

# PATHOGENESIS

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Microbiology – III

3 sem BVOC – HCT

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# Introduction

- The nature of host – pathogen (microbes) interactions results in the establishment of a disease.
- **Pathogenesis:** is the **biological mechanisms** that leads to a diseased state.
- Describes the **origin** and **development** of the disease.
- **Pathogen:** Any organism that causes **disease**.

**Pathogenesis**  **Pathogenicity / Virulence**

- **Pathogenicity:** ability of a microbial **species** to cause disease.
- **Virulence:** refers to the same property in a microbial **strain**.
- Ex. *M. tuberculosis* and polio virus – pathogenic.
- Species – contain strains of varying degree of virulence – avirulent (vaccine strains.)

- Pathogenicity and virulence depends on the susceptibility and disposition of specific host organism.
- Individual - highly disposed or resistant.
- Virulence – **not constant** – spontaneous or induced **variations**.
  
- **Exaltation**: enhancement of virulence.
  - Serial passage - susceptible host.
  
- **Attenuation**: reduction of virulence.
  - Passage – unfavourable hosts,
  - repeated cultures – artificial media,
  - growth – high temperature,
  - presence – weak antiseptics,
  - dessication
  - prolonged storage - culture

## Pathogenicity / Virulence determinants:

- ❖ Adhesion
- ❖ Invasiveness
- ❖ Toxigenicity
- ❖ Plasmids
- ❖ Bacteriophages
- ❖ Communicability
- ❖ Other bacterial products
- ❖ Bacterial appendages
- ❖ Infecting dose
- ❖ Route of infection

# Adhesion:

- Initial event – **attachment** of bacteria to the body surfaces.
- Specific reaction btw surface **receptors** host cells – **adhesins** (adhesive structures) of bacterial surface.
- Adhesins:
  - Occur as organized structures - fimbria or pili
  - Colonisation factors
  - Have host specificity
  - Made of protein
  - Antigenic in nature

## Invasiveness:

- Ability of a pathogen to **spread** in host tissue after establishing infection.
- **Highly invasive** pathogens produce – spreading or **generalized lesions**.
  - Ex. Streptococcal septicemia – wound infection.
- Less invasive – **localized** lesions.
  - Ex. Staphylococcal abscess.
- Some pathogens that cause fatal disease lack invasiveness.
  - Ex. Tetanus bacillus.

## Toxigenicity: 2 types of toxins

### Exotoxins:

- Heat labile
- Diffuse into the surrounding
- Highly potent in minute amounts
- Ex. tetanus and botulinum toxins
- Exhibits specific tissue affinity
- Pharmacological activity
- Generally produced by Gram positive bacteria
- Gram negative bacteria
  - *Vibrio cholera*,
  - enterotoxigenic *E. coli*.

### Endotoxins:

- Heat stable lipopolysaccharides (LPS)
- Form integral part of Gram –ve cell wall
- Not secreted outside
- Released by disintegrated cell wall
- Active in large doses
- Do not produce Pharmacological activity

## Plasmids:

- It contains virulence coding genes
- Ex. Surface antigens in *E. coli* – colonize intestinal mucosa
- Enterotoxin - *E. coli* and *Staph. aureus*
- **Multiple drug resistance (R)** plasmids – increase severity of disease – resistant to antibiotic therapy

## Bacteriophage:

- Diphtheria – phage directed virulence

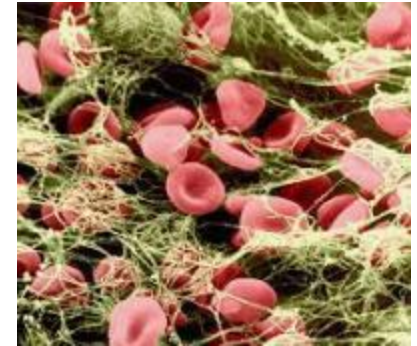
## Communicability:

- Ability of a parasite to spread from one host to another
- Determines the survival & distribution of a parasite in a community



## Other bacterial products:

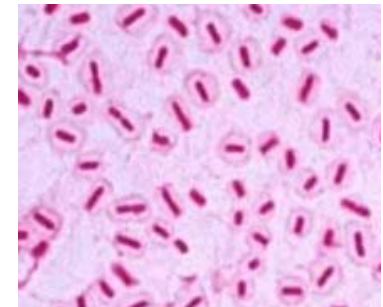
- *Staphylococci* produce thrombin-like enzyme coagulase – prevents phagocytosis – forming fibrin barrier



Thrombine

## Bacterial appendages:

- **Capsules**: capsulated bacteria are not easily phagocytosed.
- Ex. *K. pneumoniae*, *H. influenzae*.
- Bacterial **surface antigens**:
  - Vi antigen of *S. typhi*,
  - K antigens of *E. coli*
- withstand phagocytosis & lytic activity of complement.



*K. pneumoniae*

## Infecting dose:

- Adequate no. of bacteria required to cause infection in the host.
- **MID**: Minimum infecting dose
- **MLD**: Minimum lethal dose
- Min. no. of bacteria – clinical evidence of infection or death – susceptible animal – std. conditions
- **ID 50** and **LD 50** – dose required to infect or kill 50% -animals tested under std. conditions.

- **Route of infection:**
- Some bacteria initiate infections at any site of entry
  - Ex. *Streptococci*
- Others only can survive & multiply – introduced optimal routes
  - Ex. *Vibrio cholera* – oral, not – subcutaneous.

# STAGES OF BACTERIAL PATHOGENESIS

1. Transmission from the source of infection into the portal of entry.
2. Evasion of primary host defense.
3. Adherence to mucous membrane.
4. Colonization by growth of the bacteria at the site of adherence.
5. Disease symptoms caused by bacterial toxin or invasion.
6. Host immune response during steps 3,4,5
7. Progression or resolution of the disease.

# Steps in the Pathogenesis of Infectious Diseases

1. Entry.
2. Attachment.
3. Colonization.
4. Invasion.
5. Immune response Inhibitors.
6. Toxins.

# I- Ways of Pathogen Entry

## 1. Penetration of Skin.

e.g. Bilharzia

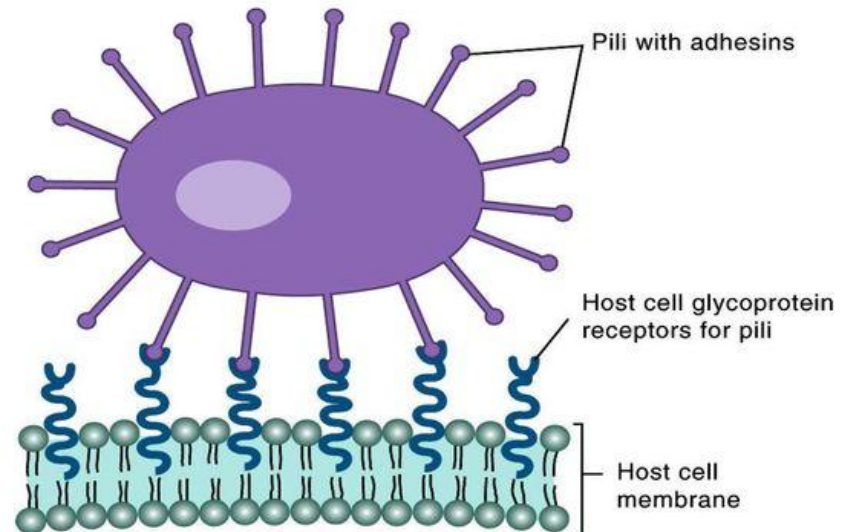
## 2. Through mucous membranes.

Ingestion (Gastrointestinal tract), Inhalation (Respiratory tract), introducing pathogen into Genitourinary tract or blood, or by insects.

e.g. E.coli, Malaria, ...

## II. Attachment (Adhesion)

- Microorganisms have macromolecules (proteins or carbohydrates) that promote attachment to tissue surfaces.
- Viruses and many bacteria must first bind to host cell surfaces.
- Prevents early clearance.
- Pathogens often bind host tissues via surface receptors. e.g. pili in bacteria.



- **Adhesins** have been shown to be important in a number of microorganisms
- *Streptococcus mutans*, a member of the normal oral flora, produces a polysaccharide, dextran, that enhances its attachment to teeth.



- Pathogenic strains of *Escherichia coli* have *pili* that aid in attachment to epithelial cells of the gastrointestinal tract or urinary tract



# III. Colonization

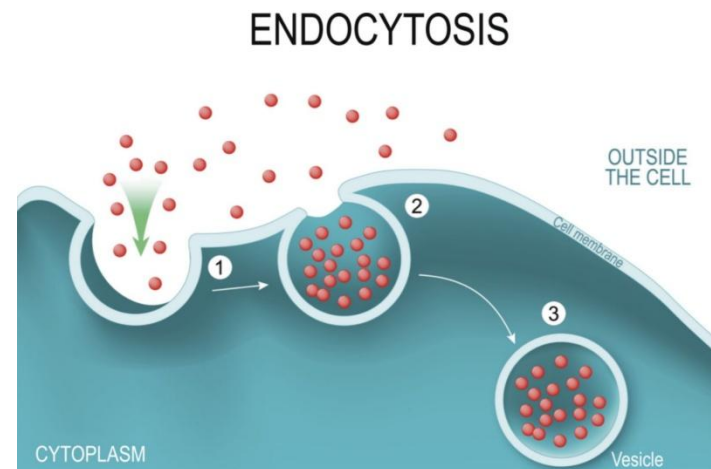
- Some virulent bacteria produce special proteins that allow them to colonize parts of the host body.
- Pathogens start multiplication and maintenance.
- Pathogens compete with normal flora for residence.
- Pathogens will resist body reactions e.g. Bile, stomach acid, skin secretions, IgA (mucosal antibodies).
- e.g.  
*Helicobacter pylori* is able to survive in the acidic environment of the human stomach by producing the enzyme **urease**.

# IV. Invasion

Some virulent bacteria produce proteins that either:

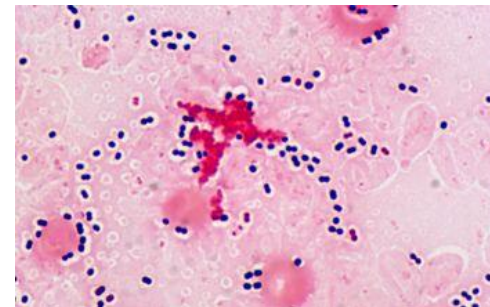
- a. Disrupt host cell membranes or
- b. Stimulate endocytosis into host cells.

*Endocytosis is the process by which cells absorb material (molecules such as proteins) from outside the cell by engulfing it with their cell membrane*



## V. Immune Response Inhibitors

- Many bacteria produce virulence factors that inhibit the host's immune system defenses.
- The polysaccharide capsule of *Streptococcus pneumoniae* inhibits phagocytosis of the bacterium by host immune cells.



# VI. Toxins

- Many virulence factors are proteins made by microorganisms that poison host cells and cause tissue damage.  
**e.g.** Bacteria that produce toxins are called toxigenic.

## Bacterial toxins

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graph TD; A[Bacterial toxins] --> B[Endotoxins]; A --> C[Exotoxins];
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**Endotoxins:** they are part of the outer membrane of the cell wall of bacteria  
-They are present **only** by Gram -ve bacteria  
- Death of the bacteria lead to the release of endotoxins.

**Exotoxins:** they are toxins produced by the bacteria to the surrounding tissue.  
-They are produced mostly by Gram +ve bacteria  
E.g. Diphtheria toxins

# Pathogenesis mechanism in Bacteria

