UNIT – 5 PATHOPHYSIOLOGY 🧬

B. PHARMACY 2ND SEMESTER

POINTS TO BE COVERED IN THIS TOPIC

- ➤ INFECTIOUS DISEASES 🦠
- ➤ SEXUALLY TRANSMITTED DISEASES 💔

INFECTIOUS DISEASES 🦠

INTRODUCTION

Infectious diseases are disorders caused by pathogenic microorganisms including bacteria, viruses, fungi, or parasites. These diseases can be transmitted from person to person through various modes including direct contact, airborne transmission, vector-borne transmission, or through contaminated food and water.

The pathophysiology of infectious diseases involves the invasion of host tissues by pathogenic organisms, followed by multiplication and spread, leading to tissue damage and clinical manifestations. The severity of infection depends on factors such as virulence of the organism, host immune status, and route of transmission.

🧠 MENINGITIS

DEFINITION

Meningitis is an acute inflammation of the protective membranes (meninges) covering the brain and spinal cord. It is characterized by inflammation of the pia mater, arachnoid mater, and subarachnoid space.

ETIOLOGY

Bacterial Meningitis:

- Streptococcus pneumoniae
- Neisseria meningitidis
- Haemophilus influenzae type b
- Listeria monocytogenes
- Group B Streptococcus

Viral Meningitis:

- Enteroviruses
- Herpes simplex virus
- Varicella-zoster virus
- Mumps virus

Fungal Meningitis:

- Cryptococcus neoformans
- Candida species
- Aspergillus species

PATHOPHYSIOLOGY

The pathophysiology of meningitis involves several sequential steps:

Initial Invasion: Pathogens reach the central nervous system through hematogenous spread, direct extension from adjacent infected sites, or through anatomical defects. The blood-brain barrier normally prevents entry of pathogens, but certain organisms have developed mechanisms to cross this barrier.

Inflammatory Response: Once pathogens enter the subarachnoid space, they multiply rapidly due to the lack of effective immune surveillance in this immunologically privileged site. The presence of bacterial components triggers an intense inflammatory response involving:

- Release of inflammatory mediators
- Activation of complement cascade
- Neutrophil recruitment and degranulation
- Increased vascular permeability

Cerebral Edema: The inflammatory process leads to three types of cerebral edema:

- Vasogenic edema (breakdown of blood-brain barrier)
- Cytotoxic edema (cellular swelling)
- Interstitial edema (obstruction of CSF flow)

Increased Intracranial Pressure: Progressive cerebral edema and impaired CSF drainage result in elevated intracranial pressure, leading to

reduced cerebral perfusion and potential herniation.

CLINICAL MANIFESTATIONS

Classic Triad:

- Fever
- Neck stiffness (nuchal rigidity)
- Altered mental status

Additional Symptoms:

- Severe headache
- Photophobia
- Nausea and vomiting
- Skin rash (particularly in meningococcal meningitis)
- Seizures
- Cranial nerve palsies

COMPLICATIONS

Acute Complications:

- Cerebral edema
- Seizures
- Stroke
- Cranial nerve palsies
- Septic shock

Long-term Sequelae:

- Hearing loss
- Cognitive impairment
- Motor deficits
- Hydrocephalus
- Epilepsy

🌡️ TYPHOID FEVER

DEFINITION

Typhoid fever is a systemic infection caused by Salmonella enterica serotype Typhi, characterized by prolonged fever, headache, and abdominal symptoms.

ETIOLOGY

Causative Organism:

- Salmonella enterica serotype Typhi
- Gram-negative, facultative anaerobic bacterium
- Exclusively human pathogen

PATHOPHYSIOLOGY

Transmission and Entry: Typhoid fever is transmitted through the fecal-oral route via contaminated food and water. The bacteria must survive the acidic gastric environment to reach the small intestine.

Intestinal Phase: After ingestion, S. Typhi invades the intestinal mucosa through M cells in Peyer's patches. The bacteria are then phagocytosed by macrophages but survive intracellularly by preventing phagosome-lysosome fusion.

Systemic Dissemination: Infected macrophages carry the bacteria to mesenteric lymph nodes, where multiplication occurs. Subsequently, bacteria enter the bloodstream, causing primary bacteremia and seeding various organs including:

- Liver and spleen
- Bone marrow
- Gall bladder
- Kidneys

Re-infection Phase: Bacteria multiply in the reticuloendothelial system and re-enter the bloodstream, causing secondary bacteremia. This phase corresponds to the clinical onset of symptoms.

Intestinal Re-invasion: Bacteria are secreted in bile and re-invade the small intestine, potentially causing ulceration of Peyer's patches, which may lead to perforation and hemorrhage.

CLINICAL MANIFESTATIONS

Week 1:

- Gradual onset of fever
- Headache
- Malaise

- Anorexia
- Relative bradycardia

Week 2:

- High fever (39-40°C)
- Rose spots on trunk
- Splenomegaly
- Abdominal distension

Week 3:

- Complications may develop
- Intestinal bleeding
- Perforation
- Encephalopathy

COMPLICATIONS

Intestinal Complications:

- Gastrointestinal bleeding
- Intestinal perforation
- Toxic megacolon

Extra-intestinal Complications:

- Typhoid encephalopathy
- Myocarditis

- Pneumonia
- Osteomyelitis
- Endocarditis

🦠 LEPROSY (HANSEN'S DISEASE)

DEFINITION

Leprosy is a chronic infectious disease caused by Mycobacterium leprae, primarily affecting the skin, peripheral nerves, and mucosa of the upper respiratory tract.

ETIOLOGY

Causative Organism:

- Mycobacterium leprae
- Acid-fast, obligate intracellular bacterium
- Cannot be cultured in artificial media

PATHOPHYSIOLOGY

Transmission: Leprosy is transmitted through prolonged close contact with infected individuals, primarily through respiratory droplets containing M. leprae.

Host Response and Disease Spectrum: The clinical manifestations of leprosy depend on the host's immune response, particularly cell-mediated immunity. The disease exists on a spectrum:

Tuberculoid Leprosy (TT):

- Strong cell-mediated immune response
- Low bacterial load
- Well-formed granulomas
- Limited skin lesions

Lepromatous Leprosy (LL):

- Poor cell-mediated immune response
- High bacterial load
- Poorly formed granulomas
- Extensive skin involvement

Borderline Forms:

- Borderline tuberculoid (BT)
- Borderline borderline (BB)
- Borderline lepromatous (BL)

Nerve Damage: M. leprae has a predilection for peripheral nerves, particularly those in cooler areas of the body. The organism invades Schwann cells, leading to:

- Demyelination
- Axonal damage
- Nerve thickening
- Loss of sensation

- Motor weakness

CLINICAL MANIFESTATIONS

Skin Lesions:

- Hypopigmented or erythematous patches
- Loss of sensation in lesions
- Thickening of peripheral nerves
- Nodules and plaques (in lepromatous form)

Nerve Involvement:

- Anesthesia
- Muscle weakness
- Deformities
- Trophic ulcers

Systemic Features:

- Nasal congestion and epistaxis
- Eye involvement (lagophthalmos, corneal anesthesia)
- Testicular involvement leading to infertility

COMPLICATIONS

Neural Complications:

- Claw hand deformity
- Foot drop

- Facial palsy
- Blindness

Reactional States:

- Type 1 reaction (reversal reaction)
- Type 2 reaction (erythema nodosum leprosum)

🫁 TUBERCULOSIS

DEFINITION

Tuberculosis is a chronic infectious disease caused by Mycobacterium tuberculosis complex, primarily affecting the lungs but can involve any organ system.

ETIOLOGY

Causative Organisms:

- Mycobacterium tuberculosis
- Mycobacterium bovis
- Mycobacterium africanum
- Mycobacterium microti

PATHOPHYSIOLOGY

Transmission: TB is transmitted through airborne droplet nuclei containing M. tuberculosis, expelled when infected individuals cough, sneeze, or speak.

Primary Infection: When inhaled, bacilli reach the alveoli where they are phagocytosed by alveolar macrophages. The bacteria can survive and multiply within macrophages due to their ability to:

- Prevent phagosome-lysosome fusion
- Resist lysosomal enzymes
- Inhibit macrophage activation

Granuloma Formation: The host immune response leads to the formation of granulomas (tubercles) consisting of:

- Epithelioid cells (activated macrophages)
- Langerhans giant cells
- Lymphocytes
- Central caseous necrosis

Primary Complex: The primary lesion (Ghon focus) plus involved hilar lymph nodes constitute the primary complex (Ranke complex).

Latent vs. Active TB:

- **Latent TB:** Contained infection with no clinical symptoms
- **Active TB:** Progressive infection with clinical manifestations

Reactivation: Latent TB can reactivate, particularly when host immunity is compromised. Reactivation typically occurs in the apical and subapical segments of the upper lobes or superior segments of the lower lobes.

CLINICAL MANIFESTATIONS

Pulmonary TB:

- Persistent cough (>2 weeks)
- Hemoptysis
- Chest pain
- Dyspnea

Constitutional Symptoms:

- Fever with night sweats
- Weight loss
- Anorexia
- Fatigue

Extra-pulmonary TB:

- Lymph node TB (scrofula)
- Pleural TB
- Miliary TB
- TB meningitis
- Genitourinary TB
- Skeletal TB

COMPLICATIONS

Pulmonary Complications:

- Cavitation
- Hemoptysis
- Pneumothorax
- Bronchiectasis
- Respiratory failure

Systemic Complications:

- Miliary dissemination
- Amyloidosis
- Cor pulmonale

💧 URINARY TRACT INFECTIONS (UTI)

DEFINITION

Urinary tract infections are bacterial infections involving any part of the urinary system, including kidneys, ureters, bladder, and urethra.

CLASSIFICATION

Based on Location:

- **Upper UTI:** Pyelonephritis (kidney infection)
- **Lower UTI:** Cystitis (bladder infection), Urethritis (urethral infection)

Based on Complexity:

- **Uncomplicated UTI:** In healthy individuals with normal urinary tract

- **Complicated UTI:** Associated with structural or functional abnormalities

ETIOLOGY

Common Bacterial Pathogens:

- Escherichia coli (80-85% of uncomplicated UTIs)
- Staphylococcus saprophyticus
- Klebsiella species
- Enterococcus species
- Proteus mirabilis
- Pseudomonas aeruginosa (complicated UTIs)

PATHOPHYSIOLOGY

Route of Infection: Most UTIs result from ascending infection, where bacteria from the intestinal flora colonize the periurethral area and ascend through the urethra to the bladder and potentially to the kidneys.

Bacterial Adherence: Pathogenic bacteria possess specific adhesins that allow them to bind to uroepithelial cells, preventing washout during urination. E. coli uses P fimbriae to bind to P blood group antigens on uroepithelial cells.

Host Defense Mechanisms:

- Complete bladder emptying
- Urine flow and micturition

- Antimicrobial properties of urine
- Immunological factors
- Anatomical factors

Bacterial Virulence Factors:

- Adhesins for epithelial binding
- Toxins causing tissue damage
- Resistance to host immune responses
- Biofilm formation

Inflammatory Response: Bacterial invasion triggers an inflammatory response characterized by:

- Neutrophil infiltration
- Release of inflammatory mediators
- Tissue damage and symptoms

UTI Classification Table
Type
Cystitis
Pyelonephritis
Urethritis

CLINICAL MANIFESTATIONS

Lower UTI (Cystitis):

- Dysuria (painful urination)

- Urinary frequency
- Urinary urgency
- Suprapubic pain
- Hematuria
- Cloudy, malodorous urine

Upper UTI (Pyelonephritis):

- High fever and chills
- Flank pain
- Nausea and vomiting
- Malaise
- Costovertebral angle tenderness

COMPLICATIONS

Acute Complications:

- Urosepsis
- Renal abscess
- Emphysematous pyelonephritis

Chronic Complications:

- Chronic pyelonephritis
- Renal scarring
- Hypertension
- Chronic kidney disease

SEXUALLY TRANSMITTED DISEASES 💔

INTRODUCTION

Sexually transmitted diseases (STDs) are infections transmitted through sexual contact, including vaginal, anal, and oral sex. These diseases can be caused by bacteria, viruses, parasites, or fungi and represent a major global health concern.

🩸 ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

DEFINITION

AIDS is the final stage of infection with Human Immunodeficiency Virus (HIV), characterized by severe immunosuppression and susceptibility to opportunistic infections and malignancies.

ETIOLOGY

Causative Agent:

- Human Immunodeficiency Virus (HIV)
- Two types: HIV-1 (worldwide) and HIV-2 (West Africa)
- RNA retrovirus belonging to lentivirus subfamily

PATHOPHYSIOLOGY

HIV Structure: HIV contains essential enzymes:

- Reverse transcriptase

- Integrase
- Protease

Cellular Entry: HIV primarily targets CD4+ T helper cells but can also infect:

- Macrophages
- Monocytes
- Dendritic cells
- Microglial cells

Viral Entry Mechanism:

1. HIV binds to CD4 receptor via gp120
2. Conformational change exposes coreceptor binding sites
3. Binding to coreceptors (CCR5 or CXCR4) via gp120
4. Conformational change in gp41 facilitates membrane fusion
5. Viral core enters the cell

Viral Replication Cycle:

- **Reverse Transcription:** Viral RNA is converted to DNA by reverse transcriptase
- **Integration:** Viral DNA integrates into host genome via integrase
- **Transcription and Translation:** Host cellular machinery produces viral proteins
- **Assembly and Budding:** New viral particles are assembled and released

Immunopathogenesis:

- Progressive depletion of CD4+ T cells
- Disruption of immune system architecture
- Chronic immune activation
- Increased susceptibility to opportunistic infections
- Development of AIDS-defining malignancies

Disease Progression:

1. **Acute HIV Syndrome:** Flu-like illness 2-4 weeks after infection
2. **Clinical Latency:** Asymptomatic period lasting years
3. **AIDS:** CD4+ count <200 cells/μL or presence of opportunistic infections

CLINICAL MANIFESTATIONS

Acute HIV Infection:

- Fever
- Lymphadenopathy
- Pharyngitis
- Rash
- Myalgia
- Headache

Clinical Latency Stage:

- Often asymptomatic

- Gradual decline in CD4+ count
- Persistent generalized lymphadenopathy

AIDS Stage:

- Opportunistic infections (Pneumocystis pneumonia, CMV retinitis)
- AIDS-defining malignancies (Kaposi's sarcoma, lymphomas)
- HIV wasting syndrome
- HIV-associated dementia

OPPORTUNISTIC INFECTIONS

Bacterial:

- Mycobacterium avium complex
- Mycobacterium tuberculosis
- Salmonella species

Viral:

- Cytomegalovirus
- Herpes simplex virus
- Varicella-zoster virus

Fungal:

- Pneumocystis jirovecii
- Cryptococcus neoformans
- Histoplasma capsulatum

Parasitic:

- Toxoplasma gondii
- Cryptosporidium species
- Microsporidium species

SYPHILIS

DEFINITION

Syphilis is a systemic sexually transmitted infection caused by the spirochete Treponema pallidum, characterized by distinct clinical stages.

ETIOLOGY

Causative Organism:

- Treponema pallidum subspecies pallidum
- Gram-negative spirochete
- Obligate parasite (cannot be cultured)

PATHOPHYSIOLOGY

Transmission: Syphilis is transmitted through:

- Sexual contact with infectious lesions
- Vertical transmission (congenital syphilis)
- Blood transfusion (rare)

Bacterial Invasion: T. pallidum penetrates intact mucous membranes or microscopic skin breaks. The organism disseminates rapidly throughout the body via lymphatics and blood vessels.

Immune Response:

- Initial inflammatory response at site of entry
- Development of both humoral and cell-mediated immunity
- Despite immune response, bacteria can persist and cause chronic infection
- Molecular mimicry may contribute to autoimmune phenomena

Disease Stages: Syphilis progresses through distinct stages if left untreated:

CLINICAL STAGES

Primary Syphilis (3-90 days after exposure):

- **Chancre:** Painless, indurated ulcer at site of infection
- Usually single lesion
- Heals spontaneously in 3-6 weeks
- Regional lymphadenopathy

Secondary Syphilis (6 weeks to 6 months):

- **Systemic dissemination**
- **Skin rash:** Maculopapular, involving palms and soles
- **Mucous patches:** Painless, gray-white lesions in mouth

- **Condyloma latum:** Broad, flat, moist lesions in genital area
- Constitutional symptoms: fever, malaise, lymphadenopathy
- **Alopecia:** Patchy hair loss

Latent Syphilis:

- **Early latent:** <1 year duration, potentially infectious
- **Late latent:** >1 year duration, non-infectious
- Asymptomatic with positive serology

Tertiary Syphilis (years to decades):

- **Neurosyphilis:**
  - Asymptomatic neurosyphilis
  - Meningovascular syphilis
  - General paresis
  - Tabes dorsalis
- **Cardiovascular syphilis:**
  - Aortitis
  - Aortic aneurysm
  - Aortic insufficiency
- **Gummatous syphilis:**
  - Granulomatous lesions in skin, bone, liver

PATHOLOGICAL FEATURES

Primary Stage:

- Plasma cell infiltration
- Endothelial swelling
- Spirochetes present in lesion

Secondary Stage:

- Perivascular lymphoplasmacytic infiltration
- Interface dermatitis
- Spirochetes in tissues

Tertiary Stage:

- **Gummas:** Granulomatous inflammation with central necrosis
- **Neurosyphilis:** Chronic meningoencephalitis, tabes dorsalis
- **Cardiovascular:** Aortitis with medial necrosis

GONORRHEA

DEFINITION

Gonorrhea is a sexually transmitted infection caused by Neisseria gonorrhoeae, primarily affecting the urogenital tract, rectum, and pharynx.

ETIOLOGY

Causative Organism:

- Neisseria gonorrhoeae
- Gram-negative diplococcus

- Obligate human pathogen

PATHOPHYSIOLOGY

Transmission: Gonorrhea is transmitted through:

- Sexual contact (genital, anal, oral)
- Vertical transmission during childbirth
- Direct contact with infected secretions

Bacterial Adherence and Invasion: N. gonorrhoeae uses several virulence factors for pathogenesis:

- **Pili:** Allow adherence to epithelial cells
- **Opacity proteins:** Facilitate invasion
- **Lipooligosaccharide:** Causes inflammatory response
- **IgA protease:** Cleaves secretory IgA

Host Response: The inflammatory response is characterized by:

- Neutrophil infiltration
- Release of inflammatory mediators
- Tissue damage and symptom development
- Limited protective immunity develops

Antigenic Variation: N. gonorrhoeae can alter its surface antigens, particularly pili and opacity proteins, allowing:

- Immune evasion
- Reinfection

- Chronic infection

Sites of Infection:

- **Men:** Urethra, epididymis, prostate
- **Women:** Cervix, urethra, fallopian tubes, ovaries
- **Both sexes:** Rectum, pharynx, conjunctiva

Clinical Manifestations of Gonorrhea
Site
Urethral
Cervical
Rectal
Pharyngeal

CLINICAL MANIFESTATIONS

Male Urethritis:

- Dysuria (painful urination)
- Purulent urethral discharge
- Urinary frequency
- Meatal erythema

Female Genital Infection:

- Often asymptomatic (up to 80%)
- Mucopurulent cervical discharge
- Dysuria

- Intermenstrual bleeding
- Lower abdominal pain

Extragenital Infections:

- **Rectal:** Anal pruritus, tenesmus, rectal discharge
- **Pharyngeal:** Usually asymptomatic, mild sore throat
- **Conjunctival:** Purulent conjunctivitis

Disseminated Gonococcal Infection (DGI):

- Arthritis-dermatitis syndrome
- Polyarthralgia
- Skin lesions (papules, vesicles, pustules)
- Tenosynovitis
- Septic arthritis

COMPLICATIONS

Male Complications:

- Epididymitis
- Prostatitis
- Urethral stricture
- Infertility (rare)

Female Complications:

- Pelvic inflammatory disease (PID)

- Tubal factor infertility
- Ectopic pregnancy
- Chronic pelvic pain
- Bartholin gland abscess

Neonatal Complications:

- Ophthalmia neonatorum
- Disseminated infection
- Arthritis
- Meningitis

Systemic Complications:

- Disseminated gonococcal infection
- Endocarditis (rare)
- Meningitis (rare)

SUMMARY TABLE: INFECTIOUS DISEASES COMPARISON

Disease	Causative Agent	Transmission	Primary Site	Key I
Meningitis	Various bacteria/viruses	Droplet/hematogenous	CNS	Inflar of m
Typhoid	S. enterica Typhi	Fecal-oral	GI tract/systemic	Rose sple

Disease	Causative Agent	Transmission	Primary Site	Key I
Leprosy	M. leprae	Respiratory droplets	Skin/nerves	Nerv dama defo
Tuberculosis	M. tuberculosis	Airborne	Lungs	Gran form
UTI	E. coli (common)	Ascending	Urinary tract	Dysu frequ
AIDS	HIV	Sexual/blood	Immune system	CD4- depl
Syphilis	T. pallidum	Sexual	Systemic	Disti stage
Gonorrhea	N. gonorrhoeae	Sexual	Urogenital	Puru disch