive of thin watery sputum; later bloody or rusty sputum.
- (4) Spontaneous recovery b/w 5th & 10th days, associated with development of type-specific antibodies.

Bacteremia & its complications

From alveolar exudate organisms reach bloodstream via lymphatics & cause bacteremia, which have a triad of serious complications:

DIAGNOSTIC LABORATORY TESTS

Specimens

Blood, sputum, pus, CSF.

Microscopy

Gram-stained smear of rusty sputum seen under microscope → G +ve diplococci, neutrophils & RBCs. Capsule can be demonstrated by “Negrosin staining or India ink”.

Culture

Specimens are cultured on blood agar & chocolate agar.

Capsule swelling test (Quelling test)

Fresh emulsified sputum (suspected of pneumococcal pneumonia) is mixed with specific anti-capsular polysaccharide antibodies (polyvalent antisera is usually used) → Capsule swell markedly → Positive test.

Note: Omni antiserum contains antibodies against all sero-types, which provide a definite identification of pneumococci in the specimen.

Optochin disks test

Differentiate b/w alpha-hemolytic pneumococci & alpha-hemolytic streptococcus viridans. Optochin disks are laid down on agar plate surface which is inoculated with unknown organisms. Pneumococci are very sensitive to it & so will fail to grow in its proximity whereas viridans are insensitive & will grow adjacent to implanted disks.

Animal inoculation test

Sputum is intraperitoneally injected into laboratory mice → Mice die within 18-48 hours b/c it is very sensitive to pneumococci → Heart blood gives pure culture of pneumococci.

IMMUNITY

Type-specific immunity to reinfection with pneumococci, develops. It is due to type-specific anticapsular antibodies.

TREATMENT

- (1) Penicillin G (drug of choice).
- (2) Erythromycin.
- (3) Cefotaxime.
- (4) Vancomycin.

PREVENTION & CONTROL

- (1) Immunization with polyvalent (23 types) polysaccharide vaccine.
- (2) Vaccine provides protection for 5 years.

Chapter >

Corynebacterium Diphtheriae

MORPHOLOGY

Shape

Individual organism is club-shaped, ie rods are swollen at one end. They have metachromatic granules that give the rod a beaded appearance.

Arrangement

Corynebacteria lie parallel or at acute angles to one another. Form L, Y & V shapes, called Chinese letter arrangement.

Capsule

Non-capsulated.

Motility

Non-motile.

Spore

Non-spore forming.



C. diphtheriae: Gram stain appearance.

STAINING

Gram's staining

Corynebacterium diphtheriae are club-shaped, beaded Gram-positive rods, appearing violet in color.

Methylene blue or toluidine blue staining

Granules in corynebacteria take on a reddish appearance. They are composed of polymer of inorganic polyphosphate & are called Babes-Ernst bodies (metachromatic granules or volutin).

CULTURE

Media

- (1) Loeffler's coagulated serum medium.
- (2) Blood agar containing potassium tellurite (inhibits growth of other organisms).
- (3) Chocolate agar containing potassium tellurite.

Colonies

- (1) Loeffler's medium → Small, granular, gray colonies with irregular edges.
- (2) Blood or chocolate agar with (K-tellurite) → Gray to black colonies.
- (3) **Biotypes' appearance on media:**
 - (a) Var gravis → Nonhemolytic, large, gray irregular, striated colonies.
 - (b) Var mitis → Hemolytic, small, black, glossy, convex colonies.
 - (c) Var intermedius → Nonhemolytic, small colonies with characteristics b/w (a) & (b).

Growth characteristics

- (1) **O₂ requirement**
Aerobe.
- (2) **Energy source**

Ferments glucose & maltose, produce acid but no gas.

(3) Temperature
37°C.

TOXINS

Diphtheria toxin

It is an exotoxin. Consists of two fragments A & B
→ Fragment B helps transport of fragment A into cell
→ Fragment A inactivates elongation factor EF-2 (transferase II)
→ Inhibits polypeptide chain elongation
→ Abrupt arrest of protein synthesis
→ Responsible for necrotizing & neurotoxic effects of diphtheria toxin.

Lethal dose: 0.1 µg/kg body weight.

HABITAT & TRANSMISSION

Habitat

C diphtheriae occurs in respiratory tract, wounds & skin of infected persons or normal carriers.

Transmission

Via respiratory droplets or by contact to susceptible persons.

PATHOGENESIS & CLINICAL FINDINGS

Pharyngeal diphtheria

Pathogenesis

Diphtheria toxin is absorbed into mucous memb. → Causes destruction of epithelium & superficial inflammatory response → Necrotic epithelium plus exuding fibrin, RBCs & WBCs form a greyish "pseudomembrane" over tonsils, pharynx & larynx.

Clinical findings

- (1) Bleeding (due to tearing of capillaries) if pseudomembrane is removed.
- (2) Enlargement of regional lymph nodes.
- (3) Edema of entire neck.
- (4) Sore throat & fever.

(5) Prostration & dyspnea & even suffocation (due to obstruction caused by pseudomembrane).

(6) Distant toxic effects

C diphtheriae in pseudomembrane continues to produce toxin → Toxin is absorbed in blood → Cause parenchymatous degeneration, fatty infiltration & necrosis in:

- (1) Heart → Arrhythmias
- (2) Liver
- (3) Kidneys
- (4) Adrenals

(7) Late findings

Difficulties with vision, speech, swallowing or movements of arms & legs (due to nerve damage).

Wound or skin diphtheria

A pseudomembrane is formed on infected wound → Wound healing is impaired.

DIAGNOSTIC LABORATORY TESTS

Specimens

Swabs from nose, throat or suspected lesions.

Microscopy

Smears stained with Gram's stain (or alkaline methylene blue) is seen under microscope → Gram-positive beaded rods in typical arrangement.

Culture

- (1) Loeffler's medium → Small, granular, gray colonies with irregular edges.
- (2) Blood agar (with K-tellurite) → Gray to black colonies.

Virulence tests

(1) Polymerase chain reaction

Used for detection of the diphtheria toxin gene (*tox*). It can be used directly on patient specimens before culture results are available.

(2) Enzyme-linked immunosorbent assays

Used to detect diphtheria toxin from clinical C diphtheriae isolates.

(3) Immunochromographic strip assay

Allows detection of diphtheria toxin in a matter of hours.

(4) Elek test

A strip of filter paper saturated with diphtheria antitoxin is placed at right angle to culture

streaks. Antitoxin from filter paper precipitates toxin from culture at the intersection of filter paper & culture streaks → Test positive.

(5) Tissue culture test

C diphtheriae is incorporated into an agar overlay of cell culture monolayers. Diphtheria toxin diffuses into cell monolayers & kills them → Test positive.

Note: In historic guinea pig test, emulsified culture is injected subcutaneously into 2 guinea pigs, of which one received diphtheria antitoxin previously. Unprotected animal dies in 2-3 days → Test positive.

IMMUNITY

Immunity against diphtheria depends upon production of specific neutralizing diphtheria antitoxin.

Tests for serum antitoxin determination

(1) Titration of serum for antitoxin content

Serum (tested for antitoxin) is mixed with varying amounts of toxin & mixture is injected into susceptible animals → See for the effects on animals → Less virulent effects means greater amount of toxin is neutralized → Antitoxin in serum is high.

(2) Schick test

One Schick test dose of diphtheria toxin is injected into skin of one forearm, & an identical dose of heated (neutralized) toxin is injected into other forearm as a control. Site of injection is examined after 24 hours, 48 hours & 6 days.

Results

(a) Positive reaction

- (i) At toxin site, redness & swelling is produced that increase for several days & then fades slowly.
- (ii) Control site shows no reaction.

(b) Negative reaction

Neither site shows any reaction.

(c) Pseudoreaction

Redness & swelling on arms: these signs disappear simultaneously on 2nd or 3rd day. It is a negative reaction.

(d) Combined reaction

Both injection sites show redness & swelling:

- (i) At toxin site reaction lasts for 5-7 days.
- (ii) At control site reaction lasts for 2-3 days.

Clinical significance

- (a) Positive & combined reaction indicate there is no antitoxin in body → Increased susceptibility to infection.
- (b) Negative & pseudoreactions indicate antitoxin is present in body → Resistance to diphtheria.

Immunization against diphtheria

Diphtheria toxoid is used for active immunization as part of a triple vaccine DPT (diphtheria, pertussis & tetanus).

Dosage

See chapter 9.

TREATMENT

- (1) Diphtheria antitoxin (20,000 - 100,000 units IM or IV after test dose).
- (2) Antibacterial drugs:
 - (a) Penicillins.
 - (b) Erythromycin.
 - (c) Vancomycin.

PREVENTION & CONTROL

- (1) Immunization with toxoid (formaldehyde-treated toxin) given in combination with tetanus toxoid & pertussis vaccine (DPT).
- (2) Immunization does not prevent nasopharyngeal carriage of the organism.

Chapter 8

Mycobacterium Tuberculosis

MORPHOLOGY

Shape

Individual organism is rod shaped, thin & usually straight (sometimes bent or club-shaped).

Arrangement

“Virulent strains” of M tuberculosis form microscopic “serpentine cords” in which acid-fast bacilli are arranged in parallel chains.

Capsule

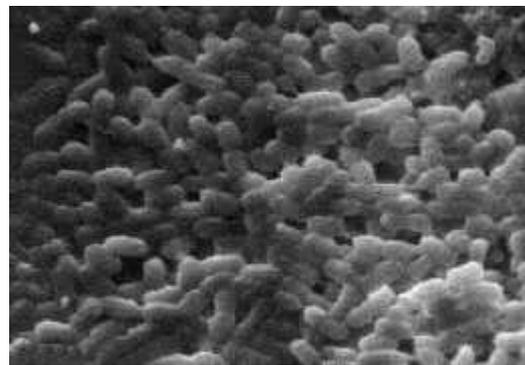
Non-capsulated.

Motility

Non-motile.

Spore

Non-spore forming.



M tuberculosis: Electron micrograph from broth culture.

mycobacteria is known as “acid-fastness”, it depends upon waxy envelop of mycobacteria.

Fluorochrome staining

Mycobacteria are stained with fluorochrome stains (eg, auramine & rhodamine) → Yellow - orange fluorescence.

STAINING

Gram's staining

Mycobacteria are Gram-positive organisms (appear violet colored).

Ziehl Neelsen (acid-fast) staining

Smear is covered with red stain carbofuchsin & heated for a few minutes. Stained smear is now washed with acid-alcohol & counterstained with methylene blue & observed under microscope → Thin rods, red in color.

Acid-Fastness of Mycobacteria

Once stained by basic dyes (carbofuchsin), mycobacteria cannot be decolorized by acid-alcohol (ie, 95% ethyl alcohol + 3% HCl). This property of

CULTURE

Media

Semisynthetic agar media

- (1) These media (eg, Middlebrook 7H10 & 7H11) contain defined salts, vitamins, cofactors, oleic acid, albumin, catalase, & glycerol; the 7H11 medium contains casein hydrolysate also.
- (2) Large inocula yield growth in several weeks.
- (3) These are used for observing colony morphology, for susceptibility testing, & with

added antibiotics & malachite green as selective media.

Inspissated egg media

- (1) These media (eg, Löwenstein-Jensen) contain defined salts, glycerol, & complex organic substances (eg, fresh eggs or egg yolks, potato flour, & other ingredients in various combinations).
- (2) Malachite green is included to inhibit other bacteria, & with added antibiotics are used as selective media.
- (3) Small inocula yield growth in 3–6 weeks.

Broth media

- (1) Broth media (eg, Middlebrook 7H9 & 7H12) support the proliferation of small inocula.
- (2) Ordinarily, mycobacteria grow in clumps or masses because of the hydrophobic character of the cell surface. If Tweens (water-soluble esters of fatty acids) are added, they wet the surface & thus permit dispersed growth in liquid media. Growth is often more rapid than on complex media.

Growth characteristics

O₂ requirement

Obligate aerobe.

Energy source

Oxidation of many simple carbon compounds.

Temperature

37°C.

Growth enhanced by

5-10% carbon dioxide.

Growth inhibited by

Heat & pasteurization.

Resistance

Mycobacteria are resistant to

- (1) Drying.
- (2) Chemicals.
- (3) Dyes, eg malachite green.
- (4) Antimicrobial agents eg penicillin.

Growth rate

Cell division requires 12 to 20 hours, taking as long as 6 weeks before colonies are visible following a small inoculation.

ANTIGENS

Lipids

Glycolipids (Mycosides)

“Mycosides” are glycolipids consisting of mycolic acid bound to carbohydrates. Following mycosides are medically important:

(1) Cord Factor

- (1) It is responsible for formation of serpentine cords, in which mycobacteria are arranged in parallel cords.
- (2) Inhibits migration of polymorphs.
- (3) Cause chronic granulomas.
- (4) Binds to mitochondrial memb. → Causing functional damage to respiration & oxidative phosphorylation.
- (5) Induces synthesis of cachectin → Responsible for cachexia observed in tuberculous patients.

(2) Phosphatides

Inhibit phagosome-lysosome fusion → Enhance survival of phagocytosed mycobacteria.

(3) Wax D

- (a) Acts as an adjuvant to increase antibody response to an antigen.
- (b) Also induce cellular immune response to mycobacteria.

Phospholipids

Induce caseation necrosis.

Proteins

Mycobacteria contain many protein antigens that are not associated with virulence.

Functions

- (1) Induce host's cellular immunity → Elicits tuberculin reaction.
- (2) Also induce antibody formation.

Polysaccharides

- (1) Their role in pathogenesis is uncertain.
- (2) Can induce immediate hypersensitivity.

HABITAT & TRANSMISSION

Habitat

Human tissues, especially lungs.

Transmission

Via droplet nuclei produced by coughing.

PATHOGENESIS & CLINICAL FINDINGS**Tuberculosis**

Organisms in droplets are inhaled & reach alveoli

→ Mycobacteria establishes in lung & proliferates

→ Produces two types of lesions:

(1) Exudative lesion

This consists of acute inflammatory reaction, with edema fluid, neutrophils & later macrophages around the tubercle bacilli. Exudative lesion may:

- Heal by resolution with absorption of exudate; or
- Lead to necrosis of lung tissue; or
- Develop into second type of lesion (productive lesion).

(2) Productive lesion

This is a chronic granuloma consisting of 3 zones:

- Central zone of multinucleated giant cell containing mycobacteria.
- Middle zone of epithelioid cells.
- Peripheral zone of fibroblasts, lymphocytes & monocytes.

Development of a tubercle

Later, central zone undergoes caseation necrosis surrounded by epithelioid cells & peripheral zone; this is called a tubercle.

A caseous tubercle may break into bronchus, empty its contents & forms a cavity that heals by fibrosis or calcification.

Spread of mycobacteria in host

By 2 methods:

- A caseous tubercle may erode into a bronchus, empty its caseous contents, & thereby spread,
 - to other parts of lungs.
 - to GIT if coughed up sputum is swallowed.
 - to other persons thru droplets.
- Also spread via lymphatics & bloodstream to many internal organs.

Site of growth

Mycobacteria grow intracellularly in monocytes, macrophages & giant cells → This makes

chemotherapy difficult & favors microbial persistence.

Reactive types of tuberculosis**(1) Primary Infection**

- After inhalation of mycobacteria, an acute exudative lesion is formed, called Ghon lesion or focus.
- Organisms from Ghon lesion spread to lymphatics & regional lymph nodes & cause acute inflammatory reaction there; combination of Ghon lesion & lymph node involvement is called Ghon complex.
- In most cases, Ghon complex undergoes progressive fibrosis & often calcification.
- Tuberculin skin test (Mantoux test) is positive.
- Significance**
 - Primary infection induces hypersensitivity & immunity.
 - May harbor viable bacilli for years, which may become reactivated.

(2) Secondary infection

It is caused by reactivation of tubercle bacilli that have survived in primary lesion, or by exogenous reinfection because of waning of immunity (induced by primary infection). It is characterized by:

- Chronic tissue lesions, formation of tubercles, caseation & fibrosis.
- Regional lymph nodes are slightly involved & do not caseate.
- Secondary infection occurs at apex of lung, where oxygen tension is highest.

Difference b/w primary & secondary infections - Koch's phenomenon

- Guinea pig is injected subcutaneously with virulent mycobacteria (primary infection);
 - Puncture wound heals quickly.
 - A nodule forms at the site of injection in 2 weeks; nodule ulcerates; & ulcer does not heal.
 - Regional lymph nodes develop tubercles & caseate.
- Same animal is later injected with virulent mycobacteria in another part of body (secondary infection);
 - Rapid necrosis of skin & tissue at the site of injection; ulcer heals rapidly.

- (b) Regional lymph nodes are either not involved or involved after some time.

Clinical findings of tuberculosis

- (1) Fever (low-grade, remittent & appear late each afternoon & then subside), night sweats, malaise & weakness.
- (2) Anorexia & weight loss.
- (3) Cough (first mucoid, later purulent & bloody sputum).
- (4) Pleuritic pain.

DIAGNOSTIC LABORATORY TESTS

Specimens

Sputum, gastric washing, urine, pleural fluid, spinal fluid, joint fluid, biopsy material, blood.

Decontamination & concentration

- (1) Non-sterile specimens eg sputum are first liquefied with *N*-acetyl-L-cysteine, decontaminated with NaOH, neutralized with buffer, & concentrated by centrifugation → Specimens then used for acid-fast stains & culture.
- (2) Sterile specimens eg CSF do not need the decontamination, but can be directly centrifuged, examined, & cultured.

Microscopy

Ziehl-Neelsen stained or auramine-rhodamine stained smear of sputum observed under simple or fluorescence microscope respectively → Reveal acid-fast bacilli.

Culture

- (1) Processed &/or centrifuged specimens are cultured onto selective & nonselective media, that yield positive results as;
 - (a) Selective broth culture → About 2 weeks.
 - (b) Löwenstein-Jensen media → About 3-6 weeks.
 - (c) Middlebrook 7H10/7H11 media → About 8 weeks.
- (2) Blood for culture of mycobacteria (usually *M* avium complex) should be anticoagulated & processed by one of the following methods:
 - (a) Commercially available lysis centrifugation system.

- (b) Inoculation into commercially available broth media specifically designed for blood cultures.
- (c) Centrifugation of the blood & inoculation of the white blood cell buffy coat layer, with or without deoxycholate lysis of the cells, into broth culture.

Mantoux (tuberculin) test

(Hypersensitivity test for early diagnosis in non-immunized individuals of tuberculosis).

0.1 ml of PPD (purified protein derivative from old tuberculin) is injected intradermally → Induration, edema & erythema develop in 24-48 hours.

(1) Positive test

- (a) Primary infection with *M* tuberculosis.
- (b) Vaccination with BCG.

(2) False negative Test

Means, -ve Mantoux test in the presence of tuberculosis:

- (a) Overwhelming tuberculosis.
- (b) Measles
- (c) Hodgkin's disease
- (d) Sarcoidosis
- (e) Immunodeficiency states
- (f) Immunosuppressive therapy

Definite identification of mycobacterial species

Conventional methods

- (1) Include observation of rate of growth, colony morphology, pigmentation, & biochemical tests (eg, positive niacin test for *M* tuberculosis, reduction of nitrate, production of urease or catalase, & arylsulfatase test).
- (2) Require 6–8 weeks for identification.
- (3) Conventional methods classify the mycobacteria into following groups (**Runyon classification**):
 - (a) TB complex → eg *M* tuberculosis, *M* africanum, *M* bovis.
 - (b) Rapid growers (growth in 7 days) → eg *M* abscessus, *M* fortuitum, *M* smegmatis.
 - (c) Photochromogens (produce pigment in light) → eg *M* asiaticum, *M* kansasii, *M* marinum.
 - (d) Scotochromogens (produce pigment in the dark) → eg *M* flavescens, *M* scrofulaceum.

- (e) Nonchromogens (nonpigmented or have light tan or buff-colored colonies) → eg *M. avium*, *M. ulcerans*.

Molecular probing

- (1) DNA probes specific for rRNA sequences of the test organism are used in a hybridization procedure. These probes are linked with chemicals that are activated in the hybrids and detected by chemiluminescence.
- (2) Mycobacteria are identified within 24 hours.

High-performance liquid chromatography

HPLC is based on development of profiles of mycolic acids, which vary from one species to another.

Susceptibility testing

Helps in selecting drugs for effective therapy;

- (1) Radiometric broth culture technique → For susceptibility to first-line drugs.
- (2) Agar-based technique → For susceptibility test to first- & second-line drugs.

DNA detection

- (1) Polymerase chain reaction (PCR) helps in rapid & direct detection of *M. tuberculosis* in specimens.
- (2) DNA fingerprinting is based on restriction fragment length polymorphism.
- (a) Many copies of the insertion sequence 6110 (IS6110) are present in the chromosome of most strains of *M. tuberculosis*.
- (b) A probe against IS6110 is used to determine the genotypes.

IMMUNITY

Cell-mediated & antibody-mediated immunity develop against mycobacteria → Localize the organisms, retard their multiplication, limit their spread & reduce lymphatic dissemination.

Immunization against tuberculosis

BCG (Bacillus-Calmette - Guerin) vaccine → 0.05 ml intradermally just after birth.

Notes

- (1) BCG vaccine contains live attenuated *M. bovis*.
- (2) BCG is not widely used for immunization in USA, because after BCG vaccination person

becomes +ve to Mantoux test & an important diagnostic tool to detect tuberculosis is lost.

- (3) In Pakistan, BCG immunization is done just after birth to save the child, although at the cost of Mantoux test (because of the much higher incidence of tuberculosis).

TREATMENT

First line drugs

- (1) Isoniazid (INH).
- (2) Rifampin.
- (3) Pyrazinamide.
- (4) Ethambutol.
- (5) Streptomycin.

Second line drugs

- (1) Kanamycin.
- (2) Capreomycin.
- (3) Ethionamide.
- (4) Cycloserine.
- (5) Ofloxacin.
- (6) Ciprofloxacin.

Note: These are more toxic &/or less effective, & used in cases of treatment failure or multiple drug resistance.

Standard 9-month regimen

- (1) First 2 months → Isoniazid, rifampin, pyrazinamide, & ethambutol (or streptomycin).
- (2) Next 7 months → Isoniazid & rifampin.

PREVENTION & CONTROL

- (1) Immunization with BCG.
- (2) Effective treatment of pts with active tuberculosis, & careful follow-up of their contacts with tuberculin test, X-ray chest, & appropriate treatment.
- (3) Eradication of tuberculosis in cattle (test & slaughter).
- (4) Pasteurization of milk.
- (5) INH prophylaxis.

MYCOBACTERIUM BOVIS

Features differentiating it from M tuberculosis

- (1) Normally a cattle pathogen.
- (2) Human infection results from ingestion of contaminated milk.
- (3) Produces lesions primarily in bone marrow of hip, knee & vertebrae & in cervical lymph nodes. If inhaled, produces pulmonary tuberculosis.
- (4) Do not form serpentine cords.
- (5) Colonies are white & flat with entire edges.
- (6) Niacin -ve.
- (7) Glycerol inhibits growth.

- (ii) Causes skin wound infections, in the form of necrotizing ulcer called "Buruli ulcer".

(4) Rapid Grower

Vary in pigment production & has a generation time of less than 1 hour & colonies become visible after 2-3 days; eg,

(a) M fortuitum

Cause wound infection, which occur either as skin abscesses or as deeper infections following surgery.

(b) M chelonae

Similar to M fortuitum.

(c) M abscessus

Similar to M fortuitum.

ATYPICAL MYCOBACTERIA**Runyon classification groups****(1) Photochromogens**

Produce yellow pigment, only if grown in light; eg.

(a) M kansasii

Cause tuberculosis (pulmonary & extrapulmonary), similar to M tuberculosis, esp. in pts with impaired immune response.

(b) M marinum

Cause infection at traumatized area in skin, manifested by draining ulcer.

(2) Scotochromogens

Produce orange pigment whether growth in light or dark, eg,

M scrofulaceum

Causes cervical lymphadenitis.

(3) Nonchromogens

Do not produce pigment under any circumstances; eg,

(a) M avium

Cause tuberculosis similar to that caused by M tuberculosis, esp. in pts with AIDS & those with preexisting pulmonary disease.

(b) M intracellulare

Similar to M avium

(c) Mycobacterium ulcerans

- (i) Closely related to M tuberculosis, but it is unable to grow above 33°C; so, cannot cause a systemic infection.

MYCOBACTERIUM LEPRAE**Pathogenesis**

Mycobacterium leprae causes "Leprosy". There are 2 main types of leprosy, with 3 intermediate forms:

- (1) Lepromatous leprosy
- (2) Boderline lepromatous leprosy
- (3) Boderline leprosy
- (4) Boderline tuberculoid leprosy
- (5) Tuberculoid leprosy

Lepromatous leprosy

- (1) Course is progressive & malignant.
- (2) Major pathogenic changes occur in skin, nerves, nose & eyes:
 - (a) Skin → Nodular (papular) lesions with abundant bacilli.
 - (b) Nerve → Bilateral symmetrical nerve involvement.
 - (c) Nose → Lesions of nasal mucous memb. cause severe nasal deformities due to destruction of cartilaginous septum.
 - (d) Eye → Infected in advanced cases with eventual blindness.
- (3) Cell mediated immunity is markedly deficient & skin is infiltrated with suppresser T cells.

Tuberculoid leprosy

- (1) Course is non-progressive & benign.
- (2) Pathogenic changes occur in nerves & skin:
 - (a) Nerve → Rapid & asymmetric nerve involvement.

- (b) Skin → Hypopigmented macular skin lesions with few bacilli.
- (3) Cell-mediated immunity is intact & skin is infiltrated with helper T cells.

Clinical findings***Lepromatous leprosy***

- (1) Multiple nodular skin lesions.
- (2) Leonine (lion-like) facies.
- (3) Fever.
- (4) Eyebrow loss.
- (5) Lepromin skin test → -ve.

Tuberculoid leprosy

- (1) Hypopigmented macular skin lesions.
- (2) Thickened superficial nerves.
- (3) Anesthesia of skin lesions.
- (4) Lepromin skin test → +ve.

Treatment

- (1) Dapsone (first line drug).
- (2) Rifampin.
- (3) Clofazimine.
- (4) Minocycline, clarithromycin, & some fluoroquinolones.
- (5) Vaccine → Killed *M leprae* + viable BCG.

Chapter 9

Clostridium Tetani

MORPHOLOGY

Shape

Individual organism is rod-shaped, containing spherical, terminal spores, which gives the cell a drum-stick or tennis-racket appearance.

Arrangement

Rods lie separately.

Capsule

Non-capsulated.

Motility

Motile with peritrichous flagella.

Spore

Spore-forming.



C tetani: Gram stain appearance from blood agar grown under anaerobic conditions.

STAINING

Gram's staining

Clostridium tetani are Gram-positive organisms. Rods appear violet colored, but the spore appear pink when the counterstain is carbolfuchsin (not stained with safranin).

CULTURE

Media

(1) Anaerobic jar

Agar plates or culture tubes are placed in anaerobic (airtight) jar from which air is removed and replaced by 10% CO₂.

(2) Anaerobic media

- (a) Robertson's cooked meat medium.
- (b) Thioglycolate medium.

Colonies

Smaller colonies that extend in a meshwork of fine filaments.

Growth characteristics

(1) O₂ requirement

Anaerobic (because they lack cytochrome and cytochrome oxidase).

(2) Energy source

Ferment sugars and can digest proteins.

(3) Temperature

37°C.

ANTIGENS

- (1) O (Somatic) antigen.
- (2) Flagellar antigen.

TOXINS

Tetanospasmin

Vegetative cells of *C. tetani* produce tetanospasmin, which is under control of plasmid gene.

Function

- (1) Inhibits release of acetylcholine, thus interfering with neuromuscular transmission.
- (2) Inhibits release of inhibitory neurotransmitters (glycine and GABA).

Tetanolysin

Causes hemolysis; is of minor importance in pathogenesis of tetanus.

HABITAT & TRANSMISSION

Habitat

Soil and feces of horse.

Transmission

Thru traumatized skin breaks, eg. wound, burn, injury, umbilical stump, surgical suture.

PATHOGENESIS & CLINICAL FINDINGS

Tetanus (lockjaw)

Pathogenesis

Spores in devitalized tissue germinate into vegetative organisms (aided by necrotic tissue, Ca salts & associated pyogenic infections, all of which provides anaerobic environment) → Produce toxins (tetanospasmin) → Reach CNS via 2 ways:

(1) Retrograde transmission

Toxin first bound to neuronal cells at neuromuscular junction → Here it inhibits acetylcholine release (interfering with neuromuscular transmission) → Toxin then crosses nerve cell memb. and is transported

retrograde to inhibitory Renshaw cell interneurons → Here it inhibits release of glycine and GABA.

(2) Via bloodstream

Toxin reaches spinal cord and brain stem and bind to ganglioside receptors 2 Inhibits release of glycine and GABA (inhibitory neurotransmitters).

Final Effect

Excitatory neurons are unopposed (i.e. uninhibited) → Generalized muscle spasms, hyper-reflexia and seizures.

Incubation period

4-5 days to 4-5 weeks.

Clinical findings

- (1) Convulsive tonic contraction of voluntary muscles.
- (2) Initially muscular spasms often involve the area of injury & infection.
- (3) Trismus or lockjaw due to rigid contraction of jaw muscle; mouth can not be opened.
- (4) Risus sardonicus (a grinning expression produced by spasm of facial muscles).
- (5) Gradually, other voluntary muscles become involved, resulting in tonic spasms. There is board-like abdominal wall, & back is usually slightly arched (opisthotonus).
- (6) Any external stimulus may precipitate tetanic convulsions, which are exhausting & painful.
- (7) Death from interference with mechanisms of respiration.

Note: Tetanus neonatorum may result from infection of umbilical stump, if childbirth takes place in an unhygienic environment.

DIAGNOSTIC LABORATORY TESTS

Specimen

Material from contaminated wounds.

Culture

Anaerobic culture of materials from contaminated wounds may yeild clostridium tetani.

Note: Clinical picture of tetanus with a history of injury provide sufficient clinical diagnosis; a complete laboratory diagnosis is not ordinarily done.

D/D: Strychnine poisoning.

IMMUNITY

Natural immunity does not develop because the amount of toxin producing serious disease is too small to induce protective antibodies.

Immunization against tetanus

Tetanus toxoid is used for active immunization as a part of tripple vaccine DPT (diphtheria, pertusis & tetanus).

Dose

Three doses of DPT 0.5 ml I/M at 2nd, 3rd and 4th month after birth.

Booster dose

- (1) 1st Booster: DPT 0.5 ml I/M at the age of 2 years.
- (2) 2nd Booster: DT (diphtheria & tetanus toxoids) 0.5 ml I/M at 5 years.

TREATMENT

- (1) Tetanus antitoxin, human type containing tetanus immune globulin (TIG) →
 - (a) 250 - 500 units I/M, immediately following potentially dangerous injury. This gives adequate systemic protection for 2-4 weeks.
 - (b) 1000 - 10,000 units I/M, in pts, who develop symptoms of tetanus.
- (2) Tetanus antitoxin, horse serum type (ATS) →
 - (a) 1500 - 3000 units I/M, immediately following potentially dangerous injury. This gives adequate systemic protection for 1-2 weeks.
 - (b) 40,000 - 60,000 units, half dose by I/M & half by I/V, in pts, who develop symptoms of tetanus.
- (3) Active immunization with tetanus toxoid (TT) →
 - (a) In a previously immunized patient, one booster should be given.
 - (b) In a non-immunized patient, two I/M inj. administered at 4-8 weeks intervals; 3rd dose after one year; booster after 5-10 years.
 - (c) Immunity lasts for 10 years.

- (4) Muscle relaxants, sedatives, assisted ventilation.
- (5) Surgical debridement of necrotic tissue.
- (6) Antibiotic → Penicillin.

PREVENTION & CONTROL

- (1) Active immunization with tetanus toxoid in childhood and every 10 years.
- (2) Tetanus toxoid booster, whenever trauma occurs.
- (3) Cleaning the soil contaminated wound under running water & then apply antiseptic.
- (4) Prophylactic use of antitoxin & a penicillin course, immediately following potentially dangerous injury.

Chapter 10

Clostridium Botulinum

MORPHOLOGY

Shape

Individual organism is rod-shaped, containing oval spores terminally or subterminally.

Arrangement

Rods lie separately.

Capsule

Non-Capsuled.

Motility

Motile with peritrichous flagella.

Spore

Spore-forming.



C botulinum: Gram stain appearance from broth grown under anaerobic conditions.

STAINING

Gram's staining

Clostridium botulinum are Gram-positive organisms. Rods appear violet colored, but the spores appear pink when the counterstain is carbolfushin (not stained with safrain).

CULTURE

Media

(1) Anaerobic jar

Agar plates or culture tubes are placed in anaerobic (airtight) jar from which air is removed & replaced by 10% CO₂.

(2) Anaerobic media

- (a) Robertson's cooked meat medium.
- (b) Thioglycolate medium.

Colonies

Colonies are translucent and either circular or irregularly shaped. Surface appears granular and swarming cells covers entire culture plate.

Growth characteristics

(1) O₂ requirements

Anaerobe (because they lack cytochrome & cytochrome oxidase).

(2) Energy source

Ferment sugars and can digest proteins.

(3) Temperature

37°C

TOXINS

Botulinum toxin

C botulinum produces exotoxins, of which there are 7 antigenic types (A → G). The toxins are neurotoxic proteins, of which types A, B, E (& occasionally F) are the principal causes of human illness.

- (1) The toxin is a 150,000-MW protein that is cleaved into 100,000-MW heavy chain & 50,000-MW light chain proteins linked by a disulfide bond.
 - (a) Toxin is absorbed from the gut, & the heavy chain binds to receptors of presynaptic membranes of motor neurons of the peripheral nervous system & cranial nerves.
 - (b) Light chain causes proteolysis of the target SNARE proteins in the neurons, inhibiting the release of acetylcholine at the synapse, resulting in lack of muscle contraction & paralysis.
Note: SNARE proteins are synaptobrevin, SNAP 25, & syntaxin. Toxins of C botulinum types A & E cleave SNAP-25, whereas Type B toxin cleaves synaptobrevin.
- (2) Lethal dose for humans is 1-2 µg.
- (3) The toxins are destroyed by heating for 20 minutes at 100 °C.
Note: Botulinum toxins are destroyed but not botulinum spores which can withstand 100°C for 3-5 hours.

Pathogenesis

Failure to sterilize food during preservation allows spores to survive → Spores germinate in anaerobic environment and produce toxin. So this form of food-poisoning is due to “pre-formed toxin” → Toxin blocks release of acetylcholine at myoneural junction → Cause flaccid paralysis.

Incubation period

18 - 24 hours.

Clinical findings

(A) Adult botulism

- (1) Visual disturbances (incoordination of eye muscles, double vision).
- (2) Inability to swallow.
- (3) Speech difficulty.
- (4) Bulbar paralysis.
- (5) Death from respiratory paralysis and cardiac arrest.
- (6) Patient remains fully conscious until shortly before death.
- (7) No fever.

(B) Infant botulism

Caused by ingestion of infected honey.

- (1) 2-3 days of constipation.
- (2) Flaccid paralysis.
- (3) Difficulty in nursing and a generalized weakness described as “overtly floppy”.
- (4) Respiratory distress.
- (5) Death (one of the causes of sudden infant death syndrome).

HABITAT & TRANSMISSION

Habitat

Soul & animal feces.

Transmission

Transmitted thru spiced, smoked, vacuum-packed or canned alkaline foods that are eaten without proper cooking.

PATHOGENESIS & CLINICAL FINDINGS

BOTULISM

DIAGNOSTIC LABORATORY TESTS

Specimens

- (1) In adults → Serum and left over food.
- (2) In infants → Feces.

Animal inoculation test

Patient's serum or implicated food is injected intraperitoneally into laboratory mice → Mice die rapidly.

Demonstration of toxin

Botulinum toxin can be demonstrated in Serum, leftover food or ipn feces by:

- (1) Hemagglutination, or
- (2) Radioimmunoassay.

IMMUNITY

Natural immunity does not develop because the lethal dose of toxin is too small to induce protective antibodies.

TREATMENT

- (1) Trivalent (A, B, E) antitoxin I/V.
- (2) Artificial respiration.

PREVENTION & CONTROL

- (1) Proper sterilization of all canned & vacuum-packed foods.
- (2) Foods must be adequately cooked to inactivate the toxin.
- (3) Swollen cans must be discarded (clostridial proteolytic enzymes cause gas formation that swells the cans).

Chapter 17

Clostridium Perfringens (C Welchii)

MORPHOLOGY

Shape

Individual organism is rod-shaped, containing large, central, oval spores which often give a swollen appearance.

Arrangement

Rods lie separately.

Capsule

Free organism is non-capsulated, but in tissue capsule is formed.

Motility

Non-motile.

Spore

Spore-forming.



C perfringens: Gram stain appearance from broth culture, grown under anaerobic conditions.

STAINING

Gram's staining

Clostridium pefringens are Gram-positive organisms. Rods appear violet colored, but the spore appear pink when the counterstain is carbolfushin (not stained with safranin).

CULTURE

Media

(1) **Anaerobic jar**

Agar plates or culture tubes are placed in anaerobic (airtight) jar from which air is removed and replaced by 10% CO₂.

(2) **Anaerobic media**

- (a) Robertson's cooked meat medium.
- (b) Thioglycolate medium.

Colonies

- (1) Large raised colonies with entire margins.
- (2) Produce multiple zones of hemolysis around colonies on blood agar.

Growth characteristics

(1) **O₂ requirements**

Anaerobic (because they lack cytochrome and cytochrome oxidase).

(2) **Energy source**

Ferment sugars & can digest proteins.

(3) **Temperature**

37°C.

ENZYMES**DNase**

Splits DNA.

Hyaluronidase

Splits hyaluronic acid of ground substance.

Collagenase

Digest collagen of subcutaneous tissue & muscle.

Fibrinolysin

Breaks down blood clots.

TOXINS**Alpha toxin****Produced by**

All types of *C. perfringens* (A → E).

Function

It is a lecithinase that splits lecithin (an important constituent of cell memb) → Damages cell memb of various cells thru-out the body, including RBCs (hemolysis).

Delta & theta toxins**Produced by**

- (1) Delta toxin → Types B & C.
- (2) Theta toxin → All types (A → E).

Function

- (1) Both have hemolytic effect (but no lecithinase activity).
- (2) Theta toxin also has necrotizing effect.

Beta & epsilon toxins**Produced by**

- (1) Beta toxin → Types B & C.
- (2) Epsilon toxin → Types B & D.

Function

Both have necrotizing effects.

Iota toxin**Produced by**

Type E.

Function

It has necrotizing & enterotoxigenic effects.

Enterotoxin**Produced by**

Types A & C.

Function

It is a powerful enterotoxin, esp. when grow in meat dishes. Cause hypersecretion in jejunum and ileum → Diarrhea.

HABITAT & TRANSMISSION**Habitat**

Soil, food, normal flora of colon & vagina.

Transmission

- (1) Gas gangrene is transmitted by war wounds, automobile accidents and septic abortions.
- (2) Food poisoning is transmitted by warmed meat dishes.

PATHOGENESIS & CLINICAL FINDINGS**Gas gangrene (myonecrosis)****Pathogenesis**

Spores reach tissue by contamination of traumatized areas with soil or feces → Spores germinate at low oxidation-reduction potential → Vegetative cells multiply → Cause following effects:

- (1) Ferment carbohydrates → Produce gas → Tissue is distended → Interfere with blood supply.
- (2) Produce toxins, esp alpha toxin → Damages cell memb, including those of RBCs → Hemolysis.
- (3) Hyaluronidase → Favor spread of infection.
- (4) Necrotizing toxins → Necrosis of infected tissues.

Clinical findings

- (1) Crepitation in subcutaneous tissue & muscle.
- (2) Foul-smelling discharge.
- (3) Rapidly progressive necrosis.
- (4) Fever.

- (5) Hemolysis.
- (6) Toxemia.
- (7) Shock & death.

immunization have been prepared, but they have not come into practical use.

Food poisoning**Pathogenesis**

During sporulation (spore formation) in gastrointestinal tract, an "enterotoxin" is produced
 → Induces hypersecretion in jejunum and ileum.

Incubation period

6-18 hours.

Clinical findings

- (1) Diarrhea with loss of fluid & electrolytes.
- (2) No vomiting.
- (3) No fever.

DIAGNOSTIC LABORATORY TESTS**Specimens**

Material from wounds, pus, tissue.

Microscopy

Gram-stained smear is seen under microscope → Gram-positive spore-forming rods seen.

Culture

- (1) Material is inoculated into Robertson's cooked meat medium, thioglycolate medium & blood agar → Incubated anaerobically → Typical colonies develop.
- (2) Growth from one of the media is transferred into milk → A clot is torn by gas in 24 hours → Clostridium perfringens is present.
- (3) **Negler's reaction:**
 This determines lecithinase activity. Precipitate is formed around colonies on egg yolk media.

Final identification

Depends upon toxin production & neutralization by specific antitoxin.

IMMUNITY

Natural immunity does not develop because quantity of toxins is not upto the level required for antibody production. Toxoids for active

TREATMENT**Gas gangrene**

- (1) Penicillin or tetracyclin.
- (2) Polyvalent antitoxin.
- (3) Surgical debridement of involved area, which may require amputation.
- (4) Hyperbaric oxygen.

Food poisoning

- (1) Symptomatic treatment.
- (2) No antimicrobial drugs.

PREVENTION & CONTROL**Gas fangrene**

- (1) Early & adequate cleansing of contaminated wounds.
- (2) Surgical debridement.
- (3) Penicillin prophylaxis.

Food poisoning

- (1) No specific preventive measure.
- (2) Food should be adequately cooked.

Chapter 12

Neisseria Gonorrhoeae (Gonococci)

MORPHOLOGY

Shape

Individual organism is kidney-shaped (cocci).

Arrangement

In pairs (diplococci), with their concave sides adjacent to each other.

Capsule

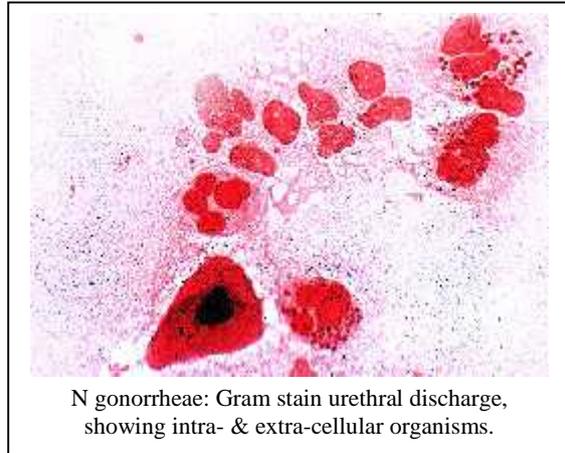
Non-capsulated.

Motility

Non-motile.

Spore

Non-spore forming.



N gonorrhoeae: Gram stain urethral discharge, showing intra- & extra-cellular organisms.

STAINING

Gram's staining

Gonococci are Gram-negative, appear pink colored due to counter-staining with safranin.

CULTURE

Media

- (1) Blood agar
- (2) Chocolate agar
- (3) Selective media:
 - (a) Mueller-Hinton medium.
 - (b) Modified Thayer-martin medium

Colonies

Convex, elevated, glistening & mucoid colonies (1-5 mm in diameter);

- (1) In selective subculture, gonococci produce small colonies containing piliated organisms, which are:
 - (a) Type 1 (P+)
 - (b) Type 2 (P++)
- (2) In nonselective subculture, gonococci produce larger colonies containing non-piliated organisms, which are:
 - (a) Type 3 (P----)
 - (b) Type 4 (P----)

Growth characteristics

(1) O₂ requirement

Aerobic or facultative anaerobic.

(2) Energy source

Ferment carbohydrates (only glucose), produce acid but no gas.

(3) Temperature

37°C.

(4) Growth promoted by

5-10% CO₂ (candle jar).

(5) Growth inhibited by

Fatty acids or salts, drying, sunlight, moist heat, & disinfectants.

(6) Growth lysed by

Autolytic enzymes that results in rapid swelling & lysis. This is prevented by destroying autolytic enzymes by heating at 65°C for 30 min, or by addition of formalin.

(4) Induces antibodies with acts as opsonins, (but gonococci goes on changing the nature PII, so this is not valuable for vaccine).

Rmp (protein III)

Present in cell memb., it is a reduction-modifiable protein (Rmp).

Function

Associates with Por in formation of pores in cell surface.

ANTIGENS

Pili (fimbriae)

Hair-like appendages that extend from gonococcal surface.

Function

- (1) Favors adherence to mucosal cells.
- (2) Inhibits phagocytosis (b/c organism is so intimately attached to host cells).
- (3) Attach to sperm.

Note: Removal of pili from virulent cell by treatment with trypsin results in their phagocytosis & destruction.

Lipopolysaccharide

Present in cell memb.

Function

- (1) Endotoxic to ciliated fallopian tube.
- (2) confer resistance to cell mediated lysis.

Other proteins

- (1) Lip (H8) → Surface-exposed protein.
- (2) Fbp (iron binding protein → Expressed when available iron supply is limited).

Por (protein I)

Extends thru gonococcal cell memb.

Function

Form pores in cell memb. thru which nutrients enter the cytoplasm.

Types

(1) P 'IA'

- (1) Associated with serotypes 1,2 & 3.
- (2) Strains possessing it are resistant to killing by normal human serum.

(2) (b) P 'IB'

Associated with serotype 4.

ENZYMES

IgA1 protease

It splits & inactivates secretory IgA1, thereby helping gonococci to attach to memb., of genital tract.

TOXINS

Endotoxin

- (1) It is the lipid A portion of gonococcal lipopolysaccharide.
- (2) It causes fever, shock, etc.

Opa (protein II)

One portion of protein II is in gonococcal outer memb., & rest is exposed on surface. A gonococcal strain can express no, one, two, or occasionally three types of Opa.

Functions

- (1) Adheres gonococci within colonies.
- (2) Attaches gonococci to host cells.
- (3) Responsible for opaque colonies.

HABITAT & TRANSMISSION

Habitat

Human genital tract.

Transmission

Via sexual contact.

Instillation of tetracycline, erythromycin or silver nitrate into conjunctival sac of newborn.

PATHOGENESIS & CLINICAL FINDINGS

Gonorrhoea

Pathogenesis

- (1) Only piliated organisms from small colonies appear to be virulent.
- (2) Gonococci attack mucosa of genitourinary tract, eye, rectum, & throat → Acute suppuration leading to tissue invasion → Chronic inflammation & fibrosis.

Clinical findings

(1) In male

- (a) Urethritis, with yellow, creamy pus & painful micturition & increased frequency.
- (b) Epididymitis.
- (c) Prostatitis.
- (d) Fibrosis & urethral strictures.

(2) In female

Primary infection is in endocervix that extends to cause:

- (a) Urethritis, with mucopurulent discharge & dysuria.
- (b) Vaginitis.
- (c) Salpingitis, fibrosis & obliteration of tubes.
- (d) Oophoritis.
- (e) Peritonitis.

Gonococcal bacteremia

This leads to:

- (1) Skin lesions (hemorrhagic papules & pustules) on hands, forearms, feet & legs.
- (2) Tenosynovitis.
- (3) Suppurative arthritis (of knee, ankles & wrists).
- (4) Gonococcal endocarditis (uncommon but severe).
- (5) Gonococcal meningitis.
- (6) Gonococcal eye-infections.

Gonococcal ophthalmia neonatorum

It is an eye infection of newborn, acquired during passage thru infected birth canal. Initial conjunctivitis rapidly progresses &, if untreated, results in blindness.

Prevention

DIAGNOSTIC LABORATORY TESTS

Specimens

Pus & secretions from urethra, cervix, rectum, conjunctiva, throat, or synovial fluid. Blood is taken in bacteremia.

Microscopy

Gram-stained smear of urethral or endocervical exudate seen under microscope → Gram-negative diplococci within pus cells.

Culture

Specimens are cultured on blood agar, chocolate agar & on selective media, ie Mueller-Hinton medium & modified Thayer- Martin medium, in an atmosphere containing 5-10% CO₂ (Candle jar) & at 37°C. To avoid overgrowth by contamination, antimicrobial drugs (eg vancomycin, amphotericin B & trimethoprim) are added → Colonies grow in 48 hrs.

Oxidase test

All Neisseria, including gonococci, are able to oxidize dimethylparaphenylene & tetramethylparaphenylene diamine, due to the presence of oxidase enzyme (Cytochrome C). Part of a suspected bacterial colony is smeared on a filter paper soaked with either di-or tetramethylparaphenylene diamine → Gonococcal (Oxidase Positive) colonies, turn dark purple, within 10-15 seconds.

Biochemical reactions

- (1) Glucose fermentation → Positive.
- (2) Maltose fermentation → Negative.

Serologic tests

Serum & genital fluid of infected individual contain IgG & IgA antibodies against gonococcal pili, outer memb. proteins & lipopolysaccharide, which can be detected by immunoblotting, radioimmunoassay & enzyme linked immunosorbent assay test.

IMMUNITY

Immunity to reinfection does not develop due to antigenic heterogeneity.

TREATMENT

- (1) Penicillin G (4.8 million units IM) + Probenicid (1 g orally).
- (2) Amoxicillin (3g) or Ampicillin (3.5g) + Probenicid (1 g). Both orally.
- (3) Ceftriaxone 250 mg IM.

PREVENTION & CONTROL

- (1) No specific immunization with toxoid or vaccine.
- (2) Use of condoms, & avoiding multiple sexual partners.
- (3) Prompt treatment of symptomatic patients & their contacts.
- (4) Gonococcal conjunctivitis in newborn is prevented by use of erythromycin ointment, tetracycline ointment or silver nitrate solution.

Chapter 13

Neisseria Meningitidis (Meningococci)

MORPHOLOGY

Shape

Individual organism is kidney-shaped.

Arrangement

In pairs (diplococci), with their concave/flat sides adjacent to each other.

Capsule

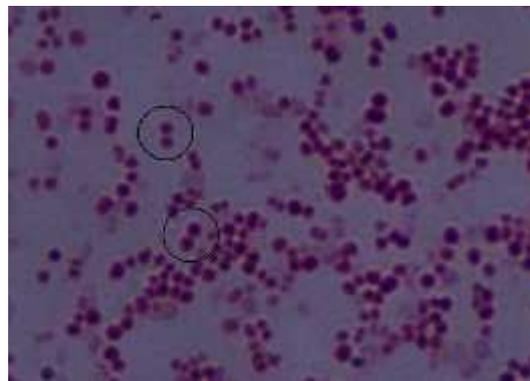
Capsulated.

Motility

Non-motile.

Spore

Non-spore forming.



N meningitidis: Gram stain appearance.

STAINING

Gram's staining

Meningococci are Gram-negative, appear pink colored due to counter-staining with safranin.

CULTURE

Media

- (1) Blood agar.
- (2) Chocolate agar.
- (3) Selective media:
 - (a) Mueller-Hinton medium.
 - (b) Modified Thayer-Martin medium.

Colonies

Convex, elevated, glistening & mucoid colonies (1-5 mm in diameter).

Growth characteristics

(1) O₂ requirements

Aerobic or facultative anaerobic.

(2) Energy source

Ferments carbohydrate (glucose & maltose), produce acid, but no gas.

(3) Temperature

37°C.

(4) Growth promoted by

5-10% CO₂ (Candle jar).

(5) Growth inhibited by

Fatty acids or salts, drying, sunlight, moist heat, & disinfectants.

(6) Growth lysed by

Autolytic enzymes that results in rapid swelling & lysis. This is prevented by destroying autolytic enzymes by heating at 65°C for 30 min. or by addition of formalin.

ANTIGENS**Capsular polysaccharides**

- (1) It is antigenically distinct & divides meningococci into "13 serogroups". Serogroups A, B, C, X, Y & W-135 are associated with human disease.
- (2) It enhances virulence by its antiphagocytic action.
- (3) It is the antigen used in vaccine.

Outer membrane proteins

- (1) Divided into 5 classes.
- (2) Each "Serogroup" of meningococcus is further subdivided into "Serotypes" on the basis of outer membrane proteins.
- (3) Class 1, 2 & 3 proteins are analogous to Por proteins of gonococci.
- (4) Class 5 protein is analogous to opa protein of gonococci.

Meningococcal lipopolysaccharide

Responsible for toxic effects of meningococci.

Pili

Help in attachment of meningococci to epithelial cells.

ENZYMES**IgA1 protease**

It splits & inactivates secretory IgA1, thereby helping meningococci to attach to memb. of upper respiratory tract.

TOXINS**Endotoxin**

- (1) It is the lipid A portion of meningococcal lipopolysaccharide.
- (2) It causes fever & shock, etc.

HABITAT & TRANSMISSION**Habitat**

Upper respiratory tract.

Transmission

Via respiratory droplets.

PATHOGENESIS & CLINICAL FINDINGS**Fulminant meningococemia**

Meningococci attach to nasopharyngeal epithelial cells with pili → Reach blood stream → Bacteremia, that may result in symptoms resembling upper respiratory tract infection, or fulminant meningococemia.

Clinical findings

- (1) High fever.
- (2) Hemorrhagic rash.
- (3) Disseminated intravascular coagulation (DIC).
- (4) Circulatory collapse.
- (5) Waterhouse-Friderichsen syndrome (massive hemorrhages in the adrenals).

Meningococcal meningitis

Occur as a complication of meningococemia.

Clinical findings

- (1) Abrupt onset.
- (2) Intense headache.
- (3) Vomiting.
- (4) Stiff neck.
- (5) Coma (within few hrs).

DIAGNOSTIC LABORATORY TESTS**Specimens**

- (1) Blood & spinal fluid for smear & culture.
- (2) Nasopharyngeal swab for carrier state.

Microscopy

Gram-stained smear of specimen seen under microscope → Gram- negative diplococci within polymorphs or extracellularly.

DIFFERENCE BETWEEN	
MENINGOCOCCI	GONOCOCCI
1) Found in upper respiratory tract & cause meningitis.	1) Found in genital tract & cause infection there.
2) Have polysaccharide capsule.	2) Do not have polysaccharide capsule.
3) Rarely have plasmids.	3) Have plasmids.
4) Ferment both glucose & maltose.	4) Ferment only glucose.
5) Do not produce beta-lactamase.	5) Some strains produce beta-lactamase.
6) Vaccine is available.	6) Vaccine is not available.

Culture

Specimens are cultured on blood agar, chocolate agar & on selective media, ie Mueller-Hinton medium & modified Thayer- Martin medium, in an atmosphere containing 5-10% CO₂ (candle jar) & at 37°C. To avoid overgrowth by contamination antimicrobials (eg vancomycin, amphotericin B & colistin) are added → Colonies grow in 48 hours.

Oxidase test

Part of a suspected bacterial colony is smeared on a filter paper soaked with either di-or tetramethyl paraphenylene diamine → Meningococcal (oxidase positive) colonies, turn dark purple, within 10-15 seconds.

Biochemical reactions

- (1) Glucose fermentation → Positive.
- (2) Maltose fermentation → Positive.

Serological tests

Antibodies to capsular polysaccharides can be measured by latex agglutination or hemagglutination tests.

Examination of CSF in meningitis

(1) Naked eye examination

CSF is turbid, cloudy or purulent.

(2) Microscopic examination

- (a) Gram-stained smear seen under microscope → G-ve meningococci.
- (b) Polymorph count is raised upto 90,000/mm³.

(3) Chemical examination

- (a) Protein level → Raised.

- (b) Sugar content → Reduced.

IMMUNITY

Group-specific, type-specific, or both types of humoral immunity (complement dependent bactericidal antibodies) develop after subclinical infections. Immunizing antigens are capsular polysaccharides.

TREATMENT

- (1) Penicillin G
- (2) Cefotaxime.
- (3) Chloramphenicol.

PREVENTION & CONTROL

- (1) Meningococcal vaccine that contains capsular polysaccharides of groups A, C, Y & W-135.
- (2) Chemoprophylaxis with rifampin in household & other close contacts.

Chapter 14

Escherichia Coli

MORPHOLOGY

Shape

Individual organism is rod shaped (bacilli).

Arrangement

Rods may form chains.

Capsule

Present.

Motility

Motile with flagella.

Spore

Non-spore forming.

STAINING

Gram's staining

E coli are Gram-negative, appear pink colored due to counterstaining with safranin.

CULTURE

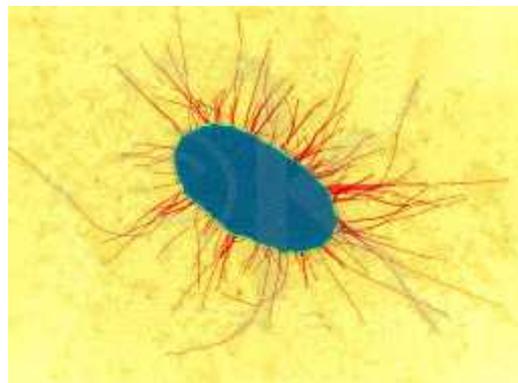
Media

(1) Differential media

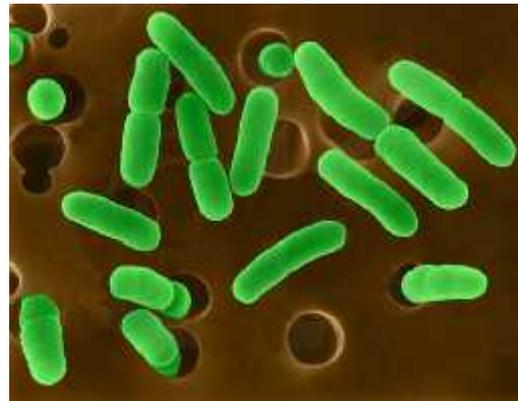
- MacConKey's medium.
- Eosin-methylene blue (EMB) medium.
- Deoxycholate medium.

(2) Media for biochemical reaction

- Triple sugar iron (TSI) agar.
- Simmon citrate medium.



E coli: Electron micrograph showing surface appendages (pili, sex pilus, & flagella).



E coli: Electron micrograph showing a few cells in division.

- Christensen's urea medium.

Colonies

- Circular, convex, & smooth with distinct edges.
- Pink colonies on MacConKey's medium (lactose fermenter).

Growth characteristics

- (1) **O₂ requirements**
Facultative anaerobes.
- (2) **Energy source**
Ferment lactose & glucose.
- (3) **Temperature**
37°C.

ANTIGENS**O (somatic) antigen**

Occur as the most external part of cell wall lipopolysaccharide & consist of repeating polysaccharide units. E coli possess more than 164 different O antigens. They are resistant to heat & alcohol.

Functions

- Cause production of IgM antibodies.
- May be associated with specific human diseases.

K (capsular) antigen

Exist as envelope polysaccharides (or proteins) & cover the O antigens when present. It is heat labile.

Functions

- Being cover the O antigens, it inhibits agglutination by specific O antiserum.
- Associated with virulence, eg K1 of E coli → Neonatal meningitis.
- Cause attachment of E coli to epithelial cells.

H (flagellar) antigen

Present in flagella as proteins. Occur in two phases, phase 1 & phase 2. Organism may change from one phase to another, called phase variation. It is heat labile.

Functions

- Cause production of IgG anti-H antibodies.
- Interfere with agglutination by anti-O antibodies.

Note: More than 164 somatic O antigens, more than 100 capsular K antigens, & more than 50 flagellar H antigens have been identified.

BACTERIOCINS

These are virus-like bactericidal substances produced by certain strains of bacteria against some other strains of same or closely related species. Their production is controlled by plasmids.

Examples

- Colicins → Produced by E coli.
- Marcescins → Produced by serratia.
- Pyocins → Produced by pseudomonas.

TOXINS**Endotoxin**

- It is the lipid A portion of lipopolysaccharides of outer membrane.
- It causes fever, hypotension, shock, etc.

Heat-labile exotoxin (LT)**Produced by**

Enterotoxigenic E coli

Mechanism of action

It consists of two subunits A & B → Subunit B attaches to GM1 ganglioside at brush border of epithelial cells of small intestine → Facilitates entry of subunit A into cell → Subunit A activates adenylate cyclase → Inc. cAMP → Hypersecretion of chlorides & water & inhibition of sodium reabsorption → Diarrhea.

Other functions

LT stimulates production of neutralizing antibodies in serum (& perhaps on gut surface) of persons with enterotoxigenic E coli infection. These persons are less prone to develop diarrhea on reexposure to enterotoxigenic E coli.

Heat-stable enterotoxin (STa)**Produced by**

Enterotoxigenic E coli.

Function

Activates guanylate cyclase in enteric epithelial cells → Stimulates fluid secretion by inhibiting NaCl reabsorption.

Heat-stable enterotoxin (STb)**Produced by**

Enterotoxigenic E coli.

Functions

Stimulates cyclic-nucleotide independent secretion (perhaps enhances net bicarbonate ion secretion).

Colonization factors (fimbriae)

Produced by

- (1) Enterotoxigenic E coli.
- (2) Enterohemorrhagic E coli.
- (3) Nephropathogenic E coli (Produces a special type of fimbriae, "P fimbria", so called b/c it binds to P blood group antigens).

Functions

Facilitate attachment of E coli to epithelium (intestinal or urinary tract epithelium).

Verocytotoxin-I (shiga-like toxin - I)

Produced by

Enterohemorrhagic E coli.

Mechanism of action

It consists of two sub-units A & B → Subunit B binds to a glycolipid in microvillus membrane → Facilitates entry of subunit A into cell → Subunit A inactivates 60S ribosomal subunit → Protein synthesis is stopped & sloughing off of dead cells occur → Bloody diarrhea.

Other functions

Produces hemolytics uremic syndrome by a similar mechanism.

Why so-called?

- (1) Verocyto-because, it is toxic for Vero cells, a line of African green monkey cells.
- (2) Shigalike - because, its many properties are similar to shiga toxin.

Verocytotoxin-II (shiga-like toxin - II)

It is biologically similar to verocytotoxin-I but they are antigenically distinct.

EIEC toxin

Produced by

Enteroinvasive E coli.

Functions

Similar to verocytotoxins, but it is produced in very small amounts.

Adhesin factor

Produced by

Enteropathogenic E coli.

Functions

It causes tight adherence of organism to enterocytes of small bowel → Destroy the normal microvillar border, resulting in disruption of epithelial cell memb. → Diarrhea.

HABITAT & TRANSMISSION

Habitat

E coli is a member of normal intestinal flora.

Transmission

- (1) Via fecal-oral route.
- (2) Ascends from urethra to cause UTI.
- (3) Acquired during birth in neonatal meningitis.

PATHOGENESIS & CLINICAL FINDINGS

Urinary tract infection (UTI)

E coli is the most common cause of UTI, responsible for about 90% of UTI in young females, in persons with urinary tract obstruction & in persons requiring urinary catheters.

Causative E coli

Nephropathogenic E coli, esp. with O antigen types 4, 7, & 75

Virulence factors

- (1) P-fimbriae
- (2) K antigen
- (3) Hemolysin

Clinical findings

- (1) Urinary frequency
- (2) Dysuria
- (3) Hematuria
- (4) Pyuria
- (5) Flank pain to upper tract infection.
- (6) Bacteremia may occur, with clinical signs of sepsis.

Traveler's diarrhea

Causative E coli

(1) Enterotoxigenic E coli

Its virulence factors are:

- (a) Heat-labile exotoxin
- (b) Heat-stable enterotoxins, STa & STb.
- (c) Colonization factors

(2) Enterohemorrhagic *E. coli*.

Its virulence factors are:

- (a) Verocytotoxins, I & II
- (b) Colonization factors

(3) Enteroinvasive *E. coli*

Its virulence factors are:

- (a) Ability to invade enteric epithelial cells
- (b) EIEC toxins.

(4) Enteropathogenic *E. coli*

Its virulence factor is:

Adhesin factor for epithelial cells

(5) Enteroadherent *E. coli*

Its virulence factor is the ability to adhere to intestinal mucosa.

Clinical findings**(1) Simple diarrhea (traveler's diarrhea)**

Caused by *E. coli* other than enterohemorrhagic strains. Gut is distended with fluid & is hypermotile → Diarrhea lasting for several days.

(2) Bloody diarrhea (hemolytic colitis)

Caused by enterohemorrhagic *E. coli*. Intestinal epithelial cells are destroyed & there is hypermotility → Copious bloody diarrhea, with severe abdominal cramps.

Why *E. coli* cause diseases inspite of being a member of normal flora?

Strains of *E. coli* capable of causing diseases possess one or more virulence factors that are not found in *E. coli* strains comprising normal flora. Such virulence factors include:

- 1) Capacity to adhere to tissue cells.
- 2) Ability to invade & grow intracellularly in enteric epithelial cells.
- 3) Secretion of toxins.
- 4) Possession of antiphagocytic capsule.
- 5) Ability to obtain iron from transferrin or lactoferrin by synthesis of iron-binding siderophores.

Sepsis

Sepsis occurs under two conditions:

- (1) When normal host defenses are inadequate, *E. coli* reach bloodstream & cause sepsis.
- (2) Secondary to UTI

Note: Newborns are highly susceptible to *E. coli* sepsis because they lack IgM antibodies.

Meningitis

E. coli having K1 antigen causes neonatal meningitis.

Hemolytic uremic syndrome

Caused by enterohemorrhagic *E. coli*, & characterized by microangiopathic hemolytic anemia, thrombocytopenia, & acute renal failure.

Other infections

- (a) Cholecystitis
- (b) Peritonitis
- (c) Wound infections

DIAGNOSTIC LABORATORY TESTS**Specimens**

Feces, urine, pus, blood, spinal fluid.

Microscopy

Gram-stained smear is seen under microscope → Gram-negative (pink colored) rods.

Culture**(1) MacConKey's medium**

Pink colonies (lactose fermenters)

(2) Eosin-methylene blue medium

Colonies are small & flat with definite metallic green sheen.

Biochemical reactions**(1) Triple sugar iron medium**

- (a) Acid on slant (yellow)
- (b) Acid & gas in butt (yellow with bubbles).

(2) Simmon citrate medium

Citrate utilization is negative color remains green.

(3) Christensen's urea medium

Urea is not hydrolyzed, so color remains pink.

(4) Voges-Proskauer reaction

Some organisms produced "Acetyl methyl carbinol" as a fermentation byproduct in glucose broth. Such organisms are called VP-positive. *E. coli* are VP-negative.

(5) Methyl-red test

If the organisms inoculated in glucose broth, produce so much acidity that pH of medium drops below 4.5 → Then on adding methyl-red indicator, the color of medium will

immediately turn red. Such organisms are called MR-Positive. E coli are MR- Positive.

(6) Indole production

Positive.

(7) Others

- (a) Lysine decarboxylase → Positive.
- (b) Mannitol fermentation test → Positive.
- (c) MUG test (detection of β -glucuronidase using substrate 4 methylumbelliferyl- β -glucuronide → Positive.

IMMUNITY

Specific antibodies to many virulence factors develop in systemic infection, but their role in protection against reinfection is uncertain. However, it appears that persons with antibodies to heat-labile exotoxin (in the serum & on gut surface) are less prone to develop diarrhea on reexposure to enterotoxigenic E coli.

TREATMENT

- (1) Sulfonamides.
- (2) Ampicillin.
- (3) Cephalosporins.
- (4) Chloramphenicol.
- (5) Tetracyclines.
- (6) Aminoglycosides.

PREVENTION & CONTROL

- (1) No specific immunization with toxoids or vaccines.
- (2) UTI is prevented by judicious use & prompt withdrawal of catheters & by prophylactic use of nitrofurantoin.
- (3) Sepsis is prevented by prompt removal or switching the site of IV lines.
- (4) Traveler's diarrhea is prevented by use of properly cooked food & boiled water & by prophylactic use of doxycycline.

Chapter 15

Klebsiella

MORPHOLOGY

Shape

Individual organism is rod shaped (bacilli).

Arrangement

Rods may form chains.

Capsule

Encapsulated. It is large & regular.

Motility

Non-motile.

Spore

Non-spore forming.



Klebsiella pneumoniae: Electron micrograph.

(c) Christensen's urea medium.

STAINING

Gram's staining

Klebsiella species are Gram-negative, appear pink colored due to counter-staining with safranin.

CULTURE

Media

(1) Differential media

- MacConkey's medium.
- Eosin-methylene blue (EMB) medium.
- Deoxycholate medium.

(2) Media for biochemical reaction

- Triple sugar iron (TSI) medium.
- Simmon citrate medium.

Colonies

- Circular, convex, mucoid colonies with distinct edges. Colonies may coalesce.
- Pink colonies on MacConkey's medium (lactose fermenter).

Growth characteristics

(1) O₂ requirements

Facultative anaerobes.

(2) Energy source

Ferment lactose, produce acid (yellow) & gas (bubbles).

(3) Temperature

37°C.

ANTIGENS

Same as *E. coli*, i.e.:

- (1) O (Somatic) antigen.
- (2) K (Capsular) antigen.
- (3) H (Flagellar) antigen.

ENZYMES

Urease

K pneumoniae produce urease that splits urea & liberates ammonia → This makes urine alkaline → Promote UTI.

TOXINS

Endotoxin

- (1) It is the complex lipopolysaccharide derived from bacterial cell wall.
- (2) It causes fever, leukopenia, hypoglycemia, hypotension and shock.

Aerobactin

- (1) Produced by K. pneumoniae.
- (2) It is a siderophore that can obtain iron from transferrin, & so, enhances virulence by making organism to grow in host tissues.

HABITAT & TRANSMISSION

Habitat

Present in respiratory tract and feces of about 5% normal individuals.

Transmission

- (1) Via respiratory droplets.
- (2) By ascending spread of fecal flora to urinary tract.

PATHOGENESIS & CLINICAL FINDINGS

K pneumoniae

It causes:

- (1) Extensive hemorrhagic necrotizing consolidation of lung.
- (2) UTI
- (3) Bacteremia with focal lesions in debilitated patients.
- (4) Hospital acquired (nosocomial) infections.

K oxytoca

Causes hospital acquired infections.

K ozaenae

Causes "ozena" (ie, a fetid, progressive atrophy of nasal mucosa).

K rhinoscleromatis

Causes "rhinoscleroma" (ie, a destructive granuloma of nose and pharynx).

DIAGNOSTIC LABORATORY TESTS

Specimens

Urine, pus, blood, spinal fluid, sputum.

Microscopy

Gram-stained smear seen under microscope → Gram-negative, capsulated bacilli.

Culture

MacConkey's medium → Pink, mucoid colonies (lactose fermenters)

Biochemical reactions

(1) Triple sugar iron medium

- (a) Acid on slant (yellow)
- (b) (ii) Acid & gas in butt (yellow with bubbles)

(2) Simmon citrate medium

Citrate is hydrolyzed (color changes from Green → Blue)

(3) Christensen's urea medium

K Pneumoniae produces urease → It hydrolyzes urea to NH₃ & CO₂ → Color changes from light pink to dark pink (or red).

- (4) Voges - Proskauer reaction → Positive.
- (5) Methyl red test → Negative.
- (6) Lysine decarboxylase test → Positive.

String test

When *Klebsiella* colonies are touched with a wire-loop, and taken up, a pink-colored string is produced.

Capsule swelling test

When *Klebsiella* colonies are mixed with specific antisera → Capsule swells.

IMMUNITY

Specific antibodies develop in systemic infections, but their role in protection against reinfection is uncertain.

TREATMENT

- (1) Sulfonamides.
- (2) Ampicillin.
- (3) Cephalosporins.
- (4) Chloramphenicol.
- (5) Tetracyclines.
- (6) Aminoglycosides.

PREVENTION & CONTROL

- (1) No specific immunization with toxoids or vaccines.
- (2) Urinary and intravenous catheters should be removed promptly.

Chapter 16

Proteus

MORPHOLOGY

Shape

Individual organism is rod-shaped (bacilli).

Arrangement

Rods may form chains.

Capsule

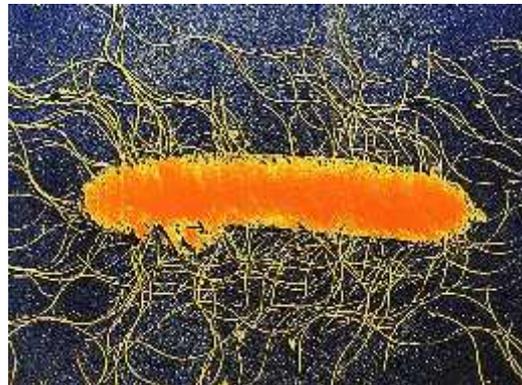
Non-capsulated.

Motility

Motile, by means of peritrichous flagella, which results in "swarming" on solid media.

Spore

Non-spore forming.



Proteus mirabilis: Electron micrograph showing peritrichous flagellation.

STAINING

Gram's staining

Proteus species are Gram-negative, appear pink colored due to counterstaining with safranin.

CULTURE

Media

- (1) Nutrient agar.
- (2) Blood agar.

(3) Differential media

- (a) MacConkey's medium.
- (b) Eosin-methylene blue (EMB) medium.
- (c) Deoxycholate medium.

(4) Media for biochemical reactions

- (a) Triple sugar iron (TSI) agar.
- (b) Simmon citrate medium.
- (c) Christensen's urea medium.

Colonies

- (1) On nutrient agar & blood agar, it produces "swarming growth"; growth occurs in successive periods which form successive waves, due to active movement of proteus by means of peritrichous flagella. They also produce "fishy smell" (or smell of ammonia).
- (2) On MacConkey's medium, it produces pale colonies (non-lactose fermenter).

Growth characteristics

(1) O₂ requirements

Facultative anaerobes or aerobes.

(2) Energy source

Ferment many sugars (but not lactose).

(3) Temperature

37°C.

ANTIGENS

Same as E coli, except K antigen; ie.,

- (1) O (Somatic antigen).
- (2) H (flagellar antigen).

ENZYMES**Urease**

Proteus species produce urease that splits urea & liberates ammonia → This makes urine alkaline → Promotes stone formation.

Phenylalanine deaminase

It deaminates phenylalanine to phenylpyruvic acid.

TOXINS**Endotoxin**

- (1) It is the lipid A portion of lipopolysaccharides of outer membrane.
- (2) It produces fever, hypotension, shock, etc.

HABITAT & TRANSMISSION**Habitat**

Proteus species are members of normal intestinal flora. Also found in sewage & soil. Cause opportunistic infections, when leave the intestinal tract.

Transmission

By ascending spread of fecal flora to urinary tract.

PATHOGENESIS & CLINICAL FINDINGS**All proteus species**

- (1) Urinary tract infections.

(2) Bacteremia → Pneumonia & focal lesions in debilitated pts or those receiving intravenous infusions.

(3) Proteus species produce urease that splits urea into ammonia → Urine becomes alkaline → Promotes stone formation.

Proteus mirabilis

Causes urinary tract infections.

Morganella morganii (P- morganii)

Causes summer diarrhea (esp, in children & travelers).

Providencia rettgeri (proteus rettgeri)

Causes nosocomial (hospital-acquired) infections.

Proteus vulgaris

Causes nosocomial infections.

DIAGNOSTIC LABORATORY TESTS**Specimens**

Urine, pus, blood, sputum.

Microscopy

Gram - stained smear seen under microscope → Gram - negative bacilli.

Culture**(1) Nutrient agar & blood agar**

Swarming growth & fishy smell.

(2) MacConkey's Medium

Pale colonies (non-lactose fermenters).

Biochemical reactions**(1) Triple sugar iron medium**

(a) Alkaline slant (red).

(b) M morganii & P rettgeri produces acid & gas in butt (yellow with bubbles).

(c) P vulgaris & P mirabilis produces H₂S in butt (black).

(2) Simmon citrate medium

Only P rettgeri gives positive reaction. Color changes from Green → Blue.

(3) Christensen's urea medium

Urease test positive (red color), within 24 hours.

(4) Voges-Proskauer reaction

Negative.

(5) Methyl red test

Positive.

IMMUNITY

Specific antibodies develop in systemic infections, but their role in protection against reinfection is uncertain.

TREATMENT

- (1) Sulfonamides.
- (2) Ampicillin.
- (3) Cephalosporins.
- (4) Chloramphenicol.
- (5) Tetracyclines.
- (6) Aminoglycosides.

PREVENTION & CONTROL

- (1) No specific immunization with toxoids or vaccines.
- (2) Prompt removal of urinary catheters.

Chapter 1 >

Salmonella

CLASSIFICATION

Kauffmann-White classification

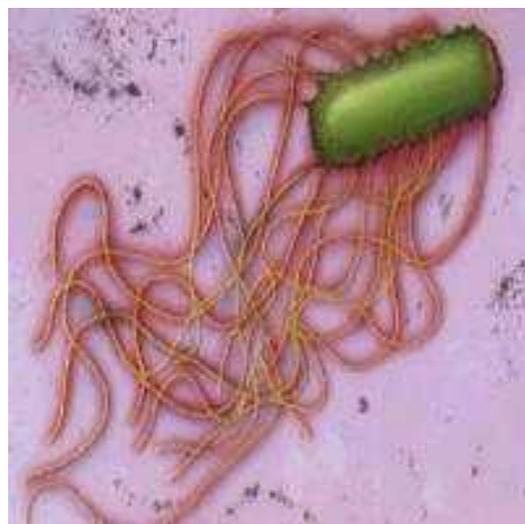
There are more than 2500 serotypes of salmonellae, including more than 1400 in DNA hybridization group I that can infect humans.

- (1) **Group A**
eg, S Paratyphi A
- (2) **Group B**
eg, S paratyphi B (S schottmuelleri), S typhimurium.
- (3) **Group C**
eg, S choleraesuis, S montevideo.
- (4) **Group C2**
eg, S manhattan
- (5) **Group D1**
eg, S typhi, S panama, S enteritidis
- (6) **Group D2**
eg, S strasbourg.
- (7) **Group E1**
eg, S anatum
- (8) **Group E2**
eg, S newbrunswick
- (9) **Group E3**
eg, S minneapolis
- (10) **Group H**
eg, S florida

MORPHOLOGY

Shape

Individual organism is rod-shaped (bacilli).



Salmonella: Electron micrograph showing peritrichous flagellation.

Arrangement

Rods may form chains.

Capsule

Present

Motility

Motile with peritrichous flagella.

Spore

Non-spore forming.

STAINING

Gram's staining

Salmonella species are gram - negative rods, appearing pink colored due to counter staining with safranin.

CULTURE

Media

(1) Enrichment media

- (a) Selenite F.
- (b) Tetrathionate broth.

(2) Selective media

- (a) Salmonella-Shigella (SS) agar.
- (b) Deoxycholate-citrate agar.
- (c) Hektoen enteric agar.

(3) Differential media

- (a) MacConkey's medium.
- (b) Eosin-methylene blue (EMB) medium.
- (c) Deoxycholate medium.
- (d) Bismuth sulfite medium.

(4) Media for biochemical reactions

- (a) Triple sugar iron (TSI) agar.
- (b) Simmon citrate medium.
- (c) Christensen's urea medium.

Colonies

(1) MacConkey's medium

Pale colonies (non-lactose fermenters); large, thick, moist & circular.

(2) Bismuth sulfite medium

Black colonies (due to H₂S production).

Growth characteristics

(1) O₂ requirements

Aerobes or facultative anaerobes.

(2) Energy source

Ferment glucose & mannose (but never lactose or sucrose).

(3) Temperature

37°C.

(4) Resistance

Salmonellae are resistant to:

- (a) Brilliant green.
- (b) Sodium tetrathionate.
- (c) Sodium deoxycholate.

(5) H₂S production

Usually most salmonellae produce H₂S from carbohydrates, except S typhi which produces very little H₂S.

ANTIGENS

Somatic (O) antigen

- (1) It is a part of outer membrane lipopolysaccharide.
- (2) More than 60 types
- (3) Its loss is associated with a change from smooth to rough colony form.

Flagellar (H) antigen

- (1) Occur in one or both of 2 phases.
- (2) Organism may lose it, & become non-motile.

Capsular (Vi) antigen

- (1) Associated with virulence (hence called Vi).
- (2) It may be lost partially or completely.

TOXINS

Endotoxin

- (1) It is the lipid A portion of outer membrane lipopolysaccharides.
- (2) It causes fever, hypertension, shock, etc.

HABITAT & TRANSMISSION

Habitat

Salmonella species (pathogenic) occur in intestinal tract of animals that constitute reservoir for human infection:

Poultry, pigs, rodents, cattle, pets (from turtles to parrots).

Transmission

Via fecal-oral route.

PATHOGENESIS & CLINICAL FINDINGS

Sources of infection

- (1) Water → Contaminated with feces.

- (2) Milk & dairy products (ice cream, cheese, custard → Contaminated with feces.
- (3) Shellfish → From contaminated water.
- (4) Eggs → From infected fowl.
- (5) Meats → From infected animals (Poultry).
- (6) Recreational drugs → eg, marijuana.
- (7) Animal dyes → eg, carmine.
- (8) Household pets → eg turtles, dogs, cats, etc.

Carriers

Carrier is a person who is symptom-free, but harbors salmonellae in gallbladder, biliary, intestinal or urinary tract.

Types

- (1) Healthy permanent carriers.
- (2) Convalescent carriers.

Enteric fever (typhoid fever)**Causative salmonella**

- (1) S typhi.
- (2) S paratyphi A.
- (3) S schottmulleri (paratyphi B).

Infective dose

$10^5 - 10^8$ salmonellae.

Host resistance

- (1) Gastric acidity.
- (2) Normal intestinal microbial flora.
- (3) Local intestinal immunity.

Portal of entry

Via oral route with contaminated food or water.

Incubation period

7-20 days (1-3 weeks).

Pathogenesis

Ingested salmonellae reach small intestine → Enter lymphatics → Enter blood → Infect many organs, eg liver, spleen, Kidneys, bone marrow, gall bladder, intestine, lung & heart → Organisms multiply in all tissues & produce lesions, eg;

- (1) Hyperplasia & necrosis of lymphoid tissue (eg, peyer's patches).
- (2) Hepatitis.
- (3) Focal necrosis of liver.
- (4) Inflammation of gallbladder, periosteum, lung & other organs.

Clinical findings

- (1) Onset → Insidious.
- (2) Fever, first gradual, then rises to high plateau.
- (3) Malaise, headache, myalgia.
- (4) Early constipation, later bloody diarrhea.

- (5) Hepatosplenomegaly.
- (6) Rose spots on skin of abdomen & chest.
- (7) Bradycardia.

Bacteremia with focal lesions**Causative salmonella**

S choleraesuis (usually), or any salmonella serotype.

Pathogenesis

Organism enters via oral route → Early invasion of bloodstream → Bacteremia, with possible focal lesions in lungs, bones & meninges.

Clinical findings

- (1) Onset → Abrupt.
- (2) Fever → Rapid rise, then spiking.
- (3) GIT symptoms → Absent.

Enterocolitis**Causative salmonella**

S typhimurium, S enteritidis.

Incubation period

8-48 hours

Pathogenesis

Organism enters via oral route → Remain Localized in gut → Produce enterotoxin & cytotoxin → Cause enterocolitis (inflammatory lesions of small & large bowel).

Clinical findings

- (1) Onset → Abrupt.
- (2) Headache.
- (3) Nausea, vomiting, diarrhea.
- (4) Low-grade fever.

DIAGNOSTIC LABORATORY TESTS**Specimens**

- (1) Blood → Culture is positive in 1st & 2nd week in enteric fever, & during high fever in bacteremia.
- (2) Stool → Culture is positive;
 - (a) In 1st week in enterocolitis.
 - (b) In 2nd week on, in enteric fevers.
- (3) Urine → Culture is positive from second week.
- (4) Bone marrow → Culture is positive from second week.

(5) Duodenal drainage → Culture is positive in biliary tract carriers.

Microscopy

Gram stained smear seen under microscope → Gram-negative rods.

Culture

- (1) MacConKey's medium → Pale colonies.
- (2) Bismuth sulfite medium → Black colonies.
- (3) Selective media → Selective growth of salmonella & shigella occur, among other enterobacteriaceae.
- (4) Enrichment media → Permit salmonella multiplication, but inhibits growth of normal intestinal bacteria.

Biochemical reactions

(1) Triple sugar iron medium

- (a) Alkaline slant (red).
- (b) Acid butt with no gas (yellow).
- (c) Later TSI turns black due to H₂S production.

(2) Simmon citrate medium

Citrate utilization → Positive (blue color).

(3) Voges - Proskauer reaction

Negative.

(4) Methyl red test

Positive.

(5) Indole production

Negative.

Serologic rests

(1) Rapid slide agglutination test

[Known antibody; Unknown antigen]

Known sera & unknown culture are mixed on a slide → Observed under microscopy → If clumping occurs → Test is positive (ie, salmonella present in culture).

(2) Tube dilution agglutination test (Widal test)

[Unknown antibody; Known antigen]

Serum agglutinating antibodies rise during 2nd & 3rd week of salmonella infection. Two serum specimens are taken at intervals of 7-10 days to see rise in antibody titer. Serial (2-fold) dilutions of unknown serum are tested against antigens from representative salmonellae.

Results

(a) High titers of antibodies to O antigen (1:160) → Active infection.

(b) High titers of antibodies to H antigen (1:160) → Past immunization or past infection.

(c) High titers of antibodies to Vi antigen → Carriers.

IMMUNITY

Infection with *S typhi*, *S paratyphi*, & *S schottmulleri* confers certain degree of immunity (circulating antibodies to O & Vi antigens & secretory IgA antibodies). However, reinfection may occur, but it is milder than first infection.

TREATMENT

- (1) Antimicrobial therapy of invasive salmonella infections is with ampicillin, trimethoprim-sulfamethoxazole, or a third-generation cephalosporin.
- (2) In severe diarrhea, replacement of fluids & electrolytes is essential.

PREVENTION & CONTROL

(1) Immunization with TAB vaccine.

Contents

Heat killed phenol preserved suspensions of *S typhi* (1000 millions/cc), *S paratyphi A* & *B* (750 millions/cc each).

Route of administration

Intramuscular.

Dosage

2 inoculations of 0.5 cc & 1 cc at interval of 1 week; booster of 0.5 cc, some months later.

Period of immunity

About one year.

- (2) Proper sewage disposal.
- (3) Chlorination of water supply.
- (4) Hand washing before food handling, & thorough cooking of animal foods.

Chapter 18

Shigellae

CLASSIFICATION

(1) Group A

Include *S dysenteriae*, having ten serotypes (1-10).

(a) Serotype 1 → *S shigae*

(b) Serotype 2 → *S schimitzii*

(c) Serotypes 3-10 → Sacch's group

(2) Group B

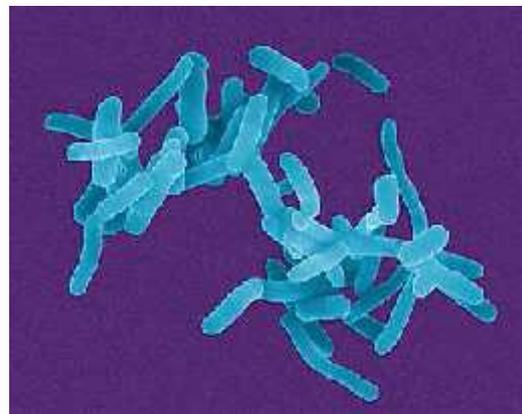
Include *S flexneri*, having six serotypes (1-6).

(3) Group C

Include *S boydii*, having fifteen serotypes (1-15).

(4) Group D

Include *S sonnei*, have only one serotype.



Shigella: Electron micrograph.

MORPHOLOGY

Shape

Individual organism is rod-shaped (bacilli); coccobacillary forms occur in young cultures.

Arrangement

Rods may form chains.

Capsule

Non-capsulated.

Motility

Non-motile.

Spore

Non-spore forming.

STAINING

Gram's staining

Shigellae are gram-negative organisms, appearing pink colored due to counterstaining with safranin.

CULTURE

Media

(1) Differential selective medium

- MacConkey's medium.
- Eosin-methylene blue (EMB) medium.
- Salmonella-Shigella agar
- Thiosulfate-citrate-bile agar.

(2) Media for biochemical reactions

- (a) Triple sugar iron (TSI) agar
- (b) Simmon citrate medium.
- (c) Christensen's urea medium

Colonies

- (1) Convex, circular, transparent colonies with intact edges.
- (2) MacConkey's medium → Pale colonies (non-lactose fermenters), except *S sonnei* which produces pink colonies after 2-3 days (late-lactose fermenters).

Growth characteristics

- (1) **O₂ requirements**
Aerobes or facultative anaerobes.
- (2) **Energy source**
Ferment glucose. *S sonnei* also ferments lactose.
- (3) **Temperature**
37°C.
- (4) **H₂S Production**
Negative.

ANTIGENS**O (somatic) antigens**

- (1) Are lipopolysaccharides.
- (2) More than 40 serotypes.

TOXINS**Endotoxin**

It is the lipopolysaccharide of outer membrane.

Functions

Contribute to irritation of bowel wall, beside its general effects, ie fever, shock etc.

Shigella dysenteriae exotoxin

S dysenteriae type 1 produces heat-labile exotoxin.

Functions

- (1) Acting as an enterotoxin → Causes bacillary dysentery & inhibits sugar & amino acid absorption in small intestine.
- (2) Acting as a neurotoxin → Causes meningismus & coma.

HABITAT & TRANSMISSION**Habitat**

Shigella occur in intestinal tracts of humans & other primates, where they produce bacillary dysentery.

Transmission

Via fecal-oral route.

PATHOGENESIS & CLINICAL FINDINGS**Bacillary dysentery****Infective dose**

10³ organisms.

Portal of entry

Organisms enter via oral route with contaminated food & water.

Incubation period

1-2 days.

Pathogenesis

- (1) *Shigella* produces enterotoxin (exotoxin) → Causes excess solute & fluid secretion → This is responsible for early non-bloody diarrhea.
- (2) *Shigella* invade mucosal epithelium → Produce micro-abscesses in walls of large intestine & terminal ileum → This leads to necrosis of mucosa, superficial ulceration, bleeding & formation of a pseudomembrane on ulcerated area → This is responsible for later dysentery with blood & pus in stool. (Later granulation tissue fills the ulcers & scar tissue forms).

Clinical findings

Sudden onset of:

- (1) Abdominal pain.
- (2) Fever.
- (3) First watery diarrhea due to exotoxin.
- (4) Later dysentery with mucus & blood due to invasion of mucosal epithelium.
- (5) Lower abdominal pain due to straining & tenesmus (rectal spasms).

Complications

- (1) Dehydration.
- (2) Acidosis.

(3) Death (if untreated).

Hemolytic - uremic syndrome

- (1) It follows blood stream carriage of exotoxin to the kidney.
- (2) Manifested by hemolytic anemia, thrombocytopenia & acute renal failure.

DIAGNOSTIC LABORATORY TESTS

Specimens

Fresh stool, mucus flecks, rectal swabs, serum (10 days apart), urine.

Microscopy

Gram's stained smear seen under microscope
→ Gram-negative rods.

Culture

- (1) Pale colonies on MacConkey's medium (non-lactose fermenters).
- (2) *S. sonnei* produce pink colonies on MacConkey's medium after 2-3 days (late-lactose fermenter).
- (3) Selective media → Selective growth of salmonella & shigella occur, among other enterobacteriaceae.
- (4) Enrichment media → Permit salmonella multiplication, but inhibits growth of normal intestinal bacteria.

Biochemical reactions

(1) Triple sugar iron medium

- (1) Alkaline slant (red)
- (2) Acid butt with no gas (yellow)

(2) Simmon citrate medium

No citrate utilization (color remain green)

(3) Christensen's urea medium

No urease production (color remain light pink)

(4) Voges-Proskauer reaction

Negative

(5) Methyl-red test

Positive

Serologic tests

(1) Slide agglutination test

Shigella culture mixed with specific shigella antisera → Clumping → Test positive.

(2) Serial determination of antibody titer

It shows rise in specific antibody titer.

DIFFERENCE BETWEEN

SHIGELLA	SALMONELLA
<ol style="list-style-type: none"> 1) Non-motile 2) H₂S not produced 3) Agglutination with shigella antisera 4) Causes bacillary dysentery 	<ol style="list-style-type: none"> 1) Motile 2) H₂S produced 3) Agglutination with salmonella antisera 4) Causes typhoid & paratyphoid fevers

IMMUNITY

Upon recovery from shigella infection, circulating type-specific antibodies to shigella develop, but they do not protect against reinfection. However, IgA antibodies in gut may play role in limiting reinfection.

TREATMENT

- (1) Specific antitoxin.
- (2) Ciprofloxacin.
- (3) Ampicillin.
- (4) Doxycycline.
- (5) Trimethoprim-Sulfamethoxazole.

PREVENTION & CONTROL

- (1) No specific immunization with toxoids or vaccines.
- (2) Sanitary control of water, food, & milk; proper sewage disposal; & fly control.
- (3) Isolation of patients & disinfection of excreta.
- (4) Detection of subclinical cases & carriers, particularly food handlers.
- (5) Antibiotic treatment of infected individuals.

Chapter 19

Vibrio Cholerae

MORPHOLOGY

Shape

Individual organism is comma-shaped, curved rod. Upon prolonged cultivation, vibrios become straight rods.

Arrangement

Rods may occur singly, or may form pairs.

Capsule

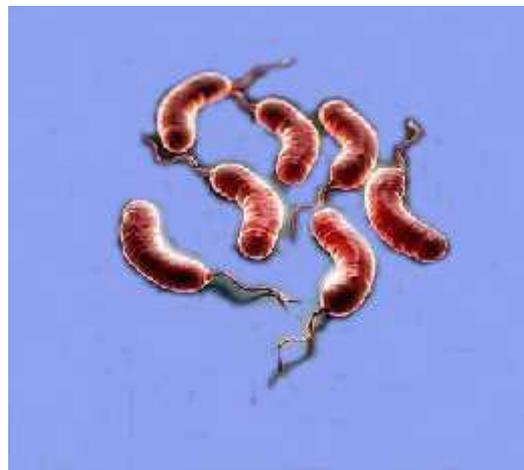
Non-capsulated.

Motility

Motile with polar flagellum.

Spore

Non-spore forming.



Vibrio cholerae: Electron micrograph.

STAINING

Gram's staining

Vibrio cholerae are Gram-negative, appear pink colored, due to counter-staining with safranin.

CULTURE

Media

- (1) Peptone agar
- (2) Blood agar
- (3) Thiosulfate-citrate-bile - sucrose (TCBS) agar.
- (4) Taurocholate - peptone broth

Colonies

- (1) Convex, smooth, round, opaque & granular colonies.
- (2) TCBS agar → Yellow colonies

Growth characteristics

- (1) **O₂ requirement**
Aerobes.
- (2) **Energy source**
Ferments sucrose & mannose.
- (3) **Temperature**
37°C.
- (4) **pH**
Grow at high pH (8.5 - 9.5).
- (5) **Growth inhibited by**
Acid & compound O/129.
- (6) **Resistance**
Vibrios are resistant to 6% NaCl.

ANTIGENS**Flagellar (H) antigen**

- (1) Heat-labile
- (2) Causes production of antibodies (but these are not involved in protection against reinfection).

'O' lipopolysaccharide antigen

Confers serologic specificity. There are 139 O antigen groups. V cholerae are divided, according to the nature of O antigens, into three groups:

(1) O1 group

Associated with classic cholera, epidemic disease. There are 3 serotypes & 2 biotypes:

Serotypes

- (a) Ogawa
- (b) Inaba
- (c) Hikojima

Biotypes

- (a) Classic
- (b) El Tor

(2) O139 group

- (a) V cholerae O139 is very similar to V cholerae O1 El Tor biotype.
- (b) Also causes classic cholera.
- (c) Has a polysaccharide capsule like other non-O1 V cholerae strains.

(3) Non-O1/non-O139 group

It includes organisms that either cause sporadic disease or are non-pathogens.

ENZYMES**Oxidase**

It differentiates vibrios from other enteric gram-negative rods grown on blood agar.

Neuraminidase

It converts other gangliosides into ganglioside GM1 → This results in increase in receptor sites to which V cholerae enterotoxin can bind.

Mucinase

It digests mucinous layer of gut wall, thus helping vibrios to adhere to & colonize the gut wall.

TOXINS**Vibrio cholera enterotoxin (cholera toxin)**

Heat-labile. Consists of subunits A & B. Subunit B binds to GM1 ganglioside on brush border of intestinal mucosa → Promotes entry of subunit A into cell → Activates adenylate cyclase → Inc. cAMP level → Hypersecretion of water & Cl⁻ & inhibition of Na⁺ absorption → Diarrhea.

HABITAT & TRANSMISSION**Habitat**

Occur in marine & water surface & human colon.

Transmission

Via fecal-oral route.

PATHOGENESIS & CLINICAL FINDINGS**Cholera****Infective dose**

10⁸ - 10¹⁰ organisms.

Portal of entry

Via oral route with contaminated food or water.

Incubation period

1-4 days.

Pathogenesis

V cholerae attach to microvilli of brush border of intestinal epithelium, being helped by mucinases → Liberate cholera enterotoxin (& probably endotoxin) → Diarrhea.

Clinical findings

Sudden onset of:

- (1) Nausea, vomiting.
- (2) Profuse diarrhea → Stools resemble "rice water", & contain mucus, epithelial cells & vibrios.
- (3) Abdominal cramps.

Complications

- (1) Dehydration.
- (2) Acidosis.

- (3) Shock & circulatory collapse.
- (4) Anuria.
- (5) Death (if untreated).

- (1) Fluid & electrolyte replacement.
- (2) Tetracyclines (orally).

DIAGNOSTIC LABORATORY TESTS***Specimens***

Mucus flecks from stool

Microscopy

- (1) Microscopic appearance of smears made from stool is not distinctive.
- (2) Dark-field or phase contrast microscopy → Motile vibrios.
- (3) Gram's stained smear made from fresh specimen, seen under microscope → Gram-negative curved rods.

Culture

Specimens are cultured on

- (1) Peptone agar (pH 9.0)
- (2) Blood agar (pH 9.0)
- (3) TCBS agar → Yellow colonies
- (4) Taurocholate - peptone broth (pH 8.0 - 9.0)
- (5) MacConkey's medium → Pink colonies after 2-3 days (late lactose fermenters).

Biochemical reactions***Triple sugar iron medium***

An acid slant (yellow) & an acid butt (yellow) without gas due to fermentation of sucrose.

Serologic tests***Slide agglutination tests***

Performed by using anti-O group 1 or group 139 antisera.

PREVENTION & CONTROL

- (1) Immunization with heat killed organisms has limited value.
- (2) Proper sewage disposal.
- (3) Chlorination of water.
- (4) Hand washing prior to food handling.

IMMUNITY

- (1) Gastric acid provides some protection against ingested vibrios.
- (2) Serum vibriocidal antibodies are associated with protection against colonization & disease.

TREATMENT

Chapter 20

Helicobacter Pylori

MORPHOLOGY

Shape

Individual organism is spiral-shaped rod.

Arrangement

Rods may occur singly, or may form pairs.

Capsule

Non-capsulated.

Motility

Actively motile with multiple flagella at one pole.

Spore

Non-spore forming.



Helicobacter pylori: Electron micrograph.

STAINING

Gram's staining

H pylori are Gram-negative, appear pink colored, due to counter-staining with safranin.

CULTURE

Media

- (1) Skirrow's medium with vancomycin, polymyxin B & trimethoprim, for primary isolation.
- (2) Chocolate medium.
- (3) Other selective media with antibiotics (eg, vancomycin, nalidixic acid, amphotericin).

Colonies

Colonies are translucent, & 1–2 mm in diameter.

Growth characteristics

(1) O₂ requirement

Microaerophilic.

(2) Energy source

Glucose is metabolized via the Entner Doudoroff pathway. Also H pylori is able to use molecular hydrogen as a respiratory substrate when grown in the laboratory.

(3) Temperature

37°C.

(4) pH

Grow at pH 6-7.

(5) Growth inhibited by

H pylori would be killed or not grow at the pH within the gastric lumen.

ANTIGENS

- (1) Flagellar (H) antigen.

- (2) 'O' lipopolysaccharide antigen.
- (3) Outer membrane proteins (OMP) eg, adhesions, porins, iron transporters.

ENZYMES**Urease**

- (1) It is a potent virulence factor for H pylori. Urease converts urea into ammonia & bicarbonate to counteract the low acidity of the stomach. The ammonia acts as an acceptor for the H⁺ to increase the local pH.
- (2) With high urease activity, H pylori can protect the bacterium from acid damage by buffering the cell & the environment.

Hydrogenase

It can be used to obtain energy by oxidizing molecular hydrogen (H₂) produced by intestinal bacteria.

Protease

Modifies the gastric mucus & further reduces the ability of acid to diffuse thru the mucus.

Other enzymes

- (1) Oxidase.
- (2) Catalase.

HABITAT & TRANSMISSION**Habitat**

Gastric mucosa of nearly half of world's population.

Transmission

Person-to-person transmission by either the oral-oral or fecal-oral route.

PATHOGENESIS & CLINICAL FINDINGS**Pathogenesis**

The exact mechanism is not well defined but probably involves both bacterial & host factors. The bacteria invade the epithelial cell surface to a limited degree. Toxins & lipopolysaccharide may damage the mucosal cells, & the ammonia produced by the urease activity may directly damage the cells also.

Clinical findings

- (1) H pylori produces duodenal & gastric ulcers;
 - (a) Acute infection may presents with epigastric pain, nausea & vomiting. Symptoms may last for less than 1 week or as long as 2 weeks.
 - (b) Chronic infection presents with milder symptoms (dyspepsia).
- (2) H pylori also may have a role in gastric carcinoma & lymphoma.

DIAGNOSTIC LABORATORY TESTS**Specimens**

- (1) Gastric biopsy specimens for histologic examination or minced in saline & used for culture.
- (2) Blood for determination of serum antibodies.

Staining

Giemsa or special silver stains can show the curved or spiraled organisms.

Culture

Skirrow's, chocolate & other selective media with antibiotics → Translucent colonies, 1–2 mm in diameter.

Serological tests

Detect serum antibodies specific for H pylori.

Note: Serum antibodies persist even if the H pylori infection is eradicated.

Special tests

- (1) Rapid tests to detect urease activity;
 - (a) Gastric biopsy material can be placed onto a urea-containing medium with a color indicator → If H pylori is present, the urease rapidly splits the urea (1–2 days) & the resulting shift in pH yields a color change in the medium.
 - (b) ¹³C- or ¹⁴C-labeled urea is ingested by the patient → If H pylori is present, the urease

activity generates labeled CO₂ that can be detected in the patient's exhaled breath.

- (2) Detection of H pylori antigen in stool specimens is used to confirm cure after treatment.

IMMUNITY

- (1) Patients infected with H pylori develop an IgM antibody response. Subsequently, IgG & IgA are produced, & these persist, both systemically & at the mucosa, in high titer in chronically infected persons.
- (2) Early antimicrobial treatment of H pylori infection blunts the antibody response; such patients suffer recurrent infection.

TREATMENT

- (1) Triple therapy with a proton pump inhibitor plus amoxicillin & clarithromycin or amoxicillin plus metronidazole, for one week.
- (2) Other option is metronidazole & either bismuth subsalicylate or bismuth subcitrate plus either amoxicillin or tetracycline for 14 days.

PREVENTION & CONTROL

Hygienic environment could help decrease the risk of H pylori infection.

Chapter 27

Pseudomonas Aeruginosa

MORPHOLOGY

Shape

Individual organism is rod-shaped (bacilli).

Arrangement

Rods may occur as single bacteria, in pairs, or in short chains.

Capsule

Present.

Motility

Motile.

Spore

Non-spore forming.



Pseudomonas aeruginosa: Electron micrograph.

STAINING

Gram's staining

Pseudomonas species are Gram-negative, appear pink colored due to counter staining with safranin.

CULTURE

Media

- (1) Nutrient Agar
- (2) Blood Agar
- (3) Differential Media
 - (a) MacConkey's medium.
 - (b) Eosin-methylene blue (EMB) medium.
 - (c) Deoxycholate medium.

Colonies

Colonies are smooth, round & mucoid.

- (1) On nutrient agar → Greenish colonies (due to production of pyoverdine) & sweet or grape-like odor.
- (2) On blood agar → Some strains produce hemolysis (beta type).
- (3) On MacConkey's medium → Pale colonies (non-lactose fermenters).

Growth characteristics

(1) O₂ requirement

Obligate aerobe.

(2) Energy source

Oxidation of sugars.

(3) Temperature

37-42 °C.

(4) Pigment production

Produce four types of pigments

- (a) Pyoverdine → Fluorescent green pigment.
- (b) Pyocyanin → Non-fluorescent blue pigment.
- (c) Pyorubin → Dark red pigment.

(d) Pyomelanin → Black pigment.

ANTIGENS

Pili (fimbriae)

Extend from cell surface.

Function

Promote attachment to host epithelial cells.

Polysaccharide capsule

- (1) It is antiphagocytic.
- (2) Acts as an adhesion.
- (3) Responsible for mucoid colonies in cultures from pts with cystic fibrosis.

ENZYMES

- (1) Oxidase.
- (2) Catalase.
- (3) Elastases.
- (4) Proteases.
- (5) Exoenzyme S.
- (6) Hemolysins;
 - (1) Heat-labile phospholipase C.
 - (2) Heat-stable glycolipid.

TOXINS

Endotoxin

It is the lipopolysaccharide. It is responsible for causing fever, shock, oliguria, leukocytosis & leukopenia, disseminated intravascular coagulation, & adult respiratory distress syndrome.

Exotoxin A

- (1) Causes tissue necrosis.
- (2) Block protein synthesis.

HABITAT & TRANSMISSION

Habitat

Occur widely in soil, water, plants & animals. Present in small numbers in normal intestinal flora & on skin of humans. Commonly present in moist environments in hospitals.

Transmission

Via water aerosols, aspiration & fecal contamination.

PATHOGENESIS & CLINICAL FINDINGS

Pathogenesis

- (1) *Pseudomonas aeruginosa* is pathogenic only when introduced into areas devoid of normal defenses, eg due to;
 - (a) Disruption of mucosa & skin, by direct tissue damage.
 - (b) Use of intravenous cannula, or urinary catheters.
 - (c) Presence of neutropenia, as in cancer chemotherapy.
- (2) Bacteria attach to & colonize mucosa or skin, invade locally or produce systemic disease.
- (3) Pili, enzymes & toxins promote the disease processes.

Clinical findings

Pseudomonas aeruginosa produces:

- (1) Meningitis.
- (2) Otitis externa (mild & malignant).
- (3) Eye infections.
- (4) Sepsis.
- (5) Necrotizing pneumonia.
- (6) UTI.
- (7) Wound infections (blue-green pus).
- (8) Ecthyma gangrenosum (hemorrhagic necrosis of skin).
- (9) Osteomyelitis.

DIAGNOSTIC LABORATORY TESTS

Specimens

Skin lesions, pus, urine, blood, CSF, sputum.

Microscopy

Gram-stained smear is seen under microscope
→ Gram-negative rods.

Culture

- (1) Nutrient agar → Greenish colonies with sweet or grape like odor.
- (2) Blood agar → Some strains produce beta hemolysis.
- (3) MacConkey's medium → Pale colonies (non-lactose fermenter).

Biochemical reactions**(1) Sugar fermentation test**

Only glucose is fermented with gas production.

(2) Citrate utilization test

Positive.

(3) Catalase test

Positive.

(4) Oxidase test

Positive.

PREVENTION & CONTROL

- (1) No specific immunization with toxoids or vaccines.
- (2) Disinfection of water-related equipments in hospitals.
- (3) Hand washing prior to food handling.
- (4) Prompt removal of urinary & intravenous catheters.

IMMUNITY

Antibodies against exotoxin A are found in some human sera, including those who have recovered from serious P aeruginosa infections, but their role in protection against reinfection is uncertain.

TREATMENT

- (1) Penicillins (ticarcillin or piperacillin) plus aminoglycoside (gentamicin, tobramycin, & amikacin).
- (2) Aztreonam.
- (3) Imipenem.
- (4) Quinolones, eg ciprofloxacin.
- (5) Cephalosporins, eg cefoperazone & ceftazidime.

Chapter 22

Chlamydiae

MORPHOLOGY

Shape

Individual organism appear as small, round to ovoid cell, which vary morphologically during replication cycle.

Replication cycle

"Elementary body", a small cell with an electron-dense nucleoid, enters host cell by endocytosis → A vacuole is formed around it → It then reorganized into "initial or reticulate body", a large cell which is devoid of an electron-dense nucleoid → Within vacuole, initial body grows in size & divides repeatedly by binary fission → Eventually entire vacuole becomes filled with small particles (elementary bodies) to form an "inclusion" in host-cell cytoplasm → Host cell ruptures & liberated elementary bodies infect new cells.

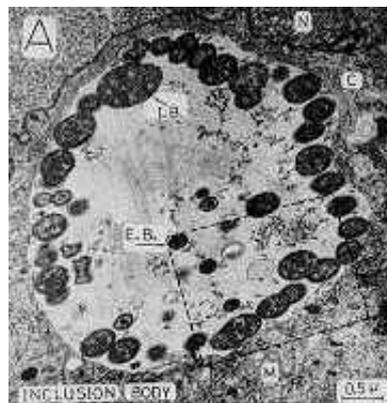
Notes

- (1) Replicating cycle takes 24-48 hours.
- (2) *Chlamydia trachomatis* form compact inclusion bodies containing glycogen.
- (3) *C. psittaci* produces diffuse inclusion bodies devoid of glycogen.

STAINING

Giemsa's staining

- (1) Elementary bodies stain purple, in contrast to blue of host cell cytoplasm.
- (2) Initial bodies stain blue.



C. trachomatis:

A. Electron micrograph showing inclusion bodies in cytoplasm (C) of infected cell. Part of nucleus (N) & mitochondria (M) can also be seen.

B. Enlarged view of inclusion body showing elementary bodies (EB) & initial bodies (IB).

(3) *C trachomatis* inclusion bodies stain dark purple.

Lugol's iodine staining

On staining with dilute Lugol's iodine solution, some of the inclusions of *C trachomatis* (but not *C pneumoniae* or *C psittaci*) appear brown because of the glycogen matrix that surrounds the particles.

Immunofluorescent staining

Chlamydiae stain brightly by immunofluorescence, with group-specific, species-specific, or immunotype-specific antibodies.

Gram's staining

Chlamydiae show gram-negative reaction, as their cell wall is similar to Gram-negative bacteria.

Macchiavello's staining

Elementary bodies stain red, in contrast to blue of host cell cytoplasm.

CULTURE

Culture

Chlamydiae are obligate intracellular bacteria; thus, can not be grown in laboratory on artificial media, but require living cells for growth. They are readily cultivated in "yolk sac of embryonated egg". Some also grow in cell cultures & in various animal tissues.

Growth characteristics

(1) Energy source

Cannot synthesize ATP nor oxidize NADP, so are dependent on host cell for energy production.

(2) Inactivated by

Heat, ether, phenol.

(3) Replication inhibited by

Tetracyclines, erythromycin, penicillins.

(4) Maintain infectivity at

-50 to -70°C for years.

ANTIGENS

Group-specific antigens

- (1) Heat-stable, lipopolysaccharides.
- (2) Shared by all chlamydiae.

(3) Antibodies to it can be detected by CF & immunofluorescence.

Species-specific antigens

- (1) Outer membrane proteins.
- (2) Are species-specific or immunotype-specific.
- (3) Best detected by immunofluorescence, esp. by monoclonal antibodies.
- (4) Fifteen immunotypes (serovars) of *C trachomatis* have been identified 2A, B, Ba, C-K, L1-L3.

HABITAT & TRANSMISSION

Habitat

- (1) *C psittaci* → Alimentary tract of birds, eg parrots.
- (2) *C trachomatis* → Human genital tract.
- (3) *C pneumoniae* → Respiratory tract.

Transmission

- (1) *C psittaci* → Via inhalation of dried bird feces.
- (2) *C trachomatis* → Via sexual contact or by passage thru birth canal.
- (3) *C pneumoniae* → Via respiratory droplets.

PATHOGENESIS & CLINICAL FINDINGS

Psittacosis

Causative chlamydia

C psittaci.

Pathogenesis

- (1) *C psittaci* enters thru respiratory tract → Causes a patchy inflammation of lungs with sharply demarcated consolidated areas, having mononuclear exudate.
- (2) Organisms may invade blood vessels → Causes enlargement & congestion of liver, spleen, heart & kidneys.

Clinical findings

Sudden onset of:

- (1) Malaise, anorexia.
- (2) Fever.
- (3) Sore-throat.

- (4) Photophobia.
- (5) Severe headache.
- (6) Cough with sputum (may occur).

Trachoma

Causative chlamydia

C trachomatis, types A, B, & C.

Pathogenesis

C trachomatis infects epithelium of conjunctiva, cornea & lacrimal apparatus → Within cytoplasm of epithelial cells, it multiplies to form basophilic inclusion bodies & produces a "soluble toxin" → This toxin spread to sub-epithelial tissues producing a chronic inflammatory cellular reaction, which may be diffuse or localized to form follicles & papillae → Healing occur by fibrous tissue formation.

Clinical findings

Insidious onset of:

- (1) Lacrimation.
- (2) Photophobia.
- (3) Mucopurulent discharge.
- (4) Conjunctival hyperemia.
- (5) Follicular hypertrophy.
- (6) Epithelial keratitis of cornea.
- (7) Corneal pannus.
- (8) Corneal ulcer.
- (9) Entropion.
- (10) Trichiasis.

Inclusion conjunctivitis

Causative chlamydia

Chlamydia trachomatis, types D-K.

Clinical findings

- (1) Purulent discharge
- (2) Follicles in lower fornix of eye

Genital chlamydial infections

Causative chlamydia

Chlamydia trachomatis, types D-K.

Clinical findings

- (1) **In male**
 - (1) Non-gonococcal urethritis
 - (2) Epididymitis
- (2) **In female**
 - (a) Urethritis
 - (b) Cervicitis
 - (c) Salpingitis
 - (d) Pelvic inflammatory disease

Lymphogranuloma venereum

Causative chlamydia

Chlamydia trachomatis, types L1-L3.

Clinical findings

- (1) Papule or vesicle on external genitalia, which may ulcerate.
- (2) Regional lymphadenopathy & lymphadenitis.
- (3) Fever.
- (4) Headache.
- (5) Meningismus.
- (6) Conjunctivitis.
- (7) Skin rashes.
- (8) Nausea & vomiting.

Chlamydial pneumonia

Causative chlamydia

Chlamydia pneumoniae.

Clinical findings

Upper & lower respiratory tract infections in young adult.

DIAGNOSTIC LABORATORY TESTS

Specimens

Serum, blood, scrapings of infected epithelial surface, biopsy from infected tissue, sputum.

Microscopy

(1) Giemsa's staining

- (a) Elementary bodies → Purple color.
- (b) Initial bodies → Blue color.
- (c) C trachomatis cytoplasmic inclusions → Dark purple color.

(2) Immunofluorescent staining

Chlamydiae stain brightly.

(3) Lugol's iodine staining

C trachomatis cytoplasmic inclusions appear brown in color.

Culture

Specimens are inoculated intra-abdominally into mice, into yolk- sacs of embryonated eggs & into cycloheximide-treated McCoy cell cultures.

Direct cytologic examination

These are used in laboratories that lack the expertise or facilities to perform culture.

(1) Direct fluorescent antibody (DFA)

DFA uses monoclonal antibodies directed against a species-specific antigen on the chlamydial major outer membrane protein (MOMP).

(2) Enzyme-linked immunoassay (EIA)

EIA detects the presence of genus-specific lipopolysaccharide antigens extracted from elementary bodies in the specimen.

Serology

Variety of antibodies develops in the course of infection, detected by following methods:

- (1) Immunofluorescence.
- (2) Complement fixation (CF) test.

Molecular methods

- (1) One commercial method uses a **chemiluminescent DNA probe** that hybridizes to a species-specific sequence of chlamydia 16S rRNA; chlamydiae have up to 10^4 copies of the 16S rRNA. Once the hybrids are formed they are absorbed onto beads, & the amount of chemiluminescence is then detected in a luminometer.
- (2) Nucleic acid amplification tests eg **polymerase chain reaction (PCR) & ligase chain reaction (LCR)**, have nearly 100% specificity. These are the tests of choice to diagnose genital C trachomatis infections.

IMMUNITY

Although antibodies are formed during infection, immunity is incomplete. A carrier state develops, which can persist for 10 years after recovery.

TREATMENT

- (1) Tetracyclines (eg, doxycycline).
- (2) Azithromycin, clarithromycin or erythromycin..

PREVENTION & CONTROL

- (1) Psittacosis is controlled by restriction on import of psittacine birds, destruction of sick birds, & addition of tetracycline to bird feed.
- (2) C trachomatis infection should be diagnosed & treated early.

Chapter 23

Rickettsiae

CLASSIFICATION

(A) Typhus group

- (1) *Rickettsia prowazekii*
- (2) *R. typhi*

(B) Scrub typhus group

Orientia tsutsugamushi

(C) Spotted fever group

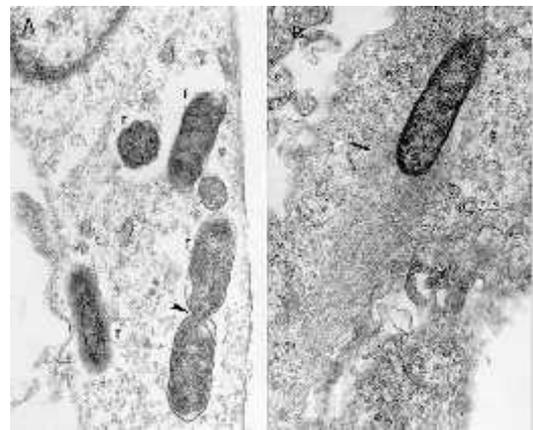
- (1) *R. rickettsii*
- (2) *R. conorii*
- (3) *R. australis*
- (4) *R. sibirica*
- (5) *R. akari*

(D) Q fever group

Coxiella burnetii

(E) Ehrlichiae

- (1) *Ehrlichia chaffeensis*
- (2) *Neorickettsia sennetsu*
- (3) *Anaplasma phagocytophilum*
- (4) *Ehrlichia ewingii*



R. conorii (r): A. Electron micrograph showing organism located free in cytosol, in a cultured human endothelial cell. One rickettsia is dividing by binary fission (arrow head).

B. These rickettsia can move inside the cytoplasm of host cell b/c of propulsive force created by tail of host cell actin filaments (arrow).

MORPHOLOGY

Shape

Rickettsiae are pleomorphic, appearing either as short rods, or as cocci.

Arrangement

May occur singly, in pairs, in short chains, or in filaments.

STAINING

Gram's staining

Rickettsiae appear as gram-negative rods (pink colored), as their cell wall is similar to gram-negative bacteria.

Giemsa's staining

Rickettsiae appear blue with Giemsa's stain.

Macchiavello's Staining

Rickettsiae appear red, in contrast with the blue-staining cytoplasm around them.

Others

- (1) Aniline dyes.

(2) Castaneda stain

CULTURE

Culture

Rickettsiae are obligate intracellular bacteria; thus, cannot be grown in laboratory on artificial media, but require living cells for growth. They are readily cultivated in “yolk sac of embryonated egg”, & pure preparations can be obtained by differential centrifugation of yolk sac suspensions.

Growth characteristics

(1) Energy source

Oxidize intermediate metabolites like pyruvic, succinic & glutamic acids, but are unable to generate sufficient energy to replicate extracellularly.

(2) Loss of biological activities

When stored at 0°C, or incubated for a few hours at 36 °C, due to progressive loss of NAD.

(3) Growth enhanced

At 32 °C & in the presence of sulfonamides.

(4) Growth inhibited

By tetracyclines or chloramphenicol, & by heat, drying or bactericidal chemicals.

(5) Site of growth

- (a) Typhus group → In the cytoplasm.
- (b) Spotted fever group → In the nucleus
- (c) Coxiellae → In cytoplasmic vacuoles

ANTIGENS

Rickettsiae produce soluble group specific antigens that are released into surrounding environment. Also each strain produces a type-specific antigen. Both group specific & type-specific antigens give rise to antibodies that can be measured by:

(1) Agglutination of proteus vulgaris (Weil Felix reaction)

Rickettsiae & P vulgaris share certain antigens → So, antibodies against rickettsial antigens agglutinate P vulgaris.

(2) Agglutination of rickettsiae

Patient's serum + Heavy rickettsial suspension → Agglutination → Positive result.

(3) Immunofluorescence test with rickettsial antigens

(4) Latex agglutination test

(5) Neutralization of rickettsial toxins

HABITAT & TRANSMISSION

Habitat

In certain arthropods like ticks, lice, fleas, & mites.

Transmission

Via bite of arthropod, or via aerosol (C burnetii).

PATHOGENESIS & CLINICAL FINDINGS

Pathogenesis

Rickettsiae multiply in endothelial cells of small blood vessels → Produce vasculitis → This results in thrombosis & disseminated intravascular coagulation, ie vascular occlusion occur with its consequent effects (eg, edema, hemorrhage, skin rash etc.).

Typhus

Epidemic typhus

Causative rickettsia

R prowazekii.

Arthropod vector

Louse.

Mammalian reservoir

Humans.

Clinical findings

- (1) Fever (last for about 2 weeks).
- (2) Headache.
- (3) Malaise & severe prostration.
- (4) Skin rash (begins on trunk & spread to extremities).
- (5) Hepato-splenomegaly.

Note: Brill-Zinsser disease is a recrudescence of an old typhus infection. The rickettsiae can persist for many years in the lymph nodes of an individual without any symptoms being manifest.

Endemic typhus (Murine typhus)

Causative rickettsia

R typhi.

Arthropod vector

Fleas.

Mammalian reservoir

Rodents.

Clinical findings

Similar to epidemic typhus, but in a milder form.

Scrub typhus

Causative rickettsia

Oriental tsutsugamushi.

Arthropod vector

Mites.

Mammalian reservoir

Rodents.

Clinical findings

- (1) Eschar (punched-out ulcer covered with black scab at bite site).
- (2) Generalized lymphadenopathy.
- (3) Lymphocytosis.
- (4) Cardiac & cerebral involvement.
- (5) Other features of epidemic typhus.

Spotted fever

Rocky mountain spotted fever

Causative rickettsia

Rickettsia.

Arthropod vector

Tick.

Mammalian reservoir

Rodents, dogs.

Clinical findings

- (1) Skin rash (appear first on wrists & ankles, then spread to trunk within a few hours).
- (2) Other features of epidemic typhus.

Rickettsial pox

Causative rickettsia

Rickettsia akari.

Arthropod vector

Mite.

Mammalian reservoir

Mice.

Clinical findings

- (1) Skin rash (first on trunk & then on face & limbs).
- (2) A firm red papule at the site of mite bite → Develop into deep seated vesicle → Finally, a black eschar.
- (3) Other features of epidemic typhus.

Q fever

Causative rickettsia

Coxiella burnetii.

Arthropod vector

None.

Mammalian rReservoir

Cattle, sheep, goats.

Clinical findings

- (1) No skin rash.
- (2) Sudden onset of fever, chills & headache.
- (3) Weil-Felix test is negative.

DIAGNOSTIC LABORATORY TESTS

Specimens

Serum, blood, skin biopsies

Serology

(1) Weil-Felix reaction

Patient's serum + Proteus vulgaris strains OX-2, OX-19 & OX-K → Agglutination → Positive reaction.

(2) Complement fixation test

Patient's serum + Rickettsiae + complement → Complement fixed → Positive test.

(3) Immunofluorescence test

Patient's serum + Fluorescein-labeled antihuman globulin + Rickettsiae → Fluorescently-labeled rickettsiae → Positive test.

Polymerase chain reaction

It has been used to diagnose Rocky Mountain spotted fever, rickettsial pox, murine typhus, scrub typhus, & Q fever.

Animal inoculation test

- (1) Whole blood (or emulsified blood clot) is inoculated into guinea pig, mice, or eggs → Rickettsiae are recovered from blood drawn soon after onset (fever, scrotal swelling, hemorrhagic necrosis, death) → Stain & observe for rickettsiae.
- (2) If guinea pig fails to show disease, serum is collected for antibody tests, to determine if it has an inapparent infection.

Skin biopsy staining

In Rocky Mountain spotted fever, skin biopsies may reveal rickettsiae by immunofluorescence stain.

IMMUNITY

Infections in humans are followed by partial immunity to reinfection from external sources, but relapses can occur.

TREATMENT

Tetracyclines are effective provided treatment is started early.

PREVENTION & CONTROL

- (1) Reducing exposure to arthropod vector by wearing protective clothing & insect repellent.
- (2) Frequent examination of skin for ticks.
- (3) Personal hygiene & delousing.
- (4) For typhus → A vaccine containing formalin-killed *R. prowazekii* is effective.
- (5) For Q fever → A vaccine that consists of killed *C. burnetii*.

Chapter 24

Treponema Pallidum

MORPHOLOGY

Shape

Slender, spiral-shaped.

Arrangement

Lie separately.

Capsule

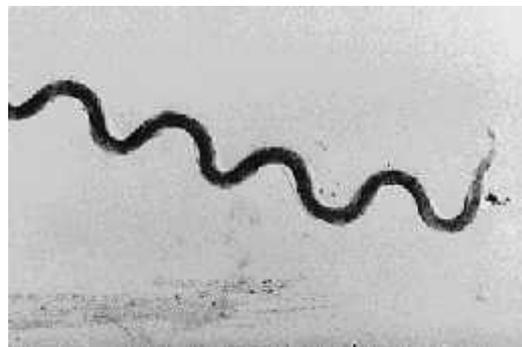
Non-capsulated.

Motility

Motile, rotating around their central axial filaments (endoflagella).

Spore

Non-spore forming.



T pallidum. Electron micrograph.

STAINING

Gram's staining

Not stained by Gram's staining.

Dark field illumination

Appear shining & refractive.

Negative staining

Spirochetes are mixed with negative dyes (eg India ink) → Appear refractile in dark background.

Tenetas antigen impregnation

Used for dry preparations & in tissue biopsy.

Levaditi silver impregnation

Spirochetes reduce silver nitrate to metallic silver that is deposited on surface → Spirochetes can be seen in tissues.

Giemsa's staining

Spirochetes appear as pink threads.

CULTURE

Culture

Treponema pallidum pathogenic for humans cannot be cultured on artificial media, in fertile eggs, or in tissue culture.

Growth characteristics

(1) O₂ requirement

Microaerophilic organism, surviving best in 1-4% O₂.

(2) Remain viable

For 24 hours if stored at 4°C in whole blood or plasma.

(3) Remain motile

For 3-6 days at 25°C.

(4) Killed by

Drying, elevation of temp to 42°C, trivalent arsenicals, mercury, bismuth & penicillin.

ANTIGENS

- (1) Characterization of T pallidum antigens is markedly limited, as the organism cannot be cultured in vitro. Probably, the followings may have a role;
 - (a) Glycosaminoglycan sheath.
 - (b) Sialic acid on the surface of T pallidum.
 - (c) Protein antigens.
 - (d) Cardioliipin.
- (2) However, they induce the production of two types of antibodies;
 - (a) Non-specific antibodies (reagins IgG & IgM) → Detected by non-treponemal antigens eg cardioliipin (a lipid antigen extracted from beef heart).
 - (b) Specific (anti-treponemal) antibodies → Detected by immunofluorescence tests.

ENZYMES

Hyaluronidase

It breaks down the hyaluronic acid in the ground substance of tissue & presumably enhances the invasiveness of the organism.

HABITAT & TRANSMISSION

Habitat

Human genital tract.

Transmission

- (1) By sexual contact.
- (2) From mother to fetus across placenta.

PATHOGENESIS & CLINICAL FINDINGS

Acquired syphilis

T pallidum penetrate intact mucosa or enter thru a break in epidermis → Multiply locally at site of

entry → Spread to nearby lymph nodes & reach bloodstream.

(1) Primary syphilis

In 2-10 weeks after infection, a papule develops at the site of infection (on penis, vulva or cervix) & breaks down to form an ulcer with a clean, hard base; this is called “hard chancre”. Inflammation is characterized by predominance of lymphocytes & plasma cells. Primary lesion heals spontaneously.

(2) Secondary syphilis

In 2-10 weeks after primary infection, secondary lesions appear. These consist of:

- (a) Red maculopapular rash anywhere on the body.
- (b) Condyloma lata (moist, pale papules) in anogenital region, axilla & mouth. Secondary lesions also subside spontaneously.

Note: Both primary & secondary lesions are rich in spirochetes, & highly infectious.

(3) Latent syphilis

All untreated patients with secondary syphilis enter latent phase; patient become asymptomatic, but serologic markers are positive. This period may last from 1 to 30 years.

(4) Tertiary syphilis

After latent period syphilis progress to tertiary stage, which is characterized by:

- (a) **Gummas (granulomas)**
In skin, bones, joints, liver (hepar lobatum), testes (painless enlargement).
- (b) **Cardiovascular lesions**
Aortitis, aortic aneurysm & aortic valve insufficiency.
- (c) **Degenerative changes in CNS**
Meningovascular syphilis, paresis & tabes.

Note: In tertiary lesions, treponemes are very rare.

Congenital syphilis

A pregnant syphilitic woman can transmit T pallidum to fetus thru placenta during 10-15th week of gestation. Stigmata of congenital syphilis develop only when fetus is infected after 4 months. Fetus may die in utero or soon after birth or may survive with following manifestations.

Clinical findings

- (1) Diffuse maculopapular rash that cause extensive desquamation of skin.
- (2) Generalized osteochondritis & perichondritis.
- (3) Destruction of vomer bone → Saddle nose.
- (4) Hutchinsonian incisors (wedge-shaped notched incisors).
- (5) Mulberry molars.
- (6) Liver failure.
- (7) Respiratory failure.
- (8) Eyes → Interstitial keratitis or choroiditis.
- (9) Saber shins (anterior bowing of tibia).

DIAGNOSTIC LABORATORY TESTS

Specimens

- (1) Tissue fluid from early surface lesion for determination of spirochetes.
- (2) Blood serum for serologic tests.

Microscopy

(1) Simple microscopy

A drop of tissue fluid or exudate is placed on a slide & a coverslip is pressed over it → Examined under oil immersion with "darkfield illumination" → Typical motile spirochetes are seen.

(2) Immunofluorescence microscopy

Tissue fluid or exudate stained with a fluorescein-labeled antitreponeme serum → Examined by means of immunofluorescence microscopy → Typical fluorescent spirochetes are seen.

Serologic tests for syphilis (STS)

(1) Non-specific serologic tests

These tests use non-treponemal antigens, eg cardiolipin (a lipid antigen extracted from beef heart). Cardiolipin cross-reacts with "reagin" (a mixture of IgG & IgM) found in serum & spinal fluid of syphilis pts.

(a) Flocculation tests (VDRL & RPR tests)

(VDRL=Venereal disease research laboratories; RPR=Rapid plasma reagin). Cardiolipin (plus lecithin & cholesterol) is mixed with pt's serum → Visible clumps develop within minutes → Test positive (ie pt serum contains "reagin").

(b) Complement fixation tests (Wassermann, Kolmer)

Cardiolipin + pt's serum + complement → Complement is fixed → Test positive.

Results

- (a) False +ve results are seen in
 - (i) Infections (malaria, leprosy, measles, infectious mononucleosis).
 - (ii) Vaccinations.
 - (iii) Collagen-vascular diseases (eg, systemic lupus erythematosus, polyarteritis nodosa, rheumatic disorders).
- (b) False -ve result is seen in "prozone phenomenon" in which antibody titer is too high & no flocculation will occur. On dilution test become +ve

(2) Specific serologic tests

These tests use treponemal antigens obtained from experimentally infected rabbits.

(a) Fluorescent treponemal antibody test (FTA-ABS)

(FTA-ABS = Fluorescent treponemal antibody absorbed test).

Killed treponema pallidum + pt's serum + labeled antihuman gamma globulin → Examined under microscope → Fluorescently labeled treponemes seen → Test positive.

(b) Treponema pallidum immobilization (TPI) Test

Motile T pallidum from testicular chancre of rabbit + pt's serum + complement → T pallidum immobilized → Test positive.

(c) Treponema pallidum complement fixation test

T pallidum + pt's serum + complement → Complement fixed → Test positive.

(d) Treponema pallidum-particle agglutination (TP-PA) test

- (i) It includes treponema pallidum hemagglutination (TPHA) & microhemagglutination for T pallidum (MHA-TP) tests.
- (ii) Particles sensitized with T pallidum subspecies pallidum antigens + pt's serum → Antibodies against T pallidum react with the sensitized particles & a mat of agglutinated particles formed → Test positive.

Results

All positive tests mean that pt's serum contains specific antitreponemal antibodies.

PREVENTION & CONTROL**IMMUNITY**

Antibody-mediated immunity develops that resist super-infection with T pallidum (in persons with active or latent syphilis). However, if early syphilis is promptly treated with complete eradication of infection, person again becomes fully susceptible.

- (1) No specific immunization with toxoid or vaccine.
- (2) Prompt treatment of all discovered cases.
- (3) Follow-up on source of infection.
- (4) Sex hygiene.
- (5) Prophylaxis at the time of exposure:
 - (a) Mechanical prophylaxis → Condoms.
 - (b) Chemoprophylaxis → Penicillin after exposure.

TREATMENT

- (1) Benzathine penicillin G (2.4 million units IM)
- (2) Tetracyclines
- (3) Erythromycin.

Chapter 25

Miscellaneous Bacteria

GRAM - POSITIVE BACTERIA

Bacillus anthracis

Individual organism is rod shaped, arranged in long



B anthracis: Gram's stain appearance.

chain, is non-motile & has central spores.

Clinical findings

It causes anthrax (two types).

(1) Malignant pustule

Infection occur thru skin by contact with hides of infected animals → A papule develops in 12-36 hours at the site of entry of organism or its spore → This changes into vesicle → Then a pustule → Finally, a necrotic ulcer, from which infection may disseminate → Septicemia.

(2) Woollorter's disease

Infection occur thru inhalation of spores from dust of wool, hair or hides → Germination of spore occur in lungs or in tracheobronchial lymph nodes → This results in pneumonia, hemorrhagic mediastinitis, & sepsis.

Bacillus cereus

Clinical findings

It causes food poisoning (two types);

- (1) Emetic type → Associated with rice dishes.
- (2) Diarrheal type → Associated with meat dishes & sauces.

Clostridium difficile

Clinical findings

- (1) It causes **pseudomembranous colitis**, a severe, necrotizing inflammation in large intestine following antibiotic therapy esp. clindamycin & ampicillin.
- (2) These antibiotics cause proliferation of drug-resistant C difficile, which produce disease by two exotoxins A & B. Toxin A is enterotoxin responsible for diarrhea while toxin B is a cytotoxin.

Clostridium septicum, histolyticum & novyi

Clinical findings

Gas gangrene (clostridial myonecrosis), similar to that caused by C perfringens.

Actinomyces

Individual organism is short & club-shaped or long, thin beaded filaments. May be branched or unbranched.

Clinical findings

Actinomycosis → A hard, red, non-tender swelling that eventually drains forming a chronic sinus tract.

Listeria monocytogenes

Individual organism is a short, spore-forming rod, having a tumbling end-over-end motility at 22°C but not at 37°C.

Clinical findings

- (1) Granulomatosis infantiseptica (a perinatal infection).
- (2) Meningoencephalitis (in adults).
- (3) Bacteremia (in adults).

Nocardia

Individual organism is a thin, branching filament, which may fragment into bacillary or coccoid forms.

Clinical findings

- (1) Nocardiosis (esp. lung & brain abscesses).
- (2) Madura foot.

GRAM - NEGATIVE BACTERIA

Pasteurella

Individual organism is non-motile coccobacilli with a bipolar appearance. Most common pasteurella causing human infection is "P multocida".

Clinical findings

Wound infection, inflicted by bites from cats & dogs.

Brucella

Individual organism vary from cocci to rods & is non-motile & non-spore forming. Species pathogenic to humans are B abortus, B suis, B canis & B melitensis.



Brucella: Electron micrograph.

Clinical findings

Brucellosis (undulant fever, Malta fever).

Yersinia

Y pestis

- (1) Small, non-motile, coccobacillus.
- (2) It causes 'plague' (a rodent infection that may be transmitted to humans by bites of fleas).

Y enterocolitica

- (1) Small, motile, rod.
- (2) It causes enterocolitis.

Francisella tularensis

Individual organism is small, pleomorphic rod.

Clinical findings

Tularemia → 4 types depending on route of entry;

- (1) Ulcerococular.
- (2) Ulceroglandular.
- (3) Pneumonic.
- (4) Typhoidal.



Francisella: Electron micrograph.

Hemophilus species

Individual organism is capsulated, short coccobacilli, sometimes occurring in short chains.

Clinical findings

- (1) *H influenzae* → Sinusitis, otitis media, laryngotracheitis, epiglottitis, meningitis & pneumonitis.
- (2) *H aegyptius* → Muco-purulent conjunctivitis, Brazilian purpuric fever (in children).
- (3) *H ducreyi* → Chancroid (soft chancre).

Bordetella pertussis

Individual organism is capsulated, short coccobacilli, having metachromatic granules.

Clinical findings

Whooping cough (pertussis).

Legionella pneumophila

Individual organism is pleomorphic rod, having flagella.

Clinical findings

Lobar, segmental or patchy pulmonary infiltration, called Legionnaires' disease (legionellosis).

Enterobacter

Individual organism is rod-shaped & motile.

Clinical findings

Hospital-acquired urinary tract infections.

Serratia

It causes hospital-acquired infections, esp. in newborn, debilitated or patient receiving immunosuppressive drugs.

Bacteroides

Individual organism appears as slender rod or coccobacilli. Most common pathogen is B fragilis.

Clinical findings

- (1) Abdominal, lung & brain abscesses.
- (2) Empyema.
- (3) Suppuration in surgical wound.
- (4) Pelvic inflammatory disease.
- (5) Bacteremia.
- (6) Endocarditis.

Fusobacterium

Individual organism is pleomorphic rod.

Clinical findings

- (1) Osteomyelitis.
- (2) Found in mixed bacterial infections

SPIROCHETES

Treponema carateum

Clinical findings

Pinta → Skin lesions, flat red or blue, that do not ulcerate, & ultimately become depigmented.

Treponema vincenti

Clinical findings

Vincent's angina (trench mouth) → Ulcerative lesion of mouth or tonsillar area.

Borrelia

Individual organism is an irregular spiral, highly flexible, & moves both by rotation & by twisting.

Clinical findings

- (1) B recurrentis → Relapsing fever.
- (2) B burgdorferi → Lyme disease (transmitted to humans by bite of tick of the genus Ixodes).

Leptospira

Individual organism is tightly coiled, thin, flexible spirals, one end of which often bent forming a hook & have rotational motion.

Clinical findings

- (1) L autumnalis → Pretibial fever (Fort Bragg fever).
- (2) L canicola → Infectious jaundice.
- (3) L grippotyphosa → Marsh fever.
- (4) L hebdomadis → Seven-day fever.
- (5) L icterohemorrhagiae → Weil's disease.
- (6) L mitis → Swineherd's disease.
- (7) L pomona → Swineherd's disease.

MYCOPLASMAS

Morphology

Individual organisms may have the shape of ring, bacillary & spiral body, filaments or granules. They are highly pleomorphic because they lack a rigid cell wall.

Clinical findings

- (1) M pneumoniae → Primary atypical pneumoniae, esp. in persons 5-20 years of age.
- (2) M hominis → Chorioamnionitis, postpartum fever, & low birth weight of infants, in pregnant women.
- (3) M genitalium → Non-gonococcal urethritis.
- (4) Ureaplasma urealyticum → Non-gonococcal urethritis.

Chapter 26

Causative Organisms of Specific Diseases

FOOD - POISONING CAUSING ORGANISMS

(A) *Toxin mediated*

- (1) Staphylococcus aureus.
- (2) Clostridium botulinum.
- (3) Clostridium perfringens.
- (4) E coli 0157 (verocytotoxin – producing).

(B) *Non-toxin mediated*

- (1) Salmonella species.
- (2) Campylobacter jejuni.
- (3) Bacillus cereus.
- (4) Some strains shigella, & proteus.
- (5) Viruses, eg Norwalk viruses.
- (6) Protozoa, eg giardia, cryptosporidium.

URINARY TRACT INFECTION (UTI) CAUSING ORGANISMS

(A) *Acute UTI*

(1) *Gram -ve bacilli*

- (a) E coli (60 - 80%)
- (b) Proteus
- (c) Klebsiella
- (d) Pseudomonas

(2) *Gram +ve cocci*

- (a) Streptococcus fecalis (enterococci)
- (b) Staphylococcus saprophyticus or epidermidis.

(B) *Chronic UTI*

Mycobacterium tuberculosis.

WOUND INFECTION CAUSING ORGANISMS

(A) *Aerobes*

(1) *Gram +ve cocci*

- (a) Staphylococci.
- (b) Streptococci.

(2) *Gram -ve bacilli*

- (a) E coli.
- (b) Proteus.
- (c) Pseudomonas.

(B) *Anaerobes*

- (1) Clostridium tetani.
- (2) Clostridium perfringens.
- (3) Bacteroides fragilis.

MENINGITIS CAUSING ORGANISMS

(A) *Pyogenic meningitis*

(1) *Neonates*

- (a) Gram –ve bacilli eg, E coli, proteus.
- (b) Group B streptococci.
- (c) Listeria monocytogenes.

(2) *Pre-school child*

- (a) Hemophilus influenza.
- (b) Neisseria meningitides.
- (c) Streptococcus pneumoniae.

(3) *Older child & adults*

- (a) Neisseria meningitidis.
- (b) Streptococcus pneumoniae.
- (c) Listeria monocytogenes.
- (d) Staphylococcus aureus (skull fracture).

(B) Chronic meningitis

- (1) Mycobacterium tuberculosis.
- (2) Cryptococcus neoformans (immunosuppressed).

PNEUMONIA CAUSING ORGANISMS**Organisms causing primary (lobar) pneumonia****(A) Most common**

Streptococcus pneumoniae.

(B) Common

- (1) Staphylococcus aureus.
- (2) Legionella pneumophila.
- (3) Mycoplasmas pneumoniae.

(C) Uncommon

- (1) Hemophilus influenzae.
- (2) Klebsiella pneumoniae.
- (3) Streptococcus pyogenes.
- (4) Pseudomonas aeruginosa.

(D) Rare

- (1) Coxiella burnetii.
- (2) Chlamydia psittaci.
- (3) Actinomyces israeli.
- (4) Viruses.

Organisms causing secondary pneumonia

- (1) Streptococci.
- (2) Certain strains of pneumococci.
- (3) Hemophilus influenzae.
- (4) Various species of anaerobic bacteria.

Organisms causing pneumonia in immunocompromised patients

- (1) Pneumocystis carinii.
- (2) Pseudomonas aeruginosa.
- (3) Staphylococcus aureus.
- (4) Aspergillus fumigatus.
- (5) Cytomegalovirus.
- (6) Herpes virus.

Organisms causing nosocomial pneumonia

- (1) Pseudomonas species.
- (2) Escherichia species.
- (3) Klebsiella species.
- (4) Staphylococcus aureus.
- (5) Anaerobic organisms.

INFECTIVE ENDOCARDITIS CAUSING ORGANISMS**(A) Acute infective endocarditis****(1) Most common cause**

- (a) Staphylococcus aureus (50%).
- (b) Streptococcus pneumoniae.
- (c) Neisseria gonorrhoea.

(2) In drug addicts

- (a) Candida
- (b) Staphylococcus epidermidis
- (c) Streptococcus viridans

(3) In patients with prosthetic heart valves

- (a) Staphylococcus albus.
- (b) Diphtheroids.
- (c) Aerobic gram -ve bacilli.

(B) Subacute infective endocarditis

- (1) Streptococcus viridans (50%)
- (2) Other streptococci eg S fecalis, S milleri, S bovis.
- (3) Gram -ve bacilli
- (4) Low-virulent organisms:
 - (a) A aerogenes
 - (b) Serratia
 - (c) Staphylococcus epidermidis
- (5) Rickettsiae
- (6) Fungi

BACTEREMIA, SEPTICEMIA, & SEPSIS CAUSING BACTERIA**Bacteremia**

Presence of bacteria in blood, without significant signs & symptoms.

Causative bacteria**(1) Gram -ve bacilli**

- (a) E coli
- (b) Klebsiella, enterobacter & serratia species
- (c) Proteus
- (d) Pseudomonas aeruginosa
- (e) Salmonella species

(2) Staphylococcus aureus**(3) Neisseria species**

- (a) N gonorrhoeae
- (b) N meningitidis

Septicemia (blood poisoning)

Presence & multiplication of bacteria or presence of its toxin in blood, associated with systemic toxic effects.

Causative bacteria**(1) Bacteroides species**

- (a) B fragilis
- (b) B melaninogenicus

(2) Clostridia species

- (a) C perfringens
- (b) C septicum

(3) Pneumococci**(4) Rickettsia****Sepsis**

Presence in blood or other tissue of bacteria or their toxins.

Causative bacteria

- (1) Streptococci
- (2) E coli
- (3) Klebsiella pneumoniae
- (4) Salmonella enteritidis
- (5) Pseudomonas aeruginosa
- (6) Listeria monocytogenes
- (7) Bacteroides fragilis

MYCETOMA (MADURA-FOOT) CAUSING ORGANISMS

Madura foot

- (1) It is characterized by chronic granulomatous inflammation, which occurs in an area of wound or abrasion contaminated with soil.
- (2) Associated with cutaneous papules or nodules with multiple draining sinuses with thick yellowish pus.
- (3) Feet & legs are the most common sites of infection.

Causative organisms**(1) Filamentous bacteria**

- (a) Nocardia
- (b) Streptomyces

(2) Fungi

- (a) Allescheria boydii.
- (b) Petriellidium boydii

NOSOCOMIAL INFECTION CAUSING ORGANISMS

(A) In the presence of urinary catheter

- (1) Serratia marcescens
- (2) Pseudomonas aeruginosa
- (3) Proteus species

(B) In the presence of foreign bodies

(eg, IV cannulas, catheters, prostheses)

- (1) Staphylococcus epidermidis
- (2) Staphylococcus aureus
- (3) Propionibacterium acnes
- (4) Candida species
- (5) Aspergillus species

(C) In surgical cases

- (1) S epidermidis
- (2) S aureus
- (3) Bacteroides species
- (4) Clostridium perfringens
- (5) P aeruginosa

(D) In burns

P aeruginosa

(E) In diabetes mellitus

- (1) S aureus
- (2) Candida albicans
- (3) P aeruginosa
- (4) Phycomycetes

Chapter 2

Mycology

CLASSIFICATION

(A) *Ascomycota (ascomycetes)*

Sexual reproduction involves a sac or ascus, producing ascospores. Asexual reproduction is via conidia. Molds have septate hyphae.

Examples

- (1) *Ajellomyces* → *Blastomyces*, histoplasma.
- (2) *Arthroderma* → *Microsporum*, trichophyton.
- (3) *Coccidioides*.
- (4) Yeasts → *Saccharomyces*, candida.

(B) *Basidiomycota (basidiomycetes)*

Sexual reproduction results in four progeny basidiospores supported by a club-shaped basidium. Hyphae have complex septa.

Examples

- (1) Mushrooms.
- (2) *Filobasidiella neoformans* → *Cryptococcus neoformans*.

(C) *Zygomycota (Zygomycetes)*

Sexual reproduction results in a zygospore; asexual reproduction occurs via sporangia. Vegetative hyphae are sparsely septate.

Examples

- (1) *Rhizopus*.
- (2) *Absidia*.
- (3) *Mucor*.
- (4) *Pilobolus*.

(D) *Chytridiomycota*

These are the smallest & simplest fungi.

Examples

- (1) *Batrachochytrium dendrobatidis*.
- (2) *Spizellomyces punctatus*.
- (3) *Rhizophyidium sphaerotheca*.

(E) *Deuteromycotina*

No sexual stage has been demonstrated.

Examples

- (1) *Epidermophyton*.
- (2) *Sporothrix*.

MORPHOLOGY

Fungi exist in three morphologic forms;

- (1) Yeasts.
- (2) Molds.
- (3) Dimorphs.

Yeasts

Unicellular forms that is spherical or ovoid in shape.

Molds

Complex, multicellular microorganisms, having variety of specialized structures with specific functions:

(1) *Hyphae*

Thread - like tubes containing cytoplasm & organelles of organism.

(2) *Septa*

Cross-walls in hyphae, forming individual cells.

(3) *Conidiophore or sporangiophore*

Specialized hypha that bears reproductive structures of some molds.

(4) *Vesicle*

Bulbous tip of conidiophore or sporangiophore.

(5) *Sterigmata*

Flask-shaped structures on vesicle that bears spores.

(6) *Sporangia*

Sac-like structures that contain spores.

(7) Conidia & spores

Conidia are asexual fungal spores, whereas spores are sexual reproductive structures.

Dimorphs

Fungi grow as molds in natural environment & in laboratory culture, & as yeasts or yeast-like structures in tissue.

Examples

- (1) Histoplasma.
- (2) Blastomyces.
- (3) Coccidioides.
- (4) Paracoccidioides.
- (5) Sporothrix schenckii.

CULTURE**Media**

- (1) Sabouraud's agar (SAB).
- (2) SAB plus antibacterial agent (SAB+).
- (3) Potato dextrose agar (PDA).

Growth characteristics**(1) O₂ requirement**

Most fungi are obligate aerobes, & only some are facultative anaerobes.

(2) pH requirement

Ranges b/w 4.0 & 6.5.

(3) Temperature

Grow better in a warm atmosphere with high humidity.

(4) Resistant to

Drying & action of antibiotics.

HABITAT & TRANSMISSION**Habitat**

Soil (esp. in association with decaying matter); exception is candida albicans, which is part of the human normal flora.

Transmission

Via inhalation, direct contact, & oral-fecal route.

PATHOGENESIS & CLINICAL FINDINGS**Superficial mycoses****Pityriasis versicolor****Causative fungi**

- (1) Malassezia globosa.
- (2) Malassezia restricta.
- (3) Malassezia furfur.

Pathogenesis

Chronic mild superficial infection of the stratum corneum.

Clinical findings

Discrete, serpentine, hyper- or hypopigmented maculae on the skin, usually on the chest, upper back, arms, or abdomen.

Tinea nigra**Causative fungi**

Hortaea werneckii.

Clinical findings

Light brown to blackish macular areas, often on the palm.

Piedra**Causative fungi**

- (1) Trichosporon species.
- (2) Piedraia hortae.

Clinical findings

- (1) Black piedra is a nodular infection of the hair shaft caused by Piedraia hortae.
- (2) White piedra, due to infection with Trichosporon species, presents as larger, softer, yellowish nodules on the hairs.

Note: Axillary, pubic, beard, & scalp hair may be infected.

Cutaneous mycoses**Dermatophytoses****Causative fungi**

- (1) Trichophyton species.
- (2) Microsporum species.
- (3) Epidermophyton floccosum.

Pathogenesis

Conidia & hyphal fragments of causative fungi invade the superficial keratinized tissue (stratum corneum of skin, hair, & nails) → Keratin is breakdown & metabolized → Cellular reactions, which produces the lesions.

Clinical findings**(1) Tinea capitis**

- (a) Caused by → *T. mentagrophytes*, *M. canis*.
- (b) Site → Scalp hair.
 - (i) Endothrix → Fungus inside hair shaft.

- (ii) Ectothrix → Fungus on surface of hair.
- (c) Clinical findings → Circular bald patches with short hair stubs or broken hair within hair follicles.
- (2) ***Tinea barbae***
- (a) Caused by → *T mentagrophytes*.
 (b) Site → Beard hairs.
 (c) Clinical findings → Edematous, erythematous lesion.
- (3) ***Tinea corporis***
- (a) Caused by → *T rubrum*, *E floccosum*.
 (b) Site → Nonhairy, smooth skin of trunk.
 (c) Clinical findings → Circular patches with advancing red, vesiculated border & central scaling, & pruritus.
- (4) ***Tinea cruris***
- (a) Caused by → *T rubrum*, *T mentagrophytes*, *E floccosum*.
 (b) Site → Groin.
 (c) Clinical findings → Erythematous scaling lesion in intertriginous area, pruritus.
- (5) ***Tinea pedis***
- (a) Caused by → *T rubrum*, *T mentagrophytes*, *E floccosum*.
 (b) Site → Interdigital spaces on feet of persons wearing shoes.
 (c) Clinical findings →
 (i) Acute → Itching, red vesicular.
 (ii) Chronic → Itching, scaling, fissures.
- (6) ***Tinea manus***
- (a) Site → hands or fingers.
 (b) Clinical findings → Dry scaly lesions.
- (7) ***Tinea unguium***
- (a) Caused by → *T rubrum*, *T mentagrophytes*, *E floccosum*.
 (b) Site → Nails.
 (c) Clinical findings → Nails thickened or crumbling distally, discolored, lusterless.

Subcutaneous mycoses

Sporotrichosis

Causative fungi

Sporothrix schenckii.

Pathogenesis

Fungus is introduced into skin thru trauma → Local chronic inflammatory cellular reaction (granulomas) occur → Spread via lymphatics, with sub-cutaneous chronic inflammatory & cellular reactions along the lymphatics.

Clinical findings

- (1) A pustule, abscess, or ulcer, at the trauma site.
- (2) Multiple sub-cutaneous nodules & abscesses, along the lymphatics.

Chromoblastomycosis

Causative fungi

- (1) *Phialophora verrucosa*.
- (2) *P pedrosoi*.
- (3) *Cladosporium carrionii*.

Pathogenesis

Fungus is introduced into skin thru trauma → Cellular reaction (granulomas) occur along the lymphatics of affected area.

Clinical findings

- (1) Wart - like growth along the lymphatics
- (2) Eventually cauliflower-like nodules with crusting abscesses.
- (3) Elephantiasis may occur.

Mycetoma

See 'chapter 26'.

Phaeohiphomycosis

Causative fungi

- (1) *Exophiala jeanselmei*.
- (2) *Phialophora richardsiae*.
- (3) *Bipolaris spicifera*.
- (4) *Wangiella dermatitidis*.

Clinical findings

- (1) Encapsulated cysts in subcutaneous tissue.
- (2) Sinusitis.
- (3) Brain abscesses.

Systemic (deep) mycoses

Coccidioidomycosis

Causative fungi

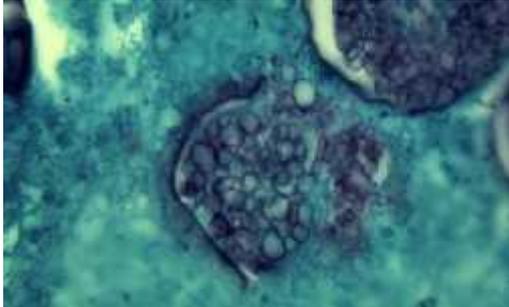
- (1) *Coccidioides immitis*.
- (2) *C posadasii*.

Pathogenesis

Infection is acquired thru inhalation of air-borne arthroconidia → In lungs, arthroconidia form spherules filled with endospores → Endospores are released upon rupture, which differentiate to form new spherules, & causes cellular reaction resulting in granulomatous lesions → Organism spread by direct extension or via bloodstream, resulting in granulomatous lesions in virtually every organs (esp. in bones & meninges).

Clinical findings

- (1) Lung infection is often asymptomatic, evident only by a positive - skin test.



Coccidioides immitis: Electron micrograph showing spherules & endospores.

- (2) Sometime, influenza - like illness with fever & cough.
- (3) Erythema nodosum (10%).

Histoplasmosis

Causative fungi

Histoplasma capsulatum.

Pathogenesis

Inhaled spores are engulfed by alveolar macrophages, & develop into budding cells → Cellular reaction occur.

Clinical findings

- (1) Asymptomatic.
- (2) Clinical pneumonia.
- (3) Chronic cavitary histoplasmosis.
- (4) Severe, disseminated histoplasmosis in infants, aged or immunosuppressed individuals. (lymphadenopathy, hepato-splenomegaly, high fever & anemia).

Blastomycosis

Causative fungi

Blastomyces dermatitidis.



Histoplasma capsulatum: Electron micrograph showing macroconidia & microconidia.

Pathogenesis

Fungus enter via respiratory tract → Causes granuloma formation

Clinical findings

- (1) Asymptomatic
- (2) With pulmonary infection → Fever, cough, & chest pain.
- (3) With dissemination → Ulcerated granulomas of skin, bone, or other sites.

Paracoccidioidomycosis

Causative fungi

Paracoccidioides brasiliensis.

Pathogenesis

Spores enter via respiratory tract → Cause granuloma formation.

Clinical findings

- (1) Asymptomatic.
- (2) Mucocutaneous & cutaneous ulcers.
- (3) Lymphadenopathy.

Opportunistic mycoses

Candidiasis

Causative fungi

Candida albicans.

Pathogenesis

Disease occurs, when local or systemic host defenses are impaired.

Clinical findings

- (1) Mouth → Thrush.
- (2) Female genitalia → Vulvovaginitis, with irritation, itching, & discharge.
- (3) Skin → Red & weeping areas, or vesicles.
- (4) Nails → Painful, red swelling of nail fold.
- (5) Secondary invasion of lungs, kidneys, & other



Candida albicans: Electron micrograph showing chlamydospore production.

organs with preexisting disease (eg, tuberculosis, cancer).

Cryptococcosis

Causative fungi

Cryptococcus neoformans.

Pathogenesis

Organism enter via inhalation → Cause granulomas in immunocompromised persons.

Clinical findings

- (1) Asymptomatic, or
- (2) Pneumonia
- (3) Meningitis

Aspergillosis

Causative fungi

Aspergillus fumigatus & other *aspergillus* species.

Pathogenesis

Organism colonize & later invade abraded skin, wounds, burns, cornea, external ear, paranasal sinuses, or lung (in immunocompromised pts).

Clinical findings

- (1) Allergic asthma.
- (2) Aspergilloma (fungus ball), in lung or in brain (rarely).
- (3) Hypopyon ulcer in cornea.
- (4) Cough, fever, night sweats.

Zygomycosis (mucormycosis)

Causative fungi

- (1) *Mucor* species.
- (2) *Rhizopus* species.
- (3) *Absidia* species.

Pathogenesis

Conidia enter via inhalation → Typical granulomas.

Clinical findings

- (1) Frontal headache.
- (2) Blindness (due to optic nerve involvement).
- (3) Rapidly progressive pulmonary infection.

DIAGNOSTIC LABORATORY TESTS

Specimens

Sputum, lung biopsy material, skin scrapings, serum, spinal fluid, pus, hair, nails.

Microscopy

Specimen placed on a slide, is covered with a drop of 10 - 20% KOH & a coverslip is placed over it → Examined immediately & then again after 20

minutes, for the presence of fungus (which may be seen as yeasts, molds, or spores).

Culture

Specimens are inoculated onto Sabouraud's agar, incubated for 1 - 3 weeks at room temperature.

Serology

Antibodies develop within 2-5 weeks in response to fungal antigens, which can be detected by:

- (1) Immunodiffusion test
- (2) Latex agglutination test
- (3) Precipitation test
- (4) CF reaction

Note: Serology tests are of value in systemic & opportunistic mycoses.

Skin test

Extract of fungus as an antigen is injected into skin → Local induration develop, due to delayed hypersensitivity → Positive test.

Skin test is positive in

- (1) *Coccidioidomycosis*
- (2) *Histoplasmosis*
- (3) *Paracoccidioidomycosis*
- (4) *Candidiasis* (candida skin test is always positive in normal adults).

IMMUNITY

Specific antibodies to fungal antigens develop in systemic infection, which provide immunity to reinfection.

TREATMENT

(A) Systemic antifungal drugs

- (1) Amphotericin B.
- (2) Flucytosine
- (3) Azoles →
 - (a) Imidazoles eg, ketoconazole.
 - (b) Triazoles eg, fluconazole, voriconazole & itraconazole.
- (4) Echinocandins eg, caspofungin.
- (5) Griseofulvin.
- (6) Terbinafine.

(B) Topical antifungal drugs

- (1) Nystatin.

- (2) Azoles → Clotrimazole, miconazole, econazole, butaconazole, tioconazole, & terconazole.
- (3) Tolnaftate.
- (4) Naftifine.
- (5) Haloprogin.
- (6) Ciclopirox

PREVENTION & CONTROL

- (1) Personal cleanliness.
- (2) Sterilization of instruments.
- (3) Reduce contact with infectious material & avoidance of exposure in endemic areas.
- (4) Effective treatment of cases.
- (5) Prevention of trauma (in subcutaneous mycoses).

Chapter 28

General Virology

DEFINITIONS

Capsid

Protein shell or coat, that encloses the nucleic acid genome.

Capsomeres

Morphologic units seen in the electron microscope on the surface of icosahedral virus particles.

Defective virus

A virus particle that is functionally deficient in some aspect of replication.

Envelope

A lipid-containing membrane that surrounds some virus particles. Virus-encoded glycoproteins are exposed on the surface of the envelope called as peplomers.

Nucleocapsid

Protein-nucleic acid complex representing the packaged form of the viral genome.

Structural units

Basic protein building blocks of the coat, referred as a protomer.

Subunit

A single folded viral polypeptide chain.

Virion

The complete virus particle.

CLASSIFICATION OF VIRUSES

Viruses are classified on the basis of virion morphology, virus genome properties,

physicochemical properties of the virion, virus protein properties, genome organization & replication, antigenic properties & biologic properties.

DNA viruses

Non-enveloped (naked)

(A) Parvoviridae

- (1) B-19 virus.
- (2) Dependovirus

(B) Polyomaviridae

- (1) JC virus.
- (2) BK virus.

(C) Papillomaviridae

Papilloma (wart) virus.

(D) Adenoviridae

Human adenoviruses (groups A-F, 51 serotypes)

Enveloped

(A) Herpesviridae

- (1) Herpes simplex virus.
- (2) Varicella-zoster virus.
- (3) Cytomegalo virus.
- (4) Epstein-Barr virus.
- (5) Human herpesviruses 6 & 7
- (6) Human herpesvirus 8

(B) Poxviridae

- (1) Variola (small pox) virus.
- (2) Vaccinia virus.
- (3) Molluscum contagiosum virus.

(C) Hepadnaviridae

Hepatitis B virus.

RNA viruses

Non-enveloped (naked) viruses

(A) Picornaviridae

- (1) Polio virus.
- (2) Cocksackie virus.
- (3) Echo virus.
- (4) Rhino virus.
- (5) Hepatitis A virus.

(B) Caliciviridae

- (1) Norwalk virus.
- (2) Hepatitis E virus.

(C) Reoviridae

- (1) Reo virus.
- (2) Rota virus.
- (3) Colti virus.

(D) Astroviridae**Enveloped viruses****(A) Flaviviridae**

- (1) Yellow fever virus.
- (2) Dengue virus.
- (3) Hepatitis C virus.

(B) Togaviridae

- (1) Rubella virus.
- (2) Alpha virus

(C) Retroviridae

- (1) Human immunodeficiency virus.
- (2) Human T-cell leukemia virus.

(D) Orthomyxoviridae

Influenza virus.

(E) Paramyxoviridae

- (1) Morbilli (measles) virus.
- (2) Mumps virus.
- (3) Parainfluenza virus.
- (4) Respiratory syncytial virus.

(F) Filoviridae

- (1) Ebola virus.
- (2) Marburg virus.

(G) Rhabdoviridae

- (1) Rabies virus.
- (2) Vesiculo virus.

(H) Coronaviridae

Corona virus.

(I) Arenaviridae

- (1) Lassa fever virus.
- (2) Lymphocytic choriomeningitis virus.

(J) Bunyaviridae

- (1) Phlebo virus.
- (2) Hanta virus.
- (3) Orthobunya virus.
- (4) Nairo virus.

(K) Bornaviridae

Borna disease virus.

PATHOGENESIS OF VIRAL INFECTION

Pathogenesis of viral infection can be viewed at two distinct levels:

(A) Changes in infected cell

Viruses may cause 4 types of effects on infected cell:

- (1) Death of cell due to inhibition of macromolecular synthesis (Proteins, DNA, & RNA).
- (2) Fusion of virus-infected cells to produce multinucleated giant cells.
- (3) Malignant transformation of virus-infected cells, characterized by unrestrained growth.
- (4) No morphologic or functional change.

(B) Changes in infected patient

Pathogenesis of viral infection in infected patient involves:

- (1) Transmission of virus & its entry into host.
- (2) Replication of virus & damage to cells.
- (3) Spread of virus to other cells & organs.
- (4) Immune responses 2 Contribute to protection against virus & also to tissue damage.
- (5) Persistence of virus in certain intances 2 cause:
 - (a) Chronic carrier infections.
 - (b) Latent infections.
 - (c) Slow virus infections.

Chapter 29

DNA Enveloped Viruses

HERPESVIRUSES

Classification

(1) Alpha herpesviruses

- (a) Fast-growing, cytolytic viruses that tend to establish latent infections in neurons.
- (b) Members → Herpes simplex virus, varicella-zoster virus.

(2) Beta herpesviruses

- (a) Slow-growing, may be cytomegalic (massive enlargements of infected cells), that become latent in secretory glands & kidneys.
- (b) Members → Cytomegalovirus, herpesviruses 6 & 7.

(3) Gamma herpesviruses

- (a) Variable growth pattern & can infect & become latent in lymphoid cells.
- (b) Members → Epstein-Barr virus, herpesvirus 8.

Important properties

- (1) **Virion** → Spherical, 150–200 nm in diameter (icosahedral).
- (2) **Genome** → Double-stranded DNA, linear, 125–240 kbp, reiterated sequences.
- (3) **Proteins** → More than 35 proteins in virion.
- (4) **Envelope** → Contains viral glycoproteins, Fc receptors.
- (5) **Replication** → Nucleus, bud from nuclear membrane.
- (6) **Outstanding characteristics** →
 - (a) Encode many enzymes.
 - (b) Establish latent infections.

- (c) Persist indefinitely in infected hosts.
- (d) Frequently reactivated in immune-suppressed hosts.
- (e) Some are cancer-causing.

HERPES SIMPLEX VIRUSES

Properties of the viruses

- (1) Two types → HSV-1, HSV-2, which can be distinguished by sequence analysis or by restriction enzyme analysis of viral DNA.
- (2) HSV growth cycle proceeds rapidly, requiring 8–16 hours for completion.
- (3) HSV genome is large (about 150 kbp) & can encode at least 70 polypeptides.
- (4) HSV produces viral glycoproteins as viral late gene products.
 - (a) Glycoprotein D (gD) is the most potent inducer of neutralizing antibodies.
 - (b) Glycoprotein C is a complement (C3b)-binding protein.
 - (c) Glycoprotein E (gE) is an Fc receptor, binding to the Fc portion of IgG.
 - (d) Glycoprotein G is type-specific & allows for antigenic discrimination between HSV-1 (gG-1) & HSV-2 (gG-2).

HABITAT & TRANSMISSION

Habitat

Worldwide in distribution.

Transmission



HSV: Electron micrograph showing thin section of virions as they leave the nucleus of an infected cell.



HSV: Electron micrograph showing envelope surrounding an icosahedral capsid.

- (1) HSV-1 infection is spread by direct contact with infected saliva or through utensils contaminated with the saliva of a virus shedder.
- (2) HSV-2 is transmitted sexually or from a maternal genital infection to a newborn.

PATHOGENESIS & CLINICAL FINDINGS

Pathogenesis

HSV causes cytolytic infections, with necrosis of infected cells & inflammatory response.

Primary infection

It enters thru mucosal surfaces or broken skin → Starts replication at the site of infection → Invades local nerve endings & transported by retrograde axonal flow to dorsal root ganglia, where, after further replication, latency is established. (**Note:** HSV-1 causes latent infections in trigeminal ganglia, whereas HSV-2 causes latently infected sacral ganglia).

Latent infection

- (1) Virus remains in a nonreplicating state; microRNA prevent cell death, maintaining the latent infection. This state may last for the lifetime of the host.
- (2) Provocative stimuli (eg axonal injury, fever, stress & exposure to ultraviolet light) can reactivate virus → Virus follows axons back to the peripheral site, & replication proceeds at the skin or mucosa.

Clinical Findings

Incubation period is about 3–5 days.

Oropharyngeal disease

- (1) Primary HSV-1 infections are usually asymptomatic.
- (1) Symptomatic disease occurs in small children (1–5 years) & involves the buccal & gingival mucosa. Symptoms include fever, sore throat, vesicular & ulcerative lesions, gingivostomatitis, & malaise.
- (2) Primary infections in adults cause pharyngitis & tonsillitis.
- (3) Localized lymphadenopathy may occur.
- (4) Recurrent disease is characterized by a cluster of vesicles at the border of the lip. Lesions progress thru the pustular & crusting stages, & heal without scarring in 8–10 days.

Keratoconjunctivitis

- (1) Appear as dendritic keratitis or corneal ulcers or as vesicles on the eyelids.
- (2) With recurrent keratitis, permanent opacification & blindness occur.

Genital herpes

- (1) Usually caused by HSV-2.
- (2) Primary infection is characterized by severe & painful vesiculoulcerative lesions of the penis (male) or of the cervix, vulva, vagina & perineum (female). Fever, malaise, dysuria, & inguinal lymphadenopathy may also be present.
- (3) Recurrences tend to be mild.

Skin infections

- (1) Localized lesions caused by HSV-1 or HSV-2 may occur in abrasions (traumatic herpes). These lesions are seen on the fingers of dentists & hospital personnel (herpetic whitlow) & on the bodies of wrestlers (herpes gladiatorum).
- (2) Eczema herpeticum is a primary infection, usually with HSV-1, in a person with chronic eczema. .

Encephalitis

HSV-1 causes sporadic, fatal encephalitis.

Neonatal herpes

- (1) HSV infection may be acquired in utero, during birth (birth canal), or after birth.
- (2) Usually caused by HSV-2.
- (3) Babies exhibit 3 types of disease:
 - (a) Lesions localized to the skin, eye & mouth.
 - (b) Encephalitis with or without localized skin involvement.
 - (c) Disseminated disease involving multiple organs. Cause of death is usually viral pneumonitis or intravascular coagulopathy.

Infections in immunocompromised hosts

Herpes lesions may spread & involve the respiratory tract, esophagus, & intestinal mucosa.

DIAGNOSTIC LABORATORY TESTS**Cytopathology**

Scrapings obtained from the base of a vesicle are stained (eg, with Giemsa's stain) → Microscopy → Multinucleated giant cells indicate the presence of HSV-1, HSV-2, or varicella-zoster.

Isolation & identification of virus

- (1) Virus may be isolated from herpetic lesions, throat washings, CSF & stool.
- (2) Inoculation of tissue cultures is used for viral isolation.
 - (a) Identified by Nt test or immunofluorescence staining with specific antiserum.
 - (b) Typing of HSV is done with monoclonal antibody or by restriction endonuclease analysis of viral DNA.

Polymerase chain reaction (PCR)

PCR amplification of viral DNA from CSF is used to diagnose HSV infections of CNS.

Serology

- (1) Antibodies appear in 4–7 days after infection & reach a peak in 2–4 weeks.
- (2) They persist with minor fluctuations for the life of the host.

IMMUNITY

- (1) Many newborns acquire passively transferred maternal antibodies, which are lost during the first 6 months of life.
- (2) HSV-1 antibodies begin to appear in the population in early childhood; by adolescence, they are present in most persons.
- (3) HSV-2 antibodies rise during adolescence & adult age.
- (4) During primary infections, IgM antibodies appear transiently & are followed by IgG & IgA antibodies that persist for long periods.
- (5) The antibodies do not prevent reinfection or reactivation of latent virus but may modify subsequent disease.

TREATMENT

- (1) Acyclovir.
- (2) Valacyclovir.
- (3) Vidarabine.

PREVENTION & CONTROL

- (1) Newborns & persons with eczema should be protected from exposure to persons with active herpetic lesions.
- (2) A recombinant HSV-2 glycoprotein vaccine prevents genital herpes in women who were sero-negative for both HSV-1 & HSV-2.

VARICELLA-ZOSTER VIRUS**Properties of the virus**

- (1) Morphologically identical to HSV.
- (2) It has no animal reservoir.
- (3) It propagates in cultures of human embryonic tissue & produces typical intranuclear inclusion bodies.

HABITAT & TRANSMISSION**Habitat**

Worldwide in distribution.

Transmission

- (1) Varicella is highly communicable & is a common epidemic disease of childhood (< 10 years of age). It spreads by airborne droplets & by direct contact.
- (2) Contact infection is less common in zoster. It occurs sporadically, chiefly in adults.

PATHOGENESIS & CLINICAL FINDINGS**Pathogenesis****Varicella**

Virus enters thru mucosa of upper respiratory tract or conjunctiva → Initial replication in regional lymph nodes → Primary viremia spreads virus & leads to replication in liver & spleen → Secondary viremia involving infected mononuclear cells transports virus to the skin → Rash & vesicle formation .

Zoster

- (1) Acute inflammation of the sensory nerves & ganglia.
- (2) Skin lesions similar to those of varicella, with characteristic distribution corresponding areas of innervation from an individual dorsal root ganglion.

Clinical Findings**Varicella (chickenpox)**

- (1) Incubation period is 10–21 days.
- (2) Malaise & fever are the earliest symptoms,
- (3) Rashes, first on the trunk & then on the face, limbs, & buccal & pharyngeal mucosa.
- (4) Successive fresh vesicles appear in crops, so that all stages of macules, papules, vesicles, & crusts may be seen at one time. The rash lasts about 5 days.
- (5) Complications → Encephalitis, dissemination, congenital varicella syndrome, pneumonia.

Zoster (shingles)

- (1) It usually starts with severe pain in the area of skin or mucosa supplied by one or more groups of sensory nerves & ganglia.

- (2) Crop of vesicles appears over the skin supplied by the affected nerves. Trunk, head, & neck are most commonly affected, with the ophthalmic division of trigeminal nerve involved in 10–15% of cases.
- (3) Complications → Postherpetic neuralgia, pneumonia.

DIAGNOSTIC LABORATORY TESTS**Cytopathology**

- (1) Stained smears of scrapings or swabs of the base of vesicles (Tzanck smear) → Multinucleated giant cells.
- (2) Intracellular viral antigens can be demonstrated by immunofluorescence staining of similar smears.

Isolation & identification of virus

- (1) Virus-specific antigens or viral DNA can be detected in vesicle fluid, skin scrapings, or biopsy material.
- (3) Virus can be isolated from vesicle fluid early in the course of illness using cultures of human cells in 3–7 days.

Polymerase chain reaction (PCR)

PCR amplification of viral DNA can detect virus in air samples from hospital rooms of patients with active varicella (82%) & zoster (70%) infections.

Serology

Rise in specific antibody titer can be detected in the patient's serum by various tests, eg fluorescent antibody & enzyme immunoassay.

IMMUNITY

- (1) Previous infection with varicella confers lifelong immunity. Antibodies induced by varicella vaccine persist for at least 20 years.
- (2) Development of varicella-zoster virus-specific cell-mediated immunity is important in recovery from both varicella & zoster.

TREATMENT

- (1) Mild varicella requires no treatment.
- (2) Varicella-zoster immune globulin can be used prophylactically in patients exposed to varicella

who are at high risk of developing severe disease.

- (3) Antiviral drugs → Acyclovir, valacyclovir, famciclovir, & foscarnet.

PREVENTION & CONTROL

- (1) Live attenuated varicella vaccine is available.
 (2) Shingles vaccine is a more potent version of the varicella vaccine.

CYTOMEGALOVIRUS

Properties of the virus

- (1) Possess largest genetic content of the human herpesviruses.
- (2) Encoded over 200 proteins, including a cell surface glycoprotein which acts as an Fc receptor that binds the Fc portion of immunoglobulins. This may help infected cells evade immune elimination by providing a protective coating of irrelevant host immunoglobulins.
- (3) Replicates in vitro only in human fibroblasts very slowly.
- (4) Produces characteristic perinuclear cytoplasmic inclusions, in addition to the intranuclear inclusions typical of herpesviruses. Multinucleated cells are also seen.

HABITAT & TRANSMISSION

Habitat

Humans are the only known host.

Transmission

- (1) Close person-to-person contact. Virus may be shed in urine, saliva, semen, breast milk & cervical secretions, & is carried in circulating WBCs.
- (2) Also spreads transplacentally, & by blood transfusion, organ transplantation & sexual contact.

Note: CMV is endemic in all parts of the world.

PATHOGENESIS & CLINICAL FINDINGS

Pathogenesis

- (1) Incubation period is 4-8 weeks.
- (2) Causes systemic infection involving lung, liver, esophagus, colon, kidneys, monocytes, & T & B lymphocytes.
- (3) Causes lifelong latent infections like all herpesviruses.
- (4) Cell-mediated immunity is depressed with primary infections, & this may contribute to the persistence of viral infection.

Clinical Findings

Normal hosts

- (1) Primary infection is usually asymptomatic but occasionally causes a spontaneous infectious mononucleosis syndrome. The disease is characterized by malaise, myalgia, fever, liver function abnormalities, & lymphocytosis. .
- (2) Subclinical hepatitis & hepatosplenomegaly can occur.
- (3) Restenosis following coronary angioplasty.

Immunocompromised hosts

- (1) Pneumonia & interstitial pneumonitis can occur.
- (2) Virus-associated leukopenia is common in solid organ transplant recipients; also seen are obliterative bronchiolitis in lung transplants, graft atherosclerosis in heart transplants, & CMV-related rejection of renal allografts.
- (3) Disseminated disease seen in untreated AIDS patients, esp. gastroenteritis & chorioretinitis.

Congenital & perinatal infections

- (1) Death of the fetus in utero.
- (2) Cytomegalic inclusion disease of newborns characterized by involvement of CNS & reticuloendothelial system.
 - (a) Clinical features include intrauterine growth retardation, jaundice, hepatosplenomegaly, thrombocytopenia, microcephaly, & retinitis.
 - (b) Mortality rates are about 20%.
 - (c) Majority of survivors will develop significant CNS defects within 2 years, eg severe hearing loss, ocular abnormalities, & mental retardation are common.
- (3) Infants may become infected at the time of delivery thru infected birth canal. They continue to excrete the virus for several years but remain healthy.

(4) Isolated pneumonia in infants < 6 months age.

DIAGNOSTIC LABORATORY TESTS

PCR & antigen detection assays

- (1) PCR assay is used for routine detection of CMV infections. It detect replicating virus, not latent viral genomes. Blood & urine are most commonly tested.
- (2) Monoclonal antibodies against viral antigens can be used to detect virus-positive leukocytes from patients.

Isolation of virus

- (1) Human fibroblasts are used for virus isolation. The virus can be recovered most readily from throat washings & urine.
- (2) In cultures, 2–3 weeks are needed for the appearance of cytologic changes, consisting of small foci of swollen, translucent cells with large intranuclear inclusions.

Serology

- (1) CMV IgG antibodies indicate past infection.
- (2) Viral IgM antibodies suggest current infection.

IMMUNITY

- (1) CMV-specific antibodies of IgM, IgA, & IgG classes have all been detected.
- (2) Reactivation of latent infection occurs in the presence of humoral immunity.
- (3) Presence of antibody in breast milk does not prevent transmission of infection to breast-feeding infants. It protects against development of serious disease.

TREATMENT

- (1) Ganciclovir is used to treat life-threatening CMV infections in immunosuppressed patients.
- (2) Foscarnet is used for CMV retinitis.
- (3) Acyclovir & valacyclovir (in bone marrow & renal transplant patients).

PREVENTION & CONTROL

- (1) Specific control measures are not available to prevent CMV spread.

- (2) Isolation of newborns with generalized cytomegalic inclusion disease from other newborns is advisable.
- (3) Screening of transplant donors & recipients for CMV antibody may prevent transmissions of primary cytomegalovirus.
- (4) Use of blood from seronegative donors.
- (5) Both live & recombinant CMV vaccines are under development.

EPSTEIN-BARR VIRUS

Properties of the virus

- (1) EBV DNA genome contains about 172 kbp, has a G + C content of 59%, & encodes about 100 genes.
- (2) Two types → EBV-1 & EBV-2, based on differences in the latency nuclear antigen genes (EBNAs, EBERs).
- (3) **Viral antigens**
 - (a) Latent phase antigens synthesized by latently infected cells (EBNAs & LMPs).
 - (b) Early antigens are nonstructural proteins whose synthesis is not dependent on viral DNA replication. It indicates the onset of viral replication.
 - (c) Late antigens are the structural components of the viral capsid (viral capsid antigen) & viral envelope (glycoproteins). They are produced abundantly in cells undergoing productive viral infection.

HABITAT & TRANSMISSION

Habitat

EBV is common in all parts of the world, with over 90% of adults being seropositive.

Transmission

Mainly by contact with oropharyngeal secretions.

PATHOGENESIS & CLINICAL FINDINGS

Pathogenesis

- (1) EBV initiates infection of B cells by binding to the viral receptor (CR2 or CD21) → Enters a

latent state in the lymphocyte without undergoing replication.

Note: EBV-immortalized B lymphocytes express immunoglobulins & B cell activation products (eg, CD23). At least 10 viral gene products are expressed including 6 EBV nuclear antigens, 2 latent membrane proteins & 2 small untranslated RNAs.

- (2) EBV genome activated to replicate in a cell by various stimuli, eg chemical inducing agents or cross-linking cell surface immunoglobulin.
- (3) EBV can replicate in vivo in epithelial cells of the oropharynx, parotid gland, & uterine cervix
- (4) Infected B cells spread the infection from the oropharynx thru-out the body.
- (5) Small numbers of latently infected lymphocytes persist for the lifetime of the host.

Clinical Findings

Most primary infections in children are asymptomatic. In adolescents & young adults, it causes classic infectious mononucleosis syndrome.

Infectious mononucleosis

- (1) Incubation period is 30–50 days.
- (2) Headache, fever, malaise, fatigue, & sore throat.
- (3) Enlarged lymph nodes & splenomegaly.
- (4) Hepatitis.

Cancer

- (1) Oral hairy leukoplakia → Wart-like growth on the tongue.
- (2) Burkitt's lymphoma → A tumor of the jaw in African children & young adults.
- (3) Nasopharyngeal carcinoma → Common in Chinese males.
- (4) Lymphoproliferative diseases in immunodeficient hosts → Polyclonal B cell proliferations, aggressive monoclonal B cell lymphomas.
- (5) Non-Hodgkin's lymphomas.
- (6) Hodgkin's disease.

DIAGNOSTIC LABORATORY TESTS

Isolation & identification of virus

- (1) Nucleic acid hybridization detects EBV in patient materials. EBER RNAs are abundantly expressed in both latently infected & lytically

infected cells, acting as a diagnostic target for detection of EBV-infected cells by hybridization.

- (2) Viral antigens can be demonstrated directly in lymphoid tissues & in nasopharyngeal carcinomas.
- (3) EBV can be isolated from saliva, peripheral blood, or lymphoid tissue by immortalization of normal human lymphocytes, usually obtained from umbilical cord blood.

Serology

- (1) Common serologic procedures include ELISA tests, immunoblot assays, & indirect immunofluorescence tests using EBV-positive lymphoid cells.
 - (a) Early in acute disease, a transient rise in IgM antibodies to viral capsid antigen occurs, replaced within weeks by IgG antibodies, which persist for life.
 - (b) Slightly later, antibodies to the early antigen develop that persist for several months.
 - (c) Several weeks after acute infection, antibodies to EBNA & the membrane antigen arise & persist thru- life.
- (2) Heterophil agglutination test → During infectious mononucleosis, most patients develop transient heterophil antibodies that agglutinate sheep cells.

IMMUNITY

- (1) EBV infections elicit an intense immune response consisting of antibodies against many virus-specific proteins, a number of cell-mediated responses, & secretion of lymphokines.
- (2) Cell-mediated immunity & cytotoxic T cells are important in limiting primary infections & controlling chronic infections.

TREATMENT

- (1) No antiviral drug is needed for uncomplicated infectious mononucleosis.
- (2) Acyclovir in life-threatening EBV infections.

PREVENTION, TREATMENT, & CONTROL

There is no EBV vaccine available.

-

Chapter 30

RNA Enveloped Viruses

TOGAVIRUS & FLAVIVIRUS

Classification & Properties

Togaviridae family

Alphavirus genus

- (1) Consists of about 30 viruses 70 nm in diameter that have a single-stranded, positive-sense RNA genome.
- (2) The envelope surrounding the particle contains two glycoproteins.
- (3) Often establish persistent infections in mosquitoes & are transmitted between vertebrates by mosquitoes or other blood-feeding arthropods.
- (4) They have a worldwide distribution.
- (5) All alphaviruses are antigenically related.
 - (a) HI, ELISA, & IF tests define eight antigenic complexes or serogroups.
 - (b) Identification of a specific virus can be made using Nt tests.
- (6) Inactivated by acid pH, heat, lipid solvents, detergents, bleach, phenol, 70% alcohol, & formaldehyde.
- (7) Most possess hemagglutinating ability.

Flaviviridae family

Flavivirus genus

- (1) Consists of about 70 viruses 40–60 nm in diameter that have a single-stranded, positive-sense RNA genome.
- (2) The viral envelope contains two glycoproteins.
- (3) Some are transmitted between vertebrates by mosquitoes & ticks, whereas others are transmitted among rodents or bats without any known insect vectors.

- (4) Many have worldwide distribution.
- (5) All flaviviruses are antigenically related.
 - (a) Nt tests identified at least eight antigenic complexes.
 - (b) Envelope (E) protein is the viral hemagglutinin & contains the group-, serocomplex-, & type-specific determinants.
- (6) Flaviviruses are inactivated similarly to alphaviruses.
- (7) Also exhibit hemagglutinating ability.

Habitat & Transmission

Habitat

In highly endemic areas, almost the entire human population may become infected with an arbovirus (mostly asymptomatic).

Transmission

Thru the bite of an infected female arthropod vector.

Pathogenesis & Clinical Findings

Pathogenesis

- (1) In susceptible vertebrate hosts, primary viral multiplication occurs either in myeloid & lymphoid cells or in vascular endothelium.
- (2) Viremia persists for several days, & arthropod vectors acquire the virus by sucking blood during this period.
- (3) Arthropod vector then causes subcutaneous inoculation, when they bite the susceptible host.
- (4) Virus replication occurs in local tissues & regional lymph nodes. Virus then enters the bloodstream & is disseminated.
- (5) Different viral agents cause virus replication in different tissues including monocyte-

- macrophages, endothelial cells, lung, liver, & muscles.
- (6) Virus crosses the blood-brain barrier & spreads. Widespread neuronal degeneration occurs in all arbovirus-induced encephalitides.
 - (7) In majority of cases, the virus is controlled before neuroinvasion occurs. Humans show an age-dependent susceptibility to CNS infections, with infants & the elderly being most susceptible.

Clinical findings

Encephalitis

- (1) Incubation period is 4 to 21 days.
- (2) Inapparent infections are common.
- (3) Some infected persons develop mild flu-like illness, whereas others develop encephalitis.
 - (a) Sudden onset with severe headache, chills, fever, nausea, vomiting, generalized pains, & malaise.
 - (b) Within 24–48 hours, marked drowsiness develops & the patient may become stuporous.
 - (c) Mental confusion, tremors, convulsions, & coma develop in severe cases.

Diagnostic Laboratory Tests

Recovery of virus & direct detection

- (1) Virus can be recovered from the blood (early), & CSF & tissue specimens (late).
- (2) Both alphaviruses & flaviviruses are able to grow in common cell lines, eg Vero, BHK, HeLa, & MRC-5.
 - (a) Mosquito cell lines are useful.
 - (b) Intracerebral inoculation of suckling mice or hamsters may also be used.
- (3) Antigen detection & PCR assays provide direct detection of viral RNA or proteins.
- (4) Virus-specific monoclonal antibodies in immunofluorescence assays results in rapid virus identification.

Serology

- (1) Neutralizing & hemagglutination-inhibiting antibodies are detectable within a few days after the onset of illness.
- (2) HI test identifies the group rather than the specific causative virus.
- (3) Virus-specific IgM in serum or CSF by ELISA is the most sensitive serologic assays.

- (4) It is necessary to establish a fourfold or greater rise in specific antibodies during infection to confirm a diagnosis.

Note: Cross-reactivity within the alphavirus or flavivirus group must be considered in making the diagnosis.

Immunity

- (1) Immunity is permanent after a single infection. Both humoral antibody & cellular immune responses are plays role in protection & recovery from infection. In endemic areas, the population may build up immunity as a result of inapparent infections.
- (2) Because of common antigens, the immune response with one virus of a group may be modified by prior exposure to another member of the same group.

YELLOW FEVER VIRUS

Properties of Virus

- (1) Based on sequence analysis, 7 genotypes are identified (5 in Africa & 2 in South America). There is a single serotype.
- (2) Virus multiplies in many different types of animals & in mosquitoes, & grows in embryonated eggs, chick embryo cell cultures, & cell lines, including those of monkey, human, hamster, & mosquito origin.

Habitat & Transmission

Habitat

- (1) Urban yellow fever is endemic in the western hemisphere & West Africa.
- (2) Jungle yellow fever is endemic in South America & Africa.

Transmission

- (1) Urban yellow fever involves person-to-person transmission by domestic Aedes mosquitoes (mainly Aedes aegypti).
- (2) Jungle yellow fever is primarily a disease of monkeys. It is transmitted from monkey to monkey by arboreal mosquitoes (ie, Haemagogus, Aedes). Persons involved in forest clearing activities can become infected.

Pathogenesis & Clinical Findings**Pathogenesis**

Virus enters via a mosquito bite → Multiplies in the skin → Spreads to regional lymph nodes, liver, spleen, kidney, bone marrow, & myocardium, where it may persist for days → Infections may result in necrotic lesions in the liver, kidney, spleen, lymph nodes, & heart.

Note: Virus is present in blood early during infection.

Clinical findings (yellow fever)

- (1) Incubation period is 3–6 days.
- (2) Abrupt onset of fever, chills, headache, dizziness, myalgia, & backache.
- (3) Nausea, vomiting, & bradycardia.
- (4) In about 15% of cases, the disease progresses to a more severe form, with fever, jaundice, renal failure, & hemorrhagic manifestations.
- (5) Complications → Hepato-renal failure, encephalitis, death.

Note: Infection may be so mild as to go unnoticed; patients either die or recover completely.

Diagnostic Laboratory Tests**Virus detection or isolation**

- (1) Virus may be recovered from the blood the first 4 days after onset, or from postmortem tissue by intracerebral inoculation of mice or by use of cell lines.
- (2) Virus antigen or nucleic acid can be identified in tissue specimens using immunohistochemistry, ELISA antigen capture, or PCR.

Serology

- (1) IgM antibodies appear during the first week of illness. This provides a presumptive diagnosis.
- (2) Diagnosis is confirmed by a fourfold or greater rise in titer of neutralizing antibody between acute phase & convalescent phase serum samples.

Immunity

Neutralizing antibodies develop in about a week of illness & are responsible for viral clearance. Neutralizing antibodies endure for life & provide complete protection from disease.

Treatment

There is no antiviral drug therapy.

Prevention & Control

- (1) Vigorous mosquito control programs can help eliminating the vector & eradicating the disease.
- (2) Proper mosquito control on airplanes & vaccination of all persons at least 10 days before arrival in or from an endemic zone.
- (3) 17D strain of yellow fever virus is an excellent attenuated live-virus vaccine. A single dose produces immunity for at least 30 years.

DENGUE VIRUS (DENV)**Properties of Virus**

- (1) Single positive-stranded RNA virus of the family flaviviridae, genus flavivirus.
- (2) Its genome encodes 3 structural proteins (capsid protein C, membrane protein M, envelope protein E), & 7 nonstructural proteins (NS1, NS2a, NS2b, NS3, NS4a, NS4b, NS5).

Habitat & Transmission**Habitat**

- (1) Dengue viruses are distributed worldwide. Most subtropical & tropical regions where Aedes vectors exist are endemic areas.
- (2) Dengue outbreak often starts during the rainy season, when the vector mosquito is abundant, as post-monsoon hot & humid climate favours its breeding. It breeds in relatively clean rain & stagnant water in drains, pots, buckets, cans & trays of potted plants.

Transmission

Transmitted between humans by female mosquitoes of genus Aedes, principally Aedes aegypti & Aedes albopictus.

Pathogenesis & Clinical Findings**Pathogenesis**

- (1) Hemorrhagic manifestations may be due to vasculopathy, thrombocytopenia, & coagulopathy.
- (2) Plasma leakage & serous effusion with high protein content (mostly albumin) occur in DHF → Ascitis, pleural effusion, & edematous &

inflammatory changes in tissues eg liver, gallbladder, appendix, pancreas & scrotum.

- (3) DSS involves preexisting dengue antibody, eg secondary infection with 2nd serotype following primary infection → Virus-antibody complexes are formed within a few days → Mononuclear release cytokines, vasoactive mediators, & procoagulants leading to the disseminated intravascular coagulation.

Clinical findings

- (1) Incubation period is 4–7 days.
- (2) Dengue infection may be asymptomatic or present as dengue fever (DF), dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS).
- (3) DF is characterized by fever, platelet count 100 000/mm³ & hemorrhagic manifestations.
 - (a) Associated features are myalgias, deep bone pain (breakbone fever), arthralgia, retro-orbital pain, headache, & rash.
 - (b) Hemorrhagic manifestations may include positive tourniquet test, petechiae, ecchymoses, purpura, mucosal bleeding, hematemesis, melena or surgical wound bleeding.
 - (c) DF is usually self-limiting, but it can lead to DHF/DSS.
- (4) DHF is characterized by 'objective evidence of plasma leakage' manifested by: elevated hematocrit (20% over baseline or a similar drop after intravenous fluid replacement), pleural effusion or ascites, or low protein.
- (5) DSS is a severe form of DHF, characterized by severe abdominal pain, hypothermia, restlessness, sweating, prostration & tender hepatomegaly. Recovery from adequately treated DSS is uneventful & survivors recover within 2 to 5 days.
- (6) Atypical manifestations → Hepatitis, encephalopathy, cardiomyopathy, glomerulonephritis, acute pancreatitis, acute appendicitis & acute cholecystitis.

Diagnostic Laboratory Tests

- (1) Reverse transcriptase-PCR results in rapid identification & serotyping of dengue virus in acute-phase serum.
- (2) Isolation of virus requires inoculation of a mosquito cell line with patient serum, coupled

with nucleic acid assays to identify a recovered virus.

- (3) Serological techniques include;
- (a) Enzyme linked immunosorbent assay (ELISA).
 - (b) Immunochromatographic test (ICT) using dengue IgG/IgM rapid test kit.
 - (c) Hemagglutination inhibition.
 - (d) Complement fixation.
 - (e) Dot-blot immunoassays.
 - (f) Neutralization (neutralizing & hemagglutination inhibiting antibodies appear within a week after onset of DF).
- (4) Blood testss → Thrombocytopenia, leucopenia, hemoconcentration & increased aminotransferase levels.

Immunity

- (1) Four serotypes of the virus (DEN1 to DEN4) exist. Infection confers lifelong protection against that serotype, but cross-protection between serotypes is of short duration.
- (2) Reinfection with a virus of a different serotype after the primary attack is more apt to result in severe disease (DHF/DSS).

Treatment

- (1) There is no antiviral drug therapy.
- (2) Symptomatic treatment is required for pain, fever & nausea/vomiting.
- (3) DHF can be treated by fluid replacement therapy.
- (4) Bleeding manifestations required transfusions of packed-RBCs, FFP &/or platelets

Note: Aspirin, NSAIDs & antibiotics should be avoided.

Prevention & Control

- (1) Control depends upon antimosquito measures, eg, elimination of breeding places & the use of insecticides.
- (2) Screened windows & doors can reduce exposure to the vectors.

ORTHOMYXOVIRUSES

Properties of Virus

- (1) 3 immunologic types → A, B, & C.
 - (a) Antigenic changes continually occur in type A & to a lesser degree in type B, whereas type C is antigenically stable.
 - (b) Influenza A strains are also known for aquatic birds, chickens, ducks, pigs, horses, & seals.
- (2) Virion → Spherical, pleomorphic, 80–120 nm in diameter (helical nucleocapsid, 9 nm).
- (3) Composition → RNA (1%), protein (73%), lipid (20%), carbohydrate (6%).
- (4) Genome → Single-stranded RNA.
- (5) Proteins → Nine structural proteins, one nonstructural. Antigenic differences exhibited by 2 structural proteins, the nucleocapsid (NP) & matrix (M) proteins, divide influenza viruses into types A, B, & C.
- (6) Envelope → Contains viral hemagglutinin (HA) & neuraminidase (NA) proteins.
 - (a) Antigenic variations in HA & NA, are used to subtype the viruses.
 - (b) HA protein binds virus particles to susceptible cells & is the major antigen against which neutralizing (protective) antibodies are directed.
 - (c) NA (a sialidase enzyme) facilitates release of virus particles from infected cell surfaces during the budding process & helps prevent self-aggregation of virions by removing sialic acid residues from viral glycoproteins.
 - (d) NA helps the virus negotiate through the mucin layer in the respiratory tract to reach the target epithelial cells.
- (7) Replication → Nuclear transcription; particles mature by budding from plasma membrane.

Habitat & Transmission**Habitat**

- (1) Influenza viruses occur worldwide & cause annual outbreaks of variable intensity.
- (2) Influenza C is least significant; it causes mild, sporadic respiratory disease but not epidemic influenza. Influenza B sometimes causes epidemics, but influenza type A can sweep across continents & around the world in massive epidemics called pandemics.
- (3) Incidence of influenza peaks during the winter.

Transmission

Spreads from person to person by airborne droplets or by contact with contaminated hands or surfaces.

Pathogenesis & Clinical Findings**Pathogenesis**

- (1) Initially a few cells of respiratory epithelium are infected if deposited virus particles escape immune mechanisms → Progeny virions are soon produced & spread to adjacent cells → Viral NA lowers the viscosity of the mucous film, laying bare the cellular surface receptors & promoting the spread of virus to lower portions of the tract → Cellular destruction & desquamation of superficial mucosa of the respiratory tract.
- (2) Viral damage to the respiratory tract epithelium lowers its resistance to secondary bacterial invaders, esp. staphylococci, streptococci, & Hemophilus influenzae.
- (3) Edema & mononuclear infiltrations in response to cell death.

Clinical findings

Incubation period varies from 1 day to 4 days.

Uncomplicated (classic) influenza

- (1) Sudden onset of chills, headache, & dry cough, followed by high fever, generalized muscular aches, malaise, & anorexia. Fever usually lasts 3-5 days, respiratory symptoms last another 3-4 days, & cough & weakness may persist for 2-4 weeks.
- (2) These symptoms may be caused by any strain of influenza A or B, whereas influenza C causes a common cold illness.

Pneumonia

- (1) Usually occur in the elderly & debilitated, & also in pregnancy.
- (2) It can be viral, secondary bacterial, or a combination of the two.

Reye's syndrome

This is an acute encephalopathy of children & adolescents.

Diagnostic Laboratory Tests**Isolation & identification of virus**

- (1) Nasal washings, gargles, & throat swabs can be used for viral isolation (within 3 days of onset).
- (2) Embryonated eggs & primary monkey kidney cells are used for viral isolation. Inoculated cell

cultures are incubated in the absence of serum, & in the presence of trypsin, which cleaves & activates the HA so that replicating virus will spread thru-ut the culture.

- (3) Cell cultures tested for the presence of virus by hemadsorption 3-5 days after inoculation, or the culture fluid can be examined for virus after 5-7 days by hemagglutination.
- (4) For rapid diagnosis, cell cultures may be inoculated & stained 1 or 2 days later with pools of monoclonal antibodies to respiratory agents. Positives are confirmed by use of single fluorescent antibodies.
- (5) Viral antigen can be identified directly in exfoliated cells in nasal aspirates using fluorescent antibodies.
- (6) Polymerase chain reaction can be used for rapid diagnosis.
- (7) Reverse-transcription polymerase chain reaction detects avian influenza A/H5 viruses.

Serology

- (1) Antibodies to several viral proteins (hemagglutinin, neuraminidase, nucleoprotein, & matrix) are produced during infection.
- (2) Routine serodiagnostic tests are based on hemagglutination inhibition (HI) & ELISA. A fourfold or greater increase in titer must occur to indicate influenza infection.

Immunity

- (1) Immunity to influenza is long-lived & subtype-specific.
- (2) Antibodies against HA & NA are important in immunity.
 - (a) Resistance to initiation of infection is related to antibody against the HA.
 - (b) Decreased severity of disease & decreased ability to transmit virus to contacts are related to antibody directed against the NA.
 - (c) Protection correlates with both serum antibodies & secretory IgA antibodies in nasal secretions.
- (3) Cell-mediated immune responses allow clearance of an established infection, eg cytotoxic T cells lyse infected cells.

Treatment

- (1) Amantadine & rimantadine (M_2 ion channel inhibitors) used for the treatment & prophylaxis of influenza A.
- (2) Zanamivir & oseltamivir (NA inhibitors) used for the treatment of both influenza A & B.

Prevention & Control

- (1) Inactivated viral vaccines are the primary means of prevention of influenza.
 - (a) Vaccine is usually a cocktail containing one or two type A viruses & a type B virus of the strains isolated in the previous winter's outbreaks.
 - (b) Vaccines are either whole virus (WV), subvirion (SV), or surface antigen preparations. All are efficacious.
- (2) Attenuated live, trivalent influenza virus vaccine administered by nasal spray.
- (3) Annual influenza vaccination is recommended for high-risk groups. These include patients with chronic heart or lung disease, children with asthma or metabolic or renal disorders, residents of nursing homes, AIDS patients, older persons (65 years or above), & persons who might transmit influenza to high-risk groups (medical personnel, employees in chronic care facilities, household members).

PARAMYXOVIRUSES

Properties of Virus

- (1) Virion → Spherical, pleomorphic, 150 nm or more in diameter (helical nucleocapsid, 13–18 nm).
- (2) Composition → RNA (1%), protein (73%), lipid (20%), carbohydrate (6%) .
- (3) Genome → Single-stranded RNA.
- (4) Proteins → Six to eight structural proteins.
- (5) Envelope → Contains viral glycoprotein (F, G, H, or HN).
- (6) Replication → Cytoplasm; particles bud from plasma membrane.
- (7) Outstanding characteristics → Antigenically stable, & particles are labile yet highly infectious

Classification

- (1) Genus respirovirus → Contains 2 serotypes of human parainfluenza viruses.
- (2) Genus rubulavirus → Contains 2 other parainfluenza viruses, as well as mumps virus.
- (3) Genus avulavirus → Contains avian parainfluenza virus.
- (4) Genus morbillivirus → Contains measles virus (rubeola).
- (5) Genus henipavirus → Contains zoonotic viruses that can infect humans.
- (6) Genus pneumovirus → Contains respiratory syncytial viruses.
- (7) Genus metapneumovirus → Contains newly recognized respiratory pathogens.

- (c) Infection may spread deeper to the lower trachea & bronchi, resulting in pneumonia or bronchiolitis, esp. with type 3.
- (2) Production of virus-specific IgE antibodies during primary infections is associated with disease severity. This causes release of mediators which alter airway function.

Clinical findings

- (1) Incubation period is 5-6 days.
- (2) Primary infections in young children result in rhinitis & pharyngitis, often with fever & some bronchitis.
- (3) Laryngotracheitis & croup.
- (4) Bronchiolitis & pneumonia.
- (5) Complication → Otitis media.

PARAINFLUENZA VIRUS

Cause common respiratory illnesses in persons of all ages.

Habitat & Transmission

Habitat

- (1) Parainfluenza viruses are widely distributed geographically.
- (2) Type 3 is most prevalent, with about two-thirds of infants infected during the first year of life. Type 1 & 2 infections occur at a lower rate, reaching prevalences of about 75% & 60%, respectively, by 5 years of age.
- (3) Type 3 is endemic, with some increase during the spring, whereas types 1 & 2 cause epidemics during the fall or winter.

Transmission

Transmitted by direct person-to-person contact or by large-droplet aerosols. Infections can occur through both the nose & the eyes.

Pathogenesis & Clinical Findings

Pathogenesis

- (1) Parainfluenza virus replication is limited to respiratory epithelia.
 - (a) Infection may involve only the nose & throat, resulting in "common cold" syndrome.
 - (b) Infection may be more extensive esp. with types 1 & 2, & may involve the larynx & upper trachea, resulting in croup (laryngotracheobronchitis).

Diagnostic Laboratory Tests

Antigen detection

Antigens may be detected in exfoliated nasopharyngeal cells by direct or indirect immunofluorescence tests.

Isolation & identification of virus

- (1) Specimens → Nasal washes, bronchoalveolar lavage fluid & lung tissue.
- (2) Primary monkey kidney cells or a continuous monkey kidney cell line (LLC-MK₂) can be used for inoculation of samples.
- (3) For rapid diagnosis, the cells are fixed & tested by immunofluorescence using monoclonal antibodies.
- (4) Viruses can also be detected by hemadsorption test using guinea pig erythrocytes.

Serology

- (1) Antibody responses can be measured using Nt, HI, or ELISA tests.
- (2) A fourfold rise in titer is indicative of infection, as is the appearance of specific IgM antibody.

Nucleic acid detection

Polymerase chain reaction assays are only used in research settings.

Immunity

- (1) Parainfluenza virus types 1-3 are distinct serotypes that lack significant cross-neutralization.
- (2) Natural infection stimulates appearance of IgA antibody in nasal secretions & concomitant resistance to reinfection. IgA antibodies are

important in providing protection against reinfection but disappear within a few months. Reinfections are thus common even in adults.

Treatment

- (1) Symptomatic treatment.
- (2) Ribavirin can be used in immunocompromised patients with lower respiratory tract disease.

Prevention & Control

- (1) Contact isolation precautions are necessary to manage nosocomial outbreaks. These include restriction of visitors, isolation of infected patients, & gowning & hand washing by medical personnel.
- (2) Both subunit vaccines & a live attenuated type 3 virus vaccine are under trial.

RESPIRATORY SYNCYTIAL VIRUS (RSV)

Habitat & Transmission

Habitat

RSV is distributed worldwide & is recognized as the major pediatric respiratory tract pathogen.

Transmission

- (1) RSV spreads by large droplets & direct contact.
- (2) It can survive on environmental surfaces for up to 6 hours.
- (3) Main portal of entry is thru the nose & eyes.
- (4) Spreads extensively occur in children every year during the winter & rainy seasons.

Pathogenesis & Clinical Findings

Pathogenesis

- (1) RSV replication occurs initially in epithelial cells of the nasopharynx → Virus may spread into the lower respiratory tract & cause bronchiolitis & pneumonia.
- (2) There is lymphocyte migration, resulting in peribronchiolar infiltration → Submucosal tissues become edematous, & plugs consisting of mucus, cellular debris & fibrin occlude the smaller bronchioles.
- (3) Patients with impaired cell-mediated immunity may become persistently infected with RSV & shed virus for months.

Clinical findings

- (1) Incubation period is 3-5 days.

- (2) Inapparent infection or common cold.
- (3) Pneumonia.
- (4) Bronchiolitis (with wheezing).
- (5) Otitis media.

Diagnostic Laboratory Tests

Antigen detection

Immunofluorescence on exfoliated cells or ELISA on nasopharyngeal secretions is commonly used.

Isolation & identification of virus

- (1) RSV can be isolated from nasal secretions. It is extremely labile, & samples should be inoculated into cell cultures immediately.
- (2) Human heteroploid cell lines HeLa & HEp-2 are inoculated → Development of giant cells & syncytia in inoculated cultures in about 10 days.
- (3) Definitive diagnosis made by detecting viral antigen in infected cells using a defined antiserum & immunofluorescence test.

Serology

Serum antibodies can be assayed via immunofluorescence, ELISA, & Nt tests.

Nucleic acid detection

Polymerase chain reaction.

Immunity

- (1) High levels of neutralizing antibody that is maternally transmitted & present during the first several months of life are important in providing immunity against lower respiratory tract illness.
- (2) Primary infection & reinfection can occur in the presence of viral antibodies.
- (3) Both serum & secretory antibodies are produced in response to RSV infection.
- (4) Primary infection with one subgroup induces cross-reactive antibodies to virus of the other subgroup.
- (5) Cellular immunity is important in recovery from infection.

Treatment

- (1) Supportive care eg, removal of secretions, administration of oxygen.
- (2) Ribavirin aerosol.

Prevention & Control

- (1) Recombinant attenuated live-virus vaccines are in clinical trials.
- (2) Control measures are necessary during outbreaks, eg contact isolation, hand washing, & restriction of visitors.

MEASLES (RUBEOLA) VIRUS

Habitat & Transmission

Habitat

- (1) Measles is endemic throughout the world.
- (2) In industrialized countries, measles occurs in 5- to 10-year-old children, whereas in developing countries it commonly infects children under 5 years of age.
- (3) Epidemics tend to occur in late winter & early spring.

Transmission

- (1) Transmission occurs mainly via the respiratory route (inhalation of large droplets of infected secretions).
- (2) Hematogenous transplacental transmission can occur.

Pathogenesis & Clinical Findings

Pathogenesis

- (1) Virus gains access to the human body via the respiratory tract, where it multiplies locally → Infection then spreads to the regional lymphoid tissue, where further multiplication occurs → Primary viremia disseminates the virus, which then replicates in the reticuloendothelial system → Finally, a secondary viremia seeds the epithelial surfaces of the body, including the skin, respiratory tract, & conjunctiva, where focal replication occurs.
- (2) Rash develops as a result of interaction of T cells with virus-infected cells in the small blood vessels.

Clinical findings

- (1) After an incubation period of 8-12 days, measles is typically a 7-11 day illness (with a prodromal phase of 2-4 days followed by an eruptive phase of 5-8 days).
- (2) Prodromal phase is characterized by fever, sneezing, coughing, running nose, redness of the eyes, Koplik's spots, & lymphopenia. Koplik's spots (pathognomonic for measles) are

small, bluish-white ulcerations on the buccal mucosa opposite the lower molars.

- (3) Rash starts on the head & then spreads progressively to the chest, trunk, & down the limbs; it appears as light pink, discrete maculopapules that coalesce to form blotches, becoming brownish in 5-10 days. The fading rash resolves with desquamation.
- (4) Complications → Otitis media, pneumonia, acute encephalitis, acute disseminated encephalomyelitis, subacute sclerosing panencephalitis.

Diagnostic Laboratory Tests

Antigen detection

Measles antigens can be detected directly in epithelial cells in respiratory secretions & urine.

Isolation & identification of virus

- (1) Specimens → Nasopharyngeal & conjunctival swabs, blood samples, respiratory secretions, & urine.
- (2) Monkey or human kidney cells or a lymphoblastoid cell line (B95-a) are inoculated;
 - (a) Typical cytopathic effects (multinucleated giant cells containing both intranuclear & intracytoplasmic inclusion bodies) take 7-10 days to develop.
 - (b) Shell vial culture tests can detect measles antigens in the inoculated cultures in 2-3 days using fluorescent antibody staining.

Serology

- (1) Depends on a fourfold rise in antibody titer between acute-phase & convalescent-phase sera or on demonstration of measles-specific IgM antibody in a single serum specimen drawn between 1 & 2 weeks after the onset of rash.
- (2) ELISA, HI, & Nt tests can be used.

Immunity

- (1) There is only one antigenic type of measles virus.
- (2) Infection confers lifelong immunity.
- (3) Presence of humoral antibodies indicates immunity, whereas cellular immunity is essential for recovery & protection:

Treatment

Symptomatic treatment is required.

Prevention & Control

Attenuated live measles virus vaccine is available in combination with live attenuated rubella vaccine (MR) & live attenuated rubella and mumps vaccines (MMR).

MUMPS VIRUS**Habitat & Transmission****Habitat**

- (1) Humans are the only natural hosts.
- (2) Mumps occurs endemically worldwide.
- (3) Cases appear throughout the year in hot climates, & peak in winter & spring in temperate climates.

Transmission

Transmitted by direct contact, airborne droplets, or fomites contaminated with saliva or urine.

Pathogenesis & Clinical Findings**Pathogenesis**

Primary replication occurs in nasal or upper respiratory tract epithelial cells → Viremia then disseminates the virus to the salivary glands & other major organ systems.

Clinical findings

- (1) Incubation period may range from 2-4 weeks, but is typically about 14-18 days.
- (2) Prodromal period of malaise & anorexia.
- (3) Rapid enlargement of parotid & other salivary glands, associated with pain.
- (4) Complications → Aseptic meningitis, Meningoencephalitis, orchitis, atrophy of testis, oophoritis, pancreatitis.

Diagnostic Laboratory Tests**Isolation & identification of virus**

- (1) Specimens → Saliva, CSF, urine.
- (2) Monkey kidney cells are inoculated with samples;
 - (a) Immunofluorescence using mumps-specific antiserum can detect mumps virus antigens as early as 2-3 days after the inoculation.
 - (b) Cytopathic effects typical of mumps virus consist of cell rounding & giant cell formation.

- (c) Mumps virus can be confirmed by hemadsorption inhibition using mumps-specific antiserum.

Serology

- (1) Using paired sera, a fourfold or greater rise in antibody titer is evidence of mumps infection.
- (2) ELISA or HI test is commonly used.

Immunity

- (1) There is only one antigenic type of mumps virus, & it does not exhibit antigenic variation.
- (2) Immunity is permanent after a single infection.
- (3) Antibodies against the HN antigen provide immunity.
- (4) Cell-mediated immune response also develops.
- (5) In immune individuals, IgA antibodies secreted in the nasopharynx exhibit neutralizing activity.
- (6) Passive immunity is transferred from mother to offspring, which is effective till 6 months of age.

Treatment

Symptomatic treatment is required.

Prevention & Control

- (1) Attenuated live-virus vaccine is available in combination with measles & rubella (MMR) live-virus vaccines.
- (2) Students & health care workers who acquire mumps illness should be excluded from school & work until 9 days after the onset of parotitis.

RUBELLA (GERMAN MEASLES) VIRUS**Habitat & Transmission****Habitat**

- (1) Rubella is worldwide in distribution.
- (2) Infection occurs thru-out the year with a peak incidence in the spring.

Transmission

Transmitted by the respiratory route, but rubella is not as contagious as measles.

Pathogenesis & Clinical Findings**Pathogenesis**

Virus enters thru the mucosa of upper respiratory tract → Initial viral replication occurs in the respiratory tract, followed by multiplication in the cervical lymph nodes → Viremia develops after 7-9 days & lasts until the appearance of antibody & rash on about day 13-15.

Clinical findings

- (1) Malaise & low-grade fever.
- (2) Morbilliform rash starting on the face, & extends over the trunk & extremities.
- (3) Complications → Arthritis, thrombocytopenic purpura, encephalitis.

Congenital rubella syndrome

- (1) Maternal viremia associated with rubella infection during pregnancy may result in infection of the placenta & fetus.
- (2) Infection may lead to deranged & hypoplastic organ development, resulting in structural anomalies in the newborn.
- (3) Infection during the first trimester results in fetal abnormalities in about 85% of cases, whereas fetal defects occur in about 16% if infection occurs during the second trimester.
- (4) Fetal death & spontaneous abortion can occur.
- (5) Classic triad of congenital rubella consists of cataracts, cardiac abnormalities, & deafness. Infants may also have growth retardation, rash, hepatosplenomegaly, jaundice, meningo-encephalitis, & mental retardation.

Diagnostic Laboratory Tests

Isolation & identification of virus

- (1) Specimens → Nasopharyngeal or throat swabs.
- (2) Various cell lines of monkey or rabbit origin may be inoculated.
 - (a) Inconspicuous cytopathic effect in most cell lines.
 - (b) Viral antigens can be detected by immunofluorescence.

Serology

- (1) A rise in antibody titer between two serum samples (taken 10 days apart) or detection of rubella-specific IgM indicates rubella infection.
- (2) ELISA or HI test can be used.

Immunity

- (1) Initial antibody response consists mostly of IgM antibodies, which do not persist beyond 6

weeks. IgG rubella antibodies usually persist for life.

- (2) One attack of the disease confers lifelong immunity, as only one antigenic type of the virus exists.
- (3) Immune mothers transfer antibodies to their offspring, who are then protected for 4-6 months.

Treatment

Symptomatic treatment is required.

Prevention & Control

Attenuated live rubella vaccines is available as a single antigen or combined with measles & mumps vaccine.

RABIES

Properties of Virus

- (1) Virion → Bullet-shaped, 75 nm in diameter & 180 nm in length.
- (2) Composition → RNA (4%), protein (67%), lipid (26%), carbohydrate (3%).
- (3) Genome → Single-stranded RNA.
- (4) Proteins → Five major proteins; one is the envelope glycoprotein.
 - (a) There is a single serotype, but different viral strains that can be distinguished by epitopes in nucleoprotein & glycoprotein (recognized by monoclonal antibodies as well as by specific nucleotide sequences).
 - (b) G glycoprotein is a major factor in rabies virus neuroinvasiveness & pathogenicity.
- (5) Envelope → Present.
- (6) Replication → Cytoplasm; virions bud from plasma membrane.

Habitat & Transmission

Habitat

Rabies is enzootic in both wild & domestic animals (dogs, bats, raccoons, skunks & foxes).

Transmission

Spread to humans by bites of rabid animals or by contact with saliva from rabid animals.

Pathogenesis & Clinical Findings**Pathogenesis**

- (1) Rabies virus multiplies in muscle or connective tissue at the site of inoculation → Enters peripheral nerves at neuromuscular junctions & spreads up the nerves to CNS → It multiplies in CNS & causes progressive encephalitis → Virus then spreads thru peripheral nerves to the salivary glands & other tissues (pancreas, kidney, heart, retina, & cornea).
- (2) Rabies virus produces a specific eosinophilic cytoplasmic inclusion, the Negri body, in infected nerve cells. Negri bodies are filled with viral nucleocapsids.

Clinical findings**Acute, fulminant encephalitis**

- (1) Incubation period is usually 1-2 months but may range from 1 week to 19 years.
- (2) Prodromal phase, lasting 2-10 days, may show malaise, anorexia, headache, photophobia, nausea, vomiting, sore throat, fever, & an abnormal sensation around the wound site.
- (3) During the acute neurologic phase, lasting 2-7 days, patients show;
 - (a) Signs of neurological dysfunction such as nervousness, apprehension, hallucinations, & bizarre behavior.
 - (b) General sympathetic overactivity eg lacrimation, pupillary dilatation, increased salivation & perspiration.
 - (c) Hydrophobia (fear of water).
 - (d) On swallowing a painful spasm of the throat muscles.
- (4) Finally, convulsive seizures or coma & death occur (from respiratory paralysis).
- (5) Disease course is slower, with some patients surviving 30 days. Recovery & survival are extremely rare.

Diagnostic Laboratory Tests**Rabies antigens or nucleic acids**

- (1) Immunofluorescence or immunoperoxidase staining of biopsy specimen (usually taken from neck skin at the hairline) using antirabies monoclonal antibodies.
- (2) A definitive diagnosis is based on the finding of Negri bodies in the brain or the spinal cord. Negri bodies contain rabies virus antigens & can be demonstrated by immunofluorescence.

- (3) Reverse transcription-polymerase chain reaction testing can be used.

Viral isolation

- (1) Specimen is inoculated intracerebrally into suckling mice →
 - (a) Infection in mice results in encephalitis & death.
 - (b) CNS is examined for Negri bodies & rabies antigen.
- (2) Hamster & mouse cell lines can be inoculated for rapid (2-4 days) growth of rabies virus.
- (3) Isolated virus is identified by fluorescent antibody tests with specific antiserum.

Serology

- (1) Serum antibodies to rabies can be detected by immunofluorescence or Nt tests.
- (2) Antibodies in CSF are produced in rabies-infected individuals but not in response to vaccination.

Animal observation

- (1) All animals considered "rabid or suspected rabid" should be sacrificed immediately for laboratory examination of neural tissues.
- (2) Other animals should be held for observation for 10 days.
 - (a) If they show any signs of encephalitis, they should be killed humanely & the tissues examined.
 - (b) If they appear normal after 10 days, decisions must be made on an individual basis.

Immunity

- (1) There is only one antigenic type of rabies virus.
- (2) Survival after the onset of rabies symptoms is extremely rare.

Mechanism of action of rabies vaccine

Rabies virus first amplified in muscle near the site of inoculation until the conc. is sufficient to accomplish infection of CNS. If immunogenic vaccine or specific antibody can be administered promptly, virus replication can be depressed & virus can be prevented from invading CNS.

Treatment

There is no successful treatment, & the outcome is almost always fatal.

Prevention & Control

It is essential that individuals at high risk receive preventive immunization, & individuals be given postexposure prophylaxis.

Types of vaccines

- (1) Human diploid cell vaccine (HDCV)
- (2) Rabies vaccine, adsorbed (RVA)
- (3) Purified chick embryo cell vaccine (PCEC)
- (4) Nerve tissue vaccine
- (5) Duck embryo vaccine

Types of rabies antibody

- (1) Rabies immune globulin, human (HRIG)
- (2) Antirabies serum, equine

Preexposure prophylaxis

- (1) Indicated for high risk persons eg research & diagnostic laboratory workers, veterinarians, animal control & wildlife workers.
- (2) Goal is to attain a protective antibody level by means of vaccine administration prior to any exposure.

Postexposure prophylaxis

- (1) Immediate & thorough cleansing of all wounds with soap & water.
- (2) Administration of rabies immune globulin.
- (3) Vaccination regimen.

Chapter 37

Hepatitis Viruses

Characteristics of Hepatitis Viruses

Virus	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
Family	Picornaviridae	Hepadnaviridae	Flaviviridae	Unclassified	Unclassified
Genus	<i>Hepatitis A virus</i>	<i>Orthohepadnavirus</i>	<i>Hepacivirus</i>	<i>Deltavirus</i>	<i>Hepevirus</i>
Virion	27 nm, icosahedral	42 nm, spherical	60 nm, spherical	35 nm, spherical	30–32 nm, icosahedral
Envelope	No	Yes (HBsAg)	Yes	Yes (HBsAg)	No
Genome	ssRNA	dsDNA	ssRNA	ssRNA	ssRNA
Genome size	7.5 kb	3.2 kb	9.4 kb	1.7 kb	7.6 kb
Stability	Heat- & acid-stable	Acid-sensitive	Ether-sensitive, acid-sensitive	Acid-sensitive	Heat-stable
Transmission	Fecal-oral	Parenteral	Parenteral	Parenteral	Fecal-oral
Prevalence	High	High	Moderate	Low, regional	Regional
Fulminant disease	Rare	Rare	Rare	Frequent	In pregnancy
Chronic disease	Never	Often	Often	Often	Never
Oncogenic	No	Yes	Yes	?	No

PROPERTIES OF VIRUSES

Hepatitis A Virus

- (1) Genome consists of single-stranded RNA.
- (2) There is only one serotype.
- (3) There is no antigenic cross-reactivity with HBV or with other hepatitis viruses.
- (4) It is stable to treatment with 20% ether, acid (pH 1.0 for 2 hours), & heat (60°C for 1 hour), & its infectivity can be preserved for one month after being dried & stored at 25°C & 42% relative humidity or for years at -20°C.
- (5) It is destroyed by autoclaving (121°C for 20 minutes), by boiling in water for 5 minutes, by dry heat (180°C for 1 hour), by ultraviolet irradiation (1 minute at 1.1 watts), by treatment

with formalin (1:4000 for 3 days at 37°C), or by treatment with chlorine (10-15 ppm for 30 minutes).

- (6) It is inactivated by heating food to > 85°C for 1 minute & disinfecting surfaces with sodium hypochlorite (1:100 dilution of chlorine bleach).

Hepatitis B Virus

- (1) Genome consists of double-stranded DNA.
- (2) Proteins consist of two polypeptides in HBsAg, & one in HBcAg.
- (3) Envelope contains HBsAg & lipid.
- (4) Replication is by means of an intermediate RNA copy of the DNA genome (HBcAg in nucleus; HBsAg in cytoplasm).

Hepatitis C Virus

- (1) Genome consists of positive-sense, single-stranded RNA.
- (2) RNA sequence analysis subdivided it into six major genotypes (clades) & >100 subtypes.
- (3) Genome encodes a core protein, two envelope glycoproteins, & several nonstructural proteins.

Hepatitis D (Delta) Virus

- (1) Genome consists of single-stranded, negative-sense RNA.
- (2) HDAg is the only protein coded by HDV RNA.
- (3) It is a defective virus that acquires an HBsAg coat for transmission.
- (4) In blood, HDV contains delta-Ag (HDAG) surrounded by an HBsAg envelope.

Hepatitis E Virus

Genome is a positive-sense, single-stranded RNA.

HABITAT & TRANSMISSION

Habitat

Hepatitis viruses are widespread thru-out the world;

- (1) HCV high-prevalence areas are found in Africa, South America & Asia.
- (2) HDV high-prevalence areas are found in Italy, Middle East, central Asia, West Africa & South America.

Transmission

Hepatitis A

- (1) Most likely mode of transmission is by the fecal-oral route thru close personal contact.
- (2) Other potential sources of transmission are nonhuman primates, usually chimpanzees.

Hepatitis B

- (1) Transmission most commonly occur thru parenteral route;
 - (a) Percutaneous injury by improperly sterilized syringes, needles, or scalpels & even by tattooing or ear piercing.
 - (b) High-risk groups include parenteral drug abusers, institutionalized persons, health care personnel, multiply transfused patients, organ transplant patients, hemodialysis patients & staff, & newborn infants born to mothers with hepatitis B.
- (2) Transmission also occur by the oral route or by sexual or other intimate exposures as HBsAg is present in saliva, nasopharyngeal washings, semen, menstrual fluid, vaginal secretions & blood.

Hepatitis C

- (1) Transmission primarily occurs thru direct percutaneous exposures to blood.
- (2) High-risk groups are same as in HBV.

Hepatitis D (Delta agent)

High-risk groups & primary routes of transmission are similar to HBV, though HDV does not appear to be a sexually transmitted disease.

PATHOGENESIS & CLINICAL FINDINGS

Pathogenesis

- (1) Acute hepatitis (inflammation of liver) →
 - (a) Spotty parenchymal cell degeneration, necrosis of hepatocytes, diffuse lobular inflammatory reaction, & disruption of liver cell cords.
 - (b) Reticuloendothelial (Kupffer) cell hyperplasia & periportal infiltration by mononuclear cells.
 - (c) Later, accumulation of macrophages near degenerating hepatocytes.
 - (d) Preservation of the reticulum framework allows hepatocyte regeneration. Damaged

hepatic tissue is usually restored in 8-12 weeks.

- (2) Chronic carriers of HBsAg may or may not have demonstrable evidence of liver disease.
- (3) Chronic active hepatitis features a spectrum of histologic changes from inflammation & necrosis to collapse of the normal reticulum framework with bridging between the portal triads or terminal hepatic veins.
- (4) Occasionally, more extensive damage may occur that prevents orderly liver cell regeneration.
- (5) Both HBV & HCV have significant roles in the development of hepatocellular carcinoma.

Clinical Findings

Clinical features of hepatitis A, B & C are summarized in table below.

- (1) Onset of jaundice is often preceded by gastrointestinal symptoms (eg nausea, vomiting, anorexia), & mild fever.
- (2) Extrahepatic manifestations in hepatitis B includes
 - (a) Transient serum sickness-like prodrome consisting of fever, skin rash, & polyarthritis.
 - (b) Necrotizing vasculitis (polyarteritis

nodosa.

- (c) Glomerulonephritis.
- (3) Diseases associated with chronic HCV infections include mixed cryoglobulinemia & glomerulonephritis.
- (4) Extrahepatic manifestations are unusual with HAV infections.
- (5) Complete recovery occurs in most hepatitis A cases; relapses can occur after 1-4 months.
- (6) Outcome after hepatitis B varies, ranging from complete recovery to progression to chronic hepatitis &, rarely, death due to fulminant disease.
 - (a) Chronic carriers are at high risk of developing hepatocellular carcinoma.
 - (b) Fulminant hepatitis consisting of hepatic encephalopathy, occasionally develops during acute viral hepatitis. It is associated with superinfection by other agents, including HDV.
- (7) Hepatitis C is usually clinically mild, with only minimal to moderate elevation of liver enzymes.
 - (a) 70-90% of cases progress to chronic liver disease.
 - (b) 20-50% patients develop cirrhosis & are at high risk for hepatocellular carcinoma.

Clinical Features of Viral Hepatitis Types A, B, & C

Feature	Hepatitis A	Hepatitis B	Hepatitis C
Incubation period	10–50 days (avg, 25–30)	50–180 days (avg, 60–90)	15–160 days (avg, 50)
Age distribution	Children, young adults	15–29 years, babies	Adults
Route of infection	Fecal-oral	Mainly parenteral	Mainly parenteral
Onset	Abrupt	Insidious	Insidious
Fever > 100.4 °F	Common	Less common	Less common
Duration of aminotransferase elevation	1-3 weeks	1-6+ months	1-6+ months
Immunoglobulins (IgM levels)	Elevated	Normal to slightly elevated	Normal to slightly elevated
Complications	Uncommon, no chronicity	Chronicity in 5-10% (95% of neonates)	Chronicity in 70-90%
Mortality rate	< 0.5%	< 1-2%	0.5-1%

DIAGNOSTIC LABORATORY TESTS

Liver biopsy gives a tissue diagnosis of hepatitis. Liver function tests (LFTs) eg, serum alanine aminotransferase (ALT) & bilirubin are supplemental.

Hepatitis A

- (1) Virus particles can be detected by immune electron microscopy in fecal extracts, from about 2 weeks prior to the onset of jaundice up to 2 weeks after.
- (2) HAV can also be detected in the liver, bile, & blood by immunoassays, nucleic acid hybridization assays, or PCR.
- (3) ELISA is the method of choice for measuring HAV antibodies;
 - (a) Anti-HAV IgM appears during the acute phase, peaking about 2 weeks after elevation of liver enzymes, & declines to non-detectable levels within 3-6 months.
 - (b) Anti-HAV IgG appears soon after the onset of disease & persists for decades.

Hepatitis B

Most useful detection methods are ELISA for HBV antigens & antibodies, & PCR for viral DNA.

- (1) DNA polymerase activity, HBV DNA & HBeAg, indicating viremic stage occurs early in the incubation period, concurrently or shortly after the appearance of HBsAg.

Interpretation of HAV, HCV, & HDV Serologic Markers in Hepatitis

Assay results	Interpretation
Anti-HAV IgM+ve	Acute infection with HAV
Anti-HAV IgG+ve	Past infection with HAV
Anti-HCV+ve	Current or past infection with HCV
Anti-HDV+ve, HBsAg+ve	Infection with HDV
Anti-HDV+ve, anti-HBc IgM+ve	Coinfection with HDV & HBV
Anti-HDV+ve, anti-HBc IgM-ve	Superinfection of chronic HBV infection with HDV

- (2) High conc. of HBV particles may be present in the blood (up to 10^{10} particles/mL) during the initial phase of infection.
- (3) HBsAg is usually detectable 2-6 weeks in advance of clinical & biochemical evidence of hepatitis & persists thru-out the clinical course, but typically disappears by 6th month after exposure.
- (4) High levels of anti-HBc IgM are detected at the onset of clinical illness, & are indicative of viral replication.
- (5) Antibody to HBsAg is detected at a variable period after the disappearance of HBsAg.
- (6) Before HBsAg disappears, HBeAg is replaced by anti-HBe, indicating the start of resolution.

Interpretation of HBV Serologic Markers in Hepatitis

HBsAg	Anti-HBs	Anti-HBc	Interpretation
Positive	Negative	Negative	Early acute HBV infection.
Positive	(±)	Positive	HBV infection, either acute or chronic.
Negative	Positive	Positive	Indicates previous HBV infection & immunity to hepatitis B.
Negative	Negative	Positive	Possibilities include: HBV infection in remote past; "low-level" HBV carrier; "window" between disappearance of HBsAg & appearance of anti-HBs; or false-positive or nonspecific reaction.
Negative	Negative	Negative	Never infected with HBV.
Negative	Positive	Negative	Vaccine-type response.

- (7) HBV chronic carriers are those in whom HBsAg persists for more than 6 months in the presence of HBeAg or anti-HBe. Low titers of IgM anti-HBc are found in chronic HBsAg carriers.

- (d) Genotype 4 has the highest frequency leading to chronic infection.

Hepatitis C

- (1) Enzyme immunoassays (EIA) detect antibodies to HCV but do not distinguish between acute, chronic, or resolved infection.
- (2) Anti-HCV antibodies can be detected in 50-70% of patients at onset of symptoms, whereas in others its appearance is delayed 3-6 weeks. Antibodies are directed against core, envelope, & NS3 & NS4 proteins.
- (3) Nucleic acid assays (eg, RT-PCR) detect the presence of circulating HCV RNA & are useful for monitoring patients on antiviral therapy.
- (4) Nucleic acid assays also are used to genotype HCV.

TREATMENT

- (1) Treatment of hepatitis is mainly supportive & directed at allowing hepatocellular damage to resolve & repair itself.
- (2) Recombinant interferon-alfa is used in the treatment of chronic HBV or HCV.
- (3) Lamivudine, a reverse transcriptase inhibitor, reduces HBV DNA levels, but viral replication resume in the majority when treatment is stopped.
- (4) Combination therapy of interferon-alfa & ribavirin is used in chronic hepatitis C.
- (5) Orthotopic liver transplantation is a treatment for HBV or HCV end-stage liver damage.

Hepatitis D

- (1) In coinfection with HBV, antibody to HDAg develops late in the acute phase of infection.
 - (a) Assays for HDAg, HDV RNA or anti-HDV IgM are preferable.
 - (b) All markers of HDV replication disappear during convalescence.
- (2) Superinfection by HDV in chronic hepatitis B usually results in persistent HDV infection. High levels of both IgM & IgG anti-HD persist, as do levels of HDV RNA & HDAg.

PREVENTION & CONTROL

- (1) Viral vaccines & protective immune globulin preparations are available against HAV & HBV.
- (2) All blood, body fluids & materials contaminated with them are treated as if they are infectious for HIV, HBV, HCV, & other blood-borne pathogens.
- (3) Specific precautions are needed to prevent contact with infected samples;
 - (a) Hand washing & double gloves.
 - (b) Protective garments should be worn & removed before leaving the work area.
 - (c) Masks & eye protection should be worn whenever splashes or droplets from infectious material pose a risk.
 - (d) Only disposable needles should be used, & needles should be discarded directly into special containers without resheathing.
 - (e) Work surfaces should be decontaminated using a bleach solution.
 - (f) Laboratory personnel should refrain from mouth-pipetting, eating, drinking, & smoking in the work area.

IMMUNITY

- (1) A single infection with any hepatitis virus confers homologous but not heterologous protection against reinfection. A possible exception may be HCV, where reinfection may occur.
- (2) HCV has 4 genotypes:
 - (a) Genotype 1 shows the poorest response to interferon therapy.
 - (b) Genotype 2 responds the best to interferon-based therapies.
 - (c) Genotype 3 shows the highest rate of spontaneous clearance.

- (4) Metal objects & instruments can be disinfected by autoclaving or by exposure to ethylene oxide gas.

Hepatitis A

- (1) Formalin-inactivated HAV vaccine is available.
- (2) Immune (gamma) globulin (IG) confers passive protection in about 90% of those exposed when given within 1-2 weeks after exposure.
- (3) Control measures are directed toward the prevention of fecal contamination of food & water.
- (4) Reasonable hygiene is essential in preventing the spread of HAV during the acute phase, eg hand washing, use of disposable plates & eating utensils, & use of 0.5% sodium hypochlorite as a disinfectant.

Hepatitis B

- (1) Plasma-derived & recombinant DNA-derived hepatitis B vaccines are available.
- (2) Preexposure prophylaxis with hepatitis B vaccine is recommended for all susceptible, at-risk groups. HBV vaccine is recommended for all children as part of their regular immunization schedule.
- (3) Passive immunization using hepatitis B immune globulin (HBIG) is protective if given soon after exposure.
- (4) Because spouses & intimate contacts are at risk of acquiring HBV, they need to be counseled about practices that might increase the risk of infection or transmission.

Hepatitis C

- (1) There is no vaccine for hepatitis C.
- (2) Control measures focus on;
 - (a) Screening & testing blood, plasma, organ, tissue, & semen donors.
 - (b) Virus inactivation of plasma-derived products.
 - (c) Counseling of persons with high-risk drug or sexual practices.
 - (d) Implementation of infection control practices in health care & other settings.
 - (e) Professional & public education.

Hepatitis D

Delta hepatitis can be prevented by vaccinating with hepatitis B vaccine. However, vaccination does not protect hepatitis B carriers from superinfection by HDV.

Chapter 32

Miscellaneous Viruses

DNA ENVELOPED VIRUSES

Poxviruses

- (1) **Variola (small pox) virus**
Causes small pox (eradicated in 1977).
- (2) **Vaccinia virus**
 - (a) Causes localized lesion.
 - (b) Used for smallpox vaccination.
- (3) **Molluscum contagiosum virus**
Causes benign skin nodules.

DNA NON-ENVELOPED VIRUSES

Parvoviruses

- (1) **B-19 virus**
Clinical manifestations
 - (a) Erythema infectiosum (fifth disease)
 - (b) Transient aplastic crisis
 - (c) Pure red cell aplasia
 - (d) Hydrops fetalis
- (2) **Dependovirus**
They are defective viruses & depend on a helper virus (an adenovirus or herpesvirus) for replication.

Polyomaviruses

- (1) **JC virus**
Causes progressive multifocal leukoencephalopathy.
- (2) **BK virus**
Causes nephropathy in transplant recipients.

Papilloma virus

Clinical manifestations

Different kind of warts, eg:

- (a) Skin warts.
- (b) Planter warts.
- (c) Flat warts.
- (d) Genital condylomas.
- (e) Laryngeal papillomas.

Adeno virus

Clinical manifestations

- (a) Upper & lower respiratory tract diseases, esp. pharyngitis & pneumonia.
- (b) Some strains cause sarcoma in animals but not in humans.

RNA ENVELOPED VIRUSES

Togaviruses

Alpha virus

Clinical manifestations

- (1) Eastern equine encephalitis.
- (2) Western equine encephalitis.
- (3) Venezuelan equine encephalitis.
- (4) Ross river fever.

Retroviruses

(1) **Human immunodeficiency virus**

Clinical manifestations

Acquired immunodeficiency syndrome (AIDS).

(2) **Human T-cell leukemia virus**

(HTLV-I & HTLV-II)

Clinical manifestations

- (a) Leukemias.
- (b) Lymphomas.

- (c) Chronic progressive myelopathy.

Filoviruses

Marburg & Ebola viruses

Clinical manifestations

They cause similar acute diseases (African hemorrhagic fevers) characterized by fever, headache, sore throat, & muscle pain, followed by abdominal pain, vomiting, diarrhea, & rash, with both internal & external bleeding, often leading to shock & death.

Coronaviruses

Causes mild acute upper respiratory tract illnesses (common cold).

Arenaviruses

Clinical manifestations

- (1) Lassa fever.
- (2) Lymphocytic choriomeningitis.

Bunyaviruses

(1) **Phlebo virus**

Serotypes

68 known serotypes are divided into 2 groups:

- (a) Phlebotomus fever viruses (sandfly group, transmitted by Phlebotominae sandflies).
- (b) Uukuniemi group (transmitted by ticks).

Clinical manifestations

- (a) Sandfly fever (phlebotomus fever).
- (b) Rift Valley fever

(2) **Hanta virus**

Clinical manifestations

- (a) Hemorrhagic fever with renal syndrome (HFRS).
- (b) Hantavirus pulmonary syndrome (HPS).

(3) **Nairo virus**

Clinical manifestations

- (a) Crimean-Congo hemorrhagic fever.
- (b) Nairobi sheep disease.

(4) **Orthobunya virus**

La Crosse virus in the genus causes California encephalitis & aseptic meningitis.

Bornaviridae

Causes Borna disease, an infectious neurological syndrome or bipolar disorder.

RNA NON-ENVELOPED VIRUSES

Picornaviruses

(1) **Polio virus**

Clinical manifestations

- (a) Paralytic poliomyelitis.
- (b) Aseptic meningitis.

(2) **Coxsackie virus**

Clinical manifestations

- (a) Aseptic meningitis.
- (b) Herpangina.
- (c) Hand-foot-&-mouth disease
- (d) Pleurodynia.
- (e) Myocarditis.
- (f) Pericarditis.

(3) **Echo virus**

Clinical manifestations

- (a) Aseptic meningitis.
- (b) Encephalitis.
- (c) Febrile illnesses with or without rash.
- (d) Common colds.
- (e) Ocular disease.

(4) **Rhino virus**

Causes upper respiratory tract infections, including the common cold syndrome.

Caliciviruses

Norwalk virus

Causes viral gastroenteritis in older children & adults.

Reoviruses

(1) **Rota virus**

Causes viral gastroenteritis in young children.

(2) **Coltivirus**

Causes Colorado tick fever (mountain fever or tick fever).

Astroviruses

Causes viral gastroenteritis in infants, young children, & the elderly.

HUMAN TUMOR VIRUSES

(1) **Human T-cell leukemia virus**

- (a) Leukemias.
- (b) Lymphomas.
- (2) Epstein-Barr virus**
 - (a) African Burkitt's lymphoma.
 - (b) Nasopharyngeal carcinoma.
 - (c) Thymic carcinoma.
 - (d) Hodgkin's disease
 - (e) B cell lymphoma
- (3) Hepatitis B virus**
Primary hepatocellular carcinoma (hepatoma).
- (4) Hepatitis C virus**
Hepatocellular carcinoma
- (5) Human papilloma virus**
 - (a) Papillomas (warts).
 - (b) Genital tumors
 - (c) Squamous cell carcinoma
 - (d) Oropharyngeal carcinoma
- (6) Human herpesvirus 8**
Kaposi's sarcoma
- (7) Human immunodeficiency virus**
AIDS-related malignancies

Section "I/I"

Parasitology

Chapter 33

General Parasitology

DEFINITIONS

Parasite

A living organism which receives nourishment & shelter from another organism where it lives.

Classes of parasites

(1) *Ecto-parasite*

Lives outside on the surface of the body of host.

(2) *Endo-parasite*

Lives inside the body of host, in the blood, tissues, body cavities, digestive tract & other organs.

(3) *Temporary parasite*

Visits its host for a short period

(4) *Permanent parasite*

Leads a parasitic life thru-out the whole period of its life.

(5) *Facultative parasite*

Lives a parasitic life when opportunity arises.

(6) *Obligatory parasite*

Cannot exist without a parasitic life.

(7) *Accidental parasite*

Attacks an unusual host.

(8) *Aberrant parasite*

Happens to reach a place where it cannot live.

Host

An organism which harbours the parasite.

Classes of hosts

(1) *Definitive host*

Either harbors the adult stage of parasite, or where the parasite utilizes sexual method of reproduction.

(2) *Intermediate host*

Harbours the larval stages of parasite; in some cases, larval development is completed in two different intermediate hosts, referred as first & second intermediate hosts.

(3) *Paratenic host*

A host where the parasite remains viable without further development.

Association Of Living Organisms That Live Together

Symbiosis

An association in which both are so dependent upon each other that one cannot live without the help of other, & none of the partners suffers any harm from the association.

Commensalism

An association in which parasite only, is deriving benefit without causing injury to its host. A commensal is capable of leading an independent life.

Parasitism

An association in which parasite derives benefit & host gets nothing in return, but always suffers some injury. Host at the same time, offers some resistance to injury done by parasite & there may be some adaptation b/w parasite & host. A parasite has lost its power of independent life.

CLASSIFICATION OF MEDICALLY IMPORTANT PARASITES

Protozoa**Sarcodina (amebas)****(1) Genus, entameba****(a) Pathogen**

Entameba histolytica

(b) Non-pathogen

(i) E gingivalis

(ii) E coli

(2) Genus, endolimax

Endolimax nana (non-pathogen)

(3) Genus, iodameba

Iodameba butschlii (non-pathogen)

(4) Genus, dientameba

Dientameba fragilis (non-pathogen)

Sporozoa (sporozoans)**(1) Genus, plasmodium**

(a) P vivax

(b) P ovale

(c) P falciparum

(d) P malariae

(2) Genus, toxoplasma

T gondii

Mastigophora (flagellates)**(1) Genus, giardia (intestinal flagellate)**

Giardia lamblia

(2) Genus, trichomonas (genital flagellate)**(a) Pathogen**

T vaginalis

(b) Non-pathogen

(i) T hominis

(ii) T tenax

(3) Genus, trypanosoma (blood & tissue flagellate)**(a) Pathogens**

(i) T brucei

(ii) T cruzi

(iii) T gambiense

(b) Non-pathogen

T rangeli

(4) Genus, leishmania (blood & tissue flagellate)

(a) L donovani

(b) L tropica

(c) L brasiliensis

(d) L mexicana

Ciliata (ciliates)

Balantidium coli

Metazoa**Platyhelminthes****(1) Trematoda****(a) Genus, schistosoma**

(i) S hematobium

(ii) S mansoni

(iii) S japonicum

(b) Genus, fasciola

Fasciola hepatica

(2) Cestoda**(a) Genus, diphyllbothrium**

Diphyllbothrium latum

(b) Genus, tenia

(i) T Saginata

(ii) T Solium

(c) Genus, echinococcus

(i) E granulosus

(ii) E multilocularis

(d) Genus, hymenolepis

(i) H nana

(ii) H diminuta

Nemathelminthes**(1) Intestinal nematoda**

(a) Ascaris lumbricoides

(b) Ancylostoma duodenale

(c) Necator americanus

(d) Strongyloides stercoralis

(e) Trichinella spiralis

(f) Capillaria philippinensis

(g) Enterobius vermicularis

(h) Trichuris trichuria

(2) Somatic nematoda

(a) Wuchereria bancrofti

(b) Loa loa

(c) Onchocerca volvulus

(d) Dracunculus medinensis

(e) Strongyloides stercoralis

Chapter 34

Entameba Histolytica

MORPHOLOGY

Trophozoite

Growing, feeding & invading form (stage) of E histolytica.

Shape

Not fixed, due to constantly changing position.

Size

18 to 40 μm .

Cytoplasm

Granular & may contain red cells.

Motility

Slow gliding movement due to pseudopodia.

Pre-cyst

Shape

Round or slightly ovoid, as the cyst wall is begin to be secreted.

Size

10-20 μm .

Cytoplasm

Granular, but devoid of red blood cells.

Motility

Blunt pseudopodium project from periphery, but the movement is negligible.

Cyst

Infective form (stage) of E histolytica.

Shape

Rounded, as it is surrounded by a highly refractile memb., the cyst wall

Size



Entameba Histolytica:

Left, Trophozoite. Right, Cyst (binucleate).

10 to 20 μm .

Cytoplasm

In early stages, it contains a glycogen vacuole & chromotoidal bodies with rounded end. These structures disappear in final quadrinucleate cyst.

Motility

Non-motile.

Nuclear Division

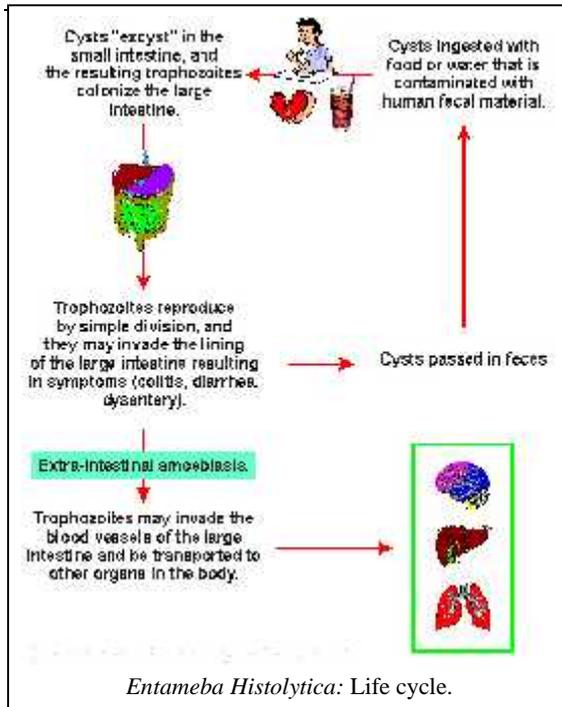
Cyst begin as a uninucleate body, but soon divides by binary fission & develops into binucleate & quadrinucleate bodies.

LIFE CYCLE

Stages in Life Cycle

Ingestion of infective form

Mature quadrinucleate cysts, the infective form, are swallowed along with contaminated food or water



→ Passed unaltered thru stomach, as the cyst wall is resistant to gastric juice.

Excystation

In terminal ileum (with alkaline pH), the cytoplasmic body retracts & loosen itself from cyst-wall, with vigorous amoeboid movements → A rent appear in cyst-wall thru which a single amoeba with four nuclei, the metacyst, comes out.

Note: Probably the digestive action of trypsin contributes in excystation.

Trophozoite phase (stage of division & invasion)

Metacysts form eight amoebulae, metacystic trophozoites, by the division of nuclei with successive fission of cytoplasm → Trophozoites being actively motile, invade the tissues, & ultimately lodge in submucus layer of large gut → Here they grow & multiply by binary fission.

Note: Trophozoites are responsible for producing lesions of amebiasis.

Encystation

Gradually the effect of parasite on host is toned down together with concomitant increase in host tolerance, making it difficult for the parasite to continue its life cycle in trophozoite phase → So, a certain number of trophozoite come from tissues

into "lumen of bowel" & are first transformed into pre-cyst forms → Pre-cysts secrete a cyst-wall & become a uninucleate cyst → Eventually, the mature quadrinucleate cysts are formed, which are the infective form.

Note: Both mature & immature cysts may be passed in feces. Immature cysts can mature in external environment & become infective.

HABITAT & TRANSMISSION

Habitat

(1) Definitive host

Human beings. Trophozoites reside in mucosa & submucosa of large intestine of man.

Note: Cysts are present in external environment (at contaminated sites).

(2) Intermediate host

None.

Transmission

Via oral-fecal route.

PATHOGENESIS & CLINICAL FINDINGS

AMEBIASIS

It means all the conditions produced in human host by infection with *E histolytica* at different areas of its invasion.

Note: "Amoebic dysentery" signifies a condition in which infection is limited to intestinal canal & is characterized by the passage of blood & mucus in stool.

Incubation period: Four to five days.

Pathogenic Lesions of Amebiasis

Intestinal (primary) lesions

Pathogenesis

Trophozoite enter thru crypts of lieberkuhn & penetrate directly thru columnar epithelium of mucosa, by their amoeboid activity & also by dissolving intestinal epithelial cells with proteolytic enzymes → They then burrow deeper & deeper by

continuous lysis of tissue cells, till they reach submucosa → In submucosa they rapidly multiply, destroy tissues & utilized cytolysed material as their food → They spread laterally till a considerable area of submucosa is destroyed, undermining the mucosa above → This invasion causes coagulative necrosis & forms abscess, which finally breaks down leading to broad base ulcers.

Intestinal lesions in acute amebic dysentery

(1) Gross appearance

(a) Distribution of ulcers

Confined to large intestine.

- (i) Generalized → Involving whole of large gut.
- (ii) Localized → Involving ileo-cecal region &/or sigmoidorectal region.

(b) Character of ulcer

Ulcers are discrete with intervening healthy mucosa b/w them.

- (i) Size → Varying from a pin's head to an inch or more in diameter.
- (ii) Shape → Round or oval.
- (iii) Margin → Ragged & undermined, formed by over hanging mucosa. This gives the ulcer, a flask shaped appearance, on vertical section.
- (iv) Base → Formed by muscular coat & filled up by yellowish or blackish slough of necrotic material.

(c) Extension of ulcer

- (i) Superficial ulcers → Limited upto the muscularis mucosa.
- (ii) Deep ulcers → Limited to the submucosa, but extend laterally in submucosa to communicate with adjacent ulcers.
- (iii) Extension beyond submucosa → Into muscular & serous coat, produces complications like peritonitis, perforation, hemorrhage, abscesses, & gangrene.

(d) Healing of ulcers

After separation of slough, granulation tissue begin to form on ulcerated floor.

- (i) In superficial ulcers → Mucosa is completely restored, with no scar formation.
- (ii) In deep ulcers → Mucosal epithelium does not grow, because of scar tissue formation. Excessive scar formation

may produce strictures, obstruction, or generalized thickening of bowel wall.

(2) Histologic appearance

(a) In early cases

- (i) Ulcer limited above the muscularis mucosa.
- (ii) Amebae may be seen marching along the interglandular spaces causing cytolysis.
- (iii) Epithelial cells of crypts of Lieberkuhn will show varying degrees of necrosis.
- (iv) A section made thru middle of an ulcer show, A central area → With necrosed tissue, having hardly any ameba; & A peripheral area → With large number of ameba, lying singly or in groups.

(b) In advanced cases

- (i) Trophozoites are seen migrating deeper & deeper, invading the inter-muscular spaces, to reach the serosa.
- (ii) Trophozoites may also enter small venules, with hyperplasia of endothelial cells, causing thrombosis.

Intestinal lesions in chronic intestinal amebiasis

Course & progress of lesions depend on the resisting power of host, with the processes of ulceration & regeneration going on simultaneously. Following points may be observed:

- (1) Small ulcers involving only the mucosa.
- (2) Extensive superficial ulcers with hyperemia.
- (3) Marked scarring of bowel wall → Thinning, dilatation & sacculatation.
- (4) Extensive adhesions with neighboring viscera.
- (5) Localized thickening of bowel wall → Narrowing of lumen.
- (6) Generalized thickening of bowel wall → Make it palpable.
- (7) Formation of tumor-like masses of granulation tissue, **ameboma**.

Metastatic (secondary) lesions

(1) Hepatic amebiasis

Pathogenesis

Trophozoites are carried as emboli by radicles of portal vein from the base of amebic ulcer in large intestine → Capillary system of liver hold

these parasites → When established, they multiply in large number → This results in thrombosis, leading to ischemic necrosis of liver cells → A solid slough of necrotic material is formed → Centre of this slough liquefy (due to cytolytic action of trophozoites), & extends radially → Many of these miliary abscess coalesce to form fairly big abscess.

Clinical findings

- (a) Size of lesion → Varies.
- (b) Site → Any part of liver, but usually postero-superior surface of right lobe.
- (c) Appearance of abscess area → Reddish brown in color, with a semi-fluid consistency.
- (d) Wall of cavity →
 - (i) Ragged & shaggy in recent abscess.
 - (ii) Smooth in an old abscess.
- (e) Signs & symptoms → Insidious onset of.
 - (i) Pain & tenderness in right hypochondrium.
 - (ii) Fever.
 - (iii) Jaundice.

(2) Cerebral amebiasis

It usually occurs as a complication of hepatic, or pulmonary abscess, or both. It is usually single, small & commonly occurs in cerebral hemispheres.

(3) Pulmonary amebiasis

It may be primary (occurring in the absence of liver abscess), or secondary (occurring as a complication of liver abscess.)

(4) Splenic amebiasis

Occur as a complication of hepatic amebiasis

(5) Cutaneous amebiasis

- (a) **Site**
Over region adjoining a visceral lesion, eg, in areas of drainage of liver abscess, or in sites of ruptured appendicular & peri-colic abscesses.
- (b) **Lesion**
 - (i) Extensive necrosis & sloughing of skin & sub-cutaneous tissues, caused by trophozoites.
 - (ii) Granulomatous ulcerations, in perianal region.

Complications

(1) Complications of intestinal amebiasis

- (a) Perforation.

- (b) Hemorrhage.
- (c) Appendicitis.
- (d) Ameboma.
- (e) Hepatic amebiasis.
- (f) Pulmonary amebiasis.
- (g) Cutaneous amebiasis.

(2) Complications of hepatic amebiasis

- (a) Pulmonary amebiasis.
- (b) Cerebral amebiasis.
- (c) Cutaneous amebiasis.
- (d) Sub-phrenic abscess.
- (e) Rupture into peritoneal cavity.
- (f) Rupture into stomach.
- (g) Rupture into inferior vena cava.
- (h) Rupture into pericardial cavity.
- (i) Rupture into transverse colon, or duodenum.

DIAGNOSTIC LABORATORY TESTS

Specimens

- (1) Fluid feces →
 - (a) Fresh & warm for immediate examination for trophozoites.
 - (b) Preserved in polyvinyl alcohol fixative or Merthiolate-iodine- formalin fixative for mailing to a diagnostic laboratory.
 - (c) After a saline purge, for cysts & trophozoites.
- (2) Formed feces → For cysts.
- (3) Scrapings & biopsies obtained thru a sigmoidoscope → For trophozoites.
- (4) Liver abscess aspirates collected from edge of abscess → For trophozoites.
- (5) Blood → For serology & cell counts.
- (6) Sputum → For trophozoites.

Microscopy

(1) Demonstration of *E histolytica*

- (a) In symptomatic pts, with diarrheic stools → Examine fresh warm feces for trophozoites.
- (b) In other cases → Stain smears with trichrome or iron- hematoxylin stain → Examined for trophozoites &/or cysts.

(2) Other microscopic features

- (a) Stool → Scant cellular exudate, clumped RBCs, & scattered charcot-lyden crystals.
 (b) Blood → Leukocytosis.

Culture

Cultures are made in a layer of fluid overlying a solid nutrient base in partial anaerobiosis: eg.

- (a) Dobell's diphasic medium.
 (b) Cleveland - Collier medium.

Serology

It is primarily for extraintestinal (metastatic) amebiasis, when stools are often negative:

- (1) Latex agglutination.
- (2) Ouchterlony double diffusion.
- (3) Counter-electrophoresis.
- (4) Complement fixation.
- (5) Immobilization.

Note: In acute intestinal amebiasis, serology is negative.

Radiology

In hepatic amebiasis, right dome of diaphragm is situated at a higher level, b/c commonest site of abscess is in postero- superior surface of liver.

IMMUNITY

Specific antibodies develop in sera of pts suffering from amebiasis. However, they do not protect the individual against reinfection.

TREATMENT

(1) Asymptomatic amebiasis

Iodoquinol, diloxanide furoate, or paromomycin.

(2) Mild to moderate intestinal amebiasis

Metronidazole (Flagyl), followed by iodoquinol.

(3) Severe intestinal amebiasis

Metronidazole or dehydroemetine, followed by iodoquinol.

DIFFERENCE BETWEEN

AMEBIC DYSENTERY	BACILLARY DYSENTERY
Cause Entameba histolytica	Cause 1) Shigella species 2) Enterohemorrhagic E coli
Macroscopy of stool 1) Number → 6-8 motions per day 2) Amount → Relatively copious 3) Color → Dark red 4) Odor → Offensive 5) Consistency → Not adherent to container 6) Nature → Blood & mucus mixed with feces 7) Reaction → Acidic	Macroscopy of stool 1) Number → Over 10 motions per day 2) Amount → Small 3) Color → Bright red 4) Odor → Odorless 5) Consistency → Adherent to bottom of container 6) Nature → Blood & mucus; no feces 7) Reaction → Alkaline
Microscopy of stool 1) RBCs → In clumps, reddish-yellow in color 2) Pus cells → Scanty 3) Macrophages → Very few 4) Eosinophils → Present 5) Charcot-Leyden crystals → Present 6) Pyknotic bodies → Very common 7) Ghost cells → Absent 8) Parasite → Trophozoites of E histolytica	Microscopy of stool 1) RBCs → Discrete or in rouleaux, bright red in color 2) Pus cells → Numerous 3) Macrophages → Large & numerous (many contain RBCs) 4) Eosinophils → Scarce 5) Charcot Leyden crystals → Absent 6) Pyknotic bodies → Absent 7) Ghost cells → Numerous 8) Parasite → Absent

(4) Hepatic or other extraintestinal amebiasis

Metronidazole followed by iodoquinol, or dehydroemetine followed by chloroquine phosphate + iodoquinol.

PREVENTION & CONTROL

- (1) Avoiding fecal contamination of food & water.
- (2) Good personal hygiene.

- (3) Purification of municipal water supplies.
- (4) Use of night soil for fertilization of crops should be discouraged.
- (5) In endemic areas, vegetables should be cooked.

Chapter 35

Plasmodia

CLASSIFICATION

- (1) *Plasmodium vivax* → Benign tertian malaria.
- (2) *P. ovale* → Benign tertian malaria.
- (3) *P. malariae* → Quartan malaria.
- (4) *P. falciparum* → Malignant tertian malaria.

MORPHOLOGY

Sporozoite

Asexual form, which is introduced into humans' skin by the bite of anopheline mosquito.

- (1) Shape → Narrow, slightly curved organism & tapers at both ends.
- (2) Size → 12 µm in length.
- (3) Nucleus → Central & elongated.
- (4) Pigment → Nil.
- (5) Motility → Slight undulatory movement.

Tissue Schizonts

Asexual form, which grow & multiply in parenchymal cells of liver.

P. vivax

Round, about 42 µm in diameter. Nucleus is divided into fragments, surrounded by very little cytoplasmic mass → This forms merozoites, about 12,000 in number.

P. ovale

Oval in shape, about 75 µm in length & 45 µm in breadth. About 15,000 merozoites are formed.

P. malariae

Round in shape, about 22 µm in dia. Contain about 2,000 merozoites.

P. falciparum

Oval in shape, about 60 x 30 µm. Contains about 40,000 merozoites.

Tissue Merozoites

Asexual form, liberated after the rupture of mature tissue schizonts. Round in shape, having a nucleus enclosed in a little cytoplasm & is about 0.7 to 1.8 µm in dia.

Trophozoites

Asexual & growing form of parasite in the blood of humans:

Small trophozoites

- (1) *P. vivax* → Large & stout ring or signet-ring shaped, about 1/3rd the dia. of red cells.
- (2) *P. ovale* → Similar to that of *P. vivax*.
- (3) *P. malariae* → Similar to that of *P. Vivax*
- (4) *P. falciparum* → Initially, small & very delicate looking ring, about 1/5th the dia. of red cell. After sometime, rings cannot be differentiated from that of other species.

Large trophozoites

- (1) *P. vivax* → Larger (as it distends the red cell), delicate, & irregular in shape with many pseudopodial processes. Fine, light brown, scattered pigments appear in its cytoplasm.
- (2) *P. ovale* → Large, solid-looking, & not amoeboid. Pigments are coarse, dark yellow-brown in color, & scattered.
- (3) *P. malariae* → Solid-looking, assuming a "band form" lying across the dia. of red cell. Pigments

Developmental stages	P vivax	P ovale	P malariae	P falciparum
Small trophozoites (ring stage)				
Growing trophozoite				
Large (mature) trophozoites				
Mature schizonts				
Macrogametocytes				
Microgametocytes				

Plasmodium species: Morphological characteristics of developmental stages in red blood cells.

- are coarse, dark brown in color, & scattered in clumps.
- (4) *P. falciparum* → Compact & solid-looking. Pigments are coarse, & collected into a single black mass.

Blood Schizonts

Asexual form, in the process of asexual multiplication.

P. vivax

Round in shape, about 9-10 μm in dia. Nucleus is divided into fragments, each enclosed in a portion

of cytoplasm, & form about 16 merozoites. Pigments collect in a clump.

P. ovale

Round in shape, about 6.2 μm in dia. Nucleus & cytoplasm are segmented into about 8 merozoites.

P. malariae

Similar to that of *P. ovale*.

P. falciparum

Round in shape, about 5 μm in dia. Mature schizont contains about 24 merozoites.

Blood Merozoites

Asexual form, being the products of division by schizogony. Round in shape, having a nucleus enclosed in a little cytoplasm & is about 0.5-2.5 μm in dia.

Gametocytes

Sexual form of the plasmodia. Male or microgametocyte, has pale blue cytoplasm, & a large & diffuse nucleus. Female or macrogametocyte, has dark blue cytoplasm & a small & compact nucleus.

- (1) *P. vivax* → Spherical, about 10 μm in dia.
- (2) *P. ovale* → Oval, about the size of red cell.
- (3) *P. malariae* → Round or oval, about the size of red cell
- (4) *P. falciparum* → Crescentic, about 10 x 2 μm in size.

LIFE CYCLE**Human Cycle****Introduction into humans**

Occur by the bite of "female anopheline" mosquito → Sporozoites enter into the blood stream.

Pre-erythrocytic schizogony

Sporozoites enter into parenchymal cells of liver → Grow into tissue schizonts → Multiplication occur in tissue schizonts, to form thousands of tiny merozoites → Merozoites, are liberated on rupture of schizonts about 7th-9th day of bite, & enter into blood stream.

Erythrocytic schizogony

Completed in 48 hours in *P. vivax*, *P. ovale* & *P. falciparum*, & 72 hours in *P. malariae*.

Merozoites attack fresh red cells & in them develop into rings → Grow into large trophozoites & then into blood schizonts → Multiplication occur in blood schizonts, to form about 8-24 merozoites → On rupture of cell, merozoites are liberated into plasma → Liberated merozoite immediately enter a fresh red cell & starts the cycle again.

Gametogony

Certain merozoites, instead of repeating the asexual cycle, develop into gametocytes (some are male & some are female), in the RBCs of capillaries of

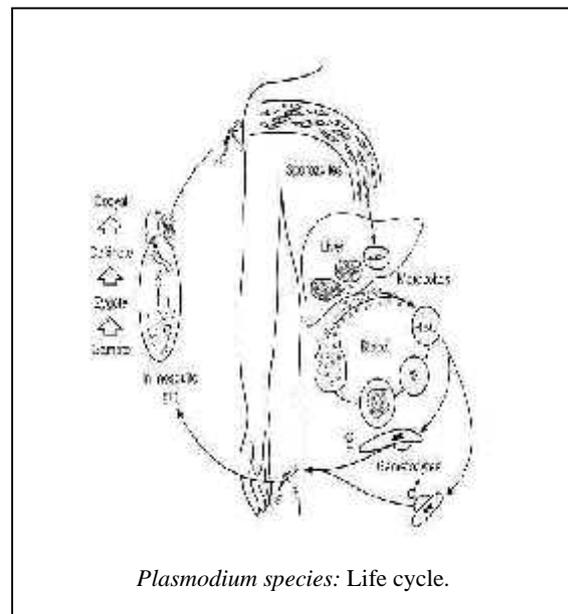
spleen & bone marrow. Only mature gametocytes are found in peripheral blood. Further development occurs only, if they are taken up by the mosquito.

Exo - erythrocytic schizogony

In *P. vivax*, *P. ovale*, & *P. malariae*, pre-erythrocytic schizogony does not end with the rupture of tissue schizont. Instead, some of the liberated merozoites invade fresh liver cells & again develop into schizonts.

Mosquito Cycle

Female anopheline mosquito ingests both sexual & asexual forms, during its blood meal → Asexual forms are destroyed in gut, while sexual forms survive → In the midgut, 4-8 thread-like filamentous microgametes are developed from one microgametocyte by ex-flagellation, while from one macrogametocyte only one macrogamete is formed → Fertilization occur b/w 1 male & 1 female gamete, to form a zygote about 20-120 minutes after blood meal → In next 24 hours zygote develop into "ookinete", with slow movements → Ookinete passes thru cells lining the insect's gut, till it reaches outer limiting memb. → Here it grows into an oocyst → Nuclear division occur in oocyst, to form thousands of sporozoites → Sporozoites are liberated on rupture of oocyst, & enter insect's haemocoel → Haemocoel circulation carries



Plasmodium species: Life cycle.

them to all parts of body, esp. in the salivary gland
 → Now, the mosquito become infective, & it injects sporozoites on its next bite to human being.

HABITAT & TRANSMISSION

Habitat

(1) *Intermediate host*

"Humans", in which parasite resides in the liver cells & RBCs, & reproduces by asexual methods.

(2) *Definitive host*

"Female anopheline mosquito", in which sexual reproduction takes place.

Transmission

Via inoculation, ie, via bite of female anopheline mosquito; across the placenta, in blood transfusions, & in I/V drug abusers.

PATHOGENESIS & CLINICAL FINDINGS

Malaria

Infective agent

Sporozoites.

Incubation period

- (1) *P. vivax* & *P. falciparum* → 10-15 days.
- (2) *P. ovale* → 15-20 days.
- (3) *P. malariae* → About 28 days.

Pathogenesis

- (1) Parasite rupture RBCs upon release of merozoites. Also spleen sequesters & destroys many RBCs → Spleen is enlarged due to congestion of sinusoids with RBCs, coupled with hyperplasia of lymphocytes & macrophages.
- (2) Malaria caused by *P. falciparum*, is characterized by infection of far more RBCs, & by occlusion of capillaries with aggregates of parasitized RBCs → This leads to hemorrhage & necrosis esp. in brain, extensive hemolysis, & kidney damage with resulting hemoglobinuria (Blackwater fever).

Clinical findings

- (1) Fever →
 - (a) Abrupt onset.
 - (b) Accompanied by chills.
 - (c) Continuous early in the disease, for several days after onset.
 - (d) Timing of fever cycle is 72 hours for *P. malariae* & 48 hours for other plasmodia.
 - (e) Fever spike can reach 104°F.
 - (f) Followed by drenching sweats.
- (2) Headache, myalgias, & arthralgias (accompanies the fever).
- (3) Nausea, vomiting, & abdominal pain (frequently accompanies the fever spike).
- (4) Anemia.
- (5) Splenomegaly (in most pts).
- (6) Hepatomegaly (in 1/3rd of pts).
- (7) Circulatory changes →
 - (a) Increased vasodilation → Decreased blood volume, & hypo-tension.
 - (b) Agglutinated RBCs → Increased blood viscosity, & capillary obstruction → Tissue hypoxia, & infarction.
- (8) Acute glomerulonephritis in falciparum malaria.
- (9) Progressive renal failure in chronic *P. malariae* infection (Quartan nephrosis).

DIAGNOSTIC LABORATORY TESTS

Specimens

Blood, serum, urine.

Microscopy

- (1) Thick blood film, stained with Giemsa's stain → Used to screen for the presence of organisms
- (2) Thin blood film, stained with Giemsa's stain → Used for species identification.
Note: Only the small trophozoites, large trophozoites, blood schizonts & gametocytes of plasmodium species are seen in peripheral blood, with the exceptions of large trophozoites & blood schizonts of *P. falciparum*.

Culture

Specimen inoculated in fluid media containing serum, RBCs, inorganic salts, various growth

factors, & amino acids → Helps in differentiating small trophozoites of *P vivax* & *falciparum*.

Blood Counts

- (1) Normocytic anemia.
- (2) Transient leukocytosis, initially.
- (3) Subsequently, leukopenia with monocytosis.

Serology

Done in highly endemic areas, for detecting latent infection in blood donors:

- (1) Complement fixation test.
- (2) Passive hemagglutination test.
- (3) Immunofluorescence test.

Urine Analysis

- (1) Presence of protein & casts in urine of children with *P malariae* → Suggests quartan nephrosis
- (2) Oliguria & appearance of protein, casts, & RBCs in urine → Suggests Blackwater fever.

- (3) Mefloquine, or a combination of quinine & Fansidar, for chloroquin resistant strains of *P falciparum*.

PREVENTION & CONTROL

- (1) Chemoprophylaxis for travelers to endemic areas
- (2) Use of mosquito netting, window screens, protective clothing, & insect repellants.
- (3) Control the population of mosquito vector
- (4) Drainage of stagnant water to reduce the breeding areas.

IMMUNITY

- (1) Acquired strain-specific immunity developed that depends upon low-level of parasitemia, which inhibits new infections or maintains the infection at a non-symptomatic level, thru both humoral & cellular components. This is called premunition or concomitant immunity, & is soon lost after the parasites disappear from blood.
- (2) Exo-erythrocytic forms are not controlled by premunition, so super-infection can occur.
- (3) Natural genetically determined partial immunity to malaria occurs in sickle cell disease, G-6-P dehydrogenase deficiency, & in thalassemia.

TREATMENT

- (1) Chloroquin, is the drug of choice for acute malaria, as it kills the erythrocytic stages of parasite.
- (2) Primaquine, to prevent relapses, as it kills the exo-erythrocytic stages.

Chapter 36

Giardia Lamblia

MORPHOLOGY

Trophozoite

Shape

Tennis racket, or heart shaped when viewed flat & resembles a longitudinally split pear when viewed side-on.

Size

10-20 μm in length, 5-15 μm in breadth, & 2-4 μm in thickness.

Body

Bilaterally symmetrical, having paired structures. Anterior end is broad & rounded, whereas posterior end tapers to a sharp point.

Axostyles

2 in number, seen in midline as vertical lines.

Nuclei

Two, one on each side of body.

Flagella

Four pairs, responsible for tumbling or falling-leaf motion.

Sucking disc

Circular in shape, situated on ventral surface.

Cyst

Shape

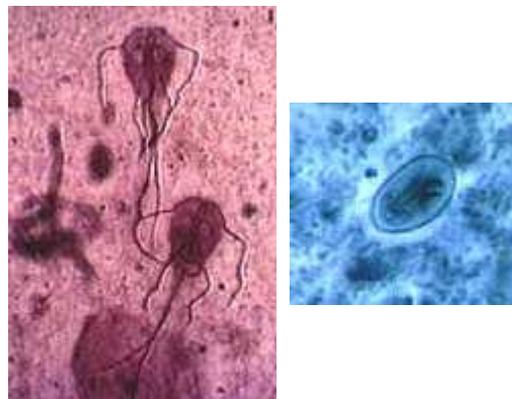
Oval or ellipsoid.

Size

12 μm in length, & 8 μm in width.

Axostyles

Lie more or less diagonally, forming a sort of dividing line within cyst wall.



Giardia lamblia: Left, Trophozoites in stool smear.
Right, Cyst in stool smear.

Nuclei

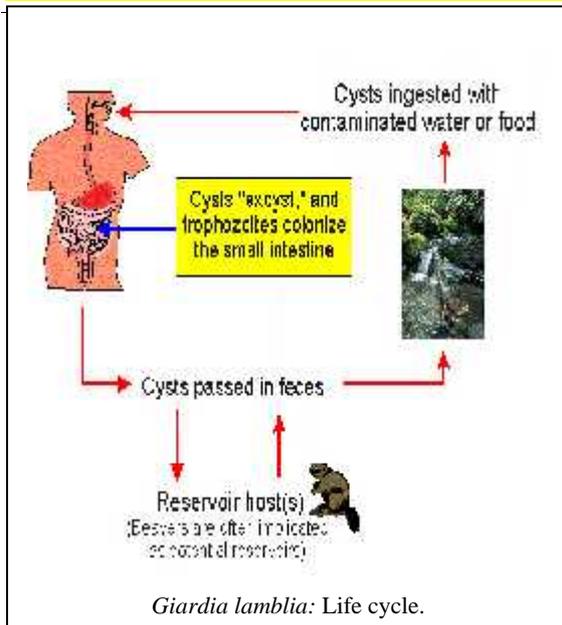
Two nuclei in immature cyst, while in mature cyst four nuclei which may remain clustered at one end.

Flagella & sucking disc

Remains may be seen in cytoplasm.

LIFE CYCLE

Trophozoites multiply by binary fission in duodenum & upper part of jejunum of humans under favorable conditions → Passes into colon under unfavorable conditions, & undergoes encystment → During encystment, a thick resistant wall is secreted & the cell then divided into 2 within the cyst → Cyst passes out in feces → Excystation occur, only when cysts are again ingested by man → Within 30 minutes of ingestion, two trophozoites



hatches out from cyst → Trophozoites then multiply in enormous numbers & colonize in the duodenum & upper jejunum (often localizes in biliary tract to avoid high acidity of duodenum).

HABITAT & TRANSMISSION

Habitat

(1) Trophozoites

- Definitive host → Man, in which *G lamblia* lives in the duodenum & upper jejunum
- Intermediate host → No.

(2) Cysts

Found in colon of man, & in contaminated materials.

Note: Beavers are often implicated as potential reservoir.

Transmission

Via fecal-oral route.

PATHOGENESIS & CLINICAL FINDINGS

Giardiasis

Infective agent

Mature cysts.

Infective dose

About 100 cysts.

Pathogenesis

Large no. of trophozoite attached to bowel wall with the help of sucking disc → Causes irritation & low-grade inflammation of duodenal or jejunal mucosa, associated with crypt hypertrophy, villous atrophy, & epithelial cell damage → Acute or chronic diarrhea.

Clinical findings

- Diarrhea, which is non-bloody & foul-smelling.
- Steatorrhea, due to malabsorption of fat.
- Malaise.
- Weakness.
- Weight loss.
- Abdominal cramps.
- Flatulence.
- Distension due to gas.
- Nausea, vomiting.
- Chronic cholecystopathy (when parasite colonizes the biliary tract).

DIAGNOSTIC LABORATORY TESTS

Specimens

Stool, duodenal aspirate.

Microscopy

- Formed stool → For cysts.
- Liquid stool → For cysts & trophozoites.
- Duodenal aspirate → For trophozoites.

Note: Both saline & Lugol's iodine preparations are examined under microscope.

IMMUNITY

Acquired immunity does develop in giardiasis, as evidenced by the fact that, immunosuppressed individuals are more liable to massive infection with severe clinical manifestations. However, its role in protecting against infection & reinfection is uncertain.

TREATMENT

- (1) Metronidazole (Flagyl).
- (2) Quinacrine hydrochloride.
- (3) Furazolidone.

PREVENTION & CONTROL

- (1) Drinking boiled, filtered, or iodine-treated water in endemic areas & while hiking.
- (2) No prophylactic drug or vaccine is available.

Chapter 3

Trichomonas Vaginalis

MORPHOLOGY

Trophozoites

Shape

Pear-shaped or ovoid, with a short undulating memb. posteriorly.

Size

About 10 x 7 μm .

Axostyle

Single, situated in midline, & runs posteriorly to the margin of body, from which it often protrudes.

Nucleus

Single, elongated, with its chromatin evenly distributed in fine granules.

Flagella

Five flagella, of which 4 are directed anteriorly & lie free, whereas 5th is directed posteriorly & is enclosed in outer margin of undulating memb. These flagella are responsible for characteristic wobbling & rotating motion.

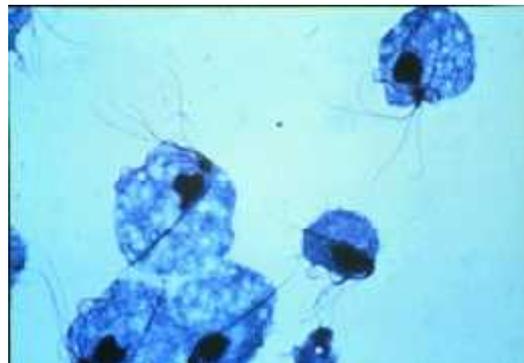
Cystosome

A depression at anterior end, thru which it ingest food particles.

Round Form

It is the form of T vaginalis, which exist shortly after the division of trophozoites, & has the same morphologic structures as that of trophozoites except for its rounded shape.

LIFE CYCLE



Trichomonas vaginalis: Organisms showing nucleus, axostyle, free flagella & an undulating memb.

Life cycle of T vaginalis consists of simple division by binary fission, under favorable conditions (35-37 °C, pH 5.5-6.0 & lack of O₂)

HABITAT & TRANSMISSION

Habitat

Genital tract of humans, both male & female (in particular).

Transmission

Via sexual contact.

PATHOGENESIS & CLINICAL FINDINGS

Trichomoniasis**Infective agent**

Trophozoites.

Incubation period

3-28 days.

Pathogenesis

Under favorable conditions, parasites multiply & penetrate b/w mucosal surface cells of lower genital tract → Induce usual tissue inflammatory reaction.

Note: Trichomoniasis often first manifests after a menstrual period & during pregnancy, because vaginal pH is raised during these conditions.

Clinical findings**(1) In females**

- (a) Discharge → Copious, frothy yellow or cream-colored vaginal discharge.
- (b) Vulvar itching & burning.
- (c) Dysuria.
- (d) Vaginal & cervical mucosa → Tender, reddened, & eroded, & petechial hemorrhages may be present.
- (e) Dyspareunia.

(2) In males

- (a) May be asymptomatic, & serves as a carrier.
- (b) In symptomatic cases, prostate, seminal vesicles & urethra may be infected:
 - (i) Discharge → Thin, white urethral discharge.
 - (ii) Dysuria.

Specimen may be inoculated in solid & fluid cell-free media, in tissue cultures, in chick embryo, & in simplified trypticase serum → May reveal organisms when microscopic examination is negative.

IMMUNITY

Natural immunity (low pH in lower genital tract) provides some degree of protection. Infection confers no apparent acquired immunity, although over time reinfections appear to cause less severe symptoms in women, suggesting that some resistance may develop.

TREATMENT

- (1) Topical & systemic metronidazole (flagyl)
- (2) Patient's sexual partner should be treated at the same time.

PREVENTION & CONTROL

- (1) Simultaneous treatment of both sexual partners
- (2) Mechanical protection (condom) should be used during intercourse until the infection is eradicated in both partners.

DIAGNOSTIC LABORATORY TESTS**Specimens**

Vaginal or urethral secretions or discharge, prostatic secretions, semen.

Microscopy

- (1) Saline preparations observed under microscope → For characteristic motility of *T. vaginalis*.
- (2) Dried smears stained with hematoxylin, is observed under microscope → For confirming *T. vaginalis*.

Culture

Chapter 38

Leishmania

CLASSIFICATION

- (1) *Leishmania donovani* → Kala-azar (Visceral leishmaniasis).
- (2) *Leishmania tropica* → Cutaneous leishmaniasis in Old World countries.
- (3) *Leishmania mexicana* → Cutaneous leishmaniasis in New World countries.
- (4) *Leishmania braziliensis* → Mucocutaneous (American) leishmaniasis.

MORPHOLOGY

Amastigote

Shape

Round or oval in shape.

Size

2-6 x 1-3 μm .

Cell membrane

Delicate, demonstrated in fresh specimens only.

Nucleus

Round or oval, situated along the side of cell wall.

Kinetoplast

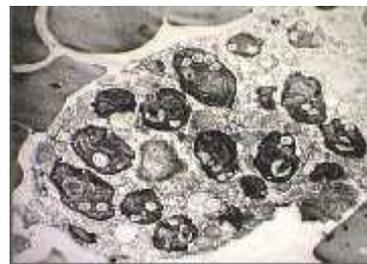
Dark-staining, rod-like structure, that lies at right angle to the nucleus.

Axoneme

A delicate filament, extending from kinetoplast to margin of body. It represents root of flagellum.

Flagellum

Absent.



Leishmania sp.: Above, electron micrograph showing multiple amastigotes in a single host cell. Below, electron micrograph showing multiple promastigotes.

Promastigote

Shape

Earlier ones are short oval, or pear-shaped bodies. Fully developed ones are long slender spindle-shaped bodies.

Size

Fully developed ones → 15-20 x 1-2 μm .

Cell membrane

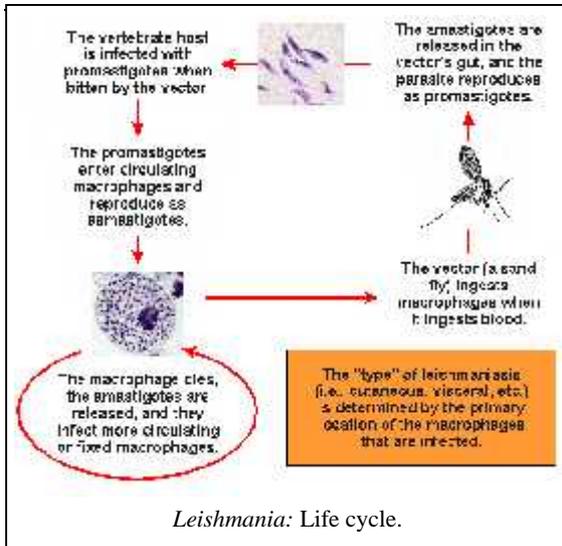
Thick (not delicate), & is always seen.

Nucleus

Round or oval, situated centrally.

Kinetoplast

Lies transversely near anterior end.



Axoneme

Form the root of flagellum, & is attached to a basal body.

Flagellum

Free, project from the anterior end, & is of same length or even longer than body.

LIFE CYCLE

In Human Being

Sandfly transmits infective promastigotes by bite to human being → Promastigotes are phagocytosed by macrophages → In macrophages, it rapidly changes into amastigotes → Amastigotes multiply, filling the cytoplasm of macrophages → Infected cells burst, & the released amastigotes are again phagocytosed by phagocytes, or are ingested by a feeding sandfly.

In Sand Fly

Amastigotes develop into promastigotes → Promastigotes multiplies by binary fission in the mid gut of sandfly → Promastigotes than proceeds towards the pharynx & buccal cavity (a heavy pharyngeal infection occur b/w 6th-9th day of its infective blood-meal) → Thru the next bite, sandfly transmit promastigotes to human being, & cycle is repeated.

HABITAT & TRANSMISSION

Habitat

- (1) Amastigotes → Occur in human beings, in the cells of reticulo-endothelial system thru-out the body, esp. in spleen, liver, & bone marrow.
- (2) Promastigotes → Occur in gut of female sandflies, mainly species of *Phlebotomus* in Old World, & species of *Lutzomyia* & *Psychodopygus* in New World.

Transmission

Via the bite of female sandflies

PATHOGENESIS & CLINICAL FINDINGS

Kala-azar

Causative leishmania

Leishmania donovani.

Incubation period

3-6 months.

Pathogenesis

Organisms multiply in reticuloendothelial cells, esp. macrophages in spleen, liver, lymph nodes, & bone marrow → This leads to cellular destruction in spleen, marked hyperplasia of spleen, reduced bone marrow activity, secondary infections, & a tendency to bleed.

Clinical findings

- (1) Fever → Initially continuous or remittent, later become intermittent.
- (2) Weakness, & weight-loss.
- (3) Massive splenomegaly.
- (4) Slight hepatomegaly.
- (5) Lymphadenopathy.
- (6) Hyperpigmentation of skin is seen in light skinned patients (black sickness).
- (7) Anemia.
- (8) Leukopenia → Secondary infections.
- (9) Thrombocytopenia → Epistaxis, GIT bleeding.
- (10) Progressive emaciation.

Cutaneous Leishmaniasis

Causative leishmania

- (1) *L. tropica* → Oriental sore in Old World.
- (2) *L. mexicana* → Chiclero ulcer in New World.

Pathogenesis

A granulomatous response occurs at the site of bite in dermis → Subsequently, the infection penetrates epidermis & causes ulceration.

Clinical findings

- (1) A red papule is formed at the bite site, usually on exposed part of the body, & is accompanied by regional lymphadenopathy.
- (2) Papule enlarges slowly to form multiple satellite nodules that coalesce & ulcerate.
- (3) Lesion heal spontaneously in 3-6 months
- (4) However, if cellular-immunity does not develop, lesion spread to involve large areas of skin & contain enormous no. of organisms.

Espundia (Mucocutaneous or Naso-oral Leishmaniasis)

Causative leishmania

Leishmania Braziliensis.

Pathogenesis

Similar to cutaneous leishmaniasis.

Clinical findings

- (1) Skin lesion is similar to cutaneous leishmaniasis.
- (2) Metastatic lesion occur, usually at mucocutaneous junction of nose & mouth → Leads to destruction of nasal cartilage & deformity of lips & cheeks.
- (3) Fever.

DIAGNOSTIC LABORATORY TESTS

Specimens

- (1) Kala-azar → Lymph node aspirates, blood, & spleen, liver or bone marrow puncture biopsies.
- (2) Cutaneous forms → Lymph node aspirates, scrapings, & biopsies from margin of lesion.

Microscopy

Giemsa-stained smears & sections are observed under microscope → For amastigotes.

Culture

Specimen inoculated into culture medium, eg, NNN medium, biphasic blood agar, Tobie's medium → Culture is then examined for promastigotes.

Serology

In Kala-azar, serologic tests may give +ve results:

- (1) Formol-gel (aldehyde) test of Napier.
- (2) Indirect hemagglutination antibody test.
- (3) Indirect fluorescent antibody test.
- (4) Enzyme-linked immunosorbent assay.

IMMUNITY

- (1) Immunity to Kala-azar may develop, but varies with the time of treatment & condition of patient
- (2) Recovery from cutaneous leishmaniasis confers a solid & permanent species-specific immunity.

TREATMENT

(1) Kala-azar

- (a) Pentavalent antimonials, eg, Na stibogluconate.
- (b) Pentamidine isothionate.

(2) Cutaneous leishmaniasis

- (a) Single lesion may be clean, curetted, treated with antibiotics if secondarily infected, & then covered & left to heal.
- (b) For larger or non-healing forms → Na stibogluconate.

(3) Espundia

- (a) Cutaneous lesion is treated as above.
- (b) Cycloguanil pamoate in oil.
- (c) Amphotericin B.

PREVENTION & CONTROL

- (1) Protection from sandfly bites by the use of netting, protective clothing, & insect repellents.
- (2) Insecticide spraying.
- (3) Vaccination significantly reduces the incidence of oriental-sore.

Chapter 39

Schistosoma (Blood Fluke)

CLASSIFICATION

- (1) *Schistosoma hematobium* → Affects urinary tract.
- (2) *Schistosoma mansoni* → Affects GIT.
- (3) *Schistosoma japonicum* → Affects GIT.

MORPHOLOGY

Adult Male Schistosoma

Shape

Cylindrical, rather broader, & tapered at both ends.

Size

1-1.5 cm in length, & 0.5-1 mm in width.

Skin (cuticle)

Colorless, & the dorsal surface is covered with small tubercles in *hematobium* & *mansoni* species, but smooth in *japonicum*.

Schist (gynecophoric canal)

Lateral margins of the body are folded ventrally, to form gynecophoric anal, in which female lives.

Suckers

Two. A small oral sucker at anterior end, & a large pedunculated ventral sucker behind the oral sucker.

Alimentary tract

Mouth at the anterior end → Esophagus extends from mouth to ventral sucker → Here, tract bifurcates, & unite again at some distance downward → Terminates blindly posteriorly.

Genital organs

(1) Testis



Schistosoma: Above, adult male & female in copula. Below, eggs of *S. hematobium* (left), *S. japonicum* (middle) & *S. mansoni* (right).

4 spherical testis in *S. hematobium*, & 8 spherical testis in *S. mansoni* & *S. japonicum*

(2) Duct system

Vas efferens arise from each testis → These unite to form vas deferens → This dilates into seminal vesicle → Finally open in genital pore just behind the ventral sucker.

Adult Female Schistosoma

Shape

Cylindrical, thread-like, & tapered at anterior end.

Size

About 2 cm in length, & 0.25 mm in width.

Skin (cuticle)

Often reddish-black, not tuberculated.

Suckers

As in male.

Alimentary tract

As in male.

Genital organs

- (1) Ovary.
- (2) Oviduct.
- (3) Vitelline glands.
- (4) Vitelline duct.
- (5) Shell-gland.
- (6) Uterus.
- (7) Genital pore.

Schistosomal Eggs***S. hematobium***

- (1) Shape → Elongated spindles, dilated in middle, with a short, stout spine at one pole.
- (2) Size → 140 μm x 50 μm.

S. mansoni

- (1) Shape → Oval, with a lateral spine.
- (2) Size → 140 μm x 60 μm.

S. japonicum

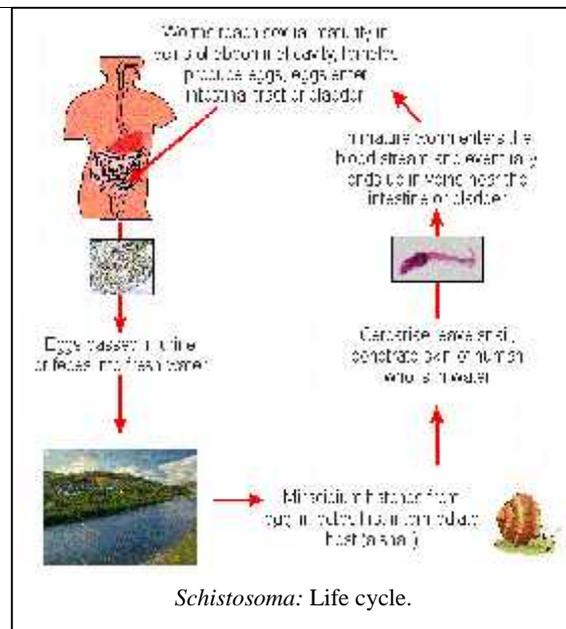
- (1) Shape → Oval, broad at each end, with a minute hook near one pole.
- (2) Size → 90 μm x 70 μm.

LIFE CYCLE**In External Environment**

Embryonated eggs of *S. hematobium* are passed with urine, while of *S. mansoni* & *S. japonicum* are passed with feces, of human being → Eggs gain access to water → 'Miracidia' (ciliated larvae), hatched out of eggs, & move freely in water in search of their intermediate host (fresh-water snail).

In Fresh-Water Snail

Miracidium enter in fresh-water snail, penetrates its soft tissues, & ultimately makes its way into liver → In liver miracidium loses its cilia & other organs, & in the course of 4-8 weeks undergoes developmental changes, to transform into a tubular sporocyst → Tubular sporocyst multiplies & forms a second generation of sporocysts → Several weeks later, when multiplication is ceased, daughter sporocyst give rise to final larval forms, 'fork-tailed cercaria', which are infective to human beings → Cercaria



break off from sporocyst & escape from snail into water.

In Human Being

Cercariae penetrates unbroken skin of human beings, while they take bath or wade in infected water → On entry, cercariae cast off its tail to become 'schistosomulae' → Schistosomulae gain access to a peripheral vein → Right-heart → Lung → Left-heart → Systemic circulation → Mesenteric artery → Portal circulation → In intrahepatic portion of portal blood-stream, it develops into 'adult schistosoma' (maturing in 3 weeks from time of entry) → After differentiated sexually, they move out of liver against blood current into inferior mesenteric vein → Rectal venous plexus, where *S. mansoni* & *S. japonicum* stay → *S. hematobium* proceeds to pelvic veins & eventually enter vesical plexus of veins (about 1-3 months after entry, adult worm reaches their places) → After maturing sexually, they copulate in "oviposition", & fertilized females lay eggs which are passed in urine or feces.

HABITAT & TRANSMISSION**Habitat**

(1) Definitive host

Human beings, in which schistosomes live in portal vein & its radicles. *S. hematobium* usually select vesical plexus, whereas *S. mansoni* & *S. japonicum* select hemorrhoidal plexuses.

(2) Intermediate host

Fresh-water snail.

Transmission

Via fecal-dermal route, or via urinal-dermal route.

PATHOGENESIS & CLINICAL FINDINGS**Bilharziasis (Urinary Schistosomiasis)****Infective agent**

Cercariae of *S. hematobium*.

Pathogenesis

- (1) Cercariae & schistosomulae → Cause immediate hypersensitivity response.
- (2) Eggs → Erode blood vessels & bladder wall, resulting in hemorrhage.
- (3) Eggs → Induce granulomatous inflammation (delayed-hypersensitivity reaction) with the formation of pseudotubercle or schistosome granuloma.

Clinical findings**(1) Early stage**

Dermatitis at the site of entrance of cercaria.

(2) Acute stage

Occur 1-2 months after cercaria entrance & lasts approx. 3 months, & is due to growing schistosomulae in systemic & portal circulation:

- (a) Fever.
- (b) Urticaria.
- (c) Cough.
- (d) Arthralgia.
- (e) Abdominal pain.
- (f) Tender, hepatomegaly.
- (g) Splenomegaly.
- (h) Eosinophilic leukocytosis.
- (i) Endophlebitis.

(3) Chronic stage

Occur within 3-9 months of infection, & is due to eggs of schistosome:

- (a) Painless hematuria.

(b) Frequency of micturition.

(c) Pain in bladder region, & in back.

(d) Granuloma formation on bladder wall → Papillomata → This may become malignant

(e) Urethra, seminal vesicles, & ureters may be involved.

(f) Subsequent fibrosis & calcification may occur in lower urinary tract → Hydronephrosis → Renal failure → Uremia.

(g) Ectopic lesions;

(i) Lung, due to eggs & worms carried there → Fibrosis, pulmonary endarteritis → Pulmonary hypertension → Cor pulmonale.

(ii) Spinal cord → Transverse myelitis-like syndrome.

Intestinal Schistosomiasis**Infective agent**

Cercariae of *S. mansoni* & *S. japonicum*.

Pathogenesis

Similar to *S. hematobium*.

Clinical findings**(1) Early stage**

Similar to *S. hematobium*.

(2) Acute stage

Similar to *S. hematobium*.

(3) Chronic stage

(a) Abdominal pain.

(b) Pronounced dysentery (as a result of eggs ulcerating thru tissue of intestine).

(c) Hepatomegaly.

(d) Periportal cirrhosis.

(e) Splenomegaly.

(f) Prolapse of rectum

(g) Ectopic lesions:

(i) Cor pulmonale.

(ii) Myelitis.

(iii) Space-occupying lesion in brain.

Note: Clinical findings in japonicum infection is more pronounced than mansoni infection.

DIAGNOSTIC LABORATORY TESTS**Specimens**

Urine, feces, blood, & biopsies from bladder wall, rectal wall & liver

- (1) Proper disposal of human waste.
- (2) Eradication of the snail host.
- (3) Swimming in endemic areas should be avoided.

Microscopy

- (1) Urine or feces, examined microscopically → For characteristic eggs.
- (2) A piece of vesicle or rectal mucosa removed by biopsy & is divided into two pieces:
 - (a) One piece is compressed b/w 2 slides & examined under microscope → For eggs.
 - (b) Other piece is placed in a fixative → For histological examination.

Blood Count

Eosinophilic count → Increased in early cases.

Serology

- (1) Complement fixation test.
- (2) Aldehyde test (often +ve due to high globulin).
- (3) Fluorescent antibody test (using cercariae or miracidia as antigens).

Skin (Fairley's) Test

Cercarial antigen is injected intradermally → Delayed hypersensitivity type reaction at the site of injection → Positive test.

IMMUNITY

Acquired immunity developed in response to the antigens of cercaria, schistosomulae, & eggs, in the form of immediate & delayed-hypersensitivity type reactions. However, besides providing protection they are also responsible for pathogenesis.

TREATMENT

- (1) Praziquantal (drug of choice).
- (2) Niridazole.
- (3) Stibocaptate.

PREVENTION & CONTROL

Chapter 40

Diphyllobothrium Latum (Fish Tapeworm)

MORPHOLOGY

Adult Worm

Shape

Long, segmented, & tape-like.

Size

3-10 meters in length, & 1-2 cm in width.

Color

Yellowish-grey, with dark central markings caused by egg-filled uterus.

Scolex (head)

Elongated & spoon-shaped, measures 2-3 mm x 1 mm, & bears 2 slit-like grooves (bothria) on dorsal & ventral surfaces respectively.

Neck

Thin, unsegmented, & longer than head.

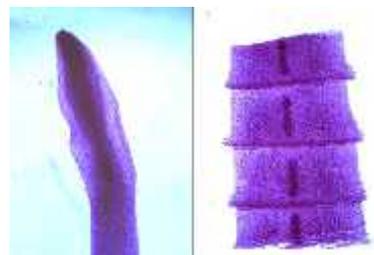
Proglottides (segments)

3,000-4,000 in number. Each segment measures 2-4 mm x 10-20 mm (ie, more wider than longer), & is filled with male & female reproductive organs.

Eggs

- (1) Shape → Oval.
- (2) Size → 70 μm x 45 μm.
- (3) Color → Brown.
- (4) Contains → Abundant yolk granules, & an unsegmented ovum.
- (5) Operculum at one end with a small knob at other end.

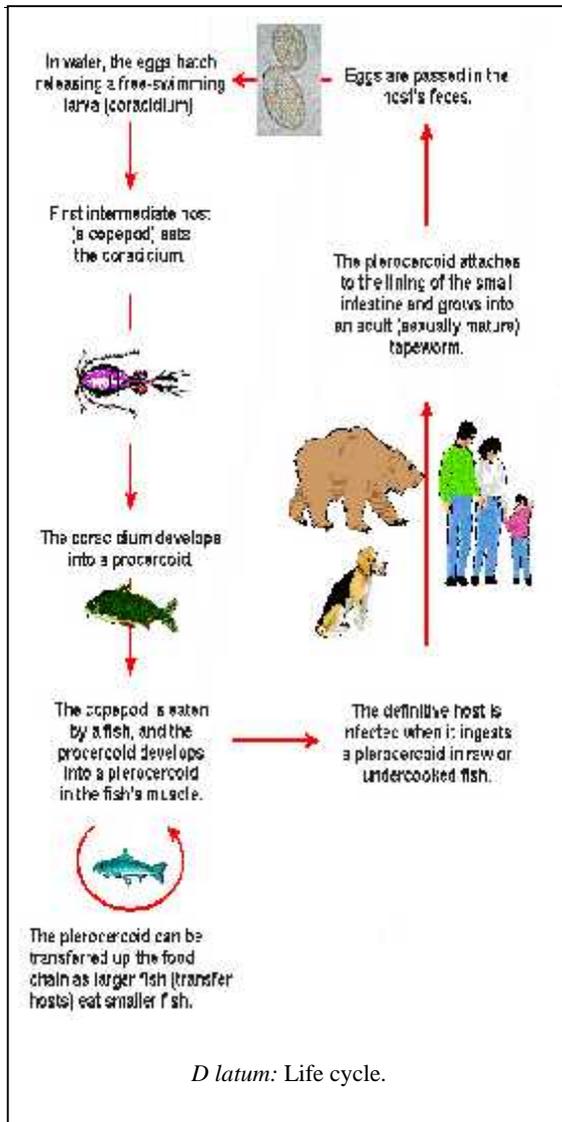
LIFE CYCLE



D latum: Above, full length adult worm. Middle, scolex (left) & gravid proglottides (right). Below, egg.

In External Environment

Operculated eggs are passed in feces of definitive hosts in water → Ovum develops into a "hexacanth embryo or oncosphere", enclosed in a delicate



memb. called embryophore, in 1-2 weeks → Cilia appear & entirely cover the embryophore → Operculum of egg is pushed off, & oncosphere enclosed in its ciliated embryophore escapes, & is now called a "coracidium" → Coracidium swims freely by means of cilia, & unless it is swallowed within 12 hours by the first larval host, cyclops, it dies.

In Cyclops (Crustacean)

In the intestine of cyclops, coracidium loses its ciliated embryophore & penetrates thru the

intestinal wall into the body cavity → In about 3 weeks in the body cavity, it is transformed into an elongated solid body with a caudal appendage containing 6 hooks, known as "proceroid larva" → Proceroid is infective to 2nd larval host, fresh-water fish.

In Fresh-Water Fish

Cyclops containing proceroid is swallowed by a fresh-water fish → Proceroid is freed from cyclops by digestive juices → It then bores its way thru the intestinal wall of fish & rests into liver, muscles, or fats in mesentery & proceeds to develop further → In 1-3 weeks proceroid changes into a "sparganum or plerocercoid" larva, with loss of caudal appendage & appearance of a depression at anterior end (for future head) & a wrinkled body → Plerocercoid is infective to human being.

In Human Being

Human being (the definitive host) is infected with the eating of raw or insufficiently cooked fish, because plerocercoid is not destroyed by ordinary salting, pickling or smoking → Plerocercoid attaches itself to the wall of intestine of humans & develops into adult worm → in about 5-6 weeks, it attained sexual maturity & starts discharging eggs → Eggs are passed, possibly along with segments, in the feces.

HABITAT & TRANSMISSION

Habitat

(1) Definitive host

Human beings, dogs, & cats; adult worms being lived in their small intestine.

(2) Intermediate host

(a) 1st intermediate host

Fresh-water crustacean or cyclops.

(b) 2nd intermediate host

Fresh-water fish, eg, pike, salmon, perch, & other fish.

Transmission

Via fecal-oral route (eggs are passed in feces, & infective plerocercoid larva is ingested).

PATHOGENESIS & CLINICAL FINDINGS**Diphyllobothriasis*****Infective agent***

Plerocercoid larva, with insufficiently cooked infective fishes.

Pathogenesis

- (1) D latum liberates unsaturated fatty acids → This interferes with intrinsic factor, which is necessary for Vit B₁₂ absorption → Pernicious anemia.
- (2) D latum may become lodged in duodenum or proximal jejunum → Here it absorbs Vit B₁₂ from intestinal contents → Megaloblastic anemia.

Clinical findings

- (1) May be asymptomatic.
- (2) Abdominal discomforts → Epigastric pain, abdominal cramps, vomiting.
- (3) Megaloblastic anemia.
- (4) Low serum level of Vit B₁₂.
- (5) Eosinophilia.

DIAGNOSTIC LABORATORY TESTS**Specimens**

Feces, blood, serum.

Microscopy

Microscopic examination of feces for → Operculated eggs, & segments (recognized by rosette-shaped uterus & positions of genital pores).

Blood Examination

- (1) RBC count & examination of size & shape of RBCs.
- (2) WBC count.
- (3) Estimation of serum Vit B₁₂ level.

IMMUNITY

Exact nature & mechanism of immunity developed against the antigens of D latum is not clear.

TREATMENT

- (1) Niclosamide (drug of choice).
- (2) Praziquantal.
- (3) Dichlorophen.

PREVENTION & CONTROL

- (1) Adequate cooking of fish.
- (2) Proper disposal of human feces.

Chapter 47

Tenia Saginata (Beef Tapeworm)

MORPHOLOGY

Adult Worm

Shape

Long, segmented, and tape-like.

Size

3-10 metres in length.

Color

White & semitransparent.

Scolex (head)

1-2mm in diameter, quadrate in shape, & has 4 circular suckers, & is not provided with any rostellum or hooklets.

Neck

Fairly long, & narrow.

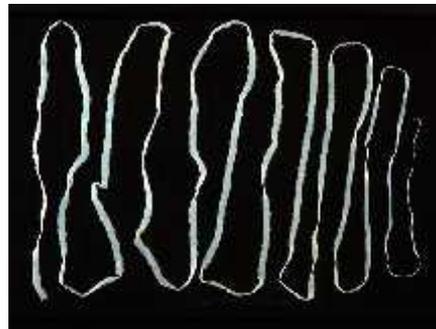
Proglottides (segments)

1,000 - 2,000 in number, & each gravid segment measures 2cm x 0.5 cm (ie, more longer than wider). Genital pore is situated near the posterior end of each segment. Gravid uterus consists of a central longitudinal stem with 15-30 lateral branches on each side.

Eggs

Liberated by the rupture of ripe proglottides. (because of lack of uterine opening):

- (1) Shape → Spherical.
- (2) Size → 31-43 μm in diameter.
- (3) Color → Brown.
- (4) Coverings →
 - (a) Inner embryophore is brown, thick-walled & radially striated.



T. saginata: Above, full length adult worm. Middle, gravid proglottid (left) & scolex (right). Below, egg.

- (b) Outer transparent shell is thin & it may be absent. When present, it causes the eggs to clump together.
- (5) Contain → An oncosphere (14-20 μm in dia) with 3 pairs of hooklets.

LIFE CYCLE

Passage of Eggs

Eggs or gravid segments are passed out with the feces of definitive host (humans) on ground → Swallowed by intermediate hosts (cow or buffalo) while grazing in the field.

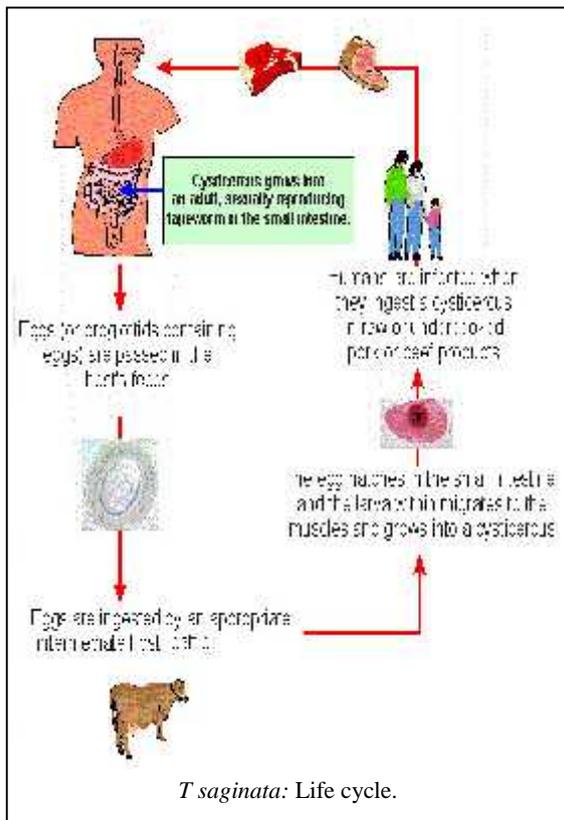
In Cattle

In the alimentary canal of intermediate host, oncospheres are liberated with the rupture of embryophore → Oncospheres penetrate the gut-wall with the help of their hooks & again entrance into

portal circulation → Liver → Right-heart → Lungs → Systemic circulation → It then filtered out from systemic circulation into muscular tissues, most commonly in muscles of tongue, neck, shoulder, & hamstrings → In the muscular tissues, oncospheres lose their hooks & cells in the centre are liquefied → An oval vesicle is formed in oncospheres (in about 8 days after infection) → Vesicle gradually increase in size & contain at its bottom, the cysticercus larva. It takes about 60 - 70 days for oncospheres to metamorphose into cysticercus bovis → Cysticercus bovis can live for about 8 months in flesh of cattle & can only develop further when ingested by human beings.

In Human Beings

Human beings are infected by eating under-cooked beef containing cysticerci → In the GIT, on coming in contact with bile, the scolex evaginates from cysticerci & anchors to gut-wall by means of its suckers → Scolex develops into an adult worm by gradual strobilisation → Worm grows to sexual maturity in 2-3 months & starts producing eggs → Eggs are passed in feces along with gravid segments, thereby repeating the cycle.



HABITAT & TRANSMISSION

Habitat

- (1) **Definitive host**
Human beings, in which adult worm lives in small intestine.
- (2) **Intermediate host**
Cattle (cow or buffalo), in which cysticercus bovis lives in muscular tissues, esp. muscles of tongue, neck, shoulder, & hamstrings.

Transmission

Via fecal-oral route.

PATHOGENESIS & CLINICAL FINDINGS

Teniasis

Infective agent

Cysticercus bovis, in undercooked meat of cattle.

Pathogenesis

It is related to the presence of adult worm in small intestine, which obtain its nourishment from intestinal wall & lumen & disturbs the intestinal functions.

Clinical findings

- (1) Asymptomatic (proglottides may pass in feces).
- (2) Abdominal discomfort.
- (3) Chronic indigestion.
- (4) Diarrhea alternating with constipation.
- (5) Anemia.
- (6) Obstruction of appendix, biliary duct, & pancreatic duct (rarely).

DIAGNOSTIC LABORATORY TESTS**Specimens**

Stool, perianal swab.

Macroscopic Examination

- (1) Whitish segments can easily be recognized against dark yellow mass of feces.
- (2) If specimen is obtained after an anthelmintic, scolex (head) may be seen in it.

Microscopy

- (1) A direct smear preparation of sample of feces → For eggs.
- (2) A smear preparation made from sample after concentrating in one of low density solution → For eggs.
- (3) Microscopic examination of proglottides → To differentiate b/w T saginata & T solium infection.

IMMUNITY

The exact nature & mechanism of acquired immunity developed against T saginata is uncertain.

TREATMENT

- (1) Niclosamide (drug of choice).
- (2) Praziquantal.
- (3) Dichlorophen.
- (4) Mebendazole.

PREVENTION & CONTROL

- (1) Adequate cooking of beef.
- (2) Adequate meat inspection in slaughter house.
- (3) Preventing cattle from consuming human feces by disposing of waste properly.

Chapter 42

Tenia Solium (Pork Tapeworm)

MORPHOLOGY

Adult Worm

Shape

Long, segmented, & tape-like.

Size

2-3 metres in length.

Color

White & semi-transparent.

Scolex (head)

1 mm in diameter, globular in shape, has 4 circular suckers, & is provided with a rostellum armed with a double row of alternating large & small hooklets.

Neck

Short & narrow.

Proglottides (segments)

800-900 in number, & each gravid segment measures 1.2cm x 0.6cm (ie. more longer than wider). Common genital pore is situated near the middle of lateral margin of each segment. Gravid uterus consists of a central longitudinal stem with 5-10 lateral branches on each side.

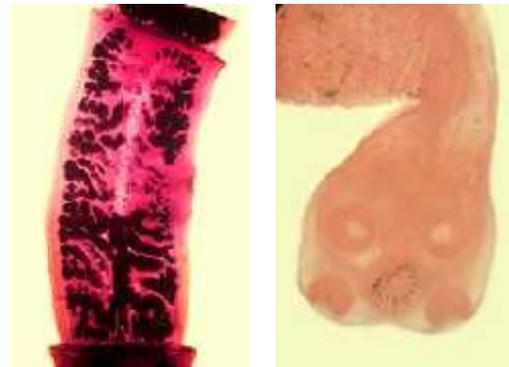
Eggs

Similar to the eggs of *Tenia saginata*.

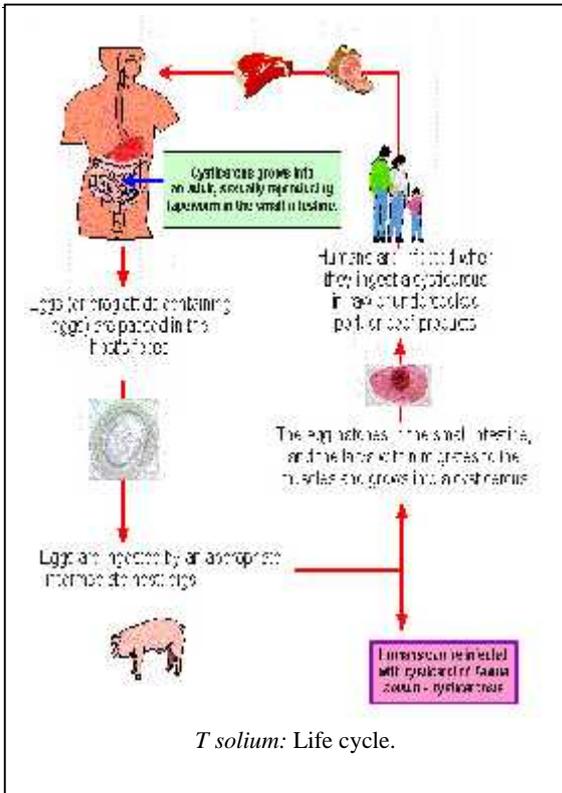
LIFE CYCLE

Same as described for *T. saginata*, with the exception of following differences:

(1) Intermediate host is pig.



T. saginata: Above, full length adult worm. Middle, gravid proglottid (left) & scolex (right). Below, egg.



- (a) Pig, in which cysticercus cellulosa lives in muscular tissues, esp. muscles of tongue, neck, shoulder, & hamstrings.
- (b) Human beings in cases of auto-infection. Cysticercus cellulosa inhabit practically every part of human body, esp. subcutaneous tissues, brain, orbit, & muscles.

Transmission

Via fecal-oral route; occasionally by regurgitation of gravid segments in stomach.

PATHOGENESIS & CLINICAL FINDINGS

Teniasis

Infective agent

Cysticercus cellulosa, in under-cooked infected pig's flesh.

Pathogenesis & clinical findings

Same as in teniasis caused by *T. saginata*.

Cysticercosis

Infective agent

- (1) Eggs, in contaminated water, or in uncooked vegetables infected with eggs.
- (2) Gravid segment, via regurgitation.

Pathogenesis

It is related to the presence of cysticercus cellulosa in the body. Cysticerci are usually found in tens of thousands but sometimes singly. It can become enlarge esp. in brain resulting in space occupying lesion. When they die they can release substances that provoke an inflammatory reaction (living cysticerci do not cause inflammation).

Clinical findings

- (1) Subcutaneous tissues → Visible or palpable nodule.
- (2) Muscles → Visible or palpable nodule.
- (3) CNS → Epilepsy, meningo-encephalitis, mental disorder.

Note: Older cysts calcify, & become obsolete in 5-6 years.

- (2) Eggs which are passed in feces of definitive host (humans) are infective to intermediate host as well as to the definitive host → Eggs hatch in small intestine of humans as it hatch in alimentary canal of pig, & liberated oncosphere larvae are disseminated thru-out the body, where they form cysticercus cellulosa.
- (3) Proglottides which are usually passed in feces are sometimes regurgitated & hatch in stomach, & this is equivalent to thousands of eggs being swallowed.

Note: Points (2) & (3) accounts for the phenomenon of "autoinfection."

HABITAT & TRANSMISSION

Habitat

- (1) **Definitive host**
Human beings, in which adult worm lives in small intestine.
- (2) **Intermediate host**

DISGNOSTIC LABORATORY TESTS**Specimens**

Stool, perianal swab, biopsies, blood, serum.

Macroscopic Examination

- (1) Whitish segments (in chain of 5-6 segments) can easily be recognized against dark yellow mass of feces.
- (2) If specimen is obtained after an antihelminthic, scolex (head) may be seen in it.

Microscopy

- (1) Smear preparations of sample of feces → For eggs.
- (2) Proglottides (segments) → To differentiate b/w *T. saginata* & *T. solium* infection.
- (3) Biopsy specimen taken from subcutaneous or muscular nodule → For *Cysticercus cellulosae*.
- (4) Blood specimen → For the evidence of eosinophilia, which occur in cysticercosis.

Serology

Indirect hemagglutination test using antigen from pig's cysticerci → Positive test indicates cysticercosis.

Radiology

X-ray examination of skull & soft tissues (buttocks & thighs) → May reveal calcified cysticerci.

CT Scan

For demonstrating the presence of cyst in tissue.

IMMUNITY

The exact nature & mechanism of acquired immunity developed against *T. solium* & *Cysticercus cellulosae* is uncertain.

TREATMENT**(A) *Teniasis***

- (1) Niclosamide (drug of choice).
- (2) Praziquantal.
- (3) Mebendazole.

(B) *Cysticercosis*

- (1) Praziquantal.
- (2) Surgery → To remove cerebral & ocular cysts.

PREVENTION & CONTROL**(A) *Teniasis***

- (1) Adequate cooking of pork.
- (2) Preventing pigs from ingesting human feces by disposing of waste properly.

(B) *Cysticercosis*

- (1) Treatment of patients to prevent auto-infection.
- (2) Observation of proper hygiene, including hand washing, to prevent contamination of food with the eggs.

Chapter 43

Echinococcus Granulosus (Hydatid Worm)

MORPHOLOGY

Adult Worm

Shape

Small, segmented, & tape-like.

Size

3-6 mm in length.

Scolex

Globular in shape, bears 4 suckers, & a protrusible rostellum with 2 circular rows of hooks.

Neck

Short & thick.

Strobila (body)

Consists of 3 segments.

- (1) 1st segment → Immature, contains no genital organ.
- (2) 2nd segment → Mature, contain testes & ovaries, & the sacculated uterus lie laterally.
- (3) 3rd segment → Gravid, sacculated uterus become filled with eggs.

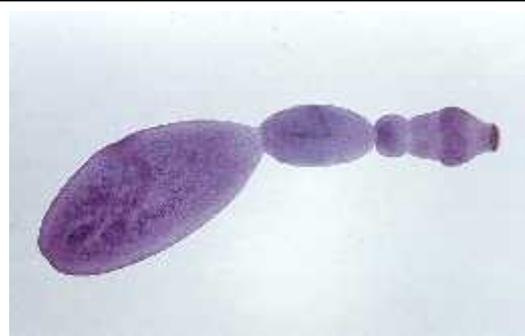
Eggs

Resembles eggs of *T. saginata*

Larval Form

It represents the structure of scolex of future adult worm that remains invaginated within a vesicular body. This is found within hydatid cyst developing inside the intermediate host.

LIFE CYCLE



E. granulosus:

Above, adult worm showing hooks on scolex as a dark ring & numerous eggs in terminal proglottid.

Middle, single egg.

Below, hydatid cyst in lung showing laminate & proliferative layers & daughter cysts containing scolices.

Passage of Eggs

Eggs are passed out with the feces of definitive hosts (dog, wolf, fox & jackal) → Swallowed by intermediate hosts, sheep & other domestic animals while grazing in field, & also by humans due to intimate handling of infected dogs.

In Intermediate Hosts

In the duodenum of intermediate hosts, oncospheres are liberated with the rupture of embryophore → About 8 hours after ingestion, oncospheres bore their way thru intestinal wall with the help of their hooks & enter the radicles of portal vein → Carried to liver to be arrested in sinusoidal capillaries (1st filter) → Some pass thru the liver, & filter out in lungs (2nd filter) → Few oncospheres enter systemic circulation & lodge in various organs → Wherever oncospheres settles, it forms hydatid cyst, young larva being transformed into a hollow bladder → From inner side of cyst, a no. of brood capsules developed → Within each brood capsule, a no. of proto-scolices (may be thousand in no.) are developed → Hydatid cyst may rupture, releasing proto-scolices (with invaginated heads) into surrounding tissue → A fully developed proto-scolex is infective to definitive hosts.

Dead end (blind alley) cycle

If humans become the intermediate host, then dogs have no access to hydatid cyst developed in viscera of humans & the life-cycle of parasite comes to a dead-end (blind alley).

In Definitive Hosts

Definitive hosts are infected by ingesting fertile hydatids or proto-scolex → In the GIT, scolex head evaginates & attaches to gut-wall by means of its suckers → Grow into adult worm in about 6-7 weeks & start producing eggs → Eggs are passed in feces, thereby repeating the cycle.

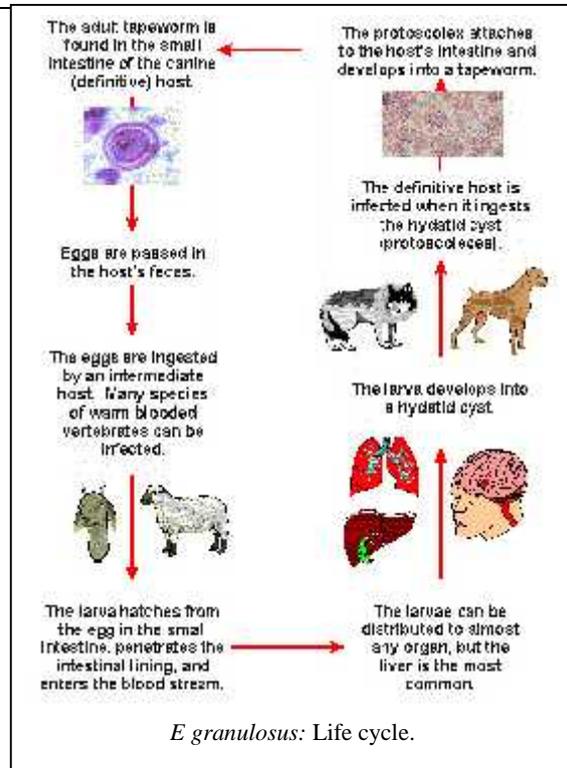
HABITAT & TRANSMISSION

Habitat

(1) Definitive hosts

Dog, wolf, fox & jackal; adult worm lives in small intestine.

(2) Intermediate hosts



Sheep, pig, cattle, horse, goat, & human beings; hydatid cysts with brood capsules & a no. of proto-scolices developed in various tissues esp. in liver & lungs.

Transmission

Via fecal-oral route.

PATHOGENESIS & CLINICAL FINDINGS

Hydatid Disease

Infecting agent

Eggs, in dog's feces.

Pathogenesis

- (1) Unilocular, large, fluid-filled cyst is formed that contains thousands of individual proto-scolices as well as many daughter cysts → Cyst acts as a space-occupying lesion, putting pressure on adjacent tissues.
- (2) Cyst fluid contains parasite antigens, which can sensitize the host.

- (3) Cysts can rupture spontaneously or during trauma or surgical removal, which results in life-threatening "anaphylaxis".

Clinical findings

- (1) May be asymptomatic.
- (2) Liver cysts → Hepatic dysfunction.
- (3) Lung cysts → Erode into a bronchus → Bloody sputum.
- (4) Cerebral cysts → Headache & focal neurologic signs.
- (5) Superficial cysts → Visible swelling.
- (6) Ruptured cysts → Anaphylactic shock, & localized or generalized secondary echinococcosis

Owing to saline contents, cyst is relatively opaque & casts a characteristic circular shadow with a sharp outline.

IMMUNITY

Innate immunity developed in the form of active cellular reaction consisting of macrophages, giant cells, & eosinophils. Humoral immunity also developed as evidenced by serologic tests, but its exact nature & mechanism is uncertain.

DIAGNOSTIC LABORATORY TESTS**Specimens**

Blood, serum, cysts enucleated surgically.

Microscopy

Cysts are observed under microscope → For the presence of brood capsules containing multiple protoscolices.

Note: Although an accurate diagnosis may be made by withdrawing only a few ml of hydatid fluid by exploratory cyst puncture, it is not advised due to the risk of anaphylactic shock.

Blood Examination

May reveal eosinophilia.

Serology

- (1) Precipitin reaction.
- (2) Complement fixation test.
- (3) Flocculation test.
- (4) Hemagglutination test.

Casoni's Reaction

0.2 ml of hydatid fluid is injected intradermally into a suspected patient → A wheal is produced in about 15 minutes, surrounded by a concentric red zone, which later disappears with wheal → Positive reaction.

Radiology**TREATMENT**

- (1) Surgical removal of cysts. Extreme care must be exercised to prevent release of protoscolices during surgery.
- (2) Protoscolicidal agent, eg hypertonic saline, should be injected into cyst to kill the organisms & to prevent accidental dissemination.
- (3) In inoperable case →
 - (a) Mebendazole (drug of choice).
 - (b) Albendazole.

PREVENTION & CONTROL

- (1) Not feeding the entrails of slaughtered sheep to dogs.
- (2) Cleaning of hands before eating.

Chapter 44

Hymenolepis Nana (Dwarf Tapeworm)

MORPHOLOGY

Adult Worm

Shape

Small, segmented, & thread-like.

Size

1-4 cm in length.

Scolex

Globular in shape, has 4 suckers, & is provided with a short retractile rostellum armed with a single row of 20-30 hooklets.

Neck

Long, & narrow

Proglottides

About 200 in number, & a mature segment measures 0.3 mm x 0.9 mm (ie, more wider than longer). Genital pores are marginal. Uterus is a transverse sac with lobulated walls, while there are 3 testes.

Eggs

Liberated by gradual disintegration of terminal segments.

- (1) Shape → Spherical or oval.
- (2) Size → 30-45 μm in diameter.
- (3) Coverings →
 - (a) Outer membrane is thin & colorless.
 - (b) Inner embryophore is thin, colorless & unstriated, & bear at each pole a minute papilla from which a few long filaments arise.
- (4) Contain → An oncosphere with 3 pairs of lancet-shaped hooklets.



H nana: Above, adult worm. Below, egg.

LIFE CYCLE

Life Cycle of Human Strain of H Nana

Humans become infected with ingestion of fully embryonated egg → A hexacanth embryo, oncosphere, is liberated in small intestine → Oncosphere burrows into villi of proximal part of

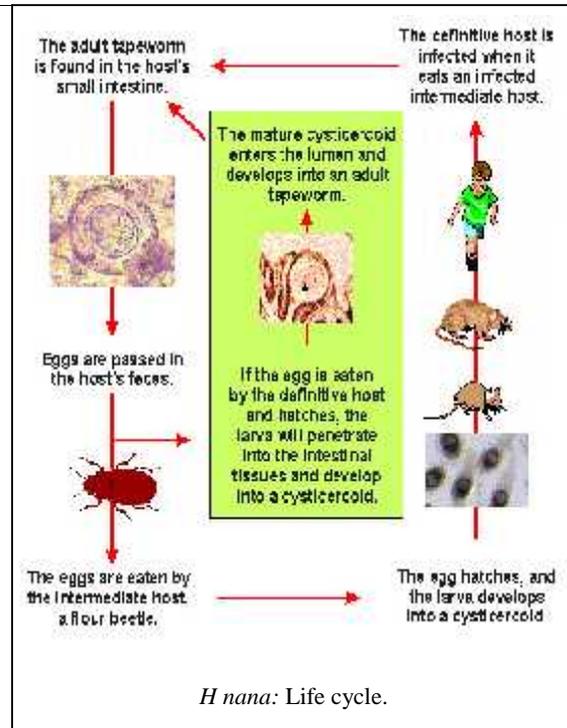
small intestine, & develops in about 4 days into cysticercoid larva → After reaching maturity, villus ruptures & cysticercoid larva re-enters the lumen of small intestine → Later, it attaches to another villus further down & in the course of a fortnight develops into an adult worm → Rapid strobilisation occur, & in about 30 days after infection, eggs begin to be released on rupture of gravid segments → Some of the eggs may remain in the bowel & starts the cycle again (autoinfection), but the majority are passed in feces → These eggs can be ingested by the same person due lack of personal cleanliness (autoinfection), or by other persons with contaminated food or water.

Notes:

- (1) Entire life cycle takes place in one definitive host, human beings.
- (2) *H. nana* can multiply in definitive host due to autoinfection, & this is against the general rule that helminths do not multiply inside the body of definitive host.

Life Cycle of Murine Strain (H Fraterna) of H Nana

It takes place in larvae of various fleas & mealworms if they swallow the eggs → A cysticercoid develops in larval body, which persists thru the metamorphosis into adult flea → Rat becomes infected by swallowing the flea, & young children may become infected with *H. fraterna* if they similarly swallow infected fleas.



HABITAT & TRANSMISSION

Habitat

- (1) Definitive host**
 - (a) Human beings are the only host (definitive host) for human strains of *H. nana*, in which both the larval & adult forms are found in small intestine.
 - (b) Humans & rats are the definitive hosts for murine strains of *H. nana*.
- (2) Intermediate host**
 - (a) For human strains → No.
 - (b) For murine strains → various fleas & mealworms.

Transmission

Via fecal-oral route (eggs being passed in feces, & ingested orally).

PATHOGENESIS & CLINICAL FINDINGS

Hymenolepiasis

Infective agent
Eggs, in contaminated food, or due to autoinfection.

Pathogenesis
It is related to the no. of parasites present in small intestine, busy in obtaining its food, damaging the villi & disturbing the intestinal function.

Clinical findings
(1) Asymptomatic (in light infections).
(2) Abdominal pain, & diarrhea (in heavy infections).
(3) Eosinophilia (variable).

DIAGNOSTIC LABORATORY TESTS

Specimens

Stool, blood.

Microscopy

- (1) Stool → For characteristic eggs.
- (2) Stool → Sometime, segments may be seen.
- (3) Blood → For the evidence of eosinophilia; however, it is variable & not pronounced.

IMMUNITY

Innate immunity developed, but its extent is protecting against infection is uncertain. Role of acquired immunity is not definitely known.

TREATMENT

- (1) Praziquantal (drug of choice).
- (2) Niclosamide.

PREVENTION & CONTROL

- (1) Avoidance of fecal contamination of food & water.
- (2) Good personal hygiene.

Chapter 45

Ascaris Lumbricoides (Common Roundworm)

MORPHOLOGY

Adult Male Worm

Shape

Elongated, cylindrical, un-segmented, & tapers at both ends (anterior end being thinner than posterior end).

Size

15-25 cm in length, with a maximum diameter of 3-4 mm.

Color

Light brown or pink in color when fresh from the intestine, but it gradually changes to white.

Anterior end

Mouth opens here, having 3 finely toothed lips (1 dorsal & 2 ventral).

Posterior end

Curved ventrally in the form of a hook having a conical tip. Genital pore opens into cloaca from which 2 curved copulatory spicules protrude.

Body cavity

Digestive & reproductive organs float inside the body cavity, containing an irritating fluid called ascarron or ascarse.

Adult Female Worm

Shape

Similar to male worm.

Size

25-40 cm in length, with a maximum diameter of 5 mm.

Color

Similar to male worm.



A lumbricoides: Above, adult worms (female upper & male lower). Below, egg.

Anterior end

Similar to male worm.

Posterior end

Conical & straight. Anus opens sub-terminally on ventral aspect.

Vulvar opening

Situated at the junction of anterior & middle thirds of body on mid-ventral aspect.

Body cavity

Similar to male worm.

Eggs

(1) Fertilized egg

- Shape → Round or oval.
- Size → 60-75 μm x 40-50 μm .
- Color → Brown (bile-stained).
- Coverings →

Habitat**(1) Definitive host**

Human beings, in which adult worm lives in small intestine.

(2) Intermediate host

None.

Transmission

Via fecal-oral route (eggs being passed in feces & ingested orally), & also via inhalation of desiccated eggs in dust.

PATHOGENESIS & CLINICAL FINDINGS**Ascariasis****Infective agent**

Embryonated eggs, in contaminated food or water or raw vegetables cultivated on a soil fertilized by infected human excreta.

Pathogenesis

- (1) Larval migration thru the tissues causes tissue reaction esp. in lungs, where inflammation with an "eosinophilic exudate" occurs in response to larval antigens.
- (2) Adults in small intestine derive their nourishment from ingested food, & so a heavy worm burden may contribute to malnutrition esp. in children.
- (3) Adults also cause effects due to its presence.

Clinical findings**(1) Due to migrating larvae**

- (a) In light infection → Asymptomatic.
- (b) In heavy infection → Ascari pneumonia (Loeffler's synd.) with fever, cough, dyspnea, urticarial rash, eosinophilia, & blood-tinged sputum (that may contain larvae).
- (c) Larvae may reach places like brain, spinal cord, heart, kidneys, & causes disturbances there.

(2) Due to adult worms

- (a) Spoliative effects → Protein malnutrition, & Vit A deficiency (night blindness).
- (b) Toxic effects → Ascari (body fluid of ascaris) when absorbed, causes typhoid-like fever & various allergic reactions like

urticaria, facial edema, conjunctivitis & upper respiratory tract irritation.

- (c) Mechanical effects → Intestinal obstruction (when a large no. of ascaris forms a bolus), & penetrance thru a GIT ulcer.
- (d) Ectopic ascariasis →
 - (i) Worms may migrate upward from intestine → May be vomited, or accidentally enter into respiratory tract causing suffocation.
 - (ii) It may enter appendix → Appendicitis.
 - (iii) It may enter biliary tract → Obstructive jaundice & acute hemorrhagic pancreatitis.

DIAGNOSTIC LABORATORY TESTS**Specimens**

Stool, vomitus, sputum, blood, serum, bile (obtained by duodenal intubation).

Macroscopic Examination

- (1) Stool → For adult worm (that may be passed out spontaneously in stool or per anum b/w stool).
- (2) Vomitus → For adult worm (in case of ectopic migration).

Microscopy

- (1) Stool → For eggs.
- (2) Bile → For eggs.
- (3) Sputum → For eggs.

Note: Fertilized eggs float in saturated solution of common salt, while unfertilized eggs do not float.

Blood Examination

For the evidence of eosinophilia (present only in early stage of invasion).

Dermal Reaction

Scratch test with powdered ascaris antigen → Often positive.

Radiology

With barium emulsion, which is ingested by worm within 4-6 hours → Casts an opaque, string-like shadow.

- (1) Proper disposal of human feces.
- (2) Treatment of parasitized individuals.
- (3) Personal hygiene.

IMMUNITY

Partial acquired immunity developed, induced by migrating larvae. Antigens are liberated during moulting period which produces protective antibodies. A severe allergic reaction occurs when larvae reach small intestine for 2nd time. Eosinophilic count is increased at the time of tissue invasion (innate immunity).

TREATMENT

- (1) Mebendazole (drug of choice).
- (2) Pyrantal pamoate.
- (3) Piperazine.
- (4) Levamisole.

PREVENTION & CONTROL

Chapter 46

Ancylostoma Duodenale (Hook Worm)

MORPHOLOGY

Adult Male Worm

Shape

Small, un-segmented & cylindrical.

Size

About 8 mm in length.

Color

Greyish-white in color, but in fresh specimen appear reddish-brown due to ingested blood in its intestinal tract.

Anterior end

Bent slightly dorsally (hence called hookworm). Buccal capsule is provided with 6 teeth, 4 hook-like on ventral surface & 2 knob-like on dorsal surface. Oral aperture is sub-terminal on dorsal surface.

Posterior end

Expanded in an umbrella-like fashion, copulatory bursa, which consists of 3 lobes supported by 3 chitinous rays.

Genital opening

Opens posteriorly with the cloaca.

Adult Female Worm

Shape

Similar, but slightly longer than male worm.

Size

12.5 mm in length.

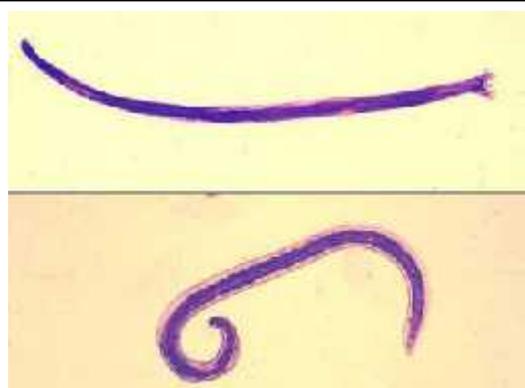
Color

Similar to male worm.

Anterior end

Similar to male worm.

Posterior end



A duodenale:

Above, adult worms (male upper & female lower).
Below, anterior of adult worm (left) & egg (right).

Tapering, with no expanded bursa.

Genital opening

Situated at the junction of posterior & middle third of body.

Eggs

- (1) Shape → Oval or elliptical.
- (2) Size → 65 μm x 40 μm .
- (3) Color → Colorless.

- (4) Covering → A transparent, hyaline, shell membrane.
 (5) Contains → A segmented ovum usually with 4 blastomeres (when passed out in feces).

LIFE CYCLE

In External Environment

Eggs, containing segmented ova with 4 blastomeres are passed out with feces of definitive host, human beings (the only host for *A. duodenale*), on ground → From each egg, a "rhabditiform larva" hatches out in soil in about 48 hours → Rhabditiform larva moults twice, 1st on the 3rd day & 2nd on 5th day, & develops into a "filariform larva" in about 8 to 10 days → Filariform larva is infective to humans.

In Human Beings (The Only Host)

Penetration & migration

Humans become infected with the filariform larva, which cast off its sheath, & enter the body by penetrating the skin → On reaching subcutaneous tissue, it enters into lymphatics or small venules →

Pass thru the venous circulation, to reach the right heart → Enter the pulmonary circulation → In the lungs, it break thru the capillary walls & enter into alveolar spaces → Then migrate on to bronchi, trachea, & larynx → Crawl over the epiglottis to the back of pharynx & are ultimately swallowed into esophagus, reaching here in about 10 days.

Note: During migration, or on entering esophagus, a 3rd moulting takes place & a terminal buccal capsule is formed.

Localization & laying of eggs

Growing larvae settle down in small intestine, & undergo a 4th moulting to develop into adult worms, with definite buccal capsule complete with teeth → In 3-4 weeks, worms become sexually matured & fertilized females begin to lay eggs, which are passed in feces in about 6 weeks, & the cycle is again repeated.

Note: 4 moultings of larva occur, 2 outside ie in soil, 1 during migration or on entering esophagus, & 1 in small intestine.

HABITAT & TRANSMISSION

Habitat

(1) Definitive host

Human beings, in which adult worm lives in small intestine.

(2) Intermediate host

None.

Transmission

Via fecal-dermal route (eggs being passed in feces & filariform larva penetrate thru the skin to enter a new host).

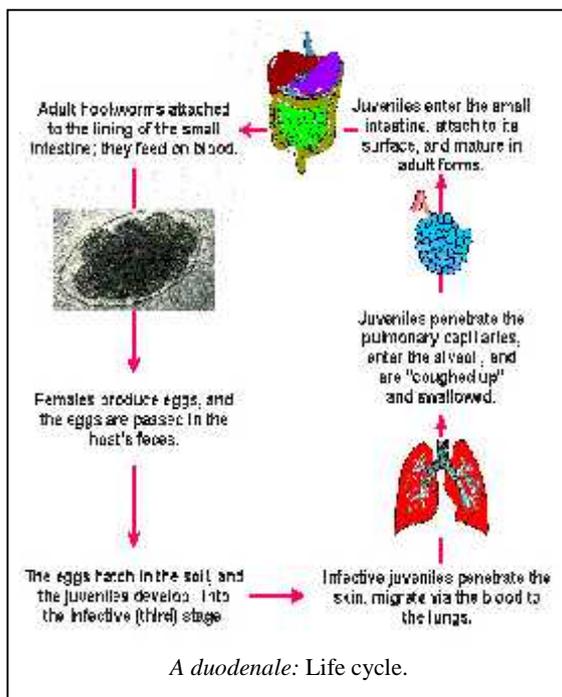
PATHOGENESIS & CLINICAL FINDINGS

Ancylostomiasis

Infective agent

Filariform larva, penetrating directly thru the skin, usually the thin skin of feet while walking bare-footed on fecally contaminated soil.

Pathogenesis



- (1) Larval migration thru tissues causes local inflammatory reaction with an eosinophilic exudate, esp. in lungs & on entry site.
- (2) Adult worms withdraw blood from intestinal wall for their food, & also cause chronic hemorrhages from punctured sites, both leading to progressive microcytic anemia. Anemia is esp. pronounced in persons whose nutrition cannot compensate for blood loss.

- (2) Duodenal content → Obtained by duodenal intubation, sometime reveals adult worms.

Clinical findings

(1) Due to migrating larva

- (a) Ground itch (dermatitis) at entry site.
- (b) Creeping eruption → A reddish itchy papule, due to wandering of larva in skin before gaining entry into lymphatics or veins (occur rarely).
- (c) Bronchitis.
- (d) Bronchopneumonia.
- (e) Eosinophilia (marked).

(2) Due to adult worm

- (a) Anemia → Usually microcytic & hypochromic due to blood loss, & this is more pronounced when there is also nutritional deficiency of iron & hemopoietic substances.
- (b) Dyspepsia.
- (c) Epigastric tenderness.
- (d) Perverted taste for things like earth, mud, or lime (pica or geophagy).
- (e) Constipation.
- (f) Pale appearance of skin, nails, & conjunctiva.
- (g) Puffy face with swelling of lower eyelids.
- (h) Edema of feet & ankle.
- (i) Koilonychia.
- (j) Protuberant abdomen.
- (k) Dry lusterless hair.

Microscopy

- (1) Stool → For eggs.
- (2) Duodenal content → Sometime reveals eggs.

Intensity of ancylostomiasis

Intensity is related to degree of anemia, & is estimated by counting the eggs in feces:

- (1) 2,000-4,000 eggs/gm of feces → Slight anemia.
- (2) 4,000-8,000 eggs/gm of feces → Marked anemia.
- (3) Over 10,000 eggs/gm of feces → Severe anemia.

Blood Examination

- (1) RBC count.
- (2) Shape & size of RBCs.
- (3) Hb%.
- (4) WBC count → For the presence of eosinophilia.

IMMUNITY

Partial acquired immunity developed, that protects against small repeated infections. Innate immunity also provides some protection as evidenced by marked eosinophilia in tissue invasion stage (by larvae).

TREATMENT

- (1) Pyrantal pamoate.
- (2) Mebendazole.

DIAGNOSTIC LABORATORY TESTS

Specimens

Stool, duodenal contents, blood.

Macroscopic Examination

- (1) Stool → For adult worms (that may be passed out spontaneously or after a vermifuge), & for occult blood.

PREVENTION & CONTROL

- (1) Proper sewage disposal.
- (2) Wearing of shoes & gloves.
- (3) Treatment of carrier & diseased persons.

Chapter 4 >

Enterobius Vermicularis (Thread or Pin Worm)

MORPHOLOGY

Adult Male Worm

Shape

Small, un-segmented, & more or less spindle shaped.

Size

2-4 mm in length

Color

White.

Anterior end

A pair of cervical alae (wing-like expansions) is present at anterior end. No buccal cavity.

Posterior end

Posterior third of body is curved & sharply truncated.

Adult Female Worm

Shape

Similar to male worm, but it is more longer & more spindle- shaped.

Size

8-12 mm in length.

Color

Similar to male worm.

Anterior end

Similar to male worm.

Posterior end

Straight, & drawn out into a long, tapering & finely pointed tail.

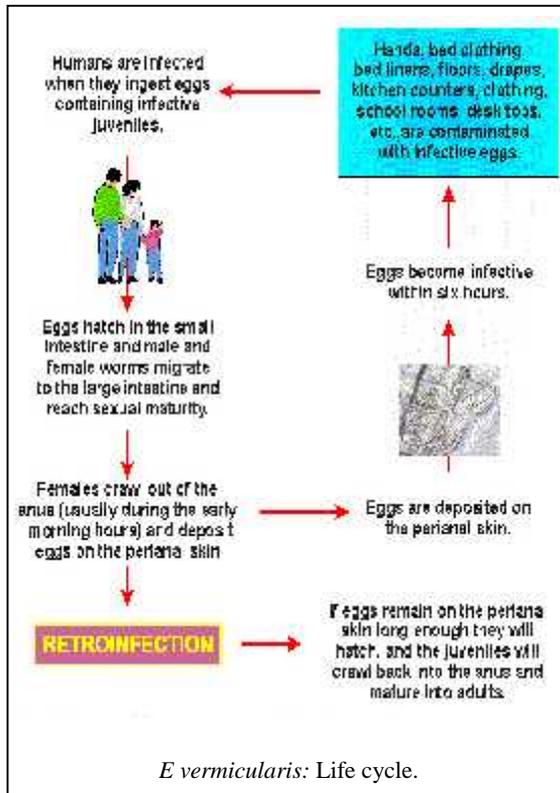
Eggs



E. vermicularis: Above, adult female worm (left) & adult male worm (right). Below, egg.

- (1) Shape → Asymmetrical, being plano-convex.
- (2) Size → 50-60 μm x 30 μm .
- (3) Color → Colorless.
- (4) Covering → A transparent shell.
- (5) Contains → A coiled tadpole-like larva.

LIFE CYCLE



HABITAT & TRANSMISSION

Habitat

(1) Definitive host

Human beings, in which adult mature worms live in terminal ileum, & gravid females in cecum, colon, & rectum.

(2) Intermediate host

None

Transmission

Via perianal-oral route.

(1) Auto-infection

Wandering of female worms at the time of egg laying causes intense itching, inducing patient to scratch affected part → Eggs containing infective larvae are carried on their fingers → Eggs are subsequently transferred to food & swallowed, or infection may result from anus-to-mouth habit of children.

(2) Retro-infection

Eggs laid on perianal skin immediately hatch into infective-stage larvae & migrate thru anus to develop into adult worms in colon.

(3) Person-to-person transmission

- Contagious, due to handling of night-clothes, & bed-linens of infected patients.
- Ingestion of eggs, in contaminated food or water.
- Occasionally, air-borne transmission.

In External Environment

Eggs are laid on perianal skin of definitive hosts, humans (the only host of *E. vermicularis*) → Contained tadpole-like larva completes its development in 24-36 hours, in the presence of O₂ → These embryonated eggs are infective to humans.

In Human Being (The Only Host)

Humans become infected with the ingestion of embryonated eggs → In GIT, egg shells gets dissolved by digestive juices & larvae escape in upper small intestine → After moulting twice, they become adult in lower ileum, in about 2-6 weeks → After attaining sexual maturation, male fertilizes the female & dies → Gravid female then migrates down to cecum & colon (also to vermiform appendix) & remains there until the eggs develop → Fertilized female then wanders down the rectum & work its way out of anus during night, to deposit eggs on perianal skin, & so, the cycle is again repeated.

Note: 3 moultings of larva occur, one outside on perianal skin, & 2 in small intestine.

PATHOGENESIS & CLINICAL FINDINGS

Enterobiasis

Infective agent

Embryonated eggs.

Pathogenesis

- Irritation caused by gravid females around anus
- Ectopic migration of females in places like female genital tract, & peritoneal cavity.

Clinical finding

- Perianal pruritus.
- Eczematous condition in perianal region.
- Salpingitis.
- Nocturnal enuresis.

- (5) Appendicitis (in 2% cases).
- (6) Secondary bacterial infections.

TREATMENT

DIAGNOSTIC LABORATORY TESTS

- (1) Pyrantal pamoate.
- (2) Mebendazole.

Specimens

Perianal swab, stool.

PREVENTION & CONTROL

Macroscopic Examination

- (1) Stool → For adult worms.
- (2) Perianal region at the commencement of itching
→ May reveal gravid female worms.

- (1) Personal hygiene.
- (2) Mass treatment of all infected cases.

Microscopy

Perianal swab → For eggs.

IMMUNITY

Role of acquired immunity in protection against infection & re- infection is uncertain.

Chapter 48

Trichuris Trichiura (Whip Worm)

MORPHOLOGY

Adult Male Worm

Shape

Resembles a whip, being composed of a hair-like anterior part 'the lash' comprising roughly 3/5th of worm length, & a much stouter part comprising remaining 2/5th representing 'the stock'.

Size

3-4 cm in length.

Anterior end

There is a minute, spear-like projection, by which worm bores into intestinal wall.

Posterior end

Spirally coiled ventrally called copulatory bursa, & a single spicule protrudes from it.

Adult Female Worm

Shape

Similar to male worm.

Size

4-5 cm in length.

Anterior end

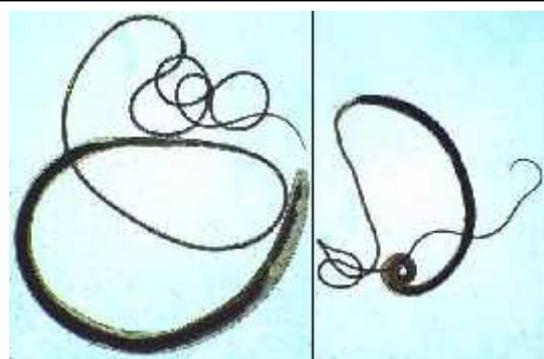
Similar to male worm.

Posterior end

Shaped like a comma or an arc.

Eggs

- (1) Shape → Barrel-shaped with a mucus plug at each pole.
- (2) Size → 50 μm x 25 μm.
- (3) Color → Brown (bile-stained).



T trichiura: Above, adult female (left) & adult male (right) worms. Below, egg.

- (4) Coverings → Double shell, outer one is bile-stained.
- (5) Contents → An un-segmented ovum, when eggs leaves the human host.

LIFE CYCLE

In External Environment

Eggs are passed with the feces of definitive host, humans (the only host for *T trichiura*) → Development proceeds slowly in water or damp soil, & a rhabditiform larva develops within egg in

about 3-6 weeks → Embryonated eggs are now infective to humans.

In Human Beings (The Only Host)

Humans become infected with the ingestion of embryonated eggs in contaminated food or water → In GIT, egg-shell is dissolved by digestive juices & larva emerges thru one of the poles of egg → Liberated larvae pass down into cecum & grow directly into adult worms → Adult worms bores into intestinal wall, in such a way that whole of its anterior part is buried in mucosa → Within a month of infection, worms become sexually matured & gravid females begin to lay eggs, & the cycle is again repeated.

HABITAT & TRANSMISSION

Habitat

(1) **Definitive host**

Human beings, in which adult worms lives in cecum, & also in ileum, appendix, & colon.

(2) **Intermediate host**

None.

Transmission

Via fecal-oral route (eggs are passed in feces, & embryonated eggs are ingested orally with contaminated food or water).

PATHOGENESIS & CLINICAL FINDINGS

Trichiuriasis

Infective agent

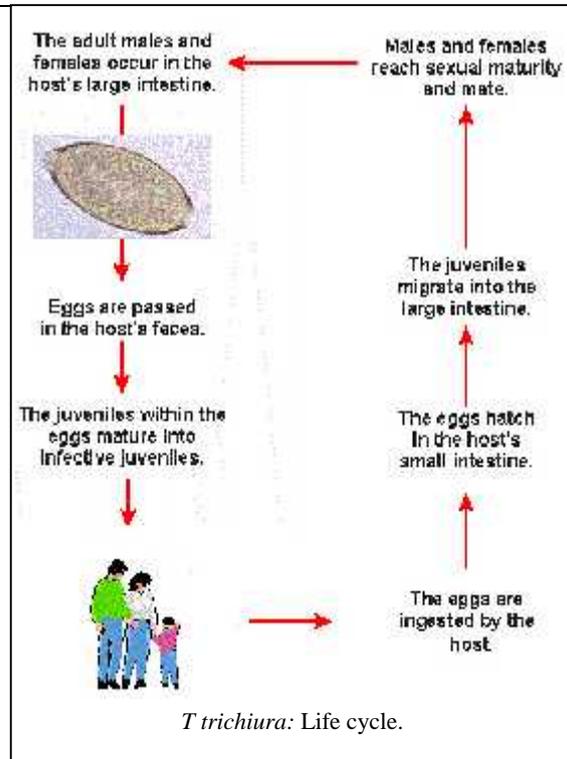
Embryonated eggs.

Pathogenesis

It is related to the burrowing effect of worm that damages the mucosa & causes hemorrhage (although slight than that caused by *A. duodenale*).

Clinical findings

- (1) In light infections → Usually asymptomatic.
- (2) In heavy infections →
 - (a) Abdominal pain.
 - (b) Diarrhea (with mucus & blood in stool).



- (c) Loss of weight.
- (d) Anemia.
- (e) Acute appendicitis (if the worms inhabit vermiform appendix).
- (f) Rectal prolapse (occur occasionally in massive infection).

DIAGNOSTIC LABORATORY TESTS

Specimen

Stool.

Macroscopic Examination

Stool → For adult worms, that may be passed in stool.

Microscopy

Stool smear is observed under microscope for:

- (1) Characteristic barrel-shaped eggs.
- (2) Eosinophils.
- (3) Charcot-Leyden crystals.

Proctoscopy & Sigmoidoscopy

May show stocks of worms attached to the mucosa.

PREVENTION & CONTROL**IMMUNITY**

Role of acquired immunity in protection against infection & re-infection is uncertain.

- (1) Proper disposal of feces.
- (2) Prevention of consumption of uncooked vegetables & fruits grown in fields having human feces used as manure.

TREATMENT

- (1) Mebendazole (drug of choice).
- (2) Pyrantal pamoate.

Chapter 49

Wuchereria Bancrofti (Bancroft's Filaria)

MORPHOLOGY

Adult Male Worm

Shape

Long hair-like or filiform in shape, & tapers at both ends.

Size

2.5-4 cm in length.

Color

Transparent or creamy-white.

Head end

Terminates in a slightly rounded swelling.

Tail end

Curved ventrally, & contains 2 spicules of unequal length.

Adult Female Worm

Shape

Similar to male worm.

Size

8-10 cm in length.

Color

Similar to male worm.

Head end

Similar to male worm.

Tail end

Narrow & abruptly pointed.

Microfilariae

Unstained



W bancrofti: Above, adult female (left) & adult male (right) worms. Below, microfilaria.

Appear as colorless & transparent bodies with blunt heads & rather pointed tails, & measures about 290 μm x 6-7 μm .

Stained with Romanowsky's stain

It shows;

- (1) A hyaline sheath, much longer (359 μm) than larval body.
- (2) Cuticula.
- (3) Somatic cells or nuclei, appearing as granules. Granules do not extend up to the tip of tail, & also the anterior end is devoid of granules.

LIFE CYCLE

In Mosquito

Microfilarial development takes place in mosquito:

(1) Blood meal

During its blood meal, mosquito ingests sheathed microfilariae → These collect round the anterior end of stomach.

(2) 1st stage larvae

Microfilariae cast off their sheaths quickly (at the anterior end of stomach) & penetrate gut-wall within 1-2 hours → Migrate to thoracic muscles, where they rest & begin to grow → In next 2 days, they change into thick, short, sausage-shaped forms with a short spiky tail & rudimentary digestive tract, called 1st stage larvae.

(3) 2nd stage larvae

In 3-7 days larvae grow rapidly, moult (sheds cuticle) once or twice, to change into 2nd stage larvae.

(4) 3rd Stage larvae

On 10th or 11th day, metamorphosis is complete, & 3rd stage larvae are formed with tail atrophies to a mere stump, & digestive system, body cavity & genital organs fully developed → 3rd stage larvae are infective to humans, which enters the proboscis sheath of mosquito on about 14th day.

In Human Beings

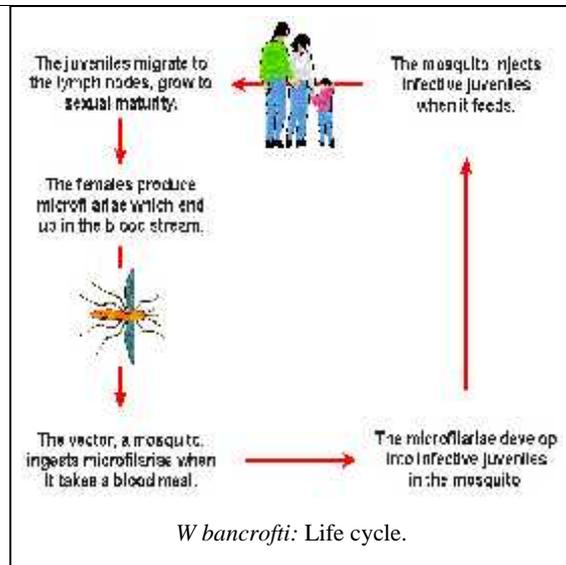
Development of adult worms takes place in humans:

(1) Entrance of 3rd stage larvae

Humans become infected with the bite of infective mosquito, which deposits the 3rd stage larvae near the site of puncture on skin → Later, attracted by skin warmth, larvae either enter thru puncture wound or penetrate thru the skin on their own.

(2) Development

3rd stage larvae gain access to the lymphatics after penetrating the skin → Settle down at some spot (inguinal, scrotal or abdominal lymph nodes) & begin to grow into adult forms → In about 5-18 months, they become sexually mature → Male fertilizes the females → Gravid females give birth to larvae, a new generation of microfilariae → Microfilariae enter venous system, either via thoracic or right lymphatic ducts → Carried to the peripheral circulation, &



wait for the next blood meal of mosquito, to repeat the cycle (microfilariae can live in peripheral circulation for up to 70 days).

HABITAT & TRANSMISSION**Habitat****(1) Definitive host**

Human beings, in which adult worms live in lymphatic system, & microfilariae in peripheral circulation.

(2) Intermediate host

Mosquitoes of genus *Culex*, *Aedes*, & *Anopheles*.

Transmission

Via mosquito bite (during bite mosquito may become infected, or it may cause the humans to become infected).

PATHOGENESIS & CLINICAL FINDINGS**Wuchereriosis (or Classical Filariasis)****Infective agent**

3rd stage larvae.

Incubation period

About one to one & half years.

Pathogenesis

It is related to adult worms, which causes inflammation in lymph nodes & lymphatics, which eventually obstructs the lymphatics causing edema.

Clinical findings

- (1) Periodic attacks of fever.
- (2) Lymphangitis.
- (3) Lymphadenitis.
- (4) Lymphangio-varix.
- (5) Thickening of skin.
- (6) Hydrocele.
- (7) Elephantiasis of legs, scrotum, & vulva, (& less commonly of arms & breasts).
- (8) Chyluria, if preaortic nodes are blocked, or when lymphatics of kidney, ureter, or bladder are blocked.
- (9) Microfilariae are present in peripheral blood.

Occult Filariasis**Infective agent**

3rd stage larvae.

Incubation period

Within a few months (three & half) after exposure.

Pathogenesis

It is related to microfilariae, the metabolites of which give rise to allergic manifestations involving lymphatic system, lungs, liver, spleen, & skin. This occurs in highly reactive individuals.

Clinical findings

- (1) Generalized lymphadenitis.
- (2) Hepatomegaly.
- (3) Splenomegaly.
- (4) Massive eosinophilia.
- (5) Pulmonary symptoms.
- (6) Absence of microfilariae in peripheral blood.

DIAGNOSTIC LABORATORY TESTS**Specimens**

Blood, chylous urine, exudate of lymph varix, hydrocele fluid, lymph node biopsy, serum.

Macroscopic Examination

Lymph node biopsies → For adult worms.

Microscopy

- (1) Blood → For sheathed microfilaria.
- (2) Chylous urine → For sheathed microfilaria.
- (3) Lymphvarix exudate → For sheathed microfilaria.
- (4) Hydrocele fluid → For sheathed microfilaria.
- (5) Blood → For eosinophils.

Skin Test

Filarial antigens injected intradermally → Immediate hypersensitivity reaction → Positive test.

Serology

Complement fixation test (a sensitive test for occult filariasis)

Radiology

May reveal calcified worms.

IMMUNITY

In earlier stages worm provokes a cellular reaction, chiefly eosinophilic, but it disappears gradually. Reticulo-endothelial system response occurs when the worm dies or undergoes degenerative changes. Antibodies develop in occult filariasis (as evidenced by positive complement fixation test).

TREATMENT

- (1) Diethylcarbamazine (effective only against microfilariae).
- (2) Surgical treatment for elephantiasis.
- (3) No drug therapy for adult worm is available.

PREVENTION & CONTROL

- (1) Mosquito control with insecticides.
- (2) Use of protective clothing, mosquito netting, & repellents.

Chapter 50

X - Borne Diseases

WATER-BORNE DISEASES

Bacterial diseases

- (1) Cholera.
- (2) Enteric fever.
- (3) Bacillary dysentery.
- (4) Diarrhea.

Viral diseases

- (1) Poliomyelitis.
- (2) Infective hepatitis.
- (3) Keratoconjunctivitis.

Protozoal diseases

Amoebic dysentery.

Helminthic diseases

- (1) Shistosomiasis.
- (2) Trichuris trichuria infestation.
- (3) Hydatid cyst.
- (4) Ascariasis.
- (5) Enterobiasis.

MILK - BORNE DISEASES

Bacterial diseases

- (1) Cholera.
- (2) Enteric fever.
- (3) Bacillary dysentery.
- (4) Diarrhea.
- (5) Diphtheria.
- (6) Bovine tuberculosis.

Viral diseases

Poliomyelitis.

Protozoal diseases

Amoebic dysentery.

MEAT-BORNE DISEASES

Bacterial diseases

- (1) Salmonellosis.
- (2) Shigellosis.
- (3) Tuberculosis.
- (4) Anthrax.
- (5) Brucellosis.
- (6) Botulism.

Helminthic diseases

- (1) Teniasis.
- (2) Trichinosis.

DROPLET-BORNE DISEASES

Bacterial diseases

- (1) Diphtheria.
- (2) Tuberculosis.
- (3) Whooping cough.
- (4) Cerebrospinal fever (meningococcal meningitis).

Viral diseases

- (1) Small pox.
- (2) Chicken pox.
- (3) Measles.
- (4) German measles.
- (5) Mumps.
- (6) Influenza.

SEX - BORNE DISEASES

Bacterial diseases

- (1) Syphilis.
- (2) Gonorrhoea.
- (3) Chancroid.
- (4) Granuloma inguinale.
- (5) Lymphogranuloma venerium.

Viral diseases

- (1) AIDS (acquired immunodeficiency syndrome).
- (2) Herpes simplex.

Section "III"

Self - Examination

Chapter 57

Self Examination (True / False)

INSTRUCTIONS

For every numbered questions, five lettered answers are given, which may be either true or false. Correct answers (T for true, & F for false) are given just before the lettered answers.

Now, what you have to do, is to,

- 1st, cover those correct answers say with a paper or scale.
- 2nd, read the question.
- 3rd, read the lettered answer.
- 4th, make up the answer in your mind.
- 5th, now bring the covering paper or scale a little down, & look at the correct answer.
- 6th, proceeds in this way.

GENERAL BACTERIOLOGY

1) Bacterial cell wall

- F = (A) Consists only of a mixed polymer called peptidoglycan.
 F = (B) Responsible for Gram reaction.
 T = (C) Uniquely flexible plastic structure.
 F = (D) G +ve bacterial cell-wall is more sensitive to lysozyme than that of G -ve cell-wall.
 T = (E) External barrier around the cell.

2) Surface structures of bacteria

- T = (A) Pili mediate interaction of bacteria with mucosal epithelium.
 T = (B) Polysaccharide capsules retard phagocytosis.

F = (C) Both G +ve & G -ve cocci have lipopolysaccharide (endotoxin) in their cell wall.

F = (D) Flagella are non-antigenic in humans b/c they closely resemble human flagella in chemical composition.

F = (E) Flagella are always present at one pole.

3) Peptidoglycan in bacterial cell wall

T = (A) Has a backbone composed of alternating units of muramic acid & acetylglucosamine.

T = (B) Cross-links b/w tetrapeptides involves D-alanine.

F = (C) Thinner in G +ve than in G -ve cells.

T = (D) Degraded by lysozyme.

T = (E) Responsible for Gram reaction.

4) Bacterial spores

F = (A) Their survival ability is based on their enhanced metabolic activity.

T = (B) Formed by G +ve rods.

T = (C) Killed by being heated to 121°C for 15 min.

T = (D) Contain much less water than bacterial cell.

F = (E) Produced outside the cells.

5) Most accurate comparison of human, bacterial, & fungal cells is,

F = (A) Human cells undergo mitosis, whereas neither bacteria nor fungi do.

F = (B) Human & fungal cells have a similar cell wall, in contrast to bacteria, whose cell wall contains peptidoglycan.

F = (C) Human & bacterial cells have plasmids, whereas fungal cells do not.

T = (D) Human & fungal cells have similar ribosomes, whereas bacterial ribosomes are different

F = (E) Cells of all 3 are characterized by spore formation.

6) Endotoxins

T = (A) Less potent (ie, less active on weight basis) than exotoxins.

T = (B) More stable on heating than exotoxins.

F = (C) Bind to specific cell receptors, whereas exotoxins are not.

T = (D) Are part of bacterial cell wall, whereas exotoxins are not.

F = (E) Vaccines can be produced from it, as well as from exotoxins.

7) Main host defense against exotoxin is

F = (A) Activated macrophages secreting proteases.

T = (B) IgG & IgM antibodies.

F = (C) Helper T cells.

F = (D) Modulation of host cell receptors in response to toxin.

F = (E) IgE antibodies & mast cells.

8) Normal flora

T = (A) Staphylococcus epidermidis is the most common organism on skin.

F = (B) E coli is a prominent member in respiratory tract.

T = (C) Bacteroides fragilis is mainly found on colon.

T = (D) Lactobacillus is the most common organism in female genital tract.

T = (E) Viridans streptococci are found in upper respiratory tract.

9) Anaerobically growing bacteria

T = (A) Require low oxidation - reduction potential such as - 300 mV.

T = (B) Require reduced O₂ tension & will not grow on surface of agar medium in air.

T = (C) Include both G +ve rods & G -ve rods.

T = (D) Facultative anaerobes can grow in presence of O₂.

T = (E) Require candle jar, or anaerobic jar to grow in laboratory.

10) For serology, following structures provide useful antigens

T = (A) Capsule.

T = (B) Flagella.

T = (C) Cell wall.

F = (D) Ribosomes.

F = (E) None.

11) Mechanism of action of antibacterial drugs

F = (A) Cephalosporins inhibit protein synthesis by blocking peptidyl transferase.

T = (B) Penicillins inhibit transpeptidase reaction & activate autolytic enzymes.

T = (C) Tetracyclines inhibit protein synthesis by blocking tRNA binding.

F = (D) Aminoglycosides inhibit protein synthesis by activating ribonuclease.

T = (E) Erythromycin inhibits protein synthesis by blocking translocation of polypeptide.

12) Resistance of bacteria to antibacterial drugs

T = (A) Resistance to chloramphenicol is due to the production of chloramphenicol acetyl transferase.

T = (B) Resistance to penicillin is due to reduced affinity of transpeptidases.

F = (C) Resistance to tetracycline is due to an enzyme that hydrolyzes the ester linkage.

T = (D) Resistance to aminoglycosides are due to alteration in receptors, & production of inactivating enzymes.

F = (E) Resistance to sulfonamides are due to enzymes that deaminates the drug.

13) Growth of bacteria

T = (A) Some bacteria grow in both presence & absence of O₂.

T = (B) Some bacteria use gaseous CO₂ as a carbon source, whereas others require carbon in organic form.

F = (C) Some bacteria grow in an exponential, logarithmic manner, whereas others undergo meiosis.

T = (D) Some bacteria have a doubling time as short as 30 minutes, whereas others have a doubling time of 10 hours or more.

F = (E) All bacteria grow best at a temperature range of 20-40°C.

14) In Gram stain, decolorization of G -ve bacteria by alcohol is MOST closely related to

F = (A) Proteins encoded by F plasmids.

T = (B) Lipids in cell wall.

F = (C) 70 C ribosomes.

F = (D) Branched polysaccharides in capsule.

F = (E) Teichoic acid in outer membrane.

15) Effects of endotoxin include

F = (A) Opsonization.

T = (B) Fever.

T = (C) Activation of coagulation cascade.

T = (D) Hypotension.

T = (E) Activation of macrophages.

16) Bacterial surface structures that show antigenic diversity include

T = (A) Pili.

T = (B) Capsules.

T = (C) Flagella.

F = (D) Peptidoglycan.

T = (E) Lipopolysaccharide.

17) Exotoxins

T = (A) When treated chemically, some exotoxins lose their toxicity & can be used as immunogens in vaccines.

T = (B) Some exotoxins are capable of causing disease in purified form, free of any bacteria.

F = (C) Toxicity destroyed by heating at 10°C.

T = (D) Some exotoxins act in GIT to cause diarrhea.

F = (E) Some contain lipopolysaccharides as toxic components.

18) Normal flora

T = (A) Of colon consists mainly of anaerobic bacteria.

T = (B) Prevents certain pathogens from colonizing upper respiratory tract.

F = (C) Include all microorganisms except fungi.

T = (D) Organisms are permanent residents of body surfaces.

F = (E) Present at birth.

19) Essential components of bacterial cell include

T = (A) Cell wall.

F = (B) Pili.

F = (C) Capsule.

T = (D) Mesosome.

T = (E) Ribosomes.

20) Portal of entry

T = (A) Genital tract.

F = (B) Liver.

T = (C) Respiratory tract.

T = (D) Skin.

T = (E) GIT.

21) Factors responsible for invasiveness of bacteria include

T = (A) Hyaluronidase.

T = (B) Capsule.

F = (C) Lipid A component of lipopolysaccharides in G -ve rods.

T = (D) Streptokinase.

F = (E) Peptidoglycan.

22) Chemical agents used as disinfectant include

T = (A) Ethanol.

T = (B) Phenols.

F = (C) Metals, eg magnesium, copper.

T = (D) Formaldehyde.

F = (E) Strong acids & weak alkalis.

23) Primary natural barrier against infection is

F = (A) Mechanical action of ciliated cells.

T = (B) Presence of intact skin.

F = (C) Acidic pH of body fluids & secretions.

F = (D) Lytic enzymes found in body fluids.

F = (E) Cell mediated immune system.

24) Following are liquid culture media

T = (A) Nutrient broth.

F = (B) MacConkey's medium.

F = (C) Lowenstein - Jensen medium.

T = (D) Christensen's urea medium.

T = (E) Simmon citrate medium.

25) Late - lactose fermenters on Mac-Conkey's medium include

F = (A) Pseudomonas.

T = (B) Vibrio cholera.

T = (C) Serratia.

T = (D) Citrobacter.

F = (E) All shigella species.

26) Microorganisms cultured on chocolate agar are

T = (A) Neisseria gonorrhoeae.

T = (B) Neisseria meningitidis.

T = (C) Streptococcus pneumoniae.

F = (D) Streptococcus viridans.

T = (E) Hemophilus influenza.

27) Color of colonies on nutrient agar

F = (A) Staphylococcus albus → Golden yellow.
 T = (B) Staphylococcus citrus → Lemon yellow.
 F = (C) Pseudomonas → Bluish green.
 F = (D) Proteus → Light yellow.
 T = (E) Staphylococcus roseus → Pink.

28) Virulence of organisms depends on

F = (A) Number of bacteria in tissues.
 T = (B) Invasion of host cells & tissues.
 T = (C) Production of enzymes.
 T = (D) Resistance to phagocytosis.
 F = (E) Decreased resistance of hosts.

29) The virulence of bacteria is related to

F = (A) Their number in the host tissues.
 T = (B) Their production of toxins.
 T = (C) Their ability to produce spreading factors.
 T = (D) Their antigenic heterogeneity.
 F = (E) Decreased resistance of the host.

30) Pathogenicity of bacteria depends on

T = (A) Invasiveness.
 F = (B) Sex of the host.
 T = (C) Portal of entry.
 F = (D) Spore formation.
 T = (E) Enzymes & toxins produced.

31) Infection within a hospital may be

T = (A) Dust-borne.
 T = (B) Water-borne.
 T = (C) Food-borne.
 T = (D) Hand-borne.
 F = (E) Endogenous.

32) Bacteria are normally found on or in the

F = (A) Blood.
 F = (B) Urinary tract.
 F = (C) Lower bronchi.
 T = (D) Gastrointestinal tract.
 T = (E) Skin, sebaceous glands & hair follicles.

SPECIAL BACTERIOLOGY**33) Classification of streptococci**

T = (A) Pneumococci are α-hemolytic, & can be serotyped on the basis of their polysaccharide capsule.
 T = (B) Enterococci are group D streptococci.

F = (C) Viridans streptococci are identified by Lancefield grouping, which is based on C carbohydrate in cell wall.
 F = (D) Streptococcus agalactiae are included in group G.
 T = (E) Peptostreptococci are anaerobic.

34) Streptococci

F = (A) Are G +ve, motile, rods.
 T = (B) On blood agar, produce α, β, or γ hemolysis.
 T = (C) Growth promoted by 10% CO₂.
 F = (D) Are always aerobic.
 T = (E) M protein are present in virulent streptococci.

35) Hemolysins of streptococci

T = (A) Streptolysin S is responsible for hemolysis on blood agar.
 F = (B) Both streptolysin O & S are antigenic.
 T = (C) Both streptolysin O & S suppresses chemotaxis.
 F = (D) Cause toxic shock syndrome.
 F = (E) Both streptolysin O & S are antiphagocytic.

36) Diseases caused by streptococci

T = (A) Sore throat.
 F = (B) Osteomyelitis.
 T = (C) Puerperal fever.
 T = (D) Infective endocarditis.
 F = (E) Hepatitis.

37) The gram negative endotoxin producing aerobic or facultative anaerobic rods include

T = (A) E. coli.
 F = (B) Clostridia.
 T = (C) Proteus species.
 T = (D) Pseudomonas aeruginosa.
 T = (E) Klebsiella pneumonia.

38) Newborn meningitis usually caused by

F = (A) Meningococci.
 F = (B) Pneumococci.
 F = (C) Dermatophytes.
 T = (D) E. coli.
 T = (E) Streptococcus agalactiae.

39) Agents recognized as cause of diarrhea include

T = (A) Clostridium perfringens.

F = (B) Streptococcus fecalis.

T = (C) Rotavirus.

T = (D) Vibrio cholerae.

T = (E) Staphylococci.

40) Organisms important in UTI are

T = (A) E coli.

T = (B) Proteus mirabilis.

T = (C) Klebsiella pneumoniae.

F = (D) Pneumococci.

F = (E) Bacteroides fragilis.

41) Mycobacterium tuberculosis

T = (A) After being stained with carbolfuchsin, it resists decolorization with acid-alcohol.

T = (B) Has a large amount of mycolic acid in its cell wall.

F = (C) Appears as red rod in Gram-stained specimens.

T = (D) Appears as red rod in acid-fast stained specimens.

F = (E) Are capsulated & motile.

42) Mycobacterium tuberculosis

T = (A) Cultivated on Lowenstein - Jensen medium.

T = (B) Cell division require 12 - 20 hours.

F = (C) Sulfatides are responsible for the formation of serpentine cord.

F = (D) BCG is a vaccine that contain formalin - treated M bovis.

T = (E) Isoniazid is an effective drug against it.

43) Staphylococci

F = (A) Are G -ve, non-motile, rods.

T = (B) Staphylococcus aureus is coagulative positive.

F = (C) On blood agar better pigmentation occur.

T = (D) Colonies are round, raised, smooth, & glistening.

T = (E) Teichoic acid is present in its cell wall.

44) Staphylococci

T = (A) Possess catalase & beta - lactamase.

T = (B) Its exotoxins damages RBCs.

F = (C) Causes toxic shock syndrome due to production of exfoliatin toxin.

T = (D) Responsible for localized infections like carbuncle, impetigo & furuncle.

T = (E) Antibodies produced against its toxins & antigens confers permanent immunity.

45) Streptococcus pneumoniae

T = (A) Produces alpha hemolysis on blood agar.

F = (B) Growth inhibited by 5 -10 % CO₂ (candle jar).

T = (C) Virulence is due to capsular polysaccharide.

F = (D) Causes pneumonia esp. bronchopneumonia.

T = (E) Causes meningitis & otitis media.

46) Following bacteria are commonly found in infected wounds following colonic operations

T = (A) Escherichia coli.

F = (B) Neisseria meningitidis.

T = (C) Streptococcus pyogenes.

T = (D) Streptococcus fecalis.

T = (E) Bacteroides fragilis.

47) Virulent treponema pallidum is used in

T = (A) Treponema pallidum immobilization test.

F = (B) Reiter protein complement fixation test.

F = (C) Wassermann complement fixation test.

F = (D) Fluorescent treponemal antibody test.

F = (E) Fluorescent treponemal antibody/absorption test.

48) Difference b/w pneumococci & strep. viridans

T = (A) Pneumococci are capsulated, whereas S viridans are not.

F = (B) S viridans lyse spontaneously in media, whereas viridans not.

T = (C) Pneumococcal growth are inhibited around optochin disks, whereas S viridans growth are not inhibited.

F = (D) Pneumococci produce beta hemolysis on blood agar, whereas S viridans produces alpha hemolysis.

T = (E) Pneumococci ferment inulin, whereas S viridans not.

49) Diseases best diagnosed by serologic means are

T = (A) Q fever.

F = (B) Pulmonary tuberculosis.

F = (C) Gonorrhoea.

F = (D) Non - gonococcal urethritis.

T = (E) Typhoid.

50) Your patient has subacute bacterial endocarditis caused by S viridans. Which

one of following sites is MOST likely to be the source of organism?

- F = (A) Skin.
 F = (B) Colon.
 T = (C) Oropharynx.
 F = (D) Urethra.
 F = (E) Small intestine.

51) Salmonella

- T = (A) Produce black colonies on Bismuth sulfite medium due H₂S production.
 F = (B) Ferment lactose & sucrose.
 T = (C) Are motile with peritrichous flagella.
 F = (D) Produce alkaline slant & acid butt with gas in triple sugar iron medium.
 T = (E) Changes color of Simmon citrate medium to blue.

52) Typhoid fever

- F = (A) Caused by salmonella typhi & S epidermidis esp.
 T = (B) Organism enter via oral route with contaminated food or water.
 F = (C) Fever remains at low level.
 T = (D) Hyperplasia & necrosis of Peyer's patches occur.
 F = (E) Rose spots appear on face & back.

53) Which one of following host defense mechanisms is MOST important for preventing dysentery caused by shigella?

- T = (A) Gastric acid.
 F = (B) Salivary enzymes.
 F = (C) Normal flora of mouth.
 F = (D) Esophageal mucosa.
 F = (E) Duodenal enzymes.

54) MOST important protective function of antibody stimulated by tetanus immunization is

- F = (A) To opsonize the pathogen (Clostridium tetani).
 F = (B) To prevent growth of pathogen.
 F = (C) To prevent adherence of pathogen.
 T = (D) To neutralize the toxin of pathogen.
 F = (E) To stimulated complement cascade.

55) Five hours after eating fried rice at a restaurant, a 24-year-old women & her husband both develop nausea, vomiting, & diarrhea. Organism most likely to be involved is,

- F = (A) Clostridium perfringens.
 F = (B) Enterotoxigenic E coli.
 T = (C) Bacillus cereus.
 F = (D) Salmonella typhi.
 F = (E) Staphylococcus aureus.

56) Following are gram -ve pathogenic diplococci

- T = (A) Neisseria meningococci.
 T = (B) Neisseria gonococci.
 T = (C) Neisseria lactamica.
 T = (D) Neisseria flavescens.
 F = (E) Streptococcus pneumoniae.

57) In diagnosis of rheumatic fever following are helpful

- T = (A) ASO titer.
 T = (B) Throat swab.
 F = (C) Blood culture.
 F = (D) Urine culture.
 T = (E) ESR.

58) Staphylococcus can cause following lesions

- T = (A) Abscess.
 T = (B) Carbuncle.
 T = (C) Boil.
 T = (D) Cellulitis.
 F = (E) Lymphangitis.

59) Pathogenic pyogenic organisms are

- T = (A) Staph. aureus.
 F = (B) Staph. albus.
 F = (C) Corynebacterium diphtheria.
 T = (D) Bacteroides.
 T = (E) Pseudomonas aeruginosa.

60) Major pathogens in post-operative chest infections are

- T = (A) Hemophilus influenza.
 F = (B) Streptococcus pyogenes.
 T = (C) Staphylococcus aureus.
 F = (D) Mycobacterium tuberculosis.
 T = (E) Streptococcus pneumoniae.

61) Pathogenesis of post-streptococcal glomerulonephritis include

- F = (A) Similarity of antigens between the bacteria & kidney tissue.
 F = (B) Hypersensitivity towards streptolysin O.
 T = (C) Formation of antigen-antibody complexes.
 F = (D) Bacteremia due to streptococcus.
 F = (E) Septicemia.

62) Actinomycosis mainly effects

- F = (A) Middle ear cavity.
 T = (B) Oral cavity.
 F = (C) Brain.
 T = (D) Liver.
 T = (E) Lungs.

63) Septic meningitidis is caused by

- T = (A) H. influenza.
 F = (B) Cryptococcus.
 F = (C) Mycobacterium tuberculosis.
 T = (D) Neisseria meningitidis.
 T = (E) Pneumococcus.

64) Actinomycosis is

- T = (A) Characterized by presence of sulphur granules in pus.
 T = (B) Characterized by abscess formation.
 T = (C) Caused by an anaerobic organism.
 T = (D) Characterized by draining sinus tracts.
 F = (E) Transmitted by personal contact.

65) Following tests are best suited for following diseases

- T = (A) Syphilis → Kahn's test.
 F = (B) Neonatal jaundice → Widal's test.
 F = (C) Myeloid leukemia → Complement fixation test.
 T = (D) SLE → Coomb's test.
 T = (E) Tuberculosis → Mantoux test.

66) Following disease cause ulcers of penis

- F = (A) Gonorrhoea.
 T = (B) Syphilis.
 T = (C) Lymphogranuloma venereum.
 T = (D) Lymphogranuloma inguinale.
 T = (E) Herpes simplex genitalis.

67) Chronic carrier state is most likely to develop in

- F = (A) Campylobacter enterocolitis.
 F = (B) Shigella enterocolitis.
 F = (C) Cholera.
 T = (D) Typhoid fever.
 F = (E) E coli UTI.

68) Clostridium botulinum

- T = (A) Contain oval, terminal or subterminal spore.
 F = (B) Possess cytochrome & cytochrome oxidase.
 F = (C) Immunity developed against its toxin.

T = (D) Found in soil & animal feces.

F = (E) Are non-motile rods.

69) Botulinum toxin

- T = (A) It is an exotoxin, with 8 antigenic types.
 F = (B) Neurotoxic protein is present in types C, D, & E.
 F = (C) Stimulate release of acetylcholine at myoneural junction.
 T = (D) Causes death in adults (adult botulism) from respiratory paralysis & cardiac arrest.
 T = (E) Trivalent (A, B, E) antitoxin, is used in treatment of botulism.

70) Zoonotic illnesses having NO arthropod vector include

- F = (A) Lyme disease.
 F = (B) Plague.
 T = (C) Brucellosis.
 F = (D) Epidemic typhus.
 T = (E) Anthrax.

71) Organisms that principally infects vascular endothelial cells

- F = (A) Salmonella typhi.
 T = (B) Rickettsia typhi.
 F = (C) Coxiella burnetii.
 F = (D) Hemophilus influenza.
 F = (E) Chlamydia psittaci.

72) Rickettsiae

- F = (A) Grown in laboratory on various artificial media.
 T = (B) Typhus group rickettsiae grow in cytoplasm.
 T = (C) Antibodies against rickettsial antigens can agglutinate proteus vulgaris.
 F = (D) R typhi causes epidemic typhus.
 T = (E) Q fever is caused by Coxiella burnetii.

73) Gram +ve cocci causes

- T = (A) Impetigo.
 T = (B) Boil.
 F = (C) Wool-sorters disease.
 T = (D) Scarlet fever.
 T = (E) Ludwig's angina.

74) B. anthracis is

- T = (A) Spore forming.
 F = (B) Motile.
 T = (C) Aerobic.

T = (D) Gram +ve.

T = (E) The causative organism of Woolsorter's disease.

75) Nocardia asteroides is

T = (A) Bacteria.

T = (B) Gram + ve.

F = (C) Gram - ve.

T = (D) Weekly AFB.

T = (E) Opportunistic.

76) Chlamydiae

T = (A) Are strict intra-cellular parasites b/c they cannot synthesize sufficient ATP.

T = (B) Possess both DNA & RNA & are bounded by a cell wall.

F = (C) Most chlamydiae are transmitted by arthropods.

F = (D) C trachomatis D -K causes trachoma.

T = (E) Lymphogranuloma venereum is caused by chlamydia trachomatis L1-L3.

77) A 65-year-old man develops dysuria & hematuria. A gram stain of a urine sample shows G -ve rods. Culture of urine on EMB agar reveals nonlactose fermenter colonies without evidence of swarming motility. Which one of following organisms is MOST likely to be the cause of his UTI?

F = (A) Streptococcus fecalis.

T = (B) Pseudomonas aeruginosa.

F = (C) Proteus vulgaris.

F = (D) E coli.

F = (E) Klebsiella ozaenae.

78) Your patient has a brain abscess that was detected one month after a dental extraction. Which one of the following organisms is MOST likely to be involved?

F = (A) Streptococcus viridans.

F = (B) Mycobacterium smegmatis.

F = (C) Lactobacillus acidophilus.

T = (D) Anaerobic streptococci.

F = (E) Mycoplasma pneumoniae.

79) Klebsiella species

F = (A) Produce pale colonies on MacConkey's medium.

F = (B) Are obligate anaerobes.

T = (C) Has large & regular capsule.

F = (D) Klebsiella produces urease.

T = (E) Produce acid slant & acid & gas in butt in triple sugar iron medium.

80) MOST important way the host circumvents the function of pneumococcal polysaccharide capsule is via

F = (A) T lymphocytes sensitized to polysaccharide antigens.

F = (B) Polysaccharide degrading enzyme.

T = (C) Anticapsular antibodies.

F = (D) Activated macrophages.

F = (E) Activation of complement cascade.

81) Diagnostic laboratory tests

T = (A) Both pneumococci & klebsiella, demonstrates +ve capsule swelling test.

F = (B) In Weil-Felix reaction, patient's serum containing anti chlamydial antibodies, agglutinates Proteus vulgaris strains OX - 2, OX - 19, & OX - K.

F = (C) In tube dilution agglutination test (Widal test) antibody is known, whereas antigens are unknown.

T = (D) Phenomenon of Mantoux test is due to delayed - type hypersensitivity response.

T = (E) Schultz Charlton reaction is used to detect erythrotoxic toxin of streptococci.

82) Toxins

T = (A) Erythrotoxic toxin is produced only by lysogenic streptococci.

F = (B) Staphylococcus aureus produces only hemolysins, & enterotoxins (A -F).

F = (C) Pneumococcal pathogenicity is related to a toxin, called pneumolysin.

F = (D) Salmonella produces no toxin.

F = (E) Toxins of Clostridium botulinum induces immunity in about 2 weeks.

83) Corynebacterium diphtheriae

T = (A) Possess Babes - Ernst bodies, that gives them a beaded appearance.

T = (B) In laboratory, cultivated in Loeffler's coagulated serum medium & blood agar containing K - tellurite.

T = (C) Diphtheria toxin is an exotoxin that inhibits poly peptide chain elongation.

T = (D) Schick test demonstrates whether immunity against diphtheria is developed or not.

T = (E) Produce gray to black colonies on blood or chocolate agar with K - tellurite.

84) Clinical findings of streptococcal sore-throat

F = (A) High fever in children, & little fever in adults.

T = (B) Enlarged cervical lymph nodes.

F = (C) Purulent discharge is always present.

T = (D) Acute & intense nasopharyngitis in adults.

F = (E) Tonsillitis in children.

85) Pathogenesis of

T = (A) *Shigella sonnei* is related to invasion of intestinal mucosa.

T = (B) *Clostridium botulinum* is related to pre-formed toxin, that blocks release of acetylcholine at myoneural junction.

F = (C) *E coli* is related to endotoxin.

T = (D) *Meninococci* is related to lipopolysaccharides, pili, & endotoxin.

T = (E) *Vibrio cholera* is related to the toxin, cholera toxin.

86) Corynebacterium diphtheria

F = (A) Is an an-aerobe.

T = (B) Produces powerful exotoxin.

T = (C) Is a gram positive bacillus.

T = (D) Causes pseudomembranous inflammation of pharynx.

T = (E) Is clubbed shaped.

87) Lymphocytosis absolute or relative is seen in

T = (A) Typhoid fever.

F = (B) Tuberculosis.

F = (C) Acute myeloid leukemia.

T = (D) Brucellosis.

T = (E) Whooping cough.

88) Bacteroides

T = (A) Are maximum in stool.

F = (B) Are spore-forming anaerobe.

T = (C) Cause peritonitis after bowel injury.

F = (D) Cause food poisoning.

T = (E) Are gram -ve coccobacillus.

89) Escherichia coli

T = (A) Produces pink colonies on MacConkey's medium.

T = (B) Motile & capsulated.

T = (C) O antigens causes production of IgM antibodies, whereas H antigens causes production of IgG antibodies.

F = (D) A member of genital flora.

T = (E) On eosin - methylene blue medium produces colonies with metallic green sheen.

90) Virulence factors involved in UTI caused by E coli are

T = (A) P - fimbriae.

F = (B) Verocytotoxin - I & II.

F = (C) Adhesin factor.

T = (D) K antigen.

T = (E) Hemolysin.

91) Vibrio cholerae

F = (A) Motile with peritrichous flagella.

T = (B) Produce yellow colonies on TCBS agar.

F = (C) Grow at low pH (4.5 - 6).

T = (D) Produces oxidase, neuraminidase, & mucinase.

F = (E) Occur only in human colon.

92) Cholera

F = (A) Incubation period is 1-2 weeks.

T = (B) Produced by *Vibrio cholerae* enterotoxin, that causes hypersecretion of water & Cl⁻, & inhibition Na⁺ absorption.

F = (C) Stool contain mucus, blood, Na⁺ & epithelial cells.

T = (D) Complication include dehydration, acidosis, shock, & circulatory collapse.

F = (E) Treatment consist only of tetracycline orally.

93) Which one of the following organisms that infects GIT is the MOST frequent cause of bacteremia?

F = (A) *Shigella flexneri*.

F = (B) *Campylobacter jejuni*.

F = (C) *Vibrio cholerae*.

T = (D) *Salmonella typhi*.

F = (E) *Clostridium difficile*.

94) Treponema pallidum

F = (A) Produces an exotoxin that stimulates adenylate cyclase.

T = (B) Cannot be cultured on artificial media.

T = (C) Infected patients produces antibodies that react with beef heart cardiolipin.

T = (D) Wassermann test is a complement fixation test.

F = (E) Motile & capsulated.

95) Diagnostic laboratory tests for syphilis

F = (A) Gram stained smears reveals pink threads on microscopy.

T = (B) In Venereal disease research laboratory (VDRL) test, cardiolipin is mixed with pt's serum, producing visible clumps within minutes.

T = (C) False ve results with VDRL test & Wassermann reaction occur in malaria, leprosy, measles, & infectious mononucleosis.

F = (D) For specific serologic tests treponemal antigens are obtained from infected patients thru biopsy

F = (E) Treponema pallidum immobilization test is a non-specific serologic test.

96) Antigens of gonococci

T = (A) Pili favors adherence to mucosal cells & inhibits phagocytosis.

T = (B) Opa induces antibodies which acts as opsonins.

F = (C) Strains possessing Por IB are resistant to killing by normal human serum .

F = (D) Lipopolysaccharides induces antibodies that confer immunity.

T = (E) Por extends thru gonococcal memb.

97) Gonococci

F = (A) In non-selective sub-culture, colonies consists of piliated organisms.

T = (B) Produces enzymes IgA 1 protease.

F = (C) In females, causes infection primarily in vagina.

T = (D) Causes ophthalmia neonatorum, that is acquired during passage thru infected birth canal.

T = (E) Penicillin G with probenidicid is used in gonorrhoea.

98) Folliculitis is caused by

F = (A) Proteus.

F = (B) Pseudomonas.

F = (C) Klebsiella.

T = (D) Staphylococci.

F = (E) E. coli.

99) Lymphogranuloma venereum

T = (A) Caused by chlamydia trachomatis.

T = (B) Occurs more in women.

F = (C) Most common in USA.

T = (D) Initial stages can be treated by tetracycline.

T = (E) Surgery may be required in later stages.

100) In lepromatous leprosy

T = (A) Dermis appears diffusely packed with vacuolated macrophages.

F = (B) There is a high level of cell mediated immunity.

F = (C) Mucous membranes are not involved.

F = (D) The commonest cause of death is renal failure.

F = (E) Lymphadenitis occurs during type I reaction.

101) Neisseria species (N gonorrhoeae, & N meningitidis)

T = (A) N meningitidis is capsulated, whereas gonococci is non- capsulated.

T = (B) Mueller - Hinton, & modified Thayer-Martin media, are selective media for them.

T = (C) Growth of both promoted by 5-10% CO₂.

F = (D) Gonococci are oxidase +ve, whereas meningococci are oxidase -ve.

F = (E) Both ferment glucose & maltose.

102) Clostridia species

T = (A) Pathogenic species are found both in soil & in normal flora of colon.

T = (B) Pseudomembranous colitis is due to a toxin produced by C difficile.

F = (C) Aerobic conditions at wound site is required to cause tetanus, b/c spores will form in presence of O₂.

T = (D) For laboratory cultivation Robertson's cooked meat medium, & thioglycolate medium are used.

T = (E) Trismus & Risus sardonicus signs are characteristic clinical findings in tetanus.

103) Acute glomerulonephritis is a nonsuppurative complication that follows infection by

F = (A) Strep. fecalis.

T = (B) Strep. pyogenes.

F = (C) Strep. pneumoniae.

F = (D) Strep. agalactiae.

F = (E) Strep. mutans.

104) Bacteria causing food poisoning include

T = (A) Staphylococcus aureus.
 T = (B) Clostridium perfringens.
 F = (C) Clostridium difficile.
 T = (D) Salmonella.
 F = (E) Pseudomonas aeruginosa.

105) Pseudomonas aeruginosa

T = (A) Produce greenish colonies with grape like odor on nutrient agar.
 T = (B) Obligate aerobes.
 T = (C) Pathogenic only when introduced into areas devoid of normal defenses.
 F = (D) Produces exotoxin S that causes tissue necrosis & block protein synthesis.
 T = (E) Citrate utilization, catalase, & oxidase tests are positive.

106) Five days ago a 65-year-old women with a lower urinary tract infection begin taking ampicillin. She now has a fever & severe diarrhea. Which one of the following organism is MOST likely to be the cause of diarrhea?

F = (A) Bacteroides fragilis.
 F = (B) Proteus mirabilis.
 F = (C) Bordetella pertussis.
 T = (D) Clostridium difficile.
 F = (E) Staphylococcus aureus.

107) Pathogenesis of which one of following diseases does not involve an exotoxin

F = (A) Scarlet fever.
 T = (B) Typhoid fever.
 F = (C) Toxic shock syndrome.
 F = (D) Botulism.
 F = (E) Diphtheria.

108) Intracellular bacteria include

T = (A) Brucella abortus.
 T = (B) R. prowazekii.
 F = (C) P. aeruginosa.
 T = (D) L. monocytogenes.
 T = (E) M. tuberculosis.

109) Dysentery is caused by

T = (A) Shigella.
 T = (B) E. histolytica.
 T = (C) B. coli.
 F = (D) V. cholera.

F = (E) H. nana.

110) Acid fast bacilli are

F = (A) Mycoplasmas.
 T = (B) M. leprae.
 T = (C) Nocardia.
 F = (D) Staphylococcus.
 F = (E) Lactobacillus.

111) Susceptibility of mycobacteria can be determined by

F = (A) Complement fixation test.
 F = (B) Radio-immuno assay.
 T = (C) Radiometric broth culture technique.
 F = (D) Skin test.
 T = (E) Agar-based culture technique.

112) Clostridium causes

T = (A) Food poisoning.
 T = (B) Botulism.
 T = (C) Gas gangrene.
 T = (D) Tetanus.
 T = (E) Pseudomembranous colitis.

113) Vibrio cholera

T = (A) Causes loss of fluid by increasing cyclic AMP level.
 T = (B) Elaborate enzymes mucinase & neuraminidase.
 F = (C) Infective dose is 10²-10⁵ organisms.
 F = (D) Causes cholera due to endotoxins.
 T = (E) Is motile & non-spore forming.

114) Regarding the effect of benzylpenicillin G on bacteria, which one is LEAST likely to be resistant

F = (A) Staph. aureus.
 F = (B) Strep fecalis.
 T = (C) Strep pyogenes.
 F = (D) Gonococci.
 F = (E) Vibrio cholerae.

115) MOST likely organism causing pneumonia in immunocompromised patients is

F = (A) Nocardia asteroides.
 F = (B) Serratia marcescans.
 T = (C) Mycoplasma pneumoniae.
 F = (D) Varicella - zoster virus.
 F = (E) Bacteroides fragilis.

116) Which one of following is NOT an important characteristic of either N gonorrhoeae or N meningitidis?

F = (A) Polysaccharide capsule.

F = (B) IgA1 protease.

T = (C) M protein.

F = (D) Pili.

F = (E) Diplococci.

117) Proteus species

F = (A) On nutrient agar, it produces swarming growth with grape-like odor.

T = (B) Produces urease & phenylalanine deaminase.

F = (C) Proteus mirabilis causes summer diarrhea esp. in children & travelers.

T = (D) All species causes UTI.

T = (E) Only P rettgeri changes the color of Simmon citrate medium from green to blue.

118) Which of the following are NOT the characteristic of Lancefield group B streptococci (S agalactiae)?

T = (A) Pyoderma.

F = (B) Vaginal carriage in 5-25% of normal women of child bearing age.

F = (C) Neonatal sepsis & meningitis.

F = (D) Beta - hemolysis.

T = (E) Infective endocarditis.

119) Three organisms, pneumococci, meningococci, & Hemophilus influenzae, cause vast majority of cases of bacterial meningitis. What is the MOST important pathogenic component they share?

F = (A) Protein A.

T = (B) Capsule.

F = (C) Endotoxin.

F = (D) Beta - lactamase.

F = (E) Pili.

120) Diarrhea caused by which agent is characterized by the presence of fecal leukocytes?

T = (A) Campylobacter jejuni.

F = (B) Rota virus.

F = (C) Clostridium perfringens.

F = (D) Enterotoxigenic E coli.

T = (E) Shigellae.

121) Clostridia that cause gas gangrene are

T = (A) C perfringens.

T = (B) C septicum.

F = (C) C difficile.

T = (D) C histolyticum.

T = (E) C novyi.

122) Mycoplasmas

F = (A) Possess rigid cell wall.

T = (B) M pneumoniae causes primary atypical pneumonia.

F = (C) M genitalium causes chorioamnionitis, postpartum fever, & low birth weight of infants, in pregnant women.

T = (D) Ureaplasma urealyticum causes non-gonococcal urethritis.

F = (E) M hominis causes UTI in men.

123) Tissue - degrading enzymes important in pathogenesis are

T = (A) Lecithinase of clostridium perfringens.

T = (B) Hyaluronidase of strep. pyogenes.

F = (C) M protein of pneumococci.

T = (D) Leukocidin of staph. aureus.

T = (E) Mucinase of vibrio cholerae.

124) Nocardiosis

F = (A) Is caused by anaerobic nocardia.

T = (B) Is acquired exogenously.

T = (C) Commonly occur in immunocompromized patients.

T = (D) Is treated by sulphonamides.

T = (E) Clinically resembles pulmonary tuberculosis.

125) Etiological agents causing septic meningitis include

F = (A) Myxovirus.

T = (B) Staphylococcus.

F = (C) Chlamydia.

T = (D) Hemophilus influenzae.

F = (E) Cryptococcus.

126) Lymphocytosis is characteristically seen in

T = (A) Typhoid.

F = (B) Parasitic infestations.

F = (C) Pyoderma gangrenosum.

F = (D) Atopic eczema.

T = (E) Brucellosis.

127) The rickettsiae

T = (A) Are morphologically pleomorphic.

T = (B) Contain both RNA & DNA.

T = (C) Multiply by binary fission.

F = (D) Are gram-positive.

T = (E) Are intracellular.

128) Soil is the natural habitat for

- T = (A) Clostridium tetani.
 T = (B) Mycobacterium intracellulare.
 T = (C) Bacillus anthracis.
 F = (D) Chlamydia trachomatis.
 T = (E) Proteus.

129) Organisms of UTI are

- T = (A) E. coli.
 T = (B) Proteus.
 F = (C) Bacteroides.
 T = (D) S. fecalis.
 T = (E) Staphylococcus aureus.

130) Food poisoning is caused by

- T = (A) Clostridium perfringens.
 T = (B) Clostridium botulinum.
 T = (C) Salmonella.
 T = (D) B. cereus.
 F = (E) P. vivax.

131) Isolated from subacute bacterial endocarditis

- T = (A) S. viridans.
 T = (B) Enterococcus fecalis.
 F = (C) Adenovirus.
 F = (D) H. influenza.
 T = (E) Candida.

132) Pure anaerobe are

- F = (A) E. coli.
 T = (B) C. tetani.
 T = (C) Bacteroides.
 F = (D) Rickettsia.
 T = (E) Peptostreptococcus.

133) Immunofluorescent technique is used in the diagnosis of

- T = (A) Syphilis.
 T = (B) Measles.
 T = (C) Rabies.
 F = (D) Tetanus.
 F = (E) Gas gangrene.

134) Exotoxins are produced by

- T = (A) S. dysenteriae.
 F = (B) S. typhi.
 T = (C) V. cholera.
 T = (D) C. diphtheria.
 T = (E) Clostridium tetani.

135) Serologic tests for syphilis are

- T = (A) VDRL.

- F = (B) Widal.
 T = (C) TPI.
 T = (D) TPHA.
 T = (E) Wasserman.

136) MOST frequent bacterial cause of pharyngitis is

- F = (A) Staph. aureus.
 F = (B) Pneumococci.
 T = (C) Strep. pyogenes.
 F = (D) Meningococci.
 F = (E) Gonococci.

137) Organism LEAST likely to be transmitted during gestation or at birth is

- T = (A) Hemophilus influenzae.
 F = (B) Treponema pallidum.
 F = (C) Gonococci.
 F = (D) Chlamydia trachomatis.
 F = (E) Strep. agalactiae.

138) Each of the following statements concerning VDRL test for syphilis is correct

- F = (A) Antigen is composed of inactivated T pallidum.
 T = (B) Test is usually +ve in secondary syphilis.
 T = (C) False +ve results are more frequent than with FTA-ABS test.
 T = (D) Antibody titer declines with adequate therapy.
 F = (E) It is a specific serologic test for syphilis.

139) Each of the following statements concerning Corynebacterium diphtheria is correct

- T = (A) It is a spore-forming, G +ve rod.
 T = (B) Toxin production is dependent on the organism's being lysogenized by a bacteriophage.
 F = (C) Diphtheria toxoid should not be given to children under the age of 3 years, b/c incidence of complications is too high.
 T = (D) Antitoxin should be used to treat patients with diphtheria.
 F = (E) In pharyngeal diphtheria, a pinkish pseudomembrane is formed over tonsils, pharynx, & larynx.

140) Each of the following statements concerning certain G - ve rods is correct

- T = (A) Pseudomonas aeruginosa causes wound infections, that are characterized by blue-

- green pus as a result of pyocyanin production.
- T = (B) Invasive disease caused by *Hemophilus influenzae* is most often due to strains possessing a type b polysaccharide capsule.
- T = (C) *Legionella pneumophila* infection is acquired by inhalation of aerosols from environmental water sources.
- F = (D) Whooping cough, caused by *Bordetella pertussis*, is on rise b/c changing antigenicity has made the vaccine relatively ineffective.
- T = (E) Colicin is a bacteriocin produced by *E. coli*.

141) Following organisms causes diarrhea by producing an enterotoxin that activates adenylate cyclase

- T = (A) *E. coli*.
- F = (B) *Bacteroides fragilis*.
- F = (C) *Staph. aureus*.
- F = (D) *Strep. fecalis*.
- T = (E) *Vibrio cholerae*.

142) Each of the following statements concerning *Clostridium perfringens* is correct

- T = (A) It is an important cause of gas gangrene.
- T = (B) It is an important cause of food poisoning.
- T = (C) It produces an exotoxin that degrades lecithin & causes necrosis & hemolysis.
- F = (D) It produces a toxin that inhibits release of acetylcholine at the synapse.
- T = (E) It is non-capsulated in free state, but in tissue capsule is formed.

143) Each of the following statements concerning *Clostridium tetani* is correct

- T = (A) Its natural habitat is primarily the soil.
- T = (B) Pathogenesis is due to the production of an exotoxin that blocks inhibitory neurotransmitters.
- F = (C) It is a facultative anaerobe; it will grow on a blood agar plate in the presence of room air.
- T = (D) It possess somatic & flagellar antigens.
- T = (E) Transmission occur thru traumatized skin breaks.

144) The characters of *Staphylococcus aureus* are

- T = (A) Golden colony pigmentation.
- T = (B) The production of coagulase.
- F = (C) The production of fibrinolysin.
- T = (D) The production of leukocidin.
- T = (E) The production of soluble hemolysin.

145) Lesions of syphilis in which large number of spirochetes can be demonstrated include

- F = (A) Neurosyphilis.
- T = (B) Primary chancre.
- F = (C) Cardiovascular syphilis.
- T = (D) Mucocutaneous lesions in secondary stage.
- F = (E) Gumma of bone.

146) Benzyl penicillin is

- F = (A) Bacteriostatic.
- T = (B) Destroyed by the enzyme penicillinase.
- F = (C) Insoluble in water.
- F = (D) Damaging to the nucleus of the bacterial cell.
- F = (E) Active against some viruses.

147) In bacterial meningococcal meningitis

- T = (A) CSF proteins are raised.
- T = (B) CSF blood sugar is decreased.
- T = (C) Bacteria can be cultured on media.
- T = (D) Bacteria can be gram stained.
- F = (E) CSF has no neutrophil.

148) Pseudomembranous colitis is caused by

- F = (A) *Clostridium perfringens*.
- F = (B) *Clostridium welchii*.
- T = (C) *Clostridium difficile*.
- F = (D) *Yersinia enterocolitis*.
- T = (E) *Staphylococci*.

149) Each of the following statements concerning *M. tuberculosis* is correct

- T = (A) Some strains isolated from individuals with previously untreated cases of tuberculosis are resistant to isoniazid.
- F = (B) It contains a small amount of lipid in its cell wall & therefore stains poorly with Gram stain.
- T = (C) Grows slowly, often requiring 3-6 weeks before colonies appear.
- T = (D) Antigen in skin test is a protein extracted from organism.
- T = (E) Wax D is a mycoside, that acts as an adjuvant to increase antibody response to an antigen.

150) Each of the following statements concerning immunization against clostridial diseases is correct

- F = (A) Antitoxin against tetanus protects against botulism as well, b/c the 2 toxins share antigenic sites.
- F = (B) Vaccines containing alpha toxin (lecithinase) are effective in protecting against gas gangrene.
- F = (C) Toxoid vaccine against C difficile infection should be administered to immuno-compromised patients.
- T = (D) Tetanus toxoid provides effective protection against tetanus toxin.
- T = (E) Tetanus toxoid is used for active immunization as a part of triple vaccine DPT.

151) Ticks are vectors for the transmission of

- T = (A) Rocky Mountain spotted fever.
- F = (B) Epidemic typhus.
- T = (C) Tularemia.
- T = (D) Lyme disease.
- F = (E) Q fever.

152) Following infections are caused by arthropods

- T = (A) Dengue fever.
- T = (B) Typhus.
- F = (C) Poliomyelitis.
- T = (D) Yellow fever.
- F = (E) Q fever.

153) Following test match the disease

- T = (A) Casoni's test for hydatid cyst.
- F = (B) Frei's test in infectious mononucleosis.
- F = (C) Schick's test in typhus.
- T = (D) Wassermann's test for syphilis.
- T = (E) Widal test for typhoid.

154) Following diseases are caused by chlamydiae

- T = (A) Lymphogranuloma venereum.
- F = (B) Typhus.
- F = (C) Yellow fever.
- T = (D) Psittacosis.
- F = (E) Herpes simplex.

155) Following diseases are viral

- T = (A) Yellow fever.
- T = (B) Mumps.
- F = (C) Legionnaires disease.
- T = (D) Herpes simplex.
- F = (E) Rocky mountain spotted fever.

156) AIDS virus

- T = (A) Is associated with increased incidence of malignancy.
- T = (B) Is a retrovirus.
- F = (C) Spread by close contact.
- T = (D) Can infect CNS.
- F = (E) Effect T suppressor cells.

157) Following diseases are transmitted by blood transfusion

- T = (A) Hepatitis B.
- F = (B) Hepatitis A.
- T = (C) Malaria.
- F = (D) Plague.
- F = (E) Kalazar.

158) Following viruses can cause neoplastic transformation

- T = (A) Hepatitis B.
- F = (B) Chicken pox.
- F = (C) Herpes simplex I.
- T = (D) Herpes simplex II.
- T = (E) Epstein Barr virus.

159) Following virus are teratogenic

- F = (A) Rubella.
- T = (B) Herpes simplex virus 2.
- F = (C) Rota virus.
- F = (D) Rhino virus.
- T = (E) Epstein-Barr virus.

160) Following organisms does not cross placenta

- F = (A) Proteus.
- F = (B) Polio virus.
- T = (C) CMV.
- T = (D) Rubella virus.
- T = (E) Listeria monocytogenes.

161) Live attenuated vaccines are

- T = (A) BCG.
- T = (B) MMR.
- F = (C) Polio salk.
- T = (D) Polio sabin.
- F = (E) Cholera.

162) Neonatal viral diseases results from

- T = (A) Rubella virus.
 T = (B) CMV.
 T = (C) RSV.
 F = (D) EB virus.
 F = (E) Measles virus.

163) Picorna viruses are

- T = (A) Poliovirus.
 T = (B) Rhinovirus.
 F = (C) Rubella virus.
 T = (D) Cocksackie virus.
 F = (E) Rabies virus.

164) DNA viruses are associated with the development of

- T = (A) Epithelial cancers.
 T = (B) Mesenchymal cancers.
 T = (C) Hemopoietic cancers.
 T = (D) T-cell leukemia.
 F = (E) T-cell lymphoma.

165) Torch complex (toxoplasma, rubella, cytomegalo virus, herpes simplex virus) infections show

- T = (A) Cataract.
 T = (B) Microcephaly.
 T = (C) Splenomegaly.
 T = (D) Hepatomegaly.
 F = (E) Pneumonia.

166) RNA viruses are

- F = (A) EBV.
 T = (B) Polio virus.
 T = (C) Influenza virus.
 F = (D) Small pox virus.
 T = (E) RSV.

167) Viruses are

- T = (A) CMV.
 F = (B) Trachoma.
 F = (C) S. typhi.
 T = (D) Hepatitis-B.
 F = (E) L. monocytogenes.

168) Human cancer causative organisms are

- F = (A) Polio virus.
 T = (B) EBV.
 T = (C) Hepatitis-B virus.
 F = (D) Yellow fever virus.
 T = (E) Herpes simplex II.

169) HBV transmission occurs via

- F = (A) Oral-fecal route.
 T = (B) Renal dialysis units.
 T = (C) Blood or blood products.
 T = (D) Sexual intercourse.
 T = (E) Saliva.

170) The hepatitis B virus

- T = (A) Is not usually transmitted by the oral route.
 T = (B) Is transmitted by sexual contact.
 T = (C) Is common in renal dialysis units.
 F = (D) Is the cause of Burkitt's lymphoma.
 T = (E) Causes immune complex disease.

171) Congenital malformation may be caused by

- T = (A) Toxoplasmosis.
 F = (B) Varicella.
 F = (C) Cytomegalovirus.
 F = (D) Herpes simplex.
 T = (E) Rubella.

172) Viruses transmitted thru mosquitoes include

- T = (A) Dengue.
 F = (B) HTLV-I.
 T = (C) Yellow fever.
 F = (D) Poliomyelitis.
 F = (E) Cytomegalovirus.

MYCOLOGY**173) Each of the following fungi exists in both yeasts & molds forms**

- T = (A) Histoplasma capsulatum.
 T = (B) Paracoccidiodes.
 F = (C) Trichophyton.
 F = (D) Cryptococcus neoformans.
 T = (E) Blastomyces.

174) Sites normally colonized by candida albicans include

- T = (A) Gut.
 T = (B) Skin.
 T = (C) Vagina.
 T = (D) Bronchial tree.
 F = (E) Prepuce.

175) Your patient is a women with vaginal discharge. You suspect on clinical grounds, that it may be due to candida albicans.

Which one of the following statements is accurate or appropriate?

- T = (A) A Gram stain of discharge should reveal budding yeasts.
 F = (B) A skin test, using candida albicans as antigen, should confirm the diagnosis.
 T = (C) Her urine should be checked for glucose.
 T = (D) You should ask whether she is taking antibiotics.
 T = (E) Disease probably occur, due to impairment of local or systemic host defenses.

176) Candida albicans

- T = (A) Is the most common species of candida.
 F = (B) Appears as branching hyphae in the tissues.
 T = (C) Is normally found in oral cavity, gastrointestinal tract & vagina.
 T = (D) Is an opportunist pathogen.
 T = (E) Is not affected by normal bacterial flora.

177) Aspergillosis

- T = (A) Is caused by a fungus.
 T = (B) May be seen in immunodeficient patient.
 T = (C) Is usually seen in pre-existing lung disease.
 F = (D) Occurs commonly in patients on antibiotic therapy.
 F = (E) Is seen in animals only.

178) Deep fungal infections are

- T = (A) Coccidioidomycosis.
 T = (B) Blastomycosis.
 F = (C) Tinea corporis & capitis.
 T = (D) Candidiasis.
 T = (E) Histoplasmosis.

179) Mucor mycosis

- T = (A) Is an opportunistic infection.
 T = (B) Occur in immunocompromised pts.
 F = (C) Is associated with hypertension.
 T = (D) Is associated with diabetes mellitus.
 F = (E) Caused by hepatitis delta virus.

180) Following antibiotics are effective against fungi

- T = (A) Nystatin.
 F = (B) Bacitracin.
 T = (C) Griseofulvin.
 F = (D) Polymyxin B.
 T = (E) Amphotericin B.

181) Each of the following statements concerning cutaneous & sub-cutaneous mycoses is correct

- F = (A) Sporotrichosis is a cutaneous mycoses caused by sporothrix schenckii.
 T = (B) In cutaneous mycoses, superficial keratinized tissue is invaded by fungi.
 T = (C) Wart-like growth along lymphatics occur in chromomycosis.
 T = (D) In tinea corporis lesion occur on trunk.
 T = (E) In madura foot, multiple draining sinuses occur, with a thick yellowish pus, commonly on feet & legs.

182) Following statements concerning systemic mycoses is correct

- T = (A) In coccidioidomycosis infection is acquired thru inhalation of air-borne arthroconidia.
 T = (B) Cellular reaction with granuloma formation is the usual lesion in all systemic mycoses.
 F = (C) In blastomycosis, primary lesion consists of ulcerated granulomas of skin & bone.
 T = (D) Serology are important in diagnosis of systemic mycoses.
 F = (E) Skin test is always negative in systemic mycoses.

183) Each of the following statements concerning fungi is correct

- T = (A) Yeasts are fungi that reproduce by budding.
 T = (B) Molds are fungi that have elongated filaments called hyphae.
 T = (C) Thermally dimorphic fungi exist as yeasts at 37 °C & as molds at 25 °C.
 F = (D) Both yeasts & molds have a cell wall made up of peptidoglycan.
 F = (E) Fungi are not cultivated on any artificial laboratory media.

184) Aspergillosis

- T = (A) May occur in immunocompromized pts.
 T = (B) Diagnosis depends on demonstration of hyphal fragments in tissue biopsies.
 T = (C) May involves the lungs.
 T = (D) Results in the formation of fungus ball in lung.
 F = (E) Is treated by surgery only.

185) Maduromycosis

- T = (A) Usually follows traumatic inoculation.
 F = (B) Has world wide distribution.
 F = (C) Occurs mainly in male adults.
 T = (D) Is contagious.
 T = (E) Is caused by fungi only.

PARASITOLOGY**186) Each of the following statements concerning Schistosoma species is correct**

- F = (A) Dorsal surface of male *S japonicum* is covered with small tubercles.
 T = (B) Schist is a gynecophoric canal in male, in which female lies.
 T = (C) Eggs of *S hematobium* are shaped like elongated spindles with dilation in middle, & a short, stout spine at one pole.
 F = (D) *S mansoni* causes inflammation primarily in lung alveoli.
 F = (E) Miracidium is a ciliated larva, that is formed inside the body of their intermediate host, fresh-water snail.

187) Following are oviparous

- T = (A) *Trichuris trichiura*.
 T = (B) *Nectar americanos*.
 T = (C) *Ascaris lumbricoides*.
 T = (D) *Ancylostoma duodenale*.
 F = (E) *Wuchereria bancrofti*.

188) Echinococcus granulosus

- F = (A) Is the shortest parasite.
 T = (B) Has 3 segments.
 F = (C) Is viviparous.
 F = (D) Examined or diagnosed by stool D/R.
 T = (E) Results in unilocular fluid-filled cysts in intermediate hosts.

189) Each of the following statement is concerning bilharziasis is correct

- T = (A) Infection occur, via direct penetration of cercariae of *S hematobium* thru skin.
 F = (B) Cercariae induce granulomatous inflammation with the formation of pseudotubercle in the bladder wall.
 T = (C) Hydronephrosis & renal failure may occur as end results.

- F = (D) Fairley's test is a skin test in which miracidial antigen is injected intradermally.
 T = (E) Praziquantal is the drug of choice.

190) Parasite having lungs as route in their life cycle are

- T = (A) *Ancylostoma duodenale*.
 T = (B) *Ascaris lumbricoides*.
 F = (C) *Diphyllobothrium latum*.
 T = (D) *Wuchereria bancrofti*.
 F = (E) *Enterobius vermicularis*.

191) Hook worm infection is characterized by

- T = (A) Ground itch.
 T = (B) Bronchitis.
 F = (C) Macrocytic anemia.
 T = (D) Eosinophilia.
 T = (E) The presence of eggs in stool of infected person.

192) In malaria, form of plasmodia that is transmitted from mosquito to human is

- F = (A) Gametocyte.
 F = (B) Merozoite.
 F = (C) Hypnozoite.
 T = (D) Sporozoite.
 F = (E) Cryptozoite.

193) Which one of the following protozoa primarily infects macrophages?

- F = (A) *Plasmodium vivax*.
 T = (B) *Leishmania donovani*.
 F = (C) *Trypanosoma cruzi*.
 F = (D) *Trichomonas vaginalis*.
 F = (E) *Giardia lamblia*.

194) Each of the following has an intermediate host as part of its life cycle

- F = (A) *Trichomonas vaginalis*.
 T = (B) *Tenia solium*.
 T = (C) *Echinococcus granulosus*.
 T = (D) *Toxoplasma gondii*.
 F = (E) *Entameba histolytica*.

195) Each of the following parasites passes thru the lung during human infection

- T = (A) *Ancylostoma duodenale*.
 T = (B) *Wuchereria bancrofti*.
 T = (C) *Ascaris lumbricoides*.
 T = (D) *Schistosoma hematobium*.
 F = (E) *Diphyllobothrium latum*.

196) Each of the following parasites is transmitted by mosquitoes

- F = (A) Leishmania donovani.
 T = (B) Wuchereria bancrofti.
 T = (C) Plasmodium vivax.
 T = (D) Plasmodium falciparum.
 F = (E) Trichuris trichiura.

197) Laboratory diagnosis of a patient with a suspected liver abscess due to Entameba histolytica should include

- T = (A) Stool examination & indirect hemagglutination test.
 F = (B) Stool examination & blood smear.
 F = (C) Indirect hemagglutination & skin test.
 F = (D) Xenodiagnosis & string test.
 T = (E) Liver biopsy & radiology.

198) Parasites passing thru human lung as a part of their life cycle are

- T = (A) Ascaris lumbricoides.
 T = (B) Schistosoma.
 T = (C) Ancylostoma duodenale.
 T = (D) Paragonimus.
 F = (E) Diphylobothrium latum.

199) Each of the following statements concerning Giardia lamblia is correct

- T = (A) G lamblia causes fat in stools as a result of malabsorption in small intestine.
 T = (B) Exist in two stages, trophozoites & cysts.
 T = (C) Transmission occur via fecal-oral route.
 F = (D) Causes inflammation of colonic mucosa, resulting in non-bloody, foul-smelling diarrhea.
 T = (E) Beside stool, trophozoites may be obtained from duodenal aspirate.

200) Entameba histolytica

- T = (A) Trophozoite show slow gliding movement due to pseudopodia.
 T = (B) Only the mature quadrinucleate cysts are infective to humans.
 F = (C) Excystation occur in duodenum of humans where the pH is low.
 T = (D) Transmission occur via oral-fecal route.
 F = (E) Humans are the intermediate host.

201) Intestinal amebiasis

- T = (A) Margin of ulcers are ragged & undermined.
 F = (B) Deep ulcers extend to the serosa.

- F = (C) In chronic cases, marked scarring of the bowel wall may cause narrowing of lumen.
 T = (D) Trophozoites are found in stool of symptomatic patients.
 T = (E) Metronidazole is an effective drug.

202) Important diseases transmitted by arthropods include

- T = (A) Leishmaniasis.
 T = (B) Plague.
 F = (C) Q fever.
 T = (D) Dracunculiasis.
 T = (E) Malaria.

203) Laboratory investigations for hydatid disease include

- F = (A) Weil-Felix reaction.
 F = (B) Paul-Bunnell test.
 F = (C) Latex agglutination.
 T = (D) Intradermal test (Casoni test).
 T = (E) Hemagglutination.

204) Each of the following statements concerning malaria is correct

- T = (A) Female anopheles mosquito is the vector.
 T = (B) Early in infection, sporozoites enter hepatocytes.
 T = (C) Release of merozoites from RBCs causes periodic fever & chills.
 F = (D) Principal site of gametocyte formation is human GIT.
 F = (E) Quartan nephrosis is caused by P falciparum.

205) Each of the following statements concerning plasmodia is correct

- F = (A) Trophozoites are the sexual & growing form of parasite in the hepatocytes of humans.
 T = (B) Gametocytes of P falciparum are crescentic in shape.
 F = (C) Exo- erythrocytic schizogony occur only in P malariae.
 F = (D) Blood in malaria, reveals microcytic anemia.
 F = (E) Chloroquin is the drug of choice against all 4 plasmodium species.

206) Each of the following statement concerning Kala-azar is incorrect

- F = (A) Caused by leishmania donovani.

- F = (B) Transmitted by bite of sandflies.
 F = (C) Can be diagnosed by finding amastigotes in bone marrow.
 T = (D) Spleen & liver remain normal in size.
 F = (E) Serology eg indirect hemagglutination test may give +ve results.

207) Hydatid disease can occur by

- F = (A) Eating hydatid cyst from goat.
 F = (B) Hydatid sac ingestion.
 T = (C) Eating ova of echinococcus.
 F = (D) Eating of fertile hydatids.
 F = (E) Inhaling ova of echinococcus.

208) Each of the following statements concerning Diphylobothrium latum is incorrect

- F = (A) D latum is transmitted by undercooked fish.
 F = (B) D latum has operculated eggs.
 F = (C) Crustaceans are intermediate hosts for D latum.
 T = (D) D latum has scolices with a circle of hooks.
 F = (E) D latum cause megaloblastic anemia.

209) Each of the following statements concerning hookworm infection is correct

- T = (A) Hookworm infection can cause anemia.
 T = (B) Hookworm infection is acquired by humans when filariform larvae penetrate the skin.
 F = (C) Hookworm infection can be diagnosed by finding trophozoite in stool.
 T = (D) Hookworm infection is caused by Ancylostoma duodenale & Nector americanus.
 T = (E) Patients with hookworm infection may show perverted taste for earth, mud, or lime.

210) Each of the following statements concerning Ascaris lumbricoides is correct

- T = (A) A lumbricoides is one of the largest nematodes.
 T = (B) A lumbricoides is transmitted by ingestion of eggs.
 F = (C) Both dogs & cats are intermediate hosts of A lumbricoides.
 T = (D) A lumbricoides can cause pneumonia.

- T = (E) Body fluid of A lumbricoides is toxic, which when absorbed cause typhoid-like fever.

211) Cutaneous larva migrans is due to

- T = (A) Ankylostoma braziliensis.
 F = (B) Ankylostoma duodenale.
 T = (C) Ankylostoma caninum.
 F = (D) Ankylostoma cutaneum.
 T = (E) Ankylostoma stenocephala.

212) Each of the following statements concerning Tenia saginata is correct

- F = (A) Scolex is provided with a rostellum, armed with double row of hooklets.
 T = (B) Cattle (cow or buffalo) are the intermediate host.
 T = (C) Humans become infected by eating undercooked beef containing cysticercus bovis.
 T = (D) Diarrhea & anemia may occur in T saginata infection.
 T = (E) Whitish segments can be recognized in feces.

213) Each of the following statements concerning Echinococcus granulosus is correct

- T = (A) Adult worm consists only three segments.
 F = (B) Humans are the definitive host in which hydatid cysts are formed.
 T = (C) Transmission occur via fecal-oral route.
 T = (D) Hydatid cyst when ruptured, caused anaphylactic shock.
 T = (E) Serology may give +ve results in hydatid disease.

214) Lymphatic & lymph node is primary site of infection in

- T = (A) Wuchereria bancrofti.
 F = (B) Onchocercus volvulus.
 F = (C) Entameba histolytica.
 F = (D) Trichuris trichiura.
 F = (E) Toxoplasma gondii.

215) Intracellular parasites are

- T = (A) Plasmodium.
 T = (B) Toxoplasmosis gondii.
 T = (C) Leishmania donovani.
 F = (D) Trypanosoma.
 F = (E) Giardia lamblia.

216) Hemoflagellates include

- T = (A) *Leishmania donovani*.
 T = (B) *Trypanosoma*.
 F = (C) *Giardia lamblia*.
 F = (D) *Trichomonas gingivalis*.
 F = (E) *Plasmodia*.

217) *Ascaris lumbricoides* can cause

- T = (A) Jaundice.
 T = (B) Bowel obstruction.
 F = (C) Severe anemia.
 T = (D) Pneumonia.
 F = (E) Anal itch.

218) Visceral leishmaniasis is caused by

- T = (A) *Leishmania donovani*.
 T = (B) *Leishmania infantum*.
 F = (C) *Leishmania mexicana*.
 F = (D) *Leishmania braziliensis*.
 F = (E) *Leishmania tropica*.

219) *Plasmodium falciparum* infection produces

- T = (A) Severe anemia.
 T = (B) Coma.
 T = (C) Uremia.
 F = (D) Pulmonary edema.
 T = (E) Cough.

220) *Entameba histolytica*

- T = (A) Is a protozoa.
 F = (B) Can cause gonorrhea.
 F = (C) Does not affect extra intestinal sites.
 T = (D) Has no intermediate host.
 T = (E) Is transmitted by oral-fecal route.

221) In amebiasis

- F = (A) Cysts in all stages is infective.
 T = (B) Serological tests may be used for metastatic cases.
 T = (C) Liver may involved.
 T = (D) Diagnosis can be made on examination of stool.
 T = (E) Flask shaped intestinal ulcers are present.

222) *Tenia solium*

- T = (A) Proglottides are more longer than wider.
 T = (B) Intermediate host is pig & humans.
 T = (C) Beside passing in feces, proglottides are sometime regurgitated to cause autoinfection.
 F = (D) Cysticercosis in humans may cause visible or palpable nodules, if occur in liver or spleen.

- T = (E) Praziquantal is a drug that can be used in both teniasis & cysticercosis.

223) *Trichuris trichiura*

- T = (A) Eggs are barrel-shaped with mucus plug at each pole.
 T = (B) Adult worms measure 2-3 metres in length.
 T = (C) Acute appendicitis may occur if the worm inhabit vermiform appendix.
 T = (D) In massive trichiuriasis prolapse of rectum may occur.
 F = (E) Diagnosis can be made only when adult worm passed in feces.

224) *Enterobius vermicularis*

- F = (A) Eggs are elliptical in shape, & brown in color.
 T = (B) Autoinfection occur due to intense itching in perianal area at the time of egg-laying, forcing the patient to scratch the area.
 F = (C) Eggs are usually demonstrated in feces.
 T = (D) Air-borne transmission may occur to cause the infection.
 F = (E) Adult worm lives in upper small intestine of man.

225) *Hymenolepis nana*

- F = (A) Scolex is globular, & is provided with a rostellum armed with double row of hooklets.
 F = (B) Proglottides are more longer than wider
 F = (C) Fresh-water snail is the intermediate host of *H nana*.
 F = (D) Adult worm lives in cecum & colon of man.
 F = (E) In *H nana* infection, anemia occur due to consumption of vit B12 by the worm.

226) Regarding *tenia echinococcus*

- T = (A) Transmitted by fecal-oral route.
 T = (B) Shortest tape worm.
 F = (C) Consists of 4-8 segments.
 F = (D) Stools of infected person is diagnostic.
 T = (E) Cow is the intermediate host.

227) Parasites transmitted via oro-fecal route include

- T = (A) *Giardia*.
 T = (B) *Entameba histolytica*.
 F = (C) *Enterobius vermicularis*.
 T = (D) *Trichuris trichiura*.

F = (E) *Trichinella spiralis*.

228) Man is the definite host in the life cycle of

F = (A) Malaria parasite.

F = (B) *Echinococcus granulosus*.

T = (C) *Entamoeba histolytica*.

T = (D) *Wuchereria bancrofti*.

T = (E) *Ascaris lumbricoides*.

229) Arthropod borne infections include

T = (A) Yellow fever.

T = (B) Dengue fever.

T = (C) Trypanosomiasis.

T = (D) Cytomegaloviral disease.

F = (E) Poliomyelitis.

230) Man is the definitive host in the life cycle of

F = (A) Malarial parasite.

T = (B) Fish tapeworm (*diphyllobothrium latum*).

T = (C) *Schistosoma* species.

F = (D) *Echinococcus granulosus*.

T = (E) *Tenia saginata*.

231) *Entamoeba histolytica*

T = (A) Is a protozoan.

F = (B) In its trophozoite form is more important from epidemiological point of view.

F = (C) Can not cause extraintestinal lesions.

F = (D) Can not be diagnosed by immunological methods in difficult cases.

F = (E) Can cause granuloma formation.

232) Following helminthes are oviparous

T = (A) *Ascaris lumbricoides*.

T = (B) *Trichuris trichiura*.

T = (C) *Nector americanos*.

F = (D) *Trichinella spiralis*.

T = (E) *Tenia saginata*.

233) Each of the following statements concerning *Wuchereria bancrofti* is correct

T = (A) Tail-end of male worm contains 2 spicules of unequal length.

T = (B) Adult worm lives in the lymphatic system of humans.

F = (C) Infection occur thru the bite of mosquito, which transmits microfilariae to the human skin.

F = (D) Occult filariasis is caused by microfilariae, which is present in large no in peripheral blood.

T = (E) Periodic attacks of fever with lymphadenitis, & lymphangitis occur in *Wuchereria*.

234) Following are the examples of meat borne disease

T = (A) Salmonellosis.

T = (B) Teniasis.

T = (C) Trichinosis.

T = (D) Tuberculosis.

T = (E) Anthrax.

235) Following are the examples of water-borne diseases

T = (A) Hydatid disease.

T = (B) Ascariasis.

F = (C) Chickenpox.

T = (D) Infective hepatitis.

T = (E) Cholera.

Chapter 52

Self Examination (Single Best)

BACTERIOLOGY

- 1 A child developing fever, hypotension, erythema, & neck stiffness; the most likely toxin involved in this case is
- (A) Endotoxin
 - (B) Erythrogenic toxin
 - (C) Exotoxin
 - (D) Neurotoxin
 - (E) Botulinum toxin

Ans = A

- 2 The structure that is found in gram-negative bacteria but not in gram-positive bacteria is
- (A) Capsule
 - (B) Cell wall
 - (C) Cytoplasmic membrane
 - (D) Endospore
 - (E) Outer membrane

Ans = E

- 3 A 40-year-old female presents with a 2-month history of cough that has recently become productive, fatigue, night sweats, & a recent weight loss of 5 pounds. Sputum samples contain many acid-fast bacilli & her PPD is positive. Appropriate initial presumptive therapy would be
- (A) Cefoxitin
 - (B) Erythromycin
 - (C) Rifabutin + clarithromycin
 - (D) Rifampin + isoniazid
 - (E) Rifampin + isoniazid + pyrazinamide + ethambutol

Ans = E

- 4 A newborn baby brought to hospital with irritability, fever, & neck rigidity; the most common cause is infection with
- (A) Group B streptococcus
 - (B) Streptococcus pneumoniae
 - (C) Staphylococcus aureus
 - (D) H. influenzae
 - (E) N. meningitidis

Ans = A

- 5 Gram-positive cocci in clusters are seen in purulent fluid drained from a skin abscess. Rapid identification of these organisms will be facilitated by evaluation of the clumping of latex beads coated with
- (A) IgG & fibrinogen
 - (B) Interleukin-1 (IL-1) & factor VIII (antihemophilic factor)
 - (C) Properdin & platelet factor 3
 - (D) Prothrombin & C3b
 - (E) Transferrin & plasminogen

Ans = A

- 6 Which of the following toxins continually stimulates adenylate cyclase to overproduce cAMP by catalyzing the binding of ADP-ribose to the Gs protein, leading to severe fluid loss?
- (A) Bordetella pertussis toxin
 - (B) Cholera toxin
 - (C) Clostridium botulinum toxin
 - (D) Diphtheria toxin
 - (E) Tetanus toxin

Ans = B

- 7 A person developed food poisoning; which of the following is fatal one

- (A) *Vibrio cholera*
- (B) *Staphylococcus aureus*
- (C) *Clostridium botulinum*
- (D) *E. coli*
- (E) *Bacillus cereus*

Ans = C

- 8** A young boy is having swelling & tenderness of the knee joint; the most likely pathogen involved is
- (A) *Streptococcus pyogenes*
 - (B) *Staphylococcus aureus*
 - (C) *Gonococcus*
 - (D) *Brucella*
 - (E) *Mycobacterium tuberculosis*

Ans = B

- 9** A 35-years-old male develops high-grade fever with rusty sputum; his chest x-ray shows right-sided consolidation. The most accurate test for diagnosis would be:
- (A) Blood culture
 - (B) Sputum gram stain
 - (C) Sputum culture
 - (D) Cold antibody titer
 - (E) Lung biopsy

Ans = C

- 10** Drug of choice for pulmonary anthrax is:
- (A) Penicillin
 - (B) Ciprofloxacin
 - (C) Erythromycin
 - (D) Tetracycline
 - (E) Ceftriaxone

Ans = B

- 11** A 17-years-old girl present on 6th day after onset of fever. She is likely to have typhoid fever. The best test for diagnosis would be:
- (A) Blood culture
 - (B) Typhi dot test
 - (C) Widal's test
 - (D) Bone marrow biopsy
 - (E) Stool culture

Ans = A

- 12** An 18-years-old boy from a poor family presents with 1-day history of severe diarrhea, 15-16 episodes. On examination he is severely dehydrated, hypotensive & tachycardiac. The most likely organism involved is:

- (A) *Staphylococcus aureus*
- (B) *E. coli*
- (C) *Salmonella typhi*
- (D) *Shigella*
- (E) *V. cholera*

Ans = E

- 13** A high degree of immunity to reinfection with the same bacterial species is seen in patients who have recovered from infections caused by
- (A) *Bordetella pertussis*
 - (B) *Chlamydia trachomatis*
 - (C) *Neisseria gonorrhoeae*
 - (D) *Staphylococcus aureus*
 - (E) *Vibrio cholerae*

Ans = A

- 14** An 18 years old girl had a thin, watery discharge few hours after a rape. She also had fever. The discharge is due to;
- (A) Herpes Simplex
 - (B) *Gonococcus*
 - (C) *Chlamydia trachomatis*
 - (D) *Trichomonas vaginalis*
 - (E) *Lactobacillus*

Ans = C

- 15** A 9-years-old male presented with high-grade fever & lethargy since last evening. Examination revealed petechial rashes on the skin. Clinical diagnosis of meningitis was suspected & lumbar puncture was performed. CSF examination showed WBC $1 \times 10^9/L$ with 94% neutrophils. No organisms were seen on gram staining. Blood cultures from outside hospital were subsequently positive for oxidase positive, gram-negative diplococci. Which bacterium is most likely to be causing this patient's illness
- (A) *E. coli*
 - (B) *Hemophilus influenza*
 - (C) *Neisseria meningitidis*
 - (D) *Pseudomonas aeruginosa*
 - (E) *Streptococcus pneumoniae*

Ans = C

- 16** A 10-year-old boy had meningitis; causative organism is
- (A) *Klebsiella*
 - (B) *E. coli*
 - (C) *Neisseria meningitidis*

- (D) *Staphylococcus aureus*
 (E) *Salmonella*

Ans = C

- 17** A previously healthy 3-month-old boy is brought to the physician by his parents because he continues to have fever & ear pain despite treatment with amoxicillin for 72 hours. Examination shows an immobile, red, & opaque tympanic membrane. Which of the following is the most likely pathogen?
 (A) *Chlamydia trachomatis*
 (B) Group A streptococcus
 (C) *Hemophilus influenzae*
 (D) *Mycoplasma pneumoniae*
 (E) *Staphylococcus aureus*

Ans = C

- 18** All of the following diseases cause ulcers of penis, except
 (A) Gonorrhoea.
 (B) Syphilis.
 (C) Lymphogranuloma venereum.
 (D) Granuloma inguinale.
 (E) Herpes simplex genitalis.

Ans = A

- 19** A 48-year-old man with alcoholism comes to the physician because of fever, a facial rash, & rapidly progressive swelling of the left side of the face. He is unable to open his left eye because of the severity of the swelling. Which of the following is the most likely causal organism?
 (A) Group A streptococcus
 (B) *Hemophilus influenzae*
 (C) Herpes simple virus
 (D) *Neisseria meningitidis*
 (E) *Streptococcus pneumoniae*

Ans = A

- 20** A 43-years-old patient in hospital acquires pseudomonas infection; the most likely pathogenesis involved in it is:
 (A) Endotoxin
 (B) Activation of cAMP
 (C) Activation of EF-2
 (D) Exotoxin
 (E) Inhibition of cGMP

Ans = A

- 21** A young previously healthy IV drug addict was admitted in the hospital with the complaints of fever & malaise for the last five days. From two sets of blood culture there was growth of gram-positive cocci arranged in clusters. Which of the following organisms is most likely to be responsible for the endocarditis in the case
 (A) *Staphylococcus*
 (B) *Streptococcus*
 (C) *Rhotococcus*
 (D) *Enterococcus*
 (E) *Streptococcus pneumoniae*

Ans = A

- 22** A 45-years-old gentleman develops deformity of nose. The biopsy of lesion shows granulomas. The most likely diagnosis is:
 (A) *M. tuberculosis*
 (B) *M. leprae*
 (C) *Nocardia*
 (D) *M. avium-intercellulare*
 (E) *Aspergilloma*

Ans = B

- 23** A patient comes to you with cervical lymphadenopathy, & histopathology of the node shows granulomatous inflammation. For TB diagnosis which is most diagnostic
 (A) Mantoux test
 (B) PCR
 (C) Caseation necrosis
 (D) AFB
 (E) X-ray chest

Ans = B

- 24** The TSST-1 toxin of *staphylococcus aureus* acts to produce disseminated intravascular coagulation & circulatory collapse by functioning as a(n)
 (A) Inducer of MHC antigen expression
 (B) Polyclonal B cell activator
 (C) Producer of endogenous pyrogens
 (D) Superantigen
 (E) T cell lectin

Ans = D

- 25** Regarding actinomycosis all of the following are true except
 (A) Characterized by presence of sulphur granules in pus.

- (B) Characterized by abscess formation.
- (C) Caused by an anaerobic organism.
- (D) Characterized by draining sinus tracts.
- (E) Transmitted by personal contact.

Ans = E

26 Gravity of diphtheria is due to

- (A) Toxin production
- (B) Dehydration
- (C) Hyperpyrexia
- (D) Bleeding
- (E) Pseudomembrane formation

Ans = A

27 A 71-year-old male patient has recent aggravation of an exfoliative skin condition. He now has a temperature of 102 degrees F. The skin of his upper chest, extremities, & neck shows erythema with diffuse epidermal peeling & many pustular lesions. Cultures of pus from the lesions yields a gram-positive organism that is highly salt (NaCl) tolerant. Which of the following laboratory data would be most helpful for the identification of this microorganism?

- (A) Bacitracin sensitivity
- (B) Bile solubility
- (C) Coagulase positivity
- (D) Optochin sensitivity
- (E) Oxidase positivity

Ans = C

28 Regarding pseudomonas, the following is true

- (A) Sensitive to tetracycline
- (B) Resistant to quinolones
- (C) Cause malignant otitis externa
- (D) Always complicated by brain abscess
- (E) Most common cause of infection in childhood

Ans = C

29 Spores will be killed by

- (A) 121°C, at 15 lb/in², for 15 minutes (moist heat)
- (B) 73°C for 2 hours (dry heat)
- (C) Pasteurization
- (D) Chlorination
- (E) Iodine application

Ans = A

30 Virulence of bacteria is related to

- (A) Toxin & enzyme production
- (B) Resistance of the patient
- (C) Number of bacteria
- (D) Age of the patient
- (E) Portal of entry

Ans = A

31 Brucellosis is transmitted by

- (A) Flies
- (B) Unboiled milk
- (C) Cats
- (D) Dogs
- (E) Feco-oral route

Ans = B

32 A sexually active woman develops pain in lumbar region with fever, & on asking she also mention about discoloration of urine; the next step will be

- (A) Blood culture
- (B) Blood & urine culture
- (C) Urine culture
- (D) Cystoscopy
- (E) Urine D/R

Ans = C

33 Gas gangrene is caused by:

- (A) Clostridia botulinum.
- (B) Clostridia difficile.
- (C) Clostridia welchii.
- (D) Vibrio cholera.
- (E) Proteus.

Ans = C

34 Immunization against tetanus is achieved by

- (A) Anti-toxin
- (B) Tetanus toxoid
- (C) Toxin
- (D) Immunoglobulin
- (E) Penicillin

Ans = B

35 Abscess containing sulphur granules is caused by

- (A) Actinomycosis
- (B) Staphylococcus aureus
- (C) Brucellosis
- (D) Amebiasis
- (E) Histoplasmosis

Ans = A

- 36** Regarding corynebacterium diphtheria, the following is true
- (A) Needs nutrient agar
 - (B) Shows pleomorphism
 - (C) Is a gram +ve bacilli
 - (D) Show complete alpha-hemolysis
 - (E) Produces mainly endotoxin

Ans = C

- 37** Exotoxins are produced by all of the following except
- (A) *S. dysenteriae*.
 - (B) *S. typhi*.
 - (C) *V. cholera*.
 - (D) *C. diphtheria*.
 - (E) *Clostridium tetani*.

Ans = B

- 38** A child has presented with ear infection; pus is greenish in color. What is the probable organism
- (A) *Pseudomonas aeruginosa*
 - (B) *Staphylococcus aureus*
 - (C) *Streptococcus pyogenes*
 - (D) *Streptococcus pneumoniae*
 - (E) *Klebsiella*

Ans = A

- 39** A child develops pharyngitis caused by group A beta-hemolytic streptococci. Five weeks following treatment, he develops impetigo, & another group A beta-hemolytic streptococcus is isolated. These results are best explained by which of the following?
- (A) Immunity to streptococcal disease is type-specific
 - (B) Immunity to streptococcus is organ-specific
 - (C) The first culture was misidentified
 - (D) The patient did not develop immunity to the initial streptococcus infection

Ans = A

- 40** Neonatal meningitis is caused by
- (A) *E coli*
 - (B) *H influenzae*
 - (C) Meningococci
 - (D) *Streptococcus pneumoniae*
 - (E) *Staphylococcus aureus*

Ans = A

- 41** In a hospital catalase +ve staphylococcal infection outbreak occur; following is least likely to be done
- (A) Sterilization of all contacts
 - (B) Isolation of organism
 - (C) Isolation of further sub-type
 - (D) Isolation of patient
 - (E) Vancomycin prophylaxis of all contacts

Ans = A

- 42** A patient has fever & murmur due to valvular heart disease; which bacteria is the causative agent
- (A) *Streptococcus viridans*
 - (B) *Staphylococcus aureus*
 - (C) *H influenza*
 - (D) *E coli*
 - (E) *Streptococcus pneumoniae*

Ans = A

- 43** A neonate develops meningitis. *Streptococcus* is isolated from the mother's vagina. The organism agglutinates with antiserum directed against type B surface carbohydrate. The virulence of this organism is related to a bacterial constituent that interferes with which of the following host phagocyte functions?
- (A) Aggregation
 - (B) Chemotaxis
 - (C) Ingestion
 - (D) Intracellular killing
 - (E) Pseudopod formation

Ans = C

- 44** A 25-years-old lady had fever, & sore-throat. On culture of throat swab, organism causes complete hemolysis of culture medium. The most likely organisms is
- (A) α -hemolytic streptococcus
 - (B) β -hemolytic streptococcus
 - (C) *Bacteroides*
 - (D) Viruses
 - (E) *E. coli*

Ans = B

- 45** A child has presented with throat infection to ENT ward. Swab from the throat was cultured, which showed complete hemolysis; which will be the most probable organism
- (A) Beta hemolytic streptococci

- (B) Staphylococcus aureus
- (C) Mycoplasma
- (D) Klebsiella pneumoniae
- (E) Streptococcus viridans

Ans = A

46 For diagnosis of TB following is most important

- (A) Caseous necrosis
- (B) Granuloma
- (C) Tubercle bacilli
- (D) Langhan's giant cell
- (E) Epithelioid aggregation

Ans = A

47 Virulent treponema pallidum is used in the following

- (A) Treponema pallidum immobilization test.
- (B) Reiter protein complement fixation test.
- (C) Wassermann complement fixation test.
- (D) Fluorescent treponemal antibody test.
- (E) Fluorescent treponemal antibody/absorption test.

Ans = A

48 A 32-year-old stockbroker returned from a skiing 10 days ago. He presents to with difficulty urinating & of a urethral discharge for the past several days. A smear of the discharge shows the presence of numerous neutrophils & intracellular gram-negative diplococci. Which of the following drugs would be the most appropriate treatment for this patient?

- (A) Ampicillin
- (B) Cefoperazone
- (C) Ceftriaxone
- (D) Penicillin
- (E) Spectinomycin

Ans = C

49 A patient has symptoms & signs of tuberculosis; what will be the confirmatory test

- (A) AFB
- (B) Granuloma
- (C) Macrophages
- (D) Urine
- (E) Stool

Ans = A

50 Which of the following laboratory tests is useful for the diagnosis of Lyme disease?

- (A) Blood culture on sheep blood agar plate
- (B) Detection of IgM/IgG antibodies to the spirochete
- (C) Detection of specific antibody to ixodes tick
- (D) Documentation of fever & arthritis
- (E) Spinal fluid culture on Thayer-Martin agar

Ans = B

51 Actinomycetes does not cause disease in:

- (A) Bone
- (B) Lung
- (C) Brain
- (D) Skin
- (E) Kidney

Ans = A

52 A 45-year-old male is hospitalized to undergo intensive chemotherapy for Hodgkin's disease. Over the past four days he has been complaining of increasing shortness of breath. He now has a temperature of 102.2 °F, productive cough, & chills. His chest X-ray shows bilateral patchy infiltrates. His white blood count is 800/mm³. A sputum smear contains abundant gram-negative bacilli. Which of the following would be the most appropriate therapy for this patient?

- (A) Ceftazidime + gentamicin
- (B) Chloramphenicol
- (C) Ciprofloxacin
- (D) Trimethoprim + sulfamethoxazole
- (E) Vancomycin + gentamicin

Ans = A

53 The least titer for Widal test to be positive is

- (A) 80
- (B) 120
- (C) 160
- (D) 320
- (E) 20

Ans = A

54 A young boy is having swelling & tenderness of the knee joint; the most likely pathogen involved is

- (A) Streptococcus pyogenes
- (B) Staphylococcus aureus

- (C) Gonococcus
- (D) Brucella
- (E) Mycobacterium tuberculosis

Ans = B

- 55** When compared to a non-pathogenic strain of *Corynebacterium diphtheriae*, pathogenic *C. diphtheriae* possess
- (A) a temperate bacteriophage
 - (B) an epitope
 - (C) an F-plasmid
 - (D) bacteriocin
 - (E) purified DNA from a eukaryotic cell

Ans = A

- 56** In the first week of typhoid fever which is the most probable diagnostic test
- (A) Widal test
 - (B) Typhi dot
 - (C) Urine culture
 - (D) Stool culture
 - (E) Blood culture

Ans = E

- 57** Approximately 35 people attending a picnic developed symptoms of food poisoning, which occurred approximately 8 hours after everyone ate lunch. Laboratory studies revealed that the causative agent is a microaerophilic gram-negative, curved rod with polar flagella, & a "seagull" or "comma" appearance. Which of the following is the most likely reservoir for this organism?
- (A) Fish
 - (B) Fried rice
 - (C) Improperly canned food
 - (D) Poultry
 - (E) Vegetables

Ans = D

- 58** Which of the following toxins stimulates adenylate cyclase by catalyzing the transfer of ADP-ribose to the inhibitory subunit of the G protein?
- (A) *Bordetella pertussis* toxin
 - (B) *Clostridium botulinum* toxin
 - (C) *Clostridium tetani* toxin
 - (D) *Corynebacterium diphtheriae* toxin
 - (E) *Staphylococcus aureus* toxin

Ans = A

- 59** In an area of Sindh afflicted by a major flood, a number of villagers develop cholera & are treated by oral rehydration therapy. The tremendous fluid loss in these patients is produced by an enterotoxin that directly targets which of the following?
- (A) Adenylate cyclase
 - (B) cGMP-gated Na⁺ channel
 - (C) Chloride channel
 - (D) Elongation factor of translation
 - (E) G-protein

Ans = E

- 60** What percentage of the time does tetracycline resistance accompanies methicillin-resistant *Staphylococcus aureus*?
- (A) Less than 5% of the time
 - (B) 5-24% of the time
 - (C) 25-74% of the time
 - (D) 50-74% of the time
 - (E) Greater than 75% of the time

Ans = E

- 61** A 37-year-old woman with a history of rheumatic fever recently had a dental extraction. She did not take prophylactic antibiotics. She now presents with a low-grade fever, malaise, & a cardiac murmur. Echocardiography is positive for a valvular lesion. Blood cultures are positive. Which of the following is the most likely causative microorganism?
- (A) Coxsackie virus
 - (B) *Enterococcus faecalis*
 - (C) *Pseudomonas aeruginosa*
 - (D) *Staphylococcus aureus*
 - (E) *Viridans streptococci*

Ans = E

- 62** Boil of the nose is caused by
- (A) *Streptococcus pneumoniae*
 - (B) *Streptococcus pyogenes*
 - (C) *Staphylococcus aureus*
 - (D) *Pseudomonas*
 - (E) *Proteus*

Ans = C

- 63** An 18-year-old student complains of fever, cough, chest pain, & weight loss. On physical exam, adenopathy is noted. Lymph node biopsy reveals caseating granulomatous

inflammation. Adjacent to the areas of necrosis, macrophages are seen, filled with multiple small oval structures that appear to have halos. This student most likely acquired his infection from which of the following sources?

- (A) Another human via respiratory secretions
- (B) Cat feces contaminated drinking water
- (C) Contaminated drinking water
- (D) Desert sand
- (E) Soil enriched with bird excrement

Ans = A

64 A 15-day-old infant presents with purulent conjunctivitis. Inclusion bodies are seen in conjunctival scrapings. Which of the following is the infectious form of the organism?

- (A) Arthrospore
- (B) Conidia
- (C) Elementary body
- (D) Endospore
- (E) Reticulate body

Ans = C

65 With an appropriately performed acid-fast staining procedure, Mycobacteria will appear

- (A) blue
- (B) brown
- (C) colorless
- (D) purple
- (E) red

Ans = E

66 A 43-year-old man presents to his physician complaining of a sore on his penis. He admits that he visited a prostitute three weeks ago. Physical examination reveals a single firm, raised, red, non-tender lesion at the base of his penis. His physician provisionally diagnoses primary syphilis. Which of the following laboratory procedures would be most likely to verify the diagnosis?

- (A) Culture on Fletcher's serum semi-solid medium
- (B) Gram's stain
- (C) Immunofluorescent stain of smear made from the active lesion
- (D) Rapid plasma reagin (RPR) assay
- (E) Special culture using charcoal-yeast extract agar

Ans = C

67 A 7-year-old child has had a high fever & a sore throat for 2 days. Examination shows pharyngeal erythema, a swollen right tonsil with a creamy exudates, & painful right submandibular lymphadenopathy. Throat culture on blood agar yields numerous small b-hemolytic colonies that are inhibited by bacitracin. Which of the following is the most likely causal organism?

- (A) Adenovirus
- (B) Candida albicans
- (C) Corynebacterium diphtheriae
- (D) Coxsackie virus
- (E) Streptococcus pyogenes {group A}

Ans = E

68 For which of the following diseases would strict isolation be indicated for a hospitalized patient?

- (A) Botulism
- (B) Cervical-facial actinomycosis
- (C) Mycobacterium kansasii pulmonary infection
- (D) Pneumococcal pneumonia
- (E) Y. pestis pneumonia

Ans = E

69 Enteric gram-negative bacteria are most resistant to penicillin G than gram-positive bacteria. Which of the following is most closely associated with this difference?

- (A) Cytoplasmic membrane
- (B) Lipoprotein
- (C) Outer membrane
- (D) Peptidoglycan
- (E) Teichoic acid

Ans = C

70 A 12-year-old girl with sickle cell disease has pain in her right arm. An x-ray film of her arm shows bony lesions consistent with osteomyelitis. Which of the following is the most likely causal organism?

- (A) Clostridium septicum
- (B) Enterococcus faecalis
- (C) Listeria monocytogenes
- (D) Proteus mirabilis
- (E) Salmonella enteritidis

Ans = E

- 71** A 18 years old girl after eating CANNED food end up in emergency department, with vomiting and a blood pressure of 80 systolic, pale and calm extremities with a pulse of 30 per minute. She is in a state of confusion. The reaction probably is due to:
- (A) Enterotoxin
 - (B) Endotoxin
 - (C) Preformed toxin
 - (D) Exotoxin
 - (E) None of above

Ans = C

- 72** During 2nd week of typhoid fever, which of the following will be the most accurately diagnostic
- (A) Widal test
 - (B) Urine culture
 - (C) Stool culture
 - (D) Blood culture only
 - (E) Blood culture + Widal test

Ans = E

- 73** A married woman has right sided tubo-ovarian abscess, & she gave history of IUCD; the causative organism is:
- (A) Chlamydia
 - (B) Gardenella
 - (C) Tuberculous
 - (D) Bacteroides
 - (E) Herpes simplex

Ans = A

- 74** Staphylococcus can cause all of the following lesions except
- (A) Abscess.
 - (B) Carbuncle.
 - (C) Boil.
 - (D) Cellulitis.
 - (E) Lymphangitis.

Ans = E

- 75** Over the past week, a previously healthy 17-year-old girl has had pruritus & an increasingly severe rash. She takes no medications. Her sister with whom she shares a room had a similar condition during the previous week. There are multiple 2- to 5-mm erythematous papules over the trunk, especially at the waistline, & over the forearms, hands, & fingers. There is no

lymphadenopathy or hepatosplenomegaly. Which of the following is the most likely causal organism?

- (A) Epstein-Barr virus
- (B) Group A streptococcus
- (C) Measles virus
- (D) Sarcoptes scabiei
- (E) Varicella-zoster virus

Ans = D

- 76** Ten days after undergoing sigmoid resection with diverting colostomy, a 64-year-old man has a temperature of 103.4 °F & shaking chills. He received gentamicin & ampicillin therapy after the operation, & his postoperative course had been uncomplicated until now. A blood culture grows gram-negative bacilli. Which of the following is the most likely causal organism?
- (A) Bacteroides fragilis
 - (B) Brucella abortus
 - (C) Escherichia coli
 - (D) Proteus mirabilis
 - (E) Pseudomonas aeruginosa

Ans = A

- 77** A child is complaining of fever & wrist joint pain; what investigation will help you to reach a diagnosis
- (A) ASO titer
 - (B) ESR
 - (C) RA factor
 - (D) Blood CP
 - (E) X-ray wrist joint

Ans = A

- 78** A young girl came with signs & symptoms of & diagnosed as meningitis. Which organism will be involved?
- (A) Hemophilus influenzae
 - (B) N. meningitides
 - (C) Staphylococcus aureus
 - (D) Streptococcus pyogenes
 - (E) Diphtheria

Ans = B

- 79** Gram negative bacteremia in hospitalized patient is due to:
- (A) Indwelling urinary catheter
 - (B) Pneumonia
 - (C) I/V cannula

- (D) Broad spectrum antibiotics
(E) Nil per oral

Ans = B

- 80** All of the following are gram -ve pathogenic diplococci except
(A) Neisseria meningococci.
(B) Neisseria gonococci.
(C) Neisseria lactamica.
(D) Neisseria flavescens.
(E) Streptococcus pneumoniae.

Ans = E

- 81** In a 7 year old boy with sickle cell anemia, the following can lead to septicemia
(A) E. coli
(B) H. influenza
(C) Pneumococci
(D) Salmonella
(E) Pseudomonas

Ans = D

- 82** The gram negative endotoxin producing aerobic or facultative anaerobic rods include all of the following except
(A) E. coli.
(B) Clostridia.
(C) Proteus species.
(D) Pseudomonas aeruginosa.
(E) Klebsiella pneumonia.

Ans = B

- 83** A 26-years-old woman came to you with history of fever & weakness. On examination temperature of 38.9°C (102°F), BP 130/70 mm Hg, marked tachycardia & change of murmur was noticed. The most common cause of infective endocarditis is
(A) Streptococcus aureus
(B) Streptococcus pneumoniae
(C) Streptococcus viridans
(D) Group B beta hemolytic streptococcus
(E) Group D streptococcus

Ans = C

- 84** Regarding corynebacterium diphtheria all of the following are true except
(A) Is an anaerobe.
(B) Produces powerful exotoxin.
(C) Is a gram positive bacillus.

- (D) Causes pseudomembranous inflammation of pharynx.
(E) Is clubbed shaped.

Ans = A

- 85** Gram +ve cocci causes all of the following except
(A) Impetigo.
(B) Boil.
(C) Wool-sorters disease.
(D) Scarlet fever.
(E) Ludwig's angina.

Ans = C

- 86** Organisms causing UTI include all of the following except
(A) E. coli.
(B) Proteus.
(C) Bacteroides.
(D) S. fecalis.
(E) Pseudomonas.

Ans = C

- 87** Food poisoning is caused by all of the following organisms except
(A) Clostridium perfringens.
(B) Clostridium botulinum.
(C) Salmonella.
(D) B. cereus.
(E) P. vivax.

Ans = E

- 88** A very frequent cause of hospital acquired infections is
(A) Klebsiella
(B) Pseudomonas
(C) S. aureus
(D) H. influenzae
(E) S. Pneumoniae

Ans = B

- 89** Serologic tests for syphilis include all of the following except
(A) VDRL.
(B) Widal.
(C) TPI.
(D) TPHA.
(E) Wasserman.

Ans = B

- 90** Intracellular bacteria include all of the following except
- (A) *Brucella abortus*.
 - (B) *R. prowazekii*.
 - (C) *P. aeruginosa*.
 - (D) *L. monocytogenes*.
 - (E) *M. tuberculosis*.

Ans = C

- 91** The characters of *Staphylococcus aureus* are all of the following except
- (A) Golden colony pigmentation.
 - (B) The production of coagulase.
 - (C) The production of fibrinolysin.
 - (D) The production of leukocidin.
 - (E) The production of soluble hemolysin.

Ans = C

- 92** Regarding bacterial meningococcal meningitis all of the following are true except
- (A) CSF proteins are raised.
 - (B) CSF blood sugar is decreased.
 - (C) Bacteria can be cultured on media.
 - (D) Bacteria can be gram stained.
 - (E) CSF has no neutrophil.

Ans = E

- 93** A patient had puerperal pyrexia, the most likely causative organism is
- (A) *E. coli*
 - (B) Gonococci
 - (C) *Bacteroides*
 - (D) Mixed bacterial infection
 - (E) Chlamydia

Ans = D

- 94** Infection within a hospital may be occur via the following route, except
- (A) Dust-borne.
 - (B) Water-borne.
 - (C) Food-borne.
 - (D) Hand-borne.
 - (E) Endogenous.

Ans = E

- 95** All of the following bacteria are commonly found in infected wounds following colonic operations, except
- (A) *Escherichia coli*.
 - (B) *Neisseria meningitidis*.
 - (C) *Streptococcus anginosus*.

- (D) *Streptococcus fecalis*.
- (E) *Bacteroides fragilis*.

Ans = B

- 96** Blood is drawn from a 14-year-old boy with bacterial meningitis for a complete blood count. The leukocyte count is elevated. Which of the following is released by the predominant type of white blood cell present
- (A) Histamine
 - (B) Leukotriene
 - (C) Vasoactive amines
 - (D) Peroxidase
 - (E) Lysozyme

Ans = E

- 97** Folliculitis is caused by the following organism
- (A) *Proteus*.
 - (B) *Pseudomonas*.
 - (C) *Klebsiella*.
 - (D) *Staphylococci*.
 - (E) *E. coli*.

Ans = D

- 98** Regarding lymphogranuloma venereum all of the following are true except
- (A) Caused by *Chlamydia trachomatis*.
 - (B) Occurs more in women.
 - (C) Most common sexually transmitted disease in USA.
 - (D) Initial stages can be treated by tetracycline.
 - (E) Surgery may be required in later stages.

Ans = E

- 99** The following is true regarding lepromatous leprosy
- (A) Dermis appears diffusely packed with vacuolated macrophages.
 - (B) There is a high level of cell mediated immunity.
 - (C) Mucous membranes are not involved.
 - (D) The commonest cause of death is renal failure.
 - (E) Lymphadenitis occurs during type I reaction.

Ans = A

- 100** Tuberculosis mostly effect the following organ
- (A) Ovary

- (B) Fallopian tubes
- (C) Uterus
- (D) Breast
- (E) Vagina

Ans = B

- 101** A patient who is admitted in hospital with one week history of fever, cough & sore-throat. Culture of throat swab on blood agar shows tiny colonies with complete hemolysis of RBC's; the causative organism is
- (A) Beta hemolytic streptococci
 - (B) Hemophilus influenza
 - (C) Staphylococcus
 - (D) Bordetella pertussis
 - (E) Corynebacterium diphtheria

Ans = A

- 102** Bacteria that grow at 42°C:
- (A) Vibrio cholera
 - (B) Pseudomonas
 - (C) Shigella
 - (D) E coli
 - (E) Salmonella

Ans = B

- 103** Spores should be killed by:
- (A) Dry heat at 100°C
 - (B) Dry heat at 60 °C
 - (C) Dry heat at 160 °C
 - (D) Cidex solution
 - (E) Moist heat

Ans = E

- 104** Following is not a disinfectant:
- (F) Derivatives of salicylic acid
 - (G) Alcohol
 - (H) Soap
 - (I) Hydrogen peroxide
 - (J) Gluteraldehyde

Ans = C

- 105** A postpartum patient developed a temperature of 104°F & a tender uterus with a foul discharge. Of the following organisms the most likely offender is
- (A) E coli
 - (B) Staphylococcus
 - (C) Beta streptococcus
 - (D) Gonococcus
 - (E) Bacteroides

Ans = C

- 106** The most common cause of puerperal infection is
- (A) Bacteroides
 - (B) Candida
 - (C) Trichomonas
 - (D) Clostridia
 - (E) HPV

Ans = A

- 107** A woman comes to you with Siamese cat; her child will get which type of infection
- (A) Rubella
 - (B) Syphilis
 - (C) CMV
 - (D) HPV
 - (E) Toxoplasmosis

Ans = E

- 108** A woman comes to you with pink purulent vaginal discharge; it may be due to
- (A) E. coli
 - (B) Chlamydia
 - (C) Gonorrhoea
 - (D) Trichomonas
 - (E) Giardia

Ans = B

- 109** Least positive titer for Widal test is
- (A) 1:80
 - (B) 1:160
 - (C) 1:260
 - (D) 1:320
 - (E) 1:640

Ans = A

- 110** A child comes to you with recurrent fever & klebsiella infection; name the disease
- (A) Chronic granulomatous disease of nose
 - (B) Progressive atrophy of nasal mucosa
 - (C) Nosocomial infection
 - (D) Bacteremia
 - (E) Hemorrhagic necrotizing consolidation of lung

Ans = E

- 111** Regarding the rickettsiae all of the following are true except
- (A) Are morphologically pleomorphic.
 - (B) Contain both RNA & DNA.

- (C) Multiply by binary fission.
- (D) Are gram-positive.
- (E) Are intracellular.

Ans = D

112 A 48-year-old diabetic male comes to the emergency room with a fever of 102 °F, chills, flank pain, & frequent urination. Urinalysis reveals glucosuria; white blood cells & bacteria are seen in the urinary sediment. A Gram's stain of urinary sediment reveals the presence of gram-negative rods. The patient is allergic to penicillins, & aztreonam is not available. Which of the following drugs would be an appropriate choice?

- (A) Ciprofloxacin
- (B) Cefotaxime
- (C) Clindamycin
- (D) Ticarcillin
- (E) Vancomycin

Ans = A

113 *Pseudomonas aeruginosa* produces all of the followings, except

- (A) Exotoxin
- (B) Endotoxin
- (C) Enterotoxin
- (D) Hemolysin
- (E) Proteases

Ans = C

114 A 19-year-old college student is brought to ER because the patient was difficult to arouse in the morning. He has had a flu-like illness with fever & muscle & joint aches for 12 hours. His temperature is 103.1 °F, blood pressure is 90/60 mm Hg, & pulse is 120/min. There is a diffuse petechial rash over the trunk & extremities. He has a stiff neck that cannot be passively flexed. Which of the following is the most likely pathogen?

- (A) Coxsackie virus B
- (B) Echovirus
- (C) *Haemophilus influenzae*
- (D) *Neisseria meningitidis*
- (E) *Streptococcus pneumoniae*

Ans = D

115 A patient came to you with sore-throat & fever; which test you will advised to confirm the diagnosis

- (A) Blood culture
- (B) Blood & sputum culture
- (C) ELISA of throat swab
- (D) Schultz Charlton reaction
- (E) B, C, D & E

Ans = C

VIROLOGY

116 An 8-month-old boy is brought to test for the HIV virus, who is born of HIV positive mother; the most specific test for HIV virus in infant is

- (A) DNA PCR detection
- (B) Schick test
- (C) Wassermann test
- (D) ELISA test
- (E) Western blot test

Ans = A

117 Most diagnostic test for viral infection is:

- (A) Immunofluorescence
- (B) Identification of virus in cell cultures
- (C) Complement fixation
- (D) Neutralization
- (E) ELISA

Ans = B

118 An old lady come with red denture sores; most common invading organism is:

- (A) EBV
- (B) *Staphylococcus*
- (C) *Streptococcus*
- (D) *Chlamydia*
- (E) Herpes

Ans = E

119 *Condylomata acuminatum* occurs due to;

- (A) HSV
- (B) Wart virus
- (C) *Chlamydia trachomatis*
- (D) *Gardnerella vaginalis*
- (E) *Gonococcus*

Ans = B

120 Feco-oral transmission causes

- (A) Hepatitis A
- (B) Hepatitis C

- (C) Hepatitis B
- (D) Hepatitis D
- (E) All of the above

Ans = A

121 A 26-years-old female presented with an ulcerated cervical lesions. On asking she gave history of multiple sexual partner. Which causative organism is most likely?

- (A) EBV
- (B) Herpes simplex type I
- (C) Herpes simplex type II
- (D) Human papilloma virus
- (E) Gonococcus

Ans = C

122 Live, attenuated vaccines exist for human diseases caused by

- (A) hepatitis A & B viruses
- (B) hepatitis A & polioviruses
- (C) influenza viruses
- (D) rabies virus & rotavirus
- (E) rubella & measles viruses

Ans = E

123 Which of the following viral gene products is required to establish the HIV provirus in an infected cell?

- (A) Gag p24 capsid protein
- (B) Pol p 10 protease
- (C) Pol p66/p51 RNA-dependent DNA polymerase
- (D) Rev p 19 posttranscriptional regulator
- (E) Tat p 14 transcriptional regulator

Ans = C

124 All are feature of AIDS except

- (A) CMV infection
- (B) Kaposi's sarcoma
- (C) Chronic myeloid leukemia
- (D) Pneumocystis carinii infection
- (E) Non-Hodgkin lymphoma

Ans = C

125 Within eight days of each other, beginning on 25th December, a man & woman & their three children (ages 11-15) develop rapid onset of fever with chills, malaise, headache, & diffuse myalgias. Cough, sore throat, & nasal congestion are also present. Which of the following is the most likely causative agent?

- (A) Coxsackie virus
- (B) Influenza A virus
- (C) Measles virus
- (D) Norwalk virus
- (E) Respiratory syncytial virus

Ans = B

126 BRONCHIOLITIS is caused by:

- (A) Measles.
- (B) EBV.
- (C) Respiratory syncytial virus.
- (D) Congo virus.
- (E) Burellia pertussis.

Ans = C

127 Which of the following viruses is most closely genetically related to hepatitis A?

- (A) Hepatitis B
- (B) Influenza
- (C) Measles
- (D) Poliovirus
- (E) Rubella virus

Ans = D

128 A patient has presented to ENT dept. with sore-throat & lymphadenopathy. His peripheral smear shows atypical lymphocytes. What is most probable etiological agent

- (A) HIV
- (B) EBV
- (C) Herpes simplex
- (D) Cytomegalovirus
- (E) HTCLV

Ans = B

129 Transfection with the naked nucleic acid of which of the following viruses would result in active viral replication in cytoplasm?

- (A) Bunyavirus
- (B) Coxsackie virus
- (C) Poxvirus
- (D) Retrovirus
- (E) Rhabdovirus

Ans = B

130 A 5-year-old presents with a fever & a generalized macular rash that is most dense on the scalp & trunk. Several waves of lesions appear in succession & evolve rapidly into vesicles, then pustules over several days. This

child most likely has which of the following diseases?

- (A) Chickenpox
- (B) Exanthem subitum
- (C) Herpetic gingivostomatitis
- (D) Herpetic whitlow
- (E) Infectious mononucleosis

Ans = A

131 Regarding hepatitis B the following is not true:

- (A) Has an incubation period less than that of hepatitis A
- (B) Caused by sexual contact
- (C) Caused by DNA virus
- (D) Is blood-borne pathogen
- (E) Vaccine is available

Ans = A

132 An individual with chronic hepatitis C viral infection has a chemistry profile performed; which serum analyte is most likely to be decreased

- (A) Gamma globulin
- (B) Albumin
- (C) Lactate dehydrogenase
- (D) Alanine aminotransferase
- (E) Aspartate aminotransferase

Ans = B

133 Three weeks after a renal transplant, a patient develops fever & leukopenia, followed by prostration & severe pulmonary & hepatic dysfunction. Which of the following is the most likely viral cause?

- (A) Adenovirus type 12
- (B) Coxsackie virus
- (C) Cytomegalovirus
- (D) Influenza virus
- (E) Parvovirus B19

Ans = C

134 A small non-enveloped virus has no virion-associated enzyme activity, the replication cycle takes place exclusively in the cytoplasm of infected cells. Purified genomic nucleic acid added to cells results in the production of low levels of infectious virus. The genome of the virus is most likely to be which of the following?

- (A) Double-stranded DNA

(B) Single-stranded, non-segmented, negative-sense RNA

(C) Single-stranded, non-segmented, positive-sense DNA

(D) Single-stranded, non-segmented, positive-sense RNA

(E) Single-stranded, segmented, negative-sense RNA

Ans = D

135 The following is a DNA virus

- (A) Measles virus
- (B) Mumps virus
- (C) Infectious mononucleosis virus
- (D) Influenza virus
- (E) HIV

Ans = C

136 A 19-year-old woman comes to the physician because of temperature 101 F, fatigue, & sore throat for 1 week. Examination shows cervical lymphadenopathy & splenomegaly. Initial laboratory studies show a leukocyte count of 5000/mm³ (80% lymphocytes with many of the lymphocytes exhibiting atypical features). Serum aspartate aminotransferase (AST, GOT) activity is 200 U/L. Serum bilirubin level & serum alkaline phosphatase activity are within normal limits. Select the most likely diagnosis?

- (A) Acute leukemia
- (B) Anemia of chronic disease
- (C) Congestive heart failure
- (D) Epstein-Barr virus infection
- (E) Hereditary spherocytosis

Ans = D

137 20 years old girl has been raped. She has now watery vaginal discharge, has painful red papules & ulcers on vagina and vulva, & also has fever & tender inguinal lymph nodes; the causative organism is:

- (F) Bacteroides
- (G) Chlamydia
- (H) Herpes simplex
- (I) Gonococcus
- (J) Trichomonas vaginalis

Ans = C

- 138** Among the hepatotropic viruses, the virus which is least likely to cause chronic hepatitis is
- (A) Hepatitis A
 - (B) Hepatitis B
 - (C) Hepatitis C
 - (D) Hepatitis D
 - (E) Hepatitis non-A & non-B

Ans = A

- 139** EPSTEIN-BARR VIRUS is related with:
- (A) Retinoblastoma.
 - (B) Nasopharyngeal carcinoma.
 - (C) Chronic lymphoid leukemia
 - (D) ALL.
 - (E) Phylloid tumors.

Ans = B

- 140** A 30-years-old pregnant woman contracted with German measles; the least likely effects on fetus of this infection is
- (A) Congenital deafness
 - (B) Congenital cataract
 - (C) Cardiac anomaly
 - (D) Mental retardation
 - (E) Gross anomaly

Ans = E

- 141** A 25-years-old male homosexual is diagnosed as case of acquired immunodeficiency syndrome. Which one of the following is the confirmatory test for AIDS
- (A) PCR
 - (B) ELISA
 - (C) Western blot
 - (D) Northern blot
 - (E) Southern blot

Ans = C

- 142** DNA viruses are associated with the development of all of the following except
- (A) Epithelial cancers.
 - (B) Mesenchymal cancers.
 - (C) Hemopoietic cancers.
 - (D) Genital cancers.
 - (E) T-cell lymphoma.

Ans = E

- 143** TORCH complex (toxoplasma, rubella, cytomegalo virus, herpes simplex virus) infections show all of the following except

- (A) Cataract.
- (B) Microcephaly.
- (C) Splenomegaly.
- (D) Hepatomegaly.
- (E) Pneumonia.

Ans = E

- 144** The patient is suffering from HEPATITIS B. The best marker for the disease progression will be:
- (A) HbsAg
 - (B) HbsAb
 - (C) HbcAg
 - (D) HbeAb
 - (E) HbeAg

Ans = E

- 145** One of the following is not a marker which helps in either diagnosis of or disease progression:
- (A) HbsAg
 - (B) HbsAb
 - (C) HbcAg
 - (D) HbeAb
 - (E) None of the Above

Ans = C

- 146** Vaccine is available for all except:
- (A) EBV
 - (B) Typhus
 - (C) Pneumococcus
 - (D) Typhoid
 - (E) Cholera

Ans = A

- 147** HBV transmission occur via all of the following except
- (A) Oral-fecal route.
 - (B) Renal dialysis units.
 - (C) Blood or blood products.
 - (D) Sexual intercourse.
 - (E) Saliva.

Ans = A

- 148** Arthropod borne infections include all of the following except
- (A) Yellow fever.
 - (B) Dengue fever.
 - (C) Trypanosomiasis.
 - (D) Leishmaniasis.
 - (E) Poliomyelitis.

Ans = E

- 149** Regarding the hepatitis B virus all of the following are true except
- (A) Is not usually transmitted by the oral route.
 - (B) Is transmitted by sexual contact.
 - (C) Is common in renal dialysis units.
 - (D) Is the cause of Burkitt's lymphoma.
 - (E) Causes immune complex disease.

Ans = D

- 150** A patient is found to have a non-reactive HbsAg but ANTI-HCV is positive. He is considered to be suffering from
- (A) Hepatitis B
 - (B) Hepatitis C
 - (C) Hepatitis D
 - (D) Chronic carrier stage
 - (E) Co-infection

Ans = B

- 151** A young female developed HbsAg & died after some days. Which unusual virus is involved in this case
- (A) Hepatitis A virus
 - (B) Hepatitis G virus
 - (C) Hepatitis C virus
 - (D) Hepatitis D virus
 - (E) Hepatitis E virus

Ans = D

- 152** A patient has HbsAg non-reactive but HbcAg positive; the case is
- (A) Vaccinated
 - (B) Chronic carrier
 - (C) In incubation period
 - (D) Viral hepatitis B
 - (E) Hepatic cirrhosis

Ans = B

- 153** A 27-year-old female with HIV has a visual disturbance with hemorrhage & retinal exudates. Which virus is responsible for the condition
- (A) Adenovirus
 - (B) Herpes virus
 - (C) Papovavirus
 - (D) Rotavirus
 - (E) Poxvirus

Ans = B

- 154** A woman with normal uterus & irregular cervix which bleeds when touch may be due to which infection
- (A) HPV
 - (B) CMV
 - (C) EBV
 - (D) HSV
 - (E) Varicella zoster virus

Ans = A

- 155** Important diseases transmitted by arthropods include all of the following except
- (A) Leishmaniasis.
 - (B) Plague.
 - (C) Q fever.
 - (D) Dracunculiasis.
 - (E) Malaria.

Ans = C**MYCOLOGY**

- 156** A 70-years-old gentleman dies of respiratory failure. Post mortem biopsy of lung showed the evidence of histoplasmosis. This fungus primarily involves which structure:
- (A) Respiratory system
 - (B) Central nervous system
 - (C) Gastrointestinal system
 - (D) Reticuloendothelial system
 - (E) Genito-urinary system

Ans = D

- 157** Which of the following is the most common portal of entry in Blastomyces dermatitidis infection?
- (A) Central nervous system
 - (B) Circulatory system
 - (C) Mouth
 - (D) Respiratory tract
 - (E) Skin

Ans = D

- 158** Mucor disease is diagnosed by:
- (A) HPLC (high performance liquid chromatography).
 - (B) Mycolic assay.
 - (C) Finding hyphae.
 - (D) Clinically

(E) Ultrasound

Ans = C

159 A 65-years-old patient of renal transplant developed fever & neck rigidity. His CSF exam. revealed high protein content, but no organism on gram stain; the most likely organism is:

- (A) Histoplasmosis
- (B) Cryptococcus
- (C) Coccidioidococcus
- (D) Candidiasis
- (E) Blastomycosis

Ans = B

160 Deep fungal infections are caused by all of the following except

- (A) Coccidioidomycosis .
- (B) Blastomycosis.
- (C) Tinea corporis & capitis.
- (D) Candidiasis.
- (E) Histoplasmosis.

Ans = C

161 A 33-year-old, HIV-positive male homosexual reports to his physician complaining of weight loss associated with chronic, persistent, watery, non-bloody diarrhea & loss of appetite. Numerous acid-fast cysts are found in his stool sample. Which of the following organisms is most likely responsible for this syndrome?

- (A) Cyrtosporidium parvum
- (B) Entamoeba histolytica
- (C) Giardia lamblia
- (D) Mycobacterium avium-intracellulare
- (E) Toxoplasma gondii

Ans = A

162 Which of the following fungi is the most common cause of ringworm of the hair & scalp transmitted by dog/cat-to-human exposure?

- (A) Aspergillus fumigatus
- (B) Candida albicans
- (C) Epidemophyton floccosum
- (D) Microsporium canis
- (E) Sporothrix schenckii

Ans = D

163 Sites normally colonized by candida albicans include all of the following except

- (A) Gut.
- (B) Skin.
- (C) Vagina.
- (D) Mouth.
- (E) Prepuce.

Ans = E

164 Regarding disseminated coccidioidomycosis the following is not true:

- (F) Infection will not provide life time immunity
- (G) Occur in peoples with defect in cell mediated immunity
- (H) Lungs are primarily affected
- (I) Dissemination occur mainly in kidneys
- (J) Dissemination occur in about 1% patients

Ans = D

165 A 60-year-old man presents to clinic in respiratory distress. He has been using high dose corticosteroids for several years for an unrelated condition. A chest radiograph shows a coin lesion accompanied by floccular infiltrates. A transbronchial biopsy reveals granulomatous inflammation & budding fungus within macrophages. Which of the following fungal organisms is the most likely causative agent of this man's infection?

- (A) Aspergillus fumigatus
- (B) Candida albicans
- (C) Coccidioides immitis
- (D) Cryptococcus neoformans
- (E) Histoplasma capsulatum

Ans = E

166 A 37-year-old drug addict has white plaque-like lesions on his tongue & thru-out his mouth. The organism grows on Sabouraud's agar as a yeast at room temperature as well as at 35 degrees C. The yeast form of this organism is readily converted to the hyphal form called germ tubes in a test tube containing animal serum. Which of the following is the most likely organism?

- (A) Candida albicans
- (B) Coccidioides immitis
- (C) Cryptococcus neoformans
- (D) Histoplasma capsulatum

(E) *Sporothrix schenckii*

Ans = A

167 Three weeks after traveling to Thar to study desert herbs, a 32-year-old man develops a fever, chest pain, & sore muscles. Two days later, red tender nodules appear on the shins, & the right ankle is painful & tender. And x-ray film of the chest shows a left pleural effusion. Which of the following is the most likely diagnosis?

- (A) Blastomycosis
- (B) Coccidioidomycosis
- (C) Histoplasmosis
- (D) *Mycobacterium marinum* infection
- (E) *Mycoplasma pneumoniae* infection

Ans = B

168 A 23-year-old woman comes to the physician because of pale spots on her back for the past 2 months. She first noted a 3 x 4-cm oval patch on her upper back, followed by smaller spots with occasional itching. She has tried tanning oils & salons with no relief. Examinations show multiple 3- to 5-mm macules on her back in a Christmas-tree distribution; the macules are paler than the surrounding skin. Select the most diagnosis.

- (A) Allergic contact dermatitis
- (B) Atopic dermatitis
- (C) Pityriasis versicolor
- (D) Irritant contact dermatitis
- (E) Lichen simplex chronicus (localized neurodermatitis)

Ans = C

169 A gynecologist prescribes metronidazole to a lady, this drug is not likely to cover which organism

- (A) *Candida albicans*
- (B) *Trichomonas vaginalis*
- (C) *Giardia lamblia*
- (D) *Entamoeba histolytica*
- (E) *Bacteroides fragilis*

Ans = A

170 Regarding aspergillosis all of the following are true except

- (A) May occur in immunocompromized pts.
- (B) Diagnosis depends on demonstration of hyphal fragments in tissue biopsies.

(C) May involve the lungs.

(D) Results in the formation of fungus ball in lung.

(E) Is treated by surgery only.

Ans = E

171 Regarding *Candida albicans* all are true, except

- (A) Is the most common species of *Candida*.
- (B) Appears as branching hyphae in the tissues.
- (C) Is normally found in oral cavity, gastrointestinal tract & vagina.
- (D) Is an opportunist pathogen.
- (E) Is not affected by normal bacterial flora.

Ans = B

172 In CSF examination if protein is elevated & sugar is decreased but no bacteria can be cultured. What is the organism of meningitis

- (A) *Candida*
- (B) *Cryptococcus*
- (C) Herpes simplex
- (D) *Pneumocystis carinii*
- (E) *Histoplasma*

Ans = B

173 Regarding nocardiosis all of the following are true except

- (A) Is caused by anaerobic nocardia.
- (B) Is acquired exogenously.
- (C) Commonly occur in immune-compromized patients.
- (D) Is treated by sulphonamides.
- (E) Clinically resembles pulmonary tuberculosis.

Ans = A

174 A 30-year-old woman comes to the physician because of an itchy, scaly rash for 1 year, the rash is the most severe over her elbows & knees. The rash occurs only in the winter months & is moderately relieved by emollients. Examination shows discrete oval plaques 4-6 cm in diameter over the knees & elbows; they have an erythematous base & the overlying scale is silvery. Select the most diagnosis.

- (A) Allergic contact dermatitis
- (B) Atopic dermatitis
- (C) Dyshidrotic eczema
- (D) Irritant contact dermatitis

(E) Psoriasis

Ans = E

PARASITOLOGY

- 175** The vaginal culture of a lady of 28 years showed non-pathogenic bacteria, but on smear under microscope numerous bacilli were seen. They were;
- (A) Gardenella vaginalis
 - (B) E coli
 - (C) Lactobacillus
 - (D) Proteus
 - (E) Pseudomonas

Ans = C

- 176** A fisherman came to the out-patient department with complaints of weakness and malaise. He is pale and shows signs of anemia. The suspicion will be anemia due to:
- (A) Iron deficiency
 - (B) Diphyllbothrium
 - (C) Tape worm
 - (D) Ascariasis
 - (E) Pyridoxine deficiency

Ans = B

- 177** Two days prior to admission, a 34-year-old man had chills, followed by a fever of 103 degrees F. He reports having these "fever attacks" frequently, always followed by complete remission. A Giemsa stain is positive for gametocytes from *P. vivax*. The patient is placed on chloroquine, & primaquine is added because
- (A) it is active against the blood form of the parasite
 - (B) it is the only drug effective against the liver form of *P. vivax*
 - (C) primaquine hemolyses the cells that contain *P. vivax*, thereby exposing the parasite
 - (D) *P. vivax* is especially sensitive to it
 - (E) *vivax malaria* is resistant to chloroquine & mefloquine

Ans = B

- 178** Regarding amebiasis all of the following are true except

- (A) Cysts in all stages is infective.
- (B) Serological tests may be used for metastatic cases.
- (C) Liver may involved.
- (D) Diagnosis can be made on examination of stool.
- (E) Flask shaped intestinal ulcers are present.

Ans = A

- 179** Among the following infections, there is specifically lymphoid hyperplasia except in

- (A) Chronic malaria
- (B) Cutaneous leishmaniasis
- (C) Kala-azar
- (D) Sub-acute bacterial endocarditis
- (E) Infections mononucleosis

Ans = B

- 180** An 8-years-old boy living in poor conditions develops anemia & malnutrition. The most likely parasite involved is:

- (A) Round worms
- (B) Hook worms
- (C) Pin worms
- (D) Ring worms
- (E) Whip worms

Ans = A

- 181** A patient has recurrent episodes of fever with chills, massive splenomegaly, & peritoneal hemorrhage; the cause of splenomegaly is

- (A) Malaria
- (B) Leukemia
- (C) Leishmaniasis
- (D) Typhoid fever
- (E) Hodgkin disease

Ans = A

- 182** A woman is suffering from parasitic infestation; which type of anemia she will have

- (A) Aplastic
- (B) Iron deficiency
- (C) Anemia of chronic disease
- (D) Hemolytic anemia
- (E) Paroxysmal nocturnal hemoglobinuria

Ans = B

183 A 23-years-old boy develops anemia; his peripheral film shows MCV of 103 & Hb of 7.5. His diet comprises mostly of fish & soups. The most likely parasite, he is infested with is:

(A) Ankylostoma duodenale
 (B) Nector americanus
 (C) Clonorchis sinensus
 (D) Schistosoma
 (E) Diphyllbothrium latum

Ans = E

184 Parasites passing thru human lung as a part of their life cycle are all of the following except

(A) Ascaris lumbricoides.
 (B) Schistosomes.
 (C) Ankylostoma duodenale.
 (D) Paragonimus.
 (E) Diphyllbothrium latum.

Ans = E

185 Drug of choice for ankylostoma duodenale is:

(A) Mabendazole
 (B) Pyrantal pamoate
 (C) Ivermectin
 (D) Sodium stibogluconate
 (E) Albendazole

Ans = B

186 A 9-year-old girl appears listless & inattentive, & has thin extremities with a "potbelly" consistent with malnutrition. The CBC reveals a microcytic hypochromic anemia & the fecal exam detects brown, oval nematode eggs. Which of the following is the most likely infective stage of the organism?

(A) Cercariae
 (B) Cyst
 (C) Egg
 (D) Filariform larva
 (E) Metacercariae

Ans = D

187 One of the following is a ECTOPARASITE:

(A) Leech
 (B) Lice
 (C) Beatle.
 (D) Anthrax
 (E) A and C

Ans = B

188 A 30-years-old woman has high grade fever with chills for the last 2 days; she give the history of black urine. This may be due to

(A) CMV
 (B) HPV
 (C) Hepatitis B
 (D) Toxoplasmosis
 (E) Falciparum malaria

Ans = E

189 A patient comes with excessive vaginal discharge, & the vaginal smear shows an organism which is pear shaped. Name it?

(A) Chlamydia
 (B) Fungus
 (C) Gonococcus
 (D) Trichomonas
 (E) Staphylococcus

Ans = D

190 A 35-years-old woman had fever with chills & rigors for 3 days, & give history of black urine. Pt came to the hospital by mobile medical team circulating in the area. After one day she died. The cause of her death is most likely

(A) Falciparum malaria
 (B) CMV
 (C) Toxoplasmosis
 (D) Hepatitis B
 (E) Typhoid fever

Ans = A

191 All of the following are oviparous except

(A) Trichuris trichiura.
 (B) Nectar americanos.
 (C) Ascaris lumbricoides.
 (D) Ankylostoma duodenale.
 (E) Wuchereria bancrofti.

Ans = E

192 Lymphatic & lymph node is primary site of infection in the following

(A) Wuchereria bancrofti.
 (B) Onchocercus volvulus.
 (C) Entameba histolytica.
 (D) Trichuris trichiura.
 (E) Toxoplasma gondii.

Ans = A

193 Hook worm infection is characterized by all of the following except

- (A) Ground itch.
- (B) Bronchitis.
- (C) Macrocytic anemia.
- (D) Eosinophilia.
- (E) The presence of eggs in stool of infected person.

Ans = C

194 A woman complains of vulvar itching with pinkish vaginal discharge. Most probably she is suffering from;

- (A) Trichomonas vaginalis
- (B) N. gonorrhoea
- (C) Lactobacillus
- (D) Chlamydia trachomatis
- (E) Hemophilus duceryi

Ans = A

195 Hydatid disease can occur by the following

- (A) Eating hydatid cyst from goat.
- (B) Hydatid sac ingestion.
- (C) Eating ova of echinococcus.
- (D) Eating of fertile hydatids.
- (E) Inhaling ova of echinococcus.

Ans = C

196 A 40-years-old woman with severe pruritus & greenish yellow vaginal discharge; the most likely organism is

- (A) Candida
- (B) Trichomonas vaginalis
- (C) Gonorrhoea
- (D) Streptococcus
- (E) Chlamydia

Ans = B

197 Regarding entameba histolytica the following is true

- (A) Is a protozoan.
- (B) In its trophozoite form is more important from epidemiological point of view.
- (C) Can not cause extraintestinal lesions.
- (D) Can not be diagnosed by immunological methods in difficult cases.
- (E) Can cause granuloma formation.

Ans = A

198 All of the following helminthes are oviparous, except

- (A) Ascaris lumbricoides.
- (B) Trichuris trichuria.
- (C) Nector americanos.
- (D) Trichinella spiralis.
- (E) Tenia saginata.

Ans = D

199 A fisherman has developed diarrhea; his diet was mainly fish & rice. On stool examination ova are found. What is the causative organism

- (A) Diphyllbothrium latum
- (B) Tenia saginata
- (C) Tenia solium
- (D) Hymenolepis nana
- (E) Ascaris lumbricoides

Ans = A

200 A patient with worm infestation has developed megaloblastic anemia. Which is the culprit

- (A) Ascaris lumbricoides
- (B) Diphyllbothrium latum
- (C) Ankylostoma duodenale
- (D) Enterobius vermicularis
- (E) Tenia solium

Ans = B

201 A patient presented to the gyne OPD with a yellowish discharge with vulvar erythema and edema. The causative organism is;

- (A) Trichomonas vaginalis
- (B) E coli
- (C) Candida
- (D) Proteus
- (E) Gardenella vaginalis

Ans = A

202 Plasmodium falciparum infection produces all of the following except

- (A) Severe anemia.
- (B) Coma.
- (C) Uremia.
- (D) Pulmonary edema.
- (E) Cough.

Ans = D

SALIENT FEATURES

- ★ **General Bacteriology**
- ★ **Special Bacteriology**
- ★ **General Virology**
- ★ **Special Virology**
- ★ **Mycology**
- ★ **Parasitology**
- ★ **True / False Type &
One Best MCQs**

ISBN 978-969-8691-16-5



Khurram & Brothers