Lecture (1)

Introduction:-

Microbial toxins are **toxins** produced by micro-organisms, including bacteria and fungi. Microbial toxins promote infection and disease by directly damaging host tissues and by disabling the immune system. A toxin [Latin *toxicum*, poison] is a substance, such as a metabolic product of the organism, that alters the normal metabolism of host cells with deleterious effects on the host.

Microorganisms use toxins to help them establish infections and multiply within the host. Alternatively, a pathogen may be restricted to a particular body site from which toxins are released to cause widespread problems throughout the body. Toxins also can cause human disease in the absence of the pathogens that produced them. This common mechanism of food poisoning that involves ingestion of preformed bacterial toxins is referred to as intoxication, a notable example of which is botulism.

Endotoxins and exotoxins are the two general types of bacterial toxins. Endotoxins are released by gram-negative bacteria and can have devastating effects on the body's metabolism, the most serious being endotoxic shock, which often results in death. The effects of exotoxins produced by gram-positive bacteria tend to be more limited and specific than the effects of gram-negative endotoxins. The activities of exotoxins range from those enzymes produced by many staphylococci and

streptococci that augment bacterial invasion by damaging host tissues and cells to those that have highly specific activities (e.g., diphtheria toxin that inhibits protein synthesis or the cholera toxin that interferes with host cell signals). Examples of other highly active and specific toxins are those that cause botulism and tetanus by interfering with neuromuscular functions.

Toxigenicity:-

Two distinct categories of disease can be recognized based on the role of the bacteria in the disease-causing process: infections and intoxications. An infectious disease results partly from the pathogen's growth and reproduction (or invasiveness) that often produce tissue alterations. **Intoxications** are diseases that result from the entrance of a specific preformed toxin (e.g., botulinum toxin) into the body of a host. The term toxemia refers to the condition caused by toxins that have entered the blood of the host.

Toxinosis is pathogenesis caused by the bacterial toxin alone, not necessarily involving bacterial infection (e.g. when the bacteria have died, but have already produced toxin, which are ingested). It can be caused by *Staphylococcus aureus* toxins, for example.

●Exotoxins

Defining Statement: -

Exotoxins are a group of soluble proteins that are secreted by the bacterium, enter host cells, and catalyze the covalent modification of a host cell component(s) to alter the host cell physiology. Both Gram-negative and Gram-positive bacteria produce exotoxins. A specific bacterial pathogen may produce

a single exotoxin or multiple exotoxins. Each exotoxin possesses a unique mechanism of action, which is responsible for the elicitation of a unique pathology. Thus, the role of exotoxins in bacterial pathogenesis is unique to each exotoxin.

Corynebacterium diphtheriae produces diphtheria toxin, which is responsible for the systemic pathology associated with diphtheria, whereas *Vibrio cholerae* produces cholera toxin, which is responsible for the diarrheal pathology associated with cholera. Exotoxins vary in their cytotoxic potency, with the clostridial neurotoxins being the most potent exotoxins of humans. Exotoxins also vary with respect to the host that can be intoxicated. Exotoxin A (ETA) of *Pseudomonas aeruginosa* can intoxicate cells from numerous species, whereas other toxins, such as diphtheria toxin, are more restricted in the species that can be intoxicated. Some bacterial toxins, such as pertussis toxin, can intoxicate numerous cell types, whereas other toxins, such as the clostridial neurotoxins, show a specific tropism and intoxicate only cells of neuronal origin.

Bacterial exotoxins catalyze specific chemical modifications of host cell components, such as the ADP-ribosylation reaction catalyzed by diphtheria toxins or the deamidation reaction catalyzed by the cytotoxic necrotizing factor (CNF) produced by *Escherichia coli*. These chemical modifications may either inhibit or stimulate the normal action of the target molecule to yield a clinical pathology. Bacterial exotoxins possess an AB structure–function organization, in which the A domain represents the catalytic domain and the B domain comprises the receptor-binding domain and the translocation domain. The translocation domain is responsible for the delivery of the catalytic A domain into an intracellular compartment of the host cell.

Many bacterial exotoxins can be chemically modified to toxoids that no longer express cytotoxicity, but retain immunogenicity. Bacterial toxins can also be genetically engineered to toxoids, which may lead to a wider range of vaccine products. Exotoxins have also been used as therapeutic agents to correct various disorders, including the treatment of muscle spasms by botulinum toxin (BT). Nontoxic forms of exotoxins have been used as carriers for the delivery of heterologous molecules to elicit an immune response and as agents in the development of cell-specific chemotherapy. In addition, bacterial toxins have been used as research tools to assist in defining various eukaryotic metabolic pathways, such as G protein- mediated signal transduction.

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