# **Bacterial Toxins**

## **I. General Principles**

### **A–B Toxins**

* **Structure**: Consist of two parts:
  + **A (Active)**: Enzymatically active component, responsible for the toxic effect.
  + **B (Binding)**: Mediates binding to host cell receptors and facilitates entry of A subunit.
* **Examples**: Diphtheria toxin, Cholera toxin, Shiga toxin, Tetanus toxin, Botulinum toxin, Pertussis toxin, Pseudomonas Exotoxin A.
* **Exam Tip**: Remember "B brings A in".

### **Superantigens**

* Non-specific activation of T cells → massive cytokine release.
* Example: TSST-1 (S. aureus), SpeA (S. pyogenes).

### **Endotoxin**

* Lipid A of LPS/LOS (Gram-negatives).
* Potent stimulator of cytokines → fever, hypotension, DIC, septic shock.
* Cannot be converted into a toxoid.

**II. Major Toxins by Type**

### **A–B Toxins**

|  |  |  |  |
| --- | --- | --- | --- |
| **Bacteria** | **Toxin** | **Mechanism / Function** | **Therapeutics / Vaccines** |
| Bordetella pertussis | Pertussis toxin | Hexamer with 5 binding subunits, ADP-ribosylates inhibitory protein G into ‘off’ > ↑cAMP, lymphocytosis | Acellular pertussis vaccine |
| E. coli (ETEC),  Vibro cholerae | Heat-labile toxin (LT) | Binds GM1 ganglioside on enterocytes > ADP-ribosylates Gsa into ‘on’ > ↑cAMP | Supportive |
| Clostridioides difficile | Toxin A (TcdA) | Enterocytes > glycosylates (activates) Rho GTPase > increased permeability of tight junctions > ↑Fluid secretion → diarrhoea | Fidaxomicin, vanc, metronidazole |
| Toxin B (TcdB) | Colonic epithelial cells > actin depolymerisation > cytotoxic necrosis | As above |
| Corynebacterium diphtheriae  Pseudomonas aeruginosa | Diphtheria toxin,  Exotoxin A | ADP-ribosylates EF-2 → blocks protein synthesis | Diphtheria toxoid vaccine |
| Clostridium botulinum | Botulinum toxin (A–G) | Blocks ACh release from presynaptic vesicles → flaccid paralysis | Antitoxin; toxoid not routine |
| Clostridium tetani | Tetanospasmin | Taken up at NMJ, moves retrograde to brainstem and blocks inhibitory neurotransmitters (GABA, glycine) → spastic paralysis | Toxoid vaccine, hTIg |
| E. coli (EHEC),  Shigella dysenteriae | Shiga-like toxins (Stx1,2) | Cleaves 28S rRNA → HUS | Supportive; avoid antibiotics |

### **Superantigens**

|  |  |  |  |
| --- | --- | --- | --- |
| **Bacteria** | **Toxin** | **Mechanism / Function** | **Therapeutics / Vaccines** |
| Staphylococcus aureus | TSST-1 | Cross-links MHC-II & TCR → cytokine storm | Supportive; no vaccine |
| Enterotoxins (A–E) |
| Streptococcus pyogenes (GAS) | SpeA, SpeC |

### **Cytolysins / Pore-forming toxins**

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| --- | --- | --- | --- |
| **Bacteria** | **Toxin** | **Mechanism / Function** | **Therapeutics / Vaccines** |
| Bacillus cereus | Diarrhoeal enterotoxins (Hbl, Nhe, CytK) | Membrane damage, ↑fluid secretion | Supportive only |
| Clostridium perfringens | α-toxin | Zn-dep phospholipase C > Gas gangrene, myonecrosis | Supportive |
|  | Enterotoxin | Food poisoning | Supportive only |
| Helicobacter pylori | VacA | Vacuolation, apoptosis | No vaccine |
| Listeria monocytogenes | Listeriolysin O | Escapes phagolysosome | No vaccine |
| Staphylococcus aureus | α-toxin | Cell lysis, necrosis | Supportive |
|  | PVL | Neutrophil lysis, tissue necrosis | No vaccine |

### **Other Enzymatic / Effector Toxins**

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| --- | --- | --- | --- |
| **Bacteria** | **Toxin** | **Mechanism / Function** | **Therapeutics / Vaccines** |
| Bacillus anthracis | Protective antigen (PA) | Forms heptamer pore > Entry of LF/EF | Anthrax vaccine (PA-based) |
|  | Lethal factor (LF) | Zn-dep metalloporotease > Cleaves MAPKK → apoptosis | Antitoxin (raxibacumab, obiltoxaximab) |
|  | Edema factor (EF) | Adenylate cyclase > ↑cAMP → edema | As above |
| Bacillus cereus | Heat-stable emetic toxin (cereulide) | Ionophore, mitochondrial dysfunction → vomiting | Supportive only |
| Bordetella pertussis | Adenylate cyclase toxin | Pore-forming haemolysin and adenylate cyclase enzyme > ↑cAMP, impairs phagocytes | Covered by vaccine |
|  | Tracheal cytotoxin | Kills ciliated epithelial cells | Supportive |
| Helicobacter pylori | CagA | Alters signalling, oncogenic | No vaccine |
| Pseudomonas aeruginosa | Elastase, phospholipase, pyocyanin | Tissue damage, ROS | No vaccine |
| Streptococcus pyogenes | Streptolysin O, S | Hemolysis, tissue necrosis | No vaccine |
|  | Streptokinase, DNase, Hyaluronidase | Facilitate tissue spread | Streptokinase used as thrombolytic |

### **Endotoxin / LOS**

|  |  |  |  |
| --- | --- | --- | --- |
| **Bacteria** | **Toxin** | **Mechanism / Function** | **Therapeutics / Vaccines** |
| Gram-negative bacilli generally | Endotoxin (LPS) | TLR4 on macrophages > Fever, shock, DIC | Supportive only |
| Neisseria gonorrhoeae  Neisseria meningtidits | Endotoxin (LOS) | TLR4 on macrophages > Fever, shock, DIC | Conjugate vaccines (A,C,W,Y; B separately) |

## **III. Clinical Groupings (for recall)**

* **Neurotoxins**: Tetanus, Botulinum.
* **Enterotoxins (diarrhoea)**: Cholera, ETEC LT/ST, Bacillus cereus, C. perfringens, C. difficile.
* **Cytotoxins**: Shiga toxin, Diphtheria toxin, Exotoxin A (Pseudomonas).
* **Superantigens**: TSST-1, SpeA/C, Staph enterotoxins.
* **Endotoxin-mediated shock**: Neisseria LOS, Gram-negative LPS.

✅ **Exam Tips**

* Know A–B structure and examples.
* Toxoid vaccines: **Diphtheria, Tetanus, Pertussis (acellular), Anthrax (PA)**.
* Endotoxin = not a protein → no toxoid possible.
* S. aureus food poisoning = preformed, heat-stable enterotoxin → rapid onset vomiting.