🦠 "Pathogenesis of Bacterial Infection" – Part I

🦠 Definition of Pathogenesis

Pathogenesis refers to the sequence of events and mechanisms by which a microorganism produces disease in the host.

In simple terms, it explains:

- How infection begins
- How it spreads within the host
- How it results in clinical disease

💡 Exam Line: Pathogenesis = *mechanism of disease development.*

🦠 Pathogen

A pathogen is a microorganism capable of causing disease in a healthy (immunocompetent) host.

Opportunistic Pathogens

- Cause disease only when host defenses are compromised
- Seen in:
    - HIV/AIDS
    - Diabetes mellitus
    - Chemotherapy
    - Burns

Example

- *Pseudomonas aeruginosa* → severe infections in burn patients

💡 Exam Tip: Opportunistic ≠ harmless; disease depends on host immunity.

⚖️ Factors Determining Pathogenesis

Disease development depends on an interaction between host, pathogen, and dose.

---

1. Host Immune Status 🧍‍♂️

- Strong immune system
  → Infection may be eliminated or remain asymptomatic
- Immunocompromised states increase susceptibility:
  - HIV/AIDS
  - Diabetes mellitus
  - Malignancy
  - Chemotherapy / steroids

💡 Same organism → mild disease in one person, severe in another.

---

2. Bacterial Characteristics

- Toxin production
  - Exotoxins

    - Endotoxins
- Ability to:
    - Invade tissues
    - Induce inflammation
    - Evade immune response

---

3. Inoculum Size

- Refers to the number of organisms entering the host
- Larger dose

  → Higher chance of disease

  → Greater severity

💡 Exam Pearl: Even low-virulence organisms can cause disease if inoculum size is high.

🧬 Definition of Infection

Infection is the entry, establishment, and multiplication of an infectious agent (bacteria, virus, fungus, protozoa) within the host.

Important Point

- Infection may or may not cause symptoms
- Many infections are:
  - Subclinical
  - Detected only by antibody titers in serum

💡 Infection ≠ Disease (disease requires tissue damage or symptoms).

🧭 Course of an Infectious Disease

Exposure to pathogen

Incubation period

→ Pathogen multiplies silently

Prodromal period

→ Nonspecific symptoms appear

Period of illness

→ Typical signs and symptoms

→ Peak infectivity

Convalescence

→ Recovery and healing

↘ In severe cases

→ Disability

→ Death

🕒 Four Periods of an Infectious Disease

Stage	Description	Key Points
Incubation	Time from entry to symptom onset	Varies by organism (Influenza: days; TB: weeks)
Prodromal	Early vague symptoms	Malaise, low-grade fever
Period of Illness	Specific disease manifestations	Most infectious stage
Convalescence	Recovery phase	May have residual tissue damage

💡 Exam Tip: Maximum transmission occurs during period of illness.

🌍 Manifestations of Infection in Communities

Most bacterial infections are communicable, but some are non-communicable.

Non-communicable examples

- Botulism
- Legionella pneumonia

Epidemiological Terms

Term	Definition	Example
Sporadic	Occasional, irregular cases	Tetanus
Endemic	Constant presence in an area	Typhoid in developing countries
Epidemic	Sudden rise above expected level	Cholera outbreak
Pandemic	Global epidemic	COVID-19

💡 High-Yield Line:

A localized epidemic is called an epidemic outbreak.

⚔️ Mechanisms of Host Damage

Disease occurs due to direct microbial effects or host immune response.

---

1. Direct Mechanisms – Toxins

Exotoxins

- Secreted proteins
- Highly potent and specific
- Heat-labile

Example

- Diphtheria toxin
- Tetanus toxin

Endotoxins

- Lipopolysaccharide (LPS)

- Present in Gram-negative bacteria
- Released on bacterial death

Effects

- Fever
- Shock
- Inflammation

---

2. Indirect Mechanisms – Immune-Mediated Damage

Hypersensitivity Reactions

Type I

→ Immediate (IgE-mediated)

→ Anaphylaxis

Type II

→ Cytotoxic

→ Cell destruction

Type III

→ Immune complex deposition

→ Tissue injury

Type IV

→ Delayed, cell-mediated

→ TB skin test reaction

💡 Exam Favorite: Type IV hypersensitivity = Delayed.

🧪 Virulence and Pathogenicity

Pathogenicity

- Ability of a microorganism to cause disease

Virulence

- Degree or severity of pathogenicity

Measured by

- MLD – Minimum Lethal Dose
- LD_{50} – Dose killing 50% of test animals

💡 Lower LD_{50} → higher virulence.

🔑 Virulence Factors

Factor	Function	Example
Capsule	Prevents phagocytosis	*Streptococcus pneumoniae*
Exotoxins	Tissue damage	*Clostridium tetani*
Endotoxins	Fever, inflammation	*E. coli* LPS

🔬 Koch's Postulates (Proof of Causation)

1️⃣ The organism must be found in every case of the disease

2️⃣ It must be isolated and grown in pure culture

3️⃣ The cultured organism must reproduce the disease in a healthy host

4️⃣ The same organism must be re-isolated from the infected host

🧠 Significance:
Together, Koch's postulates establish a relationship between a microbe and a disease.

🦠 Steps in Pathogenesis of Infectious Diseases

Pathogenesis follows a logical sequence of events that allows microorganisms to enter the host, survive, multiply, and cause disease.

🧭 Overall Flowchart: Steps in Pathogenesis

Entry of pathogen → Attachment to host tissues → Multiplication → Invasion / spread → Evasion of host defenses → Damage to host tissues → Progression or resolution of disease

💡 Exam Tip: Any disruption in these steps may prevent disease development.

🚪 A. Transmission

Transmission refers to the movement of microorganisms from their source to a new host.

Transmission may occur:

- Human → Human
- Nonhuman → Human (zoonotic or environmental)

---

1. Horizontal Transmission (same generation)

Direct transmission

- Physical contact
- Respiratory droplets
- Sexual contact

Indirect transmission

- Fomites (contaminated objects)
- Vectors (mosquitoes, ticks)

- Contaminated food and water

---

2. Vertical Transmission (parent → offspring)

- Transplacental

→ Rubella

- During birth

→ Gonococcal conjunctivitis

- Through breast milk

→ HIV

💨 Common Modes of Transmission

- Droplet → coughing, sneezing
- Direct contact → touch, sexual exposure
- Indirect contact → contaminated soil or surfaces
- Airborne → organisms suspended in air
- Fecal-oral → contaminated food or water
- Vector-borne → insects (mosquitoes, ticks)

💡 High-Yield: Fecal-oral route is common in enteric infections.

🧷 B. Adherence to Cell Surfaces

After entry, bacteria must attach to host tissues to avoid being washed away.

Structures Used for Adherence

- Pili
- Fimbriae
- Capsule
- Glycocalyx

Adhesins

- Specific bacterial molecules that bind to host cell receptors
- Determine tissue tropism and host specificity

🧫 Biofilm Formation

After adherence, bacteria may form biofilms:

- Organized communities embedded in a polysaccharide-protein matrix
- Protect bacteria from:
    - Antibiotics
    - Host immune defenses

Common sites

- Catheters
- Prosthetic valves
- Joint implants

💡 Exam Pearl: Biofilm-associated infections are chronic and difficult to eradicate.

🧬 C. Penetration and Spread

Once attached, bacteria may remain localized or spread throughout the body.

Types of Infection

Type	Description	Example
Local	Limited to entry site	*Shigella* (intestinal mucosa)
Systemic	Spread via blood/lymph	*Salmonella typhi* (typhoid)

Enzymes Facilitating Invasion

- Hyaluronidase
  → Degrades connective tissue
  → Facilitates spread 🧩
- Collagenase
  → Breaks down collagen
  → Tissue penetration
- IgA protease
  → Destroys mucosal IgA
  → Enhances mucosal adherence

- Coagulase (S. aureus)
  → Forms fibrin clot
  → Protects bacteria from phagocytes
- Leukocidins
  → Destroy neutrophils and macrophages

💡 Mnemonic: *"CHIL"* – Collagenase, Hyaluronidase, IgA protease, Leukocidins.

🛡️ D. Survival in the Host

Pathogens must overcome host defense mechanisms to persist.

---

1. Defense Against Phagocytes & Complement

- Capsule
  → Prevents phagocytosis (virulent strains)
- O antigen (LPS)
  → Resists complement-mediated lysis

- Agressins

→ Leukocidins & hemolysins kill host immune cells

---

2. Neutralization of Gastric Acid

- *Helicobacter pylori* produces urease
- Urease → urea → ammonia

→ Neutralizes gastric acid barrier

---

3. Survival Inside Phagocytes

Obligate intracellular organisms

- *Rickettsia*
- *Chlamydia*

Facultative intracellular organisms

- *Salmonella*
- *Shigella*
- *Yersinia*

💡 Exam Favorite: Intracellular survival = protection from antibodies.

---

4. Avoidance of Host Immune Response

- Immune-privileged sites
  → CNS, testes
- Immune suppression
  - Mumps → activates suppressor T-cells
  - HIV → destroys helper T-cells
- Molecular mimicry
  - *E. coli* K1 antigen mimics brain polysialic acid
    → neonatal meningitis
- Masking with host antigens
  - Schistosomes
- Antigenic variation
  - Influenza virus (antigenic drift & shift)

💢 E. Tissue Injury

Tissue damage results from both microbial factors and host responses.

Mechanisms

- Exotoxins 🧪
- Endotoxins ☠️
- Non-specific immunity
  → inflammation, phagocytosis
- Specific immunity
  → humoral and cell-mediated responses

💡 Key Concept: Much tissue damage is immune-mediated, not directly bacterial.

🔥 Types of Inflammation

Type	Description	Example
Pyogenic	Acute, pus-forming, neutrophil-dominant	*Staphylococcus aureus*

Granulomatous	Chronic, macrophage-dominant	*Mycobacterium tuberculosis*

🧾 Summary Flowchart: Pathogenesis of Bacterial Infection

Transmission → Direct / Indirect / Vertical → Entry into body → Adherence via pili / adhesins → Multiplication & colonization → Invasion using enzymes → hyaluronidase, collagenase, IgA protease → Evasion of host defenses → capsule, antigenic variation, immune suppression → Tissue damage → toxins, inflammation → Clinical disease → Recovery or chronicity or death