**Lec . 1**

**Introduction**

**The first attempts to demonstrate experimentally the production of bacterial poisons were undertaken by :**

**Edwin Klebs ( 1834 – 1913 ) for staphylococci**

**Robert Koch ( 1843 – 1910 ) for *V. cholera***

**Friendrich Loeffler ( 1852 – 1915 ) for diphtheria .**

**Klebs ( 1872 ) suggested that chemical substances named ʺsepsinsʺ were responsible for the lesions caused by staphylococci .**

**The first experimental demonstrations of staphylococcal toxin (s) were reported by :**

**Von Leber ( 1888 ) ,**

**De Christmas ( 1888 ) &**

**Van de velde ( 1894 ) .**

**As concerns cholera , Koch ( 1884 ) expressed the view that the disease was a toxicosis , since the causative organism proliferated in the gut without appearing to invade or damage this organ or any of the neighboring tissues .**

**Seventy five years later , in ( 1959 ) , Kochʼs hypothesis was confirmed when two Indian researchers**

**De ( 1959 ) & Dutta *et al .* , ( 1959 ) working independently of one another , showed that cell free preparation from *V. chalera* cause relevant symptomatology in animal models**

**( Adult rabbit ligated loop and infant rabbit ).**

**In 1969 , the putative toxin was purified and biochemically characterized .**

**Fourteen years later , in ( 1983 ) , the cloning and nucleotides sequence of cholera toxin was determined**

**In the same year of Kochʼs hypothesis , Loeffler ( 1884 ) :**

* **Suggested that a soluble poison was the causative agent of diphtheria .**
* **Roported that in animals that died after experimented infection , the M.O. remained at the site of inoculation and totally absent from internal organs**
* **Concluded that a poison at the site of inoculation must have circulated in the blood .**

**Discovery of the first bacterial protein toxins**

* **Roux and Yersin ( 1889 ), at Pasteur institute discovered the first bacterial toxin , namely diphtheria toxin .**
* **Tetanus was recognized since ancient times and described by Hippocrates who first reported the syndroms characterized by hypercontraction of skeletal muscles . He termed such spastic paralysis ʺtetanusʺ**

**The toxin was discovered in ( 1890 ) in culture supernatant in :**

**Denmark by Knud Feber**

**Italy by Tizzoni and Cattani**

**Feber showed that it is possible to reproduce the spastic symptoms of tetanus in experimental animals by injecting them with sterile filtrates of cultures of the bacillus .**

**Active immunization with formaldehyde – treated toxins was undertaken by Roman and Descombey ( 1925 ) , the development of toxoid .**

**Botulism ( sausage poisoning in Latin ) is the term given to an acute food poisoning caused by the ingestion of spoiled sausage ( botulus ).**

**An outbreak of botulism occurred in ( 1793 ) affected 13 persons , six of whom died .**

**Although botulism has been known as long as 1000 years ago , the discovery of the causative toxin ( Botulinum toxin ) in ( 1896 )**