### **Therapeutic areas – Part 1**



Module 4 Topic 3

# Microbiology

#### **Introduction to Microbiology**

- Microorganisms organisms seen only through a microscope
  - Bacteria (singular bacterium) are unicellular microorganisms that possess a cell wall & multiply by cell division
  - Virus is a tiny, infectious particle that can reproduce only by infecting a host cell
  - Fungi



## Microbiology

**Classification of bacteria** 

- Aerobes and anaerobes
- Pathogens and non-pathogens
- Gram positive and Gram negative
- Cocci or Bacilli



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Organism	Diseases
A] Aerobes	
Gram positive Cocci	
Staphylococcus aureus	boils, cellulitis, endocarditis, eye infections, food poisoning,
	hospital-acquired infections, impetigo, osteomyelitis, otitis
	externa, pneumonia, septicaemia, toxic shock syndrome
Staphylococcus epidermidis	abscess, endocarditis, endometritis, hospital-acquired
	infections, neonatal meningitis, urinary tract infections,
	wound infections
Streptococcus pyogenes	cellulitis, erysipelas, glomerulonephritis, impetigo, pyoderma,
(grp A)	respiratory tract infections, rheumatic fever, septicaemia,
	toxic shock syndrome, wound infections
Streptococcus agalactiae	endocarditis, neonatal meningitis, respiratory tract infections,
(grp B)	urinary tract infections, wound infections
Streptococcus faecalis	endocarditis, urinary tract infections
(grp D)	
Streptococcus pneumoniae	bronchitis, eye infections, meningitis, otitis media,
	pneumonia, septicaemia

Organism	Diseases
A] Aerobes	
Gram positive Bacilli	
Bacillus anthracis	Anthrax
Corynebacterium	Diphtheria
diphtheriae	
Listeria monocytogenes	meningitis, meningoencephalitis, septicaemia

Organism	Diseases
A] Aerobes	
Gram negative Cocci	
Neisseria meningitides	Meningitis, septicaemia
Neisseria gonorrhoeae	Gonorrhoea, endocarditis, meningitis, ophthalmia
	neonatorum, septic arthritis, septicaemia

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Organism	Diseases
A] Aerobes	
Gram negative Bacilli	
Escherichieae coli	Cholecystitis, gastroenteritis, liver abscess, neonatal
	meningitis, peritonitis, septicaemia, urinary tract infections
Haemophilus influenzae	Arthritis, cellulitis, chronic bronchitis, conjunctivitis,
	meningitis, otitis media, pneumonia, sinusitis
Haemophilus ducreyi	Chancroid
Klebsiella pneumoniae	Cholecystitis, pneumonia, infections in immunocompromised
	patients
Pseudomonas aeruginosa	Abscess, burns infections, endocarditis, hospital-acquired
	infections, malignant otitis externa, meningitis, pneumonia,
	urinary tract infections, wound infections
Salmonella spp.	Typhoid, paratyphoid, gastroenteritis
Shigella spp.	Bacillary dysentery
Vibrio cholerae	Cholera
Yersinia pestis	Plague
Bordetella pertusis	Whooping cough

Organism	Diseases	
B] Anaerobes		
Gram positive cocci		
Peptostreptococcus spp.	Abdominal infections, acute necrotising gingivitis, aspiration	
	pneumonia, brain abscess, periodontitis, wound infections	
Gram positive bailli		
Clostridium botulinum	Botulism	
Clostridium welchii	Gas gangrene, food poisoning, necrotic enteritis, septic	
	abortion	
Clostridium tetani	Tetanus	
Clostridium difficile	Antibiotic-associated colitis	
Actinomyces spp.	Actinomycosis	
Gram negative cocci		
Veillonella spp.	Periodontitis, lung infections	
Gram negative bacilli		
Bacteroides fragilis	Abscess, intra-abdominal infections	
Fusobacterium spp.	Aspiration pneumonia, necrotising gingivitis	



#### **Antibacterial Agents (contd)**

 Agents that act against Mycobacterium tuberculosis, the microbe that causes tuberculosis, including <u>streptomycin</u>, <u>rifampicin</u>, <u>isoniazid</u>, <u>ethambutol</u>, and <u>pyrazinamide</u>



#### **Antibacterial Agents**

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Mode of action	Chemical group	Antibacterial agents
	Penicillins (beta lactam)	Benzylpenicillin, ampicillin, amoxycillin, cloxacillin, piperacillin
Inhibition of cell wall synthesis	Cephalosporins (beta lactam)	Cephalexin, cefadroxil, cefuroxime, cefotaxime, ceftazidime, ceftriaxone
	Glycopeptides	Vancomycin, teicoplanin

#### **Antibacterial Agents (Contd)**

Mode of action	Chemical group	Antibacterial agents
Inhibition of protein synthesis	Aminoglycosides	Streptomycin, gentamicin, amikacin, tobramycin
	Macrolides	Erythromycin, roxithromycin, clarithromycin, azithromycin
	Tetracyclines	Tetracycline, doxycycline
	Chloramphenicol	Chloramphenicol
	Lincosamides	Clindamycin



#### **Antibacterial Agents (Contd)**

Mode of action	Chemical group	Antibacterial agents
	Quinolones	Norfloxacin, ciprofloxacin, ofloxacin, gatifloxacin
Inhibition of bacterial DNA synthesis	Sulphonamides	Sulphadoxine, sulphmethoxazole, co- trimoxazole
	Metronidazole	Metronidazole



# **Viral Infection**

A virus is smaller than a bacteria. It has a protective capsule (Capsid), the nucleic acid and the membrane. Viral infection

- Attachment Virus binds to receptor on cell surface
- Entry Virus enters cell by endocytosis
- Replication and gene expression The genome is copied and translated into viral proteins using a host ribosome
- Assembly Capsid proteins and genomes come together to make new viral particles
  - **Release** The cell bursts releasing viral particles, which then infect other host cells

- Tinea is the name of a group of diseases caused by a fungus. It is also called as "ringworm" or "dermatophytosis."
  - tinea pedis or "athlete's foot": red, swollen, peeling, itchy skin between the toes
  - tinea capitis: scaly, itchy, red, circular bald spot on scalp
  - tinea cruris or "jock itch": scaly, itchy, red spots in the groin
  - tinea barbae: scaly, itchy, red spots on the cheeks, chin, and upper neck filled with pus, affected hair might fall out
  - Onychomycosis nail infection
- Treatment

<sup>9</sup>cade<sup>r</sup>

- over-the-counter topical antifungal products clotrimazole, terbinafine
- Chronic or extensive disease may require oral antifungal agents such as terbinafine, itraconazole, or fluconazole

#### Candidiasis

- Fungal infection caused by yeasts that belong to the genus *Candida*, most commonly *Candida albicans*.
- *Candida* yeasts normally reside in the intestinal tract and can be found on mucous membranes and skin



#### Oropharyngeal candidiasis or "thrush"

- Seen commonly in people who -
  - Wear dentures
  - Have diabetes
  - Have cancer
  - Have HIV/AIDS
  - Take inhaled corticosteroids for conditions like asthma
  - Smoke
- Treatment

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 Antifungal medicines like clotrimazole, miconazole, or nystatin applied to the inside of the mouth for 7 to 14 days

Vaginal Candidiasis

- More likely in women who -
  - Are pregnant
  - Use hormonal contraceptives (for example, birth control pills)
  - Have diabetes
  - Have a weakened immune system (for example, due to HIV infection or treatment with steroids or chemotherapy)
  - Are taking or have recently taken antibiotics
- Treatment
  - Topical antifungal applied inside the vagina or a single dose of fluconazole taken by mouth

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### Pain

- An unpleasant sensation usually associated with tissue damage
- Chemicals like prostaglandins, histamine etc. released following tissue damage stimulate the pain receptors
- Pain sensation transmitted via spinal cord to thalamus and cerebral cortex



- Response of living tissue to injury
- Injury may be due to
  - Physical agents
  - Chemical agents
  - Microorganisms
  - Immunological



- Pathophysiology
  - Increase in the local blood flow
  - Outpouring of fluid from the capillaries
  - Migration of leukocytes (WBCs) into the tissue
- Chemical mediators of inflammation
  - Arachidonic acid derivatives PG, leukotrienes
  - Histamine
  - Bradykinin

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- Prostaglandins
- These chemicals cause
  - Potentiation of pain
  - Vasodilation, attraction of WBCs to the area
  - Formation of inflammatory exudate



- Signs of inflammation
  - Pain (dolor)
  - Redness (rubor)
  - Local heat (calor)
  - Swelling (tumor)
  - Loss of function (functio laesa)



Management of Pain & Inflammatory Disorders

- Management of Pain
  - Narcotic Analgesics e.g. morphine, codeine, pethidine
  - Non-narcotic Analgesics e.g. paracetamol
- Management of inflammatory disorders
  - Anti-inflammatory drugs
    - Corticosteroids
    - Non-steroidal anti-inflammatory drugs (NSAIDs)



### Immune system

- First line of defense skin (nonspecific defense)
- Second line of defense inflammatory response
- Adaptive immune system "remembers" the antigen / pathogen, allowing for a faster response on next exposure



### Immune system

### Humoral immunity

Activated B cells grow rapidly

- producing plasma
  cells, which release
  antibodies into the
  bloodstream
- and memory B cells

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### Immune system

### **Cell-mediated immunity**

- Killer T cells (cytotoxic T cells) assist with the elimination of infected body cells by releasing toxins into them and promoting apoptosis
- Helper T cells act to activate other immune cells

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### **Overview of Blood Disorders**

- Some blood disorders cause the number of cells in the blood to decrease:
  - A decreased number of red blood cells is called <u>anemia</u>
  - A decreased number of white blood cells is called <u>leukopenia</u>
  - A decreased number of platelets is called <u>thrombocytopenia</u>

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- Other blood disorders cause the numbers of blood cells to increase:
  - An increased number of red blood cells is called <u>erythrocytosis</u>
  - An increased number of white blood cells is called <u>leukocytosis</u>
  - An increased number of platelets is called thrombocytosis or <u>thrombocythemia</u>

### **Blood Disorders**

- Symptoms of Blood Disorders
  - Decreased RBCs and hemoglobin can cause symptoms of anemia, such as <u>fatigue</u>, weakness, and shortness of <u>breath</u>
  - Decreased white blood cells or immune system proteins can cause <u>recurrent fever</u> and <u>infections</u>
  - Decreased platelets or blood clotting factors can cause <u>abnormal bleeding</u> and <u>bruising</u>



### **Blood Disorders**

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#### Symptoms suggestive of a blood disorder :

- <u>Blood clot</u> (phlebitis), usually in a leg causing swelling, redness, and/or warmth of the leg or shortness of breath
- Petechiae a fine pin-point red skin rash caused by low platelet count
- Blood blisters in the mouth caused by too few platelets or clotting problems
- Swollen lymph nodes caused by white blood cell cancers leukemias, lymphomas
- Pallor (pale skin) caused by anemia
- Pica (eating of ice, dirt, or clay) suggests iron deficiency anemia

### Leukemias

#### Leukemia

- Cancer of the WBCs involving bone marrow, circulating WBCs, and organs such as the spleen and lymph nodes
- Abnormal proliferation, clonal expansion at the pluripotent stem cell level, and diminished apoptosis (programmed cell death) lead to replacement of normal blood elements with malignant cells
- Inhibitory factors produced by leukemic cells suppress normal hematopoiesis, leading to anemia, thrombocytopenia, and granulocytopenia
  - Organ infiltration results in enlargement of the liver, spleen, and lymph nodes



### Lymphoma

#### Lymphoma

- A heterogeneous group of tumors arising in the reticuloendothelial and lymphatic systems
- The major types are -
  - Hodgkin lymphoma
  - Non-Hodgkin lymphoma



The common ENT disorders include

- Otorrhea or ear discharge, e.g. Acute otitis media,
- Tonsillopharyngitis,
- Sore throat,
- Rhinorrhea,
- Sinusitis
- Dizziness and Vertigo etc.



#### Otorrhea or Ear discharge

- Most common causes are
  - <u>Acute otitis media</u> with perforation of ear drum
  - <u>Chronic otitis media</u> (with a perforation of the eardrum, cholesteatoma, or both)
  - Otitis externa

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- Malignant External Otitis
  - Occurs mainly in elderly patients with diabetes or in immunocompromised patients
  - Often due to *Pseudomonas* or methicillin-resistant Staphylococcus aureus (MRSA)
  - Treatment is with fluoroquinolone e.g. ciprofloxacin 400 mg IV q 8 h and/or a penicillin (piperacillin–tazobactam or piperacillin)/aminoglycoside combination

#### Sinuses

• Paranasal sinuses are mucus-lined bony cavities that connect to the nasopharynx





### Sinusitis

<sup>9</sup>cade<sup>n</sup>

- Inflammation of paranasal sinuses due to viral, bacterial, or fungal infections or allergic reactions
- Symptoms include nasal obstruction and congestion, purulent rhinorrhea, facial pain; malaise, headache, and/or fever
- Local measures to enhance drainage e.g. steam, topical vasoconstrictors
- Treatment of suspected bacterial infection is with antibiotics, such as amoxicillin/clavulanate or doxycycline or levofloxacin or cefixime
- Recurrent sinusitis may require surgery to improve sinus drainage

Upper GI complaints include -

- Chronic and recurrent abdominal pain
- Dyspepsia
- Nausea and vomiting
- Regurgitation



Lower GI complaints include -

- Constipation
- Diarrhea
- Gas and bloating
- Abdominal pain
- Rectal pain or bleeding



#### Dyspepsia

- Dyspepsia is a sensation of pain or discomfort in the upper abdomen
- May be described as indigestion, gassiness, fullness, or burning
- Treatment
  - Proton Pump Inhibitors (PPIs), H<sub>2</sub> blockers, or a cytoprotective agent e.g. sucralfate



#### **Nausea and Vomiting**

- Nausea unpleasant feeling of need to vomit
- Vomiting forceful expulsion of gastric contents caused by involuntary contraction of the abdominal muscles
- Most common causes:
  - Gastroenteritis
  - CNS Injury / infections / labyrinthitis / motion sickness
  - Drugs / Toxins
- Complications
  - dehydration and electrolyte imbalance
- Treatment

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- Motion sickness: Antihistamines like Dimenhydrinate, scopolamine patches, Prochlorperazine or metoclopramide
- Severe or refractory vomiting and vomiting caused by chemotherapy: 5-HT<sub>3</sub> antagonists e.g. ondansetron, granisetron

#### Constipation

- Difficult or infrequent passage of stool, hardness of stool, or a feeling of incomplete evacuation
- Associated with sluggish movement of stool through the colon due to diet, pelvic floor dysfunction or drugs
- Treatment

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- Discontinuation of causative drugs (some may be necessary)
- Increase in dietary fiber
- Brief course of laxatives

## Management of constipation

#### Laxatives -

- Bulking agents (eg, psyllium, calcium polycarbophil, methylcellulose)
- Osmotic agents contain poorly absorbed polyvalent ions (eg, magnesium phosphate, sulfate), polymers (eg, polyethylene glycol), or carbohydrates (eg, lactulose, sorbitol) increasing intraluminal osmotic pressure and thereby drawing water into the intestine
- Secretory or stimulant cathartics (eg, phenolphthalein, bisacodyl, senna, castor oil,) act by irritating the intestinal mucosa or by directly stimulating the submucosal and myenteric plexus

#### Enemas



**Emollient agents** e.g. docusate, a surfactant, which softens the fecal mass and increase its bulk; making stools them easier to pass

Constipation ( contd)

- **Enemas** including tap water and commercially prepared hypertonic solutions.
- Emollient agents e.g. docusate, a surfactant, which allows water to enter the fecal mass to soften and increase its bulk; act slowly to soften stools, making them easier to pass



#### Diarrhea

- Passing frequent and/or watery stools
- Causes of diarrhoea
  - Increased secretions
    - Causes include infections, unabsorbed dietary fat and bile acids (malabsorption syndrome), and certain drugs viz., quinidine, quinine, orlistat
    - Infections combined with food poisoning are the most common causes of acute diarrhea
  - Reduced contact time/surface area
    - Impair fluid absorption and cause diarrhea
    - Inflammatory bowel disease, celiac disease



#### Diarrhea (contd)

- Treatment
  - Fluid and electrolytes for dehydration
  - Possibly antidiarrheals for nonbloody diarrhea in patients without systemic toxicity
  - Oral rehydration solution (ORS) should contain
    - Complex carbohydrate or 2% glucose
    - 50 to 90 mEq/L of sodium



#### **Acid - Peptic Disorders**

- Gastro-oesophageal Reflux Disease (GERD) or Reflux Oesophagitis
- Duodenal Ulcer
- Gastric Ulcer
- Stress Ulcers- Occur in seriously ill hospitalized patients due to a decrease in blood flow the mucosal surface leading to ulceration



#### Therapeutic approach to acid-peptic disorders

- Antacids primary treatment for most acid-peptic disorders as they are inexpensive, readily available, and safe in most populations
  - Antacids work nearly instantaneously and find utility for rapid relief of mild or sporadic symptoms
  - Commonly used antacids are <u>aluminum hydroxide and</u> <u>magnesium hydroxide</u>
- **Proton Pump Inhibitors** e.g. <u>omeprazole</u>, <u>esomeprazole</u>, <u>pantoprazole</u>



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#### Therapeutic approach to acid-peptic disorders (Contd)

• H. pylori eradication regimens

Regimen	Comment
Triple therapy	First line treatment
PPI; amoxicillin 1 g BID; clarithromycin	
500mg BID for 10–14 days	
Sequential therapy	
PPI and amoxicillin 1 g BID for 5 days	May be first line where macrolide
followed by PPI, clarithromycin 500mg	resistance is common
BID, tinidazole 500mg BID for 5 days	
Quadruple therapy	
PPI; bismuth 525mg QID; metronidazole	Treatment for failure
500mg QID; and tetracycline 500mg QID	
for 14 days	