**Lec. 2**

**Bacterial Toxigenesis :**

* **It is the ability to produce toxins :**
* **Cell – associated lipopolysaccharide (LPS) toxins are referred to as endotoxins.**
* **Extracellular diffusible toxins are reffered to as exotoxins .**

**Bacterial Toxins**

**Some definitions of bacterial toxins**

* **Substances that are toxic to eukaryotic cells as measured in a variety of ways .**
* **A microbial substance that able to induce host damage.**
* **Any organic microbial product or substance that is harmful or lethal to cell , tissue cultures or organisms .**
* **Toxins are a common and series cause of tissue damage especially in bacterial infection .**
* **Bacterial toxins are important determinants of bacterial virulence .**

**Microbial toxins are components or products of m.0s which , when extracted and introduced into host animals , can reproduce disease symptoms normally associated with infection .**

**Terms :**

**Exotoxin = extracellular protein toxin**

**Endotoxin = a portion of gram –ve bacterial outer membrane**

**Enterotoxins = toxins those act on gastrointestinal tract , producing typical food poisoning symptoms .**

**Exotoxins : Bacterial protein toxins**

* **are typically soluble proteins secreted by living bacteria.**
* **both Gram –ve and G+ve bacteria produce soluble protein toxins.**
* **a specific toxin is generally specific to a particular bacterial species .**

**e.g. only *Clostridium tetani* produces tetanus toxin &**

**only *Corynebacterium diphtheria* produces diphtheria toxin.**

**Exotoxins and virulence:**

**Usually , virulent strains of the bacteria produce the toxin while non – virulent strains do not .**

**(( The toxin is the major determinant of virulence . ))**

**Certain protein toxins have very specific cytotoxic activity , i. e. , attack specific types of cells .**

**e.g. tetanus or botulinum toxins attack only neurons .**

**Some toxins have fairly broad cytotoxic activity and cause non–specific death of all sorts of cells and tissues eventually resulting in necrosis**

**e.g. Staphylococci , streptococci and clostridia .**

**Anthrax toxin (( LF )) is broadly lethal but with unknown specifics .**

**Protein toxin resemble enzymes :**

1. **Denatured by heat , acid and proteolytic enzymes .**
2. **High biologic activity .**
3. **Most act catalytically .**
4. **Highly specific in the substrate utilized tissue cells , organs or body fluid .**
5. **High specific mode of action**
6. **Site of damage caused by the toxin indicates the location of the substrate .**

**Entertoxin → inner lining cells of intestine .**

**neurotoxin → neurons .**

**leukocidin → WBCs .**

**hemlysin → RBCs .**

**Protein toxins are strongly antigenic :**

***In vivo* antibody ( antitoxin ) neutralizes the toxicity of bacterial proteins .**

**Toxoids :**

**Toxoids are detoxified toxins which retain their antigenicity and their immunizing capacity .**

**The formation of toxoids can be accelerated by treating toxins with a variety of reagents**

**- Formalin , iodine , pepsin , ascorbic acid etc at 37˚c , PH 6 – 9 for several weeks .**

**Resulting toxoids can be used for artificial immunization where the primary determinant of bacterial virulence is toxin productions .**

**e.g. diphtheria and tetanus .**

**Table (2) :Exotoxin lethal toxicity comparison**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Toxin** | **Toxic dose** | **Host** | **Endotoxin relation** | **Snake venom relation** |
| **Botulinum t.** |  | **Mouse** |  |  |
| **Tetanus t.** |  | **Mouse** |  |  |
| **Diphtheria t.** |  | **Guinea pig** |  |  |

**Bacterial protein toxins are the most potential human poisons known and retain high activity at very high dilutions.**

**Endotoxins**

**An important part of the toxicity of the Gram –ve bacteria is conferred through the release of endotoxins .**

**Endotoxins = lipopolysaccharides, a part of cell envelopes.**

**Killed bacteria can release endotoxin as they decay .**

**e.g. *E. coil , Salmonella , Shigella , Pseudomonas , Neisseria* … etc .,**

**Table (2): Characteristics of endotoxin and exotoxins.**

|  |  |  |
| --- | --- | --- |
| **Property** | **Endotoxin** | **Exotoxin** |
| **Chemical nature** | **Lipopolysaccharide**  **MW= 10-1000 KDs** | **Protein**  **MW=50-1000KDs** |
| **Relationship to cell** | **Part of the outer membrane.** | **Extracellular product** |
| **Denatured by boiling** | **No** | **Usually** |
| **Antigenic** | **Weakly** | **Yes** |
| **Form toxoid** | **No** | **Yes** |
| **Potency** | **Relatively low**  **( ˃ 100 μg )** | **Relatively high**  **( 1μg )** |
| **Spesificity** | **Low degree** | **High degree** |
| **Enzymatic activity** | **No** | **Usually** |
| **Pyrogenicity** | **Yes** | **Occasionally** |