🦠 "Pathogenesis of Bacterial Infection" - II

🧪 Bacterial Toxins, Immunopathogenesis & Cancer Association

🧪 Exotoxins

📘 Definition

Exotoxins are polypeptide toxins actively secreted by certain bacteria (both Gram-positive and Gram-negative) that interfere with specific host cell functions, leading to disease manifestations.

🔑 Key Characteristics

- Highly potent
- Heat-labile
- Antigenic → stimulate formation of antitoxins (IgG)
- Can be converted to toxoids (non-toxic but antigenic)

👉 Clinical Application:

Used in vaccines such as:

- Tetanus toxoid
- Diphtheria toxoid

⚙️ Mechanisms of Action of Exotoxins

❑ Exotoxins Acting on Extracellular Matrix

These enzymes facilitate local tissue destruction and spread of bacteria.

- Proteases
- Collagenases
- Hyaluronidases

  → "Loosen" connective tissue fibers → bacterial dissemination 🧩

Example

- *Staphylococcus aureus* Exfoliatin (epidermolytic toxin)
  → Causes Staphylococcal Scalded Skin Syndrome (SSSS) 🩹

2️⃣ A-B Type Exotoxins

Structure

- B (Binding) subunit → attaches toxin to host cell receptor
- A (Active) subunit → enzymatic activity

Mechanism

B subunit binds
→ A subunit enters cell
→ ADP-ribosylation of host proteins
→ altered cellular function
→ disease symptoms

📊 Important A-B Toxins

Toxin	Target / Mechanism	Result
Diphtheria toxin	ADP-ribosylates EF-2	⛔ Protein synthesis inhibited
Pseudomonas exotoxin A	ADP-ribosylates EF-2	Cell death
Cholera toxin	ADP-ribosylates Gs protein	↑ cAMP → watery diarrhea 💧
E. coli enterotoxin (LT)	ADP-ribosylates Gs protein	Secretory diarrhea
Pertussis toxin	ADP-ribosylates Gi protein	↑ cAMP → lymphocytosis, cough

💡 Mnemonic:

"EF-2 dies, cAMP flies"

3️⃣ Toxins Inhibiting Protein Biosynthesis

- Shiga toxin – *Shigella dysenteriae*
- Shiga-like toxin – *E. coli* O157:H7

Mechanism

Bind to 28S rRNA → inhibit protein synthesis → cell death

Clinical Effects

- Bloody diarrhea
- May cause Hemolytic-Uremic Syndrome (HUS) 🩸 (hemolytic anemia + thrombocytopenia + renal failure)

4️⃣ Superantigens ⚠️

Superantigens bypass normal antigen processing.

Mechanism

Bind directly to:

- MHC-II on macrophages
- T-cell receptors

→ Massive, non-specific T-cell activation

→ Excessive cytokine release (IL-1, IL-2, TNF-α)

🔥 Effects

- High fever
- Rash
- Hypotension
- Shock

Examples

- TSST-1 – *Staphylococcus aureus*
- Streptococcal pyrogenic exotoxin – *S. pyogenes*

Staphylococcal enterotoxin

→ Acts as superantigen in gut

→ Vomiting + diarrhea within 1–6 hours 🍽️

🇸 Neurotoxins 🧠

Toxin	Organism	Mechanism	Effect
Tetanus toxin	*Clostridium tetani*	Blocks GABA & glycine release	Spastic paralysis

Botulinum toxin	*Clostridium botulinum*	Blocks acetylcholine release at NMJ	Flaccid paralysis ⚡

💡 Exam Pearl:

Botulinum toxin = most potent natural toxin known.

6️⃣ Membrane-Damaging Toxins

- Act like detergents
- Disrupt host cell membranes
- Cause cell lysis

Example

- *Clostridium perfringens* α-toxin (lecithinase)
  → Cell membrane destruction
  → Gas gangrene ⛓️

☠️ Endotoxins

📘 Definition

Endotoxins are lipopolysaccharides (LPS) present in the outer membrane of Gram-negative bacteria.

- Not secreted
- Released only upon bacterial lysis

⚡ Clinical Effects

- Fever
- Hypotension
- Septic (endotoxic) shock
- DIC (Disseminated Intravascular Coagulation)
- Multi-organ failure

🧩 Mechanism of Action

Lipid A (toxic component)
→ Activates macrophages
→ Cytokine storm

Mediator Release

- TNF-α, IL-1, NO → fever, vasodilation, hypotension
- Complement (C3a, C5a) → vascular leakage
- Coagulation cascade → DIC

🧠 Key Point:

Endotoxins are poorly antigenic, cannot form toxoids → no vaccine available.

🧾 Comparison: Exotoxins vs Endotoxins

Property	Exotoxin	Endotoxin
Source	Gram-positive & Gram-negative	Gram-negative only
Location	Secreted extracellularly	Outer membrane (LPS)
Chemical nature	Polypeptide	Lipopolysaccharide (Lipid A)
Toxicity	Very high (µg)	Low (mg)
Mode of action	Specific enzymatic targets	Cytokine-mediated
Antigenicity	Highly antigenic	Poorly antigenic

Toxoid formation	Possible	Not possible
Heat stability	Heat-labile	Heat-stable
Diseases	Tetanus, Diphtheria	Gram-negative sepsis

⚔️ Immunopathogenesis

Sometimes host immune response, not bacteria, causes tissue injury.

🌡️ Rheumatic Fever

- Follows *Streptococcus pyogenes*
- Antibodies against M protein cross-react with:
  - Heart
  - Joints
  - Brain

→ Autoimmune inflammation

→ Carditis, arthritis, chorea ❤️🧠

🌊 Acute Glomerulonephritis

- Immune complex deposition in glomeruli
- Complement activation
- Renal inflammation and damage

🎗️ Bacterial Infections Associated With Cancer

Bacterium	Associated Malignancy
Helicobacter pylori	Gastric carcinoma, MALT lymphoma 🍽️
Campylobacter jejuni	Small intestinal MALT lymphoma

🧠 Mechanism: Chronic inflammation + prolonged antigenic stimulation.

🧭 Summary Flowchart: Tissue Injury in Bacterial Infections

Bacterial infection

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Toxin production or release

Exotoxins → enzyme inhibition / neural blockade / superantigen effects

Endotoxins → cytokine storm → shock

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Host immune response

→ Non-specific (inflammation, phagocytosis)
→ Specific (antibodies, T-cells)

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Tissue damage

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Clinical disease

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Recovery / Complications / Death