Bacterial Pathogenesis

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INTENDED LEARNING OUTCOMES

- To define the pathogenesis
- To describe Koch's Postulates.
- To list bacterial virulence factors
- Described bacterial replication cycle
- Know the bacterial portal of entry and exit
- Described and differentiate bacterial toxins
- Understand basic terms used in Pathogenesis

Introduction

What is Pathogenicity ?

Mechanism

- ability to cause disease

* Microorganism can cause disease = Pathogenic

Virulence is: درجة الخطورة

e.g: B. anthrax (Can easily cause disease & death) vs. Typoid, Pneumonia, common cold (less easy to cause disease or death)

The degree of pathogenicity

High virulent vs. Low virulent vs. avirulent

- Analysis of infection and disease through the application of principles such as Koch´s postulates leads to classification of bacteria as pathogenic or non-pathogenic.

→ First to discover the concept of pathogenicity

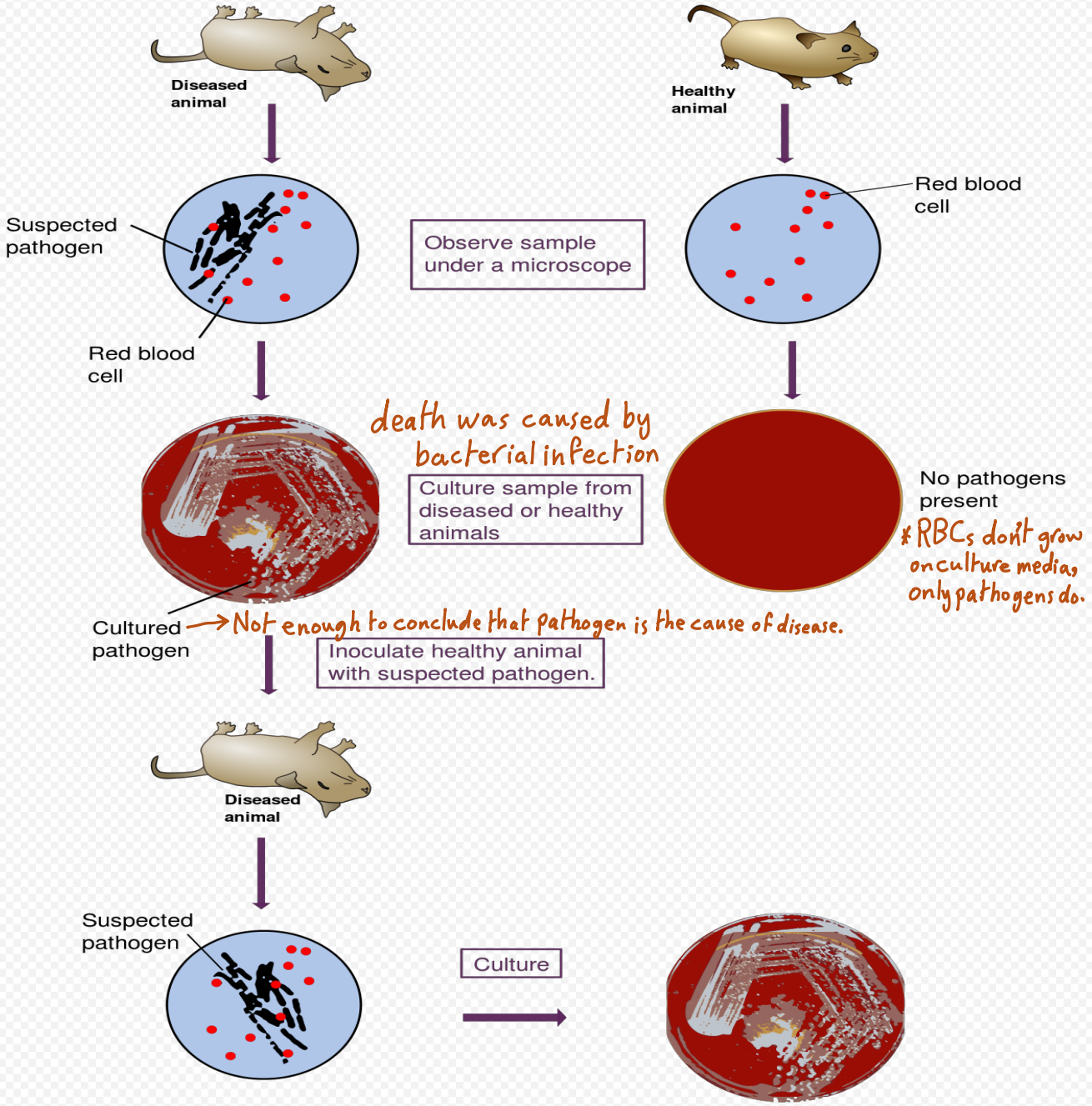
Koch's Postulates

① The microorganism must be found in abundance in all organisms suffering from the disease, but should not be found in healthy organisms.

② The microorganism must be isolated from a diseased organism and grown in pure culture.

③ The cultured microorganism should cause disease when introduced into a healthy organism.

④ The microorganism must be reisolated from the inoculated, diseased experimental host and identified as being identical to the original specific causative agent.



Modern-day Koch's Postulates

- Microbial genetics has opened new frontiers to study pathogenic bacteria and differentiate them from non-pathogens.
- The ability to study genes associated with virulence led to a proposed modern Koch´s postulates

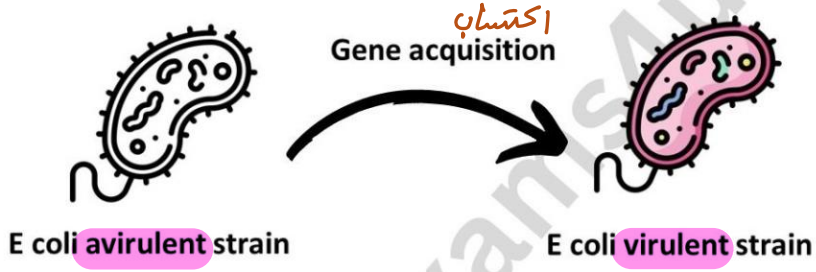
original Koch's

- The phenotype, or property, under investigation should be associated with pathogenic strains of a species.
- Specific inactivation of the gene(s) associated with the suspected virulence trait should lead to loss in pathogenicity or virulence. *No expression of "virulent gene" = No pathogenicity
- Reversion of the mutated gene should lead to restoration of pathogenicity.

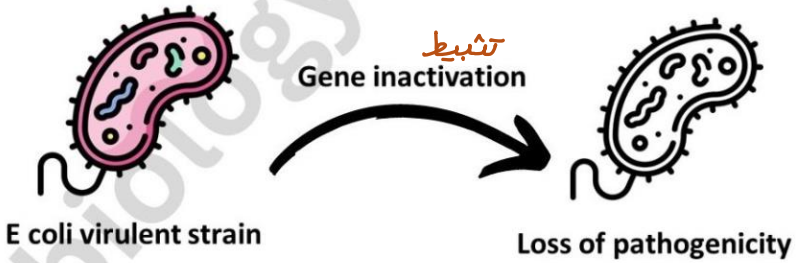
* It's all about genes!!

Molecular Koch's Postulate

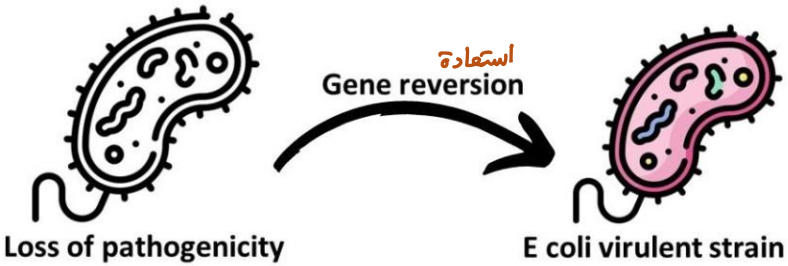
Postulate 1:The phenotype (sign or symptom of disease) should be associated only with pathogenic strains of a species.



Postulate 2: Inactivation of the suspected gene(s) associated with pathogenicity should result in a measurable loss of pathogenicity



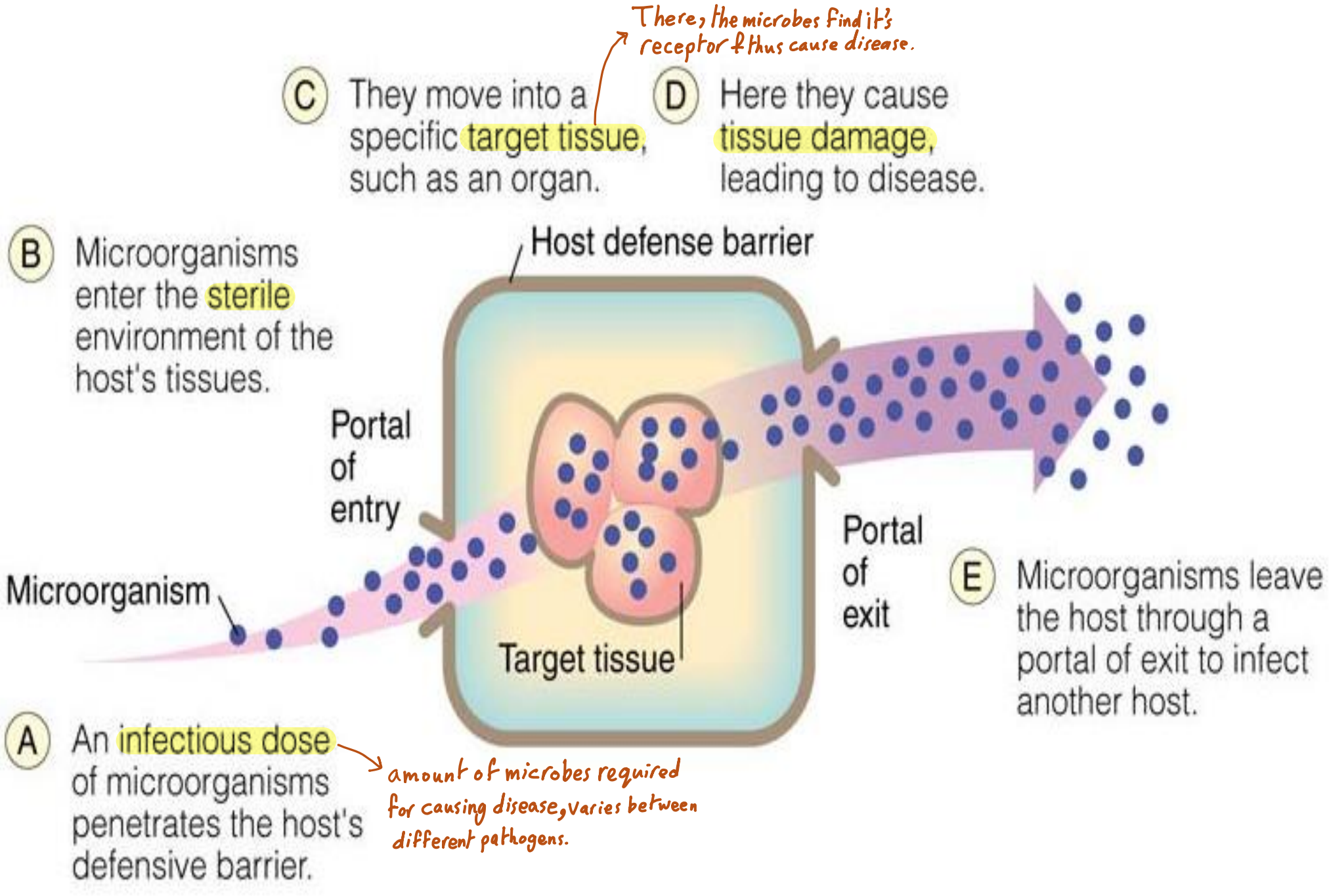
Postulate 3: Reversion of the inactive gene should restore the disease phenotype



Stages of the Infectious Process

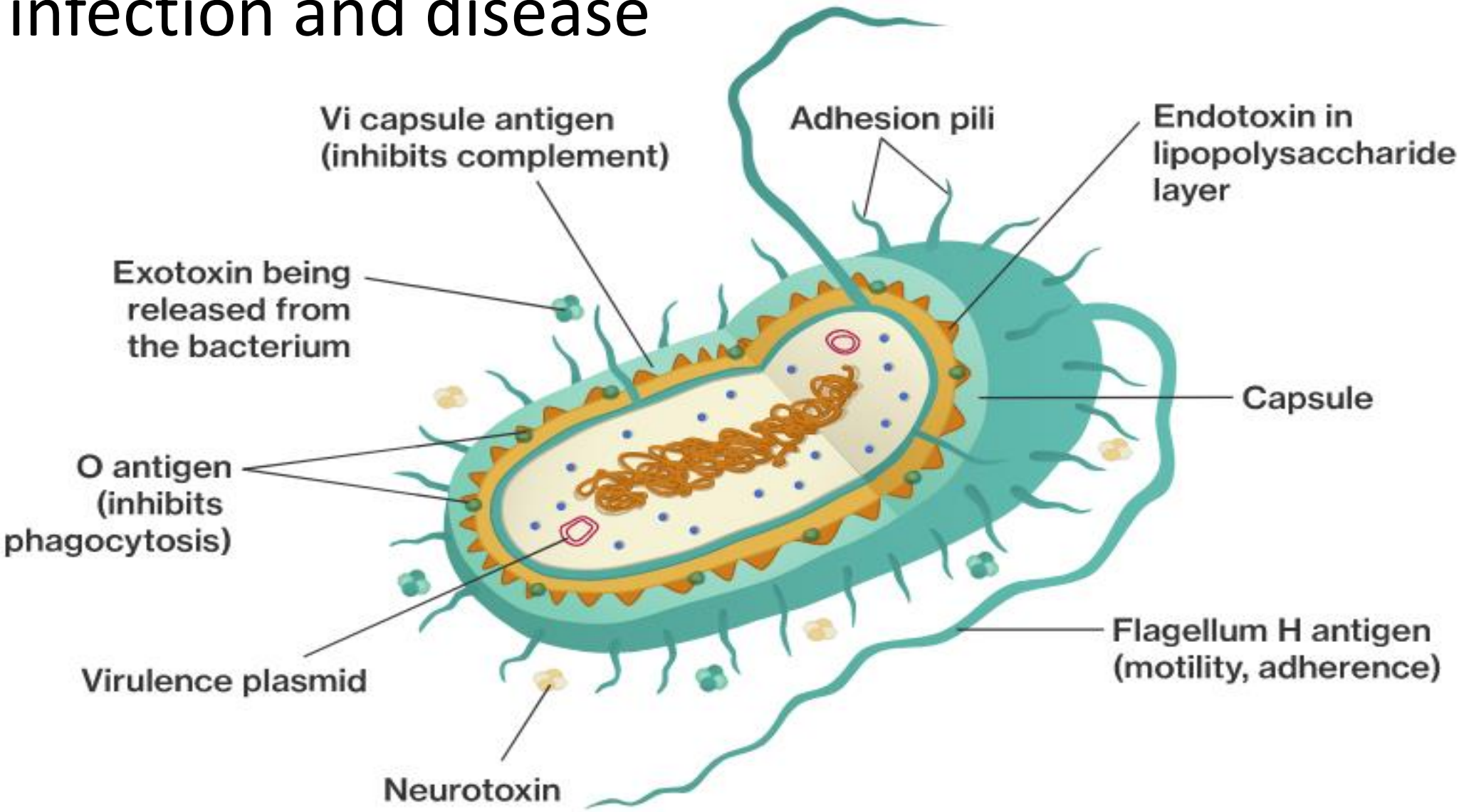
- **Source of infection** which may be man (case or carrier), animal or soil
- **Mode of transmission** e.g. droplet, inhalation, ingestion, injection, insects, contact and transplacental
- **Portal of entry** e.g. respiratory tract, gastrointestinal tract, skin
- **Portal of exit** e.g. urine, stools, blood, respiratory or genital discharge, from which the organism is transmitted to a new host.

Bacterial Infection Cycle



Bacterial virulence factors

Determine the ability of bacteria to cause infection and disease



Bacterial virulence factors

A) Adherence factors : التصاق

help bacterial adhesion to host cell membranes

1. Pili of N.gonorrhea → adhesion
2. Glycocalyx of strept. mutans
   → made of polysacharrides

اختراق/توغّل

B) Invasive factors :

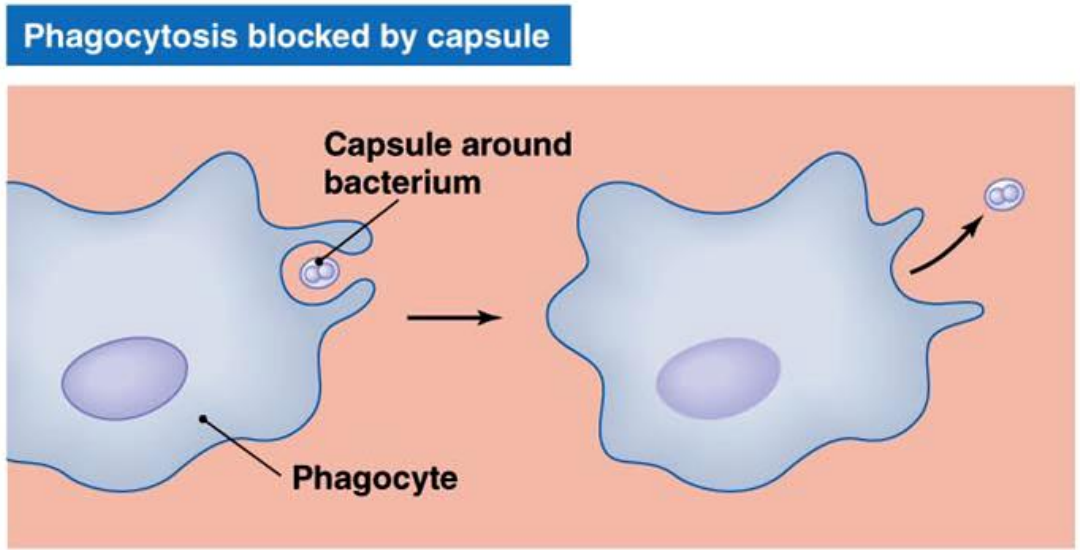
help bacteria to invade tissue through :

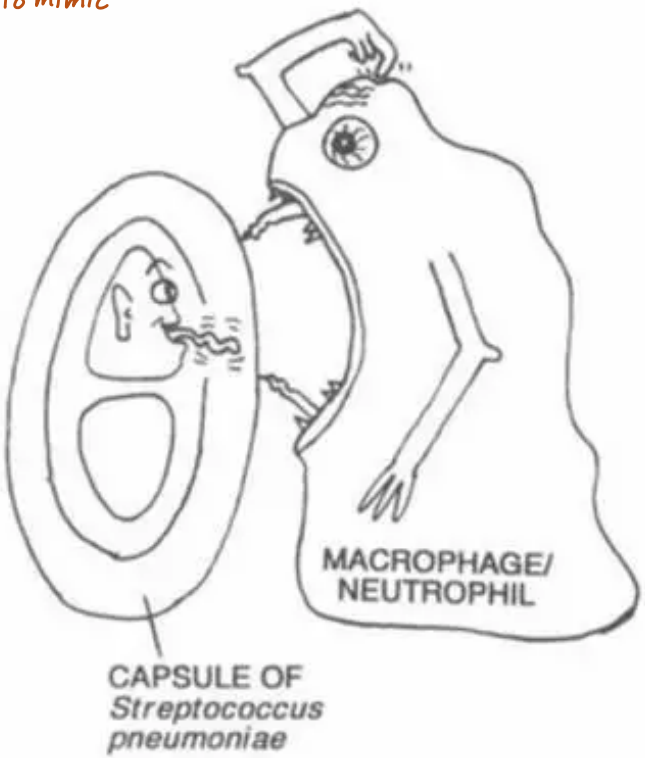
- A) Antiphagocytic factors :

protect bacteria from phagocytosis as :

- capsule of pneumococci
- protein " A " of staph.aureus
- protein " M " of strept.pyogenes

bacteria use capsule to mimic normal body cells.





- B) Extracellular enzymes :
- Substances produced by bacteria help them in spread and invasion as:

1- Fibrinolysin : produced by strept.pyogenes and cause lysis of fibrin → involved in blood clotting

3- Lecithinase : break down lecithin in cell membrane

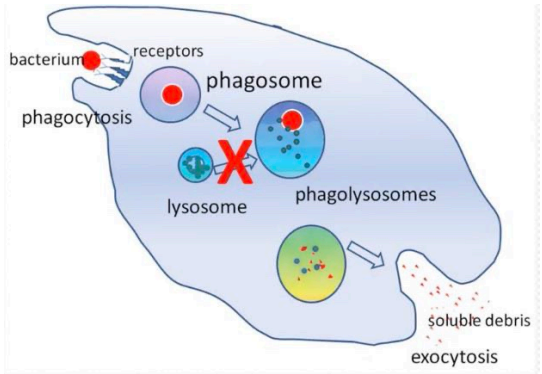
4- Collagenase : break down collagen

- C) Ability to survive intracellularly:

M.tuberculosis (inhibit formation of phagosome – lysosome fusion so escape killing by phagocytic cells.

→ Macrophage with bacteria inside it

↳ cell organelle containing hydrolytic enzymes.



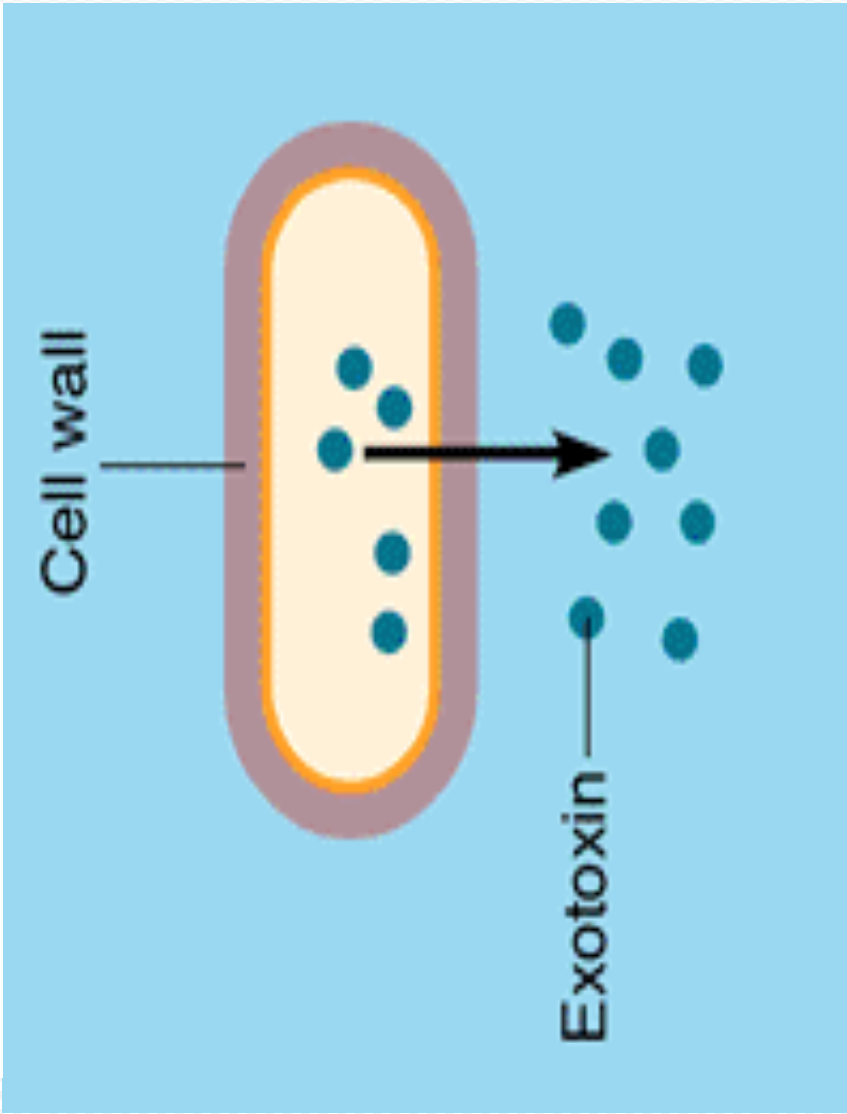
C) Production of toxins سموم

- Toxin production is another mechanism by which bacteria can produce disease.
- Bacterial toxins are either **exotoxins** or **endotoxins**.
- Treatment of exototoxin with formalin (or other agents) removes its toxicity and retains its antigenicity converting it into **toxoid**.

Exotoxins

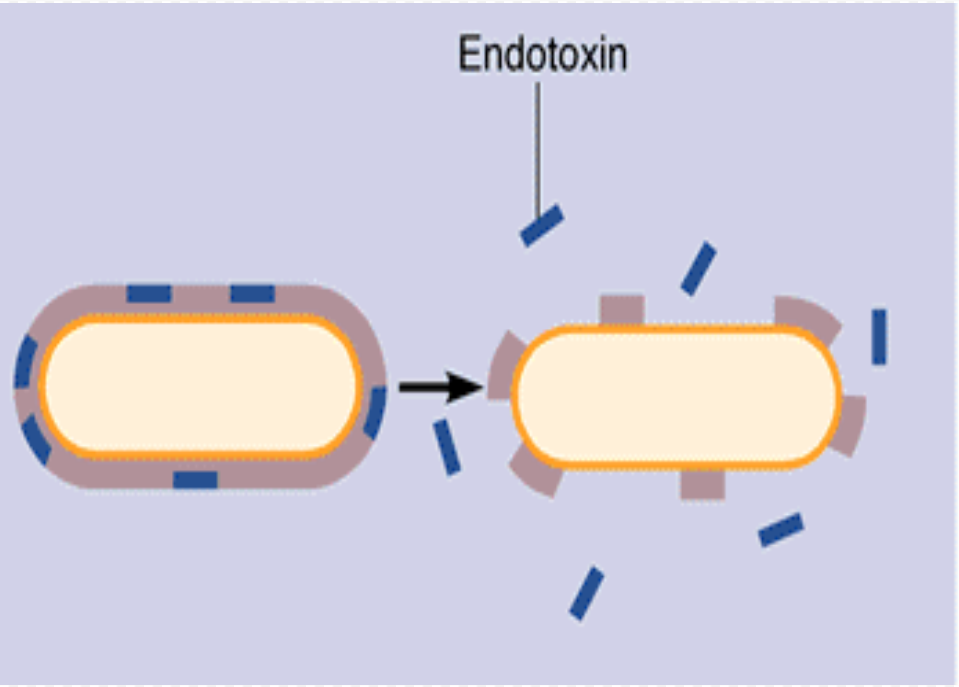
Outside

- Produced inside some bacteria as part of growth and metabolism and then secreted
- Diffuse easily within blood and rapidly travel throughout body
- Destroy parts of host cells or inhibit metabolic functions



Endotoxins

inside



- ✓ part of the outer cell wall of Gram (-) bacteria.
- ✓ Liberated when the cell wall breaks apart

* while bacteria is intact, endotoxin can't be secreted.

Exotoxins Vs Endotoxins

	Exotoxins	Endotoxins
Source	Secreted by living organisms both Gram-positive (mainly) and Gram-negative	Integral part of the cell wall of Gram-negative organisms. Liberated upon cell disintegration
Coding genes	Encoded by chromosomes, plasmids, bacteriophages or PAI	Encoded by genes on the chromosome
Examples	*C. diphtheriae* (phage) *Cl. tetani* (plasmid) *B. pertussis* (chromosome) *H. pylori* (PAI)	*E.coli* and meningococcal endotoxins
Nature	Protein	Lipopolysaccharide (lipid A)
Antigenicity	Highly antigenic	Poorly antigenic
Heat stability	Unstable to temp. above 60°C	Stable to temp. above 60°C for several hours
Detoxification	Can be converted into **toxoid***	Can not
Specificity	Every toxin has specific action	Same generalized effect (non-specific action), all give **fever** and shock
Toxicity	High	Low

ability to cause immune response

more dangerous

Basic terms used in Pathogenesis

- Disease and Infectious Disease
  - Disease
    - Any deviation from a condition of good health and well-being
  - Infectious Disease
- A disease condition caused by the presence or growth of infectious microorganisms or parasites

Basic terms used in Pathogenesis

- Acute infection vs. chronic infection
  - Acute Infection
    - An infection characterized by sudden onset, rapid progression, and often with severe symptoms ما بتلحق المريض!!
  - Chronic Infection
    - An infection characterized by delayed onset and slow progression

Basic terms used in Pathogenesis

- Primary infection vs. secondary infection
  - Primary Infection
    - An infection that develops in an otherwise healthy individual
  - Secondary Infection
    - An infection that develops in an individual who is already infected with a different pathogen

* first infection weakened the immune system
↳ second infection occured

Basic terms used in Pathogenesis

- Localized infection vs. Systemic infection
  - Localized Infection
    - An infection that is restricted to a specific location or region within the body of the host

* Some infections start as localized, if They were not treated they become systemic.

  - Systemic Infection
    - An infection that has spread to several regions or areas in the body of the host

Basic terms used in Pathogenesis

- Clinical infection vs. Subclinical infection
  - Clinical Infection
    - An infection with obvious observable or detectable symptoms
  - Subclinical Infection
    - An infection with few or no obvious symptoms

Thank You