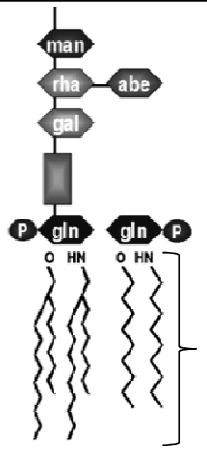


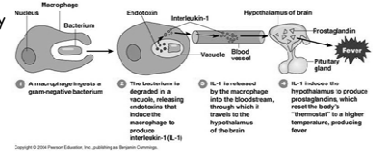
## 2. Endotoxin

- integral part of the cell wall of **Gram-negative** bacteria
- it is released during **cell degradation**
- **lipid A** portion of the cell wall >>> **lipid** >>> **heat stable, resistant to proteolytic enzymes; weak antigen**
- **not converted** to toxoid
- affects after **short incubation period**
- **less potent**
- **same biological effect** of LPSs from different species
- stimulating effect in small doses, while toxic in large amount
- target cells: mononuclear phagocytes, neutrophils, B-lymphocytes and platelet
- encoded by bacterial chromosome



## Biological effects of endotoxin

- binds to the specific receptors of macrophages, B-lymphocytes and other cells
  - ⇒ stimulates release of some lymphokines (IL-1, TNF- $\alpha$ , IFN- $\gamma$ , IL-6, histamine, prostaglandins)
  - ⇒ stimulates growth of B-cells
- fever and inflammation
- activation of complement system via alternative pathway: C3a, C5a
- leukopenia followed by leukocytosis
- hypotension - increased vascular permeability, vasodilatation
- decreased peripheral circulation, decreased perfusion of blood to major organs
- capillary leakage, formation of petechiae
- disseminated intravascular coagulation (DIC; activation of factor XII)
- thrombosis
- thrombocytopenia
- decreased iron availability
- hypoglycaemia
- cytotoxicity
- necrosis
- shock; death



## Unique endotoxins

- In *Bacteroides fragilis* the beta-hydroxy-myristinic-acid component is missing from the lipid A >>> lower toxicity, low level fever, **abscess formation**, higher risk to coagulation

## Exotoxins versus endotoxins

EXOTOXIN	ENDOTOXIN
protein	lipid
produced by living bacteria	cell wall component, free after death of bacteria
Gram+ and Gram-	only Gram-
good antigen	poor antigen
heat labile	heat stable
convertable to toxoid	not convertable to toxoid
highly toxic	moderately toxic
specific effect	similar effect
binds to specific receptors	no specific receptor
acts after incubation period	no incubation period
no fever	usually cause fever
encoded by plasmid and bacteriophage	encoded by bacterial genome

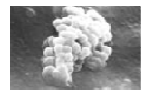
## Non toxic virulence factors

1. extracellular enzymes
2. cell surface components
  - antiphagocytic factor
  - adhesion factors (adhezins)
3. invasion factors (invazins)
4. siderophores

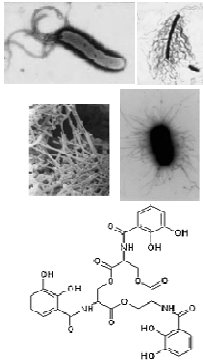
## Non toxic virulence factors

Extracellular enzymes: survival and invasion

- ✓ Coagulase (*Staphylococcus aureus*)
- ✓ Plasminogen activators - fibrinolysines/ streptokinase (*Streptococcus pyogenes*)
- ✓ DNase, RNase (*Streptococcus pyogenes*)
- ✓ Hyaluronidase (*Streptococcus, Staphylococcus, Clostridium*)
- ✓ Proteases - collagenase, elastase (*Streptococcus pyogenes, Pseudomonas aeruginosa*)
- ✓ Lipase (*Staphylococcus aureus*)
- ✓ IgA protease (*Neisseria meningitidis, Haemophilus influenzae, S. pneumoniae*)
- ✓ Urease (*Proteus, Helicobacter*)



- Antiphagocytic molecules - LPS (O-specific side chain), polysaccharide capsule (*S. pneumoniae*, *K. pneumoniae*, *H. influenzae*, *N. meningitidis*, *B. anthracis*, Cord-factor (*Mycobacterium tuberculosis*), protein M (*S. pyogenes*), protein A (*S. aureus*); soluble chemotaxis inhibiting factor (*B. pertussis*)
- Colonization factors - pili (*N. gonorrhoeae*); afimbrial adhesins (*Chlamydia*, *Mycoplasma*, *S. pyogenes*), adhesive fimbriae (*E. coli*, *V. cholerae*, *S. dysenteriae*, *B. pertussis*), outer membrane proteins, capsule, glycocalyx, LPS, teichoic acid, lipoteichoic acid
- Invasion - ingress and real invasion; enzymes and cytotoxins
  - invasins
    - invasive plasmid antigen - shigella, *E. coli*
    - plasminogen activator - yersinia
    - penetration helping factor - *L. monocytogenes*
  - flagellae (monotrich, lophotrich, peritrich)
  - enzymes (lecithinase, hyaluronidase stb.)
  - S. fimbriae* (bind to sialic receptors - sepsis, meningitis *E. coli*)
  - Flagella - motility
- Bacterial siderophores - aerobactin (*E. coli*), enterobactin (enterobacteriaceae)

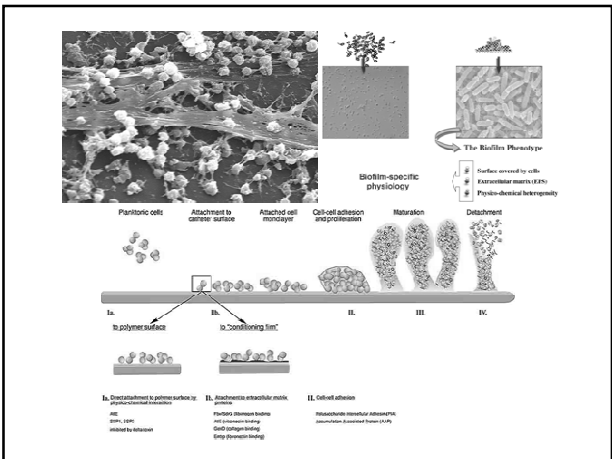


### Bacteria capable of cell invasion

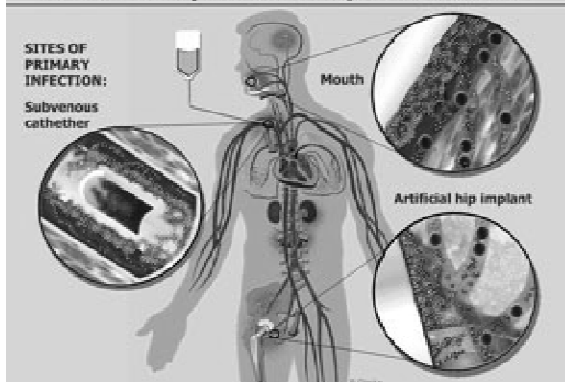
- Obligate intracellular bacteria:** chlamydia, rickettsia, coxiella
- Facultative intracellular bacteria:** mycobacterium, salmonella, shigella, *Listeria monocytogenes*, legionella

### Biofilm producing microorganisms

- Streptococcus mutans*
- Staphylococci (*S. aureus*, *S. epidermidis*)
- Pseudomonas aeruginosa*
- Candida parapsilosis*



### Sites of Primary and Secondary Biofilm Infection



**SITES OF PRIMARY INFECTION:**

- Subvenous catheter
- Mouth
- Artificial hip implant

### Infection and infectious disease

- Susceptibility of the host - age, immunosuppression
- Properties of microorganism - infective dose, characteristics, virulence
- Source and reservoir of infection
  - Source
  - Reservoir
  - Carrier
  - Zoonoses
- Mode of transmission (air, direct contact, vectors)
- Portals of entry (respiratory tract, GI-tract, urogenital tract, conjunctiva, transplacental transmission); nosocomial infections
- Mode of release of infectious agents

### The role of the host during infection

- genetic factors
- age (neonates, elderly patients)
- malnutrition (protein, vitamin )
- hormonal status (insulin, oestrogen)
- skin, mucosal membranes (pH, cilia lysosim)
- phagocytosis, complement cascade

### Source of infection

- **Source of infection:** animate and inanimate with **direct** or **indirect** contamination
  - human
  - animal
  - Vector
  - water
  - soil
- **Reservoirs:** animate or inanimate environment in which the microorganisms can persist and maintain their ability to cause infection.
  - human (carrier)
  - animal (zoonoses)
  - soil (tetanus, gas gangrene, anthrax, fungal infections)
  - water (cholera, amoebic dysentery)
  - food (food poisoning)

The source of the infection and the reservoir can be the same organism.

### Human carriers

- Human reservoirs of infection that fail to show significant outward signs of infection are termed **carriers**.
- Carriers may also be termed chronic where a **chronic carrier** continues to serve as a reservoir even after apparent recovery from a disease.
  
- incubation carrier
- active carrier
- convalescent carrier
- healthy carrier

### Transmission

- droplets (cough, sneeze)
- contact
  - direct (fingers, sexual)
  - indirect (equipments)
- water (drink, bath)
- food
- placenta
- nosocomial (iatrogenic)
- vectors (mosquito, tick, flea, lice, mite)

### Vectors

- **mechanical** transmission: fly (dysentery)
- **biological** transmission:
  - flea (plague)
  - mosquito (malaria)
  - tick (Lyme-disease)
  - louse (ricketsial typhus)
  - mite (scrub typhus)

### Portals of entry

- skin
- mucous membranes
  - respiratory tract
  - GI
  - genito-urinary tract
  - conjunctiva
- placenta (vertical transmission)
- blood (transfusion, infusion)

### Course of infectious disease in the host

1. According to clinical manifestation of the disease, it can be
  - ✓ asymptomatic or subclinical
  - ✓ manifest
2. According to course of infection, disease can be
  - ✓ acute
  - ✓ subacute
  - ✓ chronic
  - ✓ latent
3. Stages of acute infection
  - ✓ incubation period
  - ✓ prodromal phase
  - ✓ specific illness period - acute phase
  - ✓ recovery period

### Course of infectious disease in the population

- ✓ sporadic, endemic and epidemic form, pandemics
- ✓ Morbidity: the *total* number of cases in a particular population at a particular point in time (cases/100 000 individuals/year)
- ✓ Incidence: number of *new* cases of a disease in a given time interval per population size (new cases/100 000 individuals/year)
- ✓ Prevalence: the *total* (new and old cases) number of cases of the disease in the population at a given time or the total number of cases in the population
- ✓ Mortality rate: a measure of the number of deaths in the population (per 100 000 individuals/year)
- ✓ Lethality: number of death among diseased individuals
- ✓ Infectivity: infection (% of all exposed people)