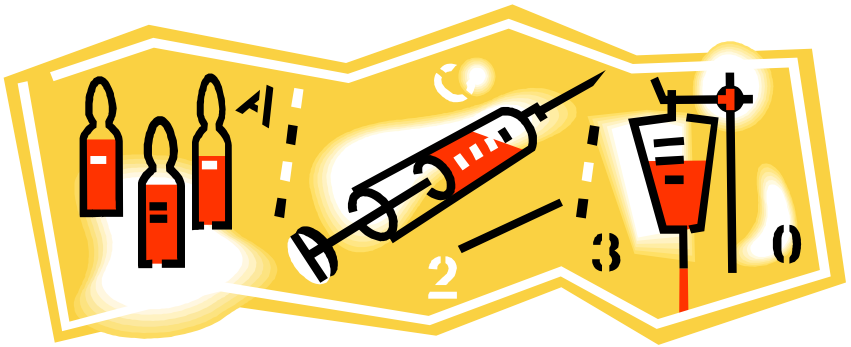
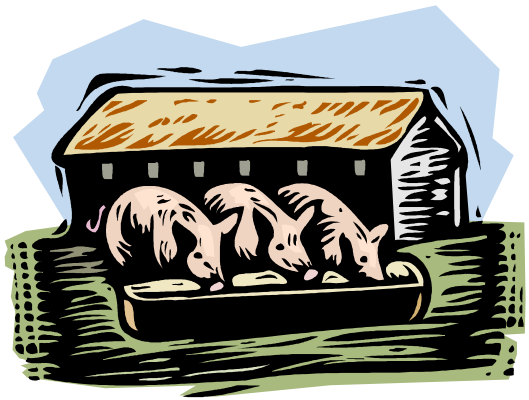
Virulence factors





Slides made by Special Consultant Henrik Hasman,

Statens Serum Institut

Who am I

Johanne Ahrenfeldt

johah@cbs.dtu.dk

- PhD student in Genomic Epidemiology
- Graduate engineer in Bioinformatics and Systems Biology from DTU – 2014
- Mainly work with Whole Genome based Phylogeny

Bacterial pathogenecity and virulence

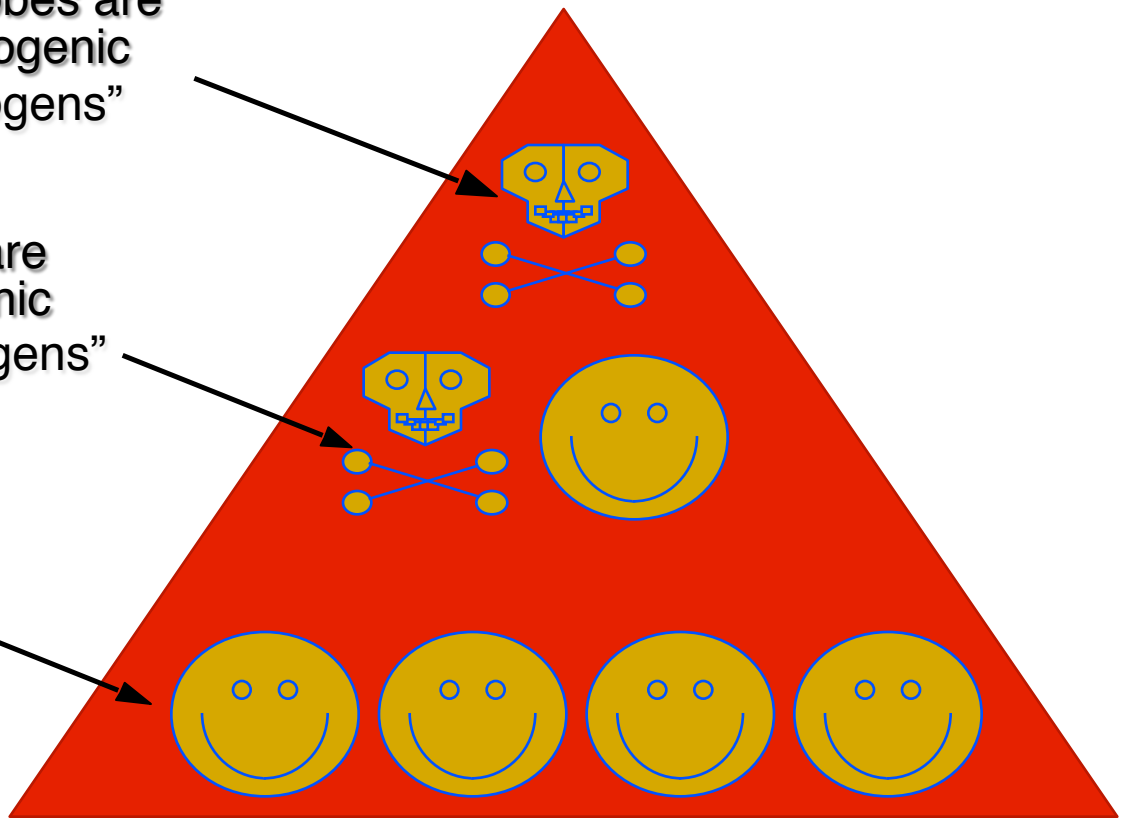
- **Pathogenicity.** This is the potential capacity of certain species of microbes to cause an infectious process.
- **Virulence.** signifies the degree of pathogenicity of the given strain. Virulence, therefore, is an index of the qualitative individual nature of the pathogenic microorganism.

Microbes and humans

Very few microbes are always pathogenic
"Strict pathogens"

Many microbes are potentially pathogenic
"Opportunistic pathogens"

Most microbes are never pathogenic
"Non-pathogenic"



Student activation

- Give an example on a strict pathogen
- Give an example on an opportunistic pathogen
- Give an example on a non-pathogen

How do we know that a given pathogen causes a specific disease?

- Koch's postulates
  - the pathogen must be present in every case of the disease
  - the pathogen must be isolated from the diseased host & grown in pure culture
  - the specific disease must be reproduced when a pure culture of the pathogen is inoculated into a healthy susceptible host
  - the pathogen must be recoverable from the experimentally infected host

Use 2 minutes to discuss in small groups how you would conquer the island.

Include:

- **How to get on to and how to stay on the island**

Back-paddle, throw an anchor, use a rope, swim from the boat (might require more than one swimmer!!)

- **How to avoid being detected by the island defense**

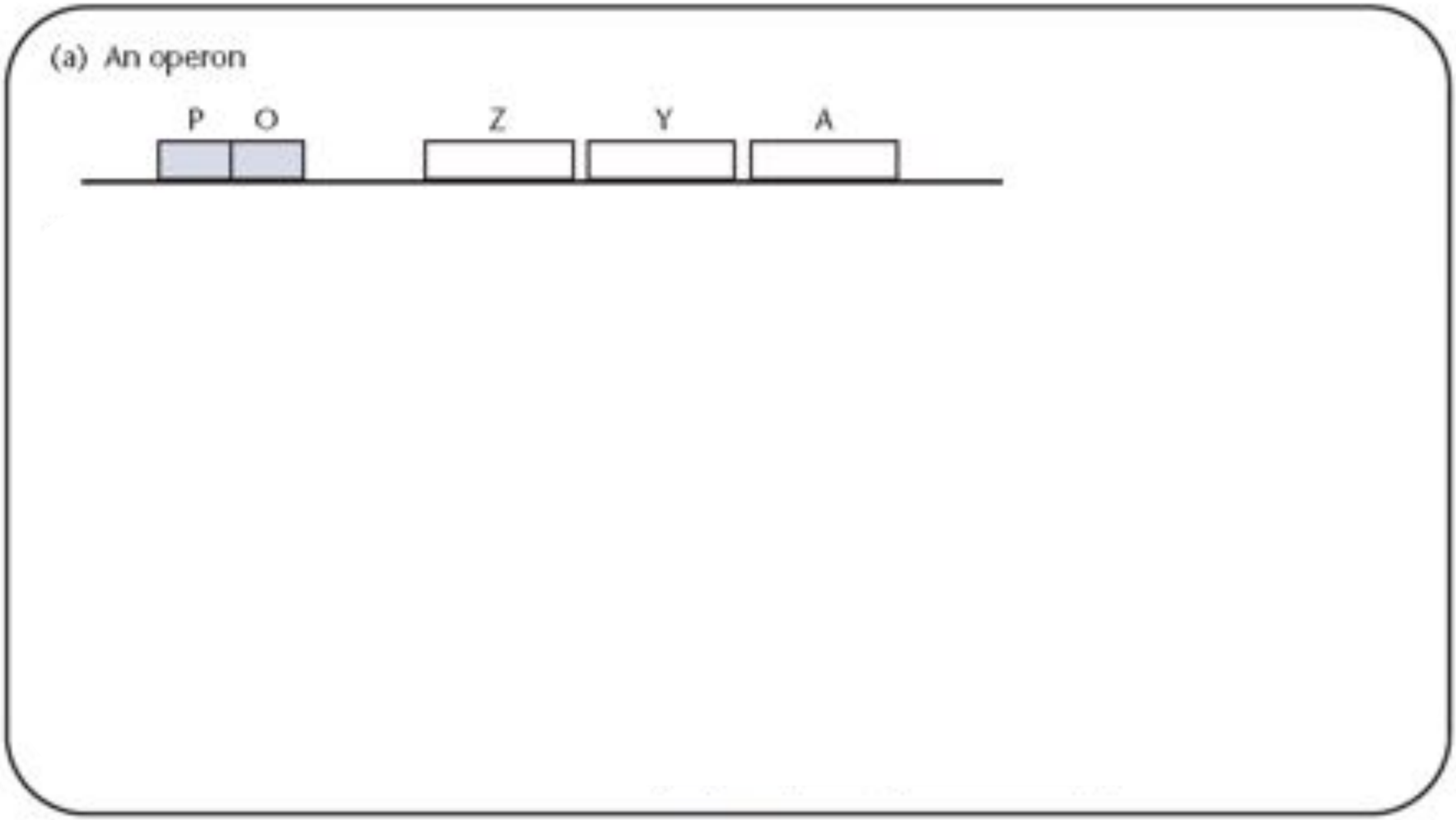
Camouflage, hide, dig-in, costume

- **How to eliminate the island defense**

Poison, weapon, scare to perform suicide

Coordinated attack

Gene regulation – A tool for a coordinated attack

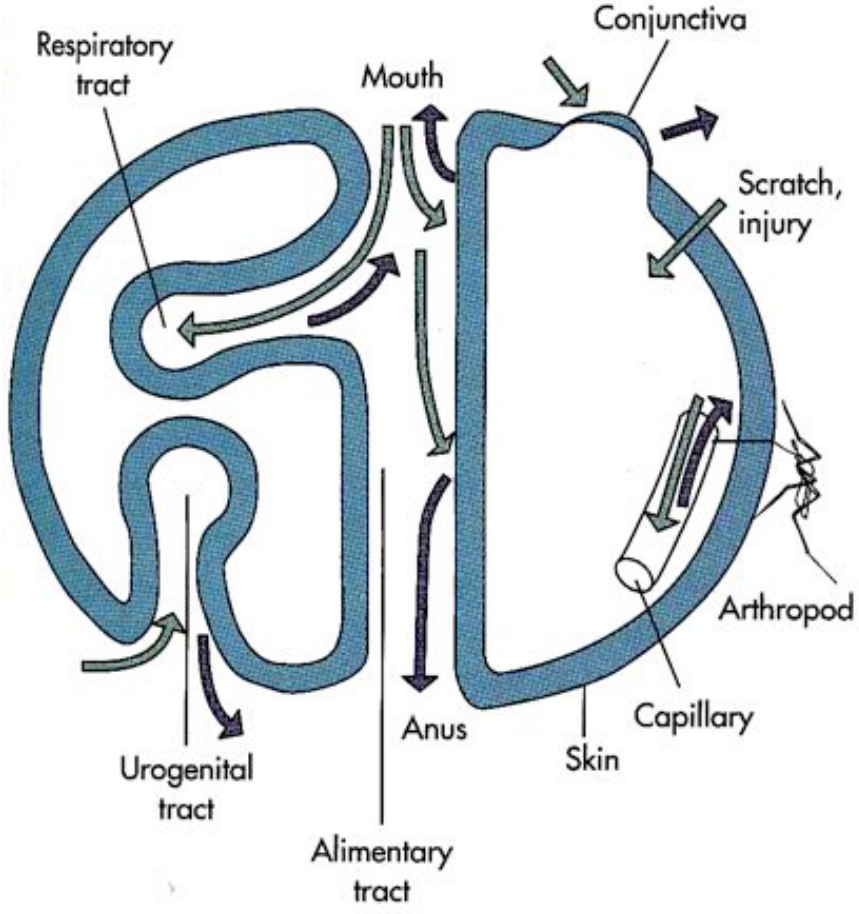


Entry into the human body

The most frequent **portals of entry**
- Mucus
- Skin

Routes:

Ingestion, inhalation, trauma, needles, catheters, arthropod bite, sexual transmission



Bacterial pathogenicity and virulence

The virulence of pathogenic microorganisms is associated with

- adherence
- invasiveness
- capsule production
- toxin production
- aggressiveness
- and other factors

”Anchor”

”Ropes”

”Camouflage”

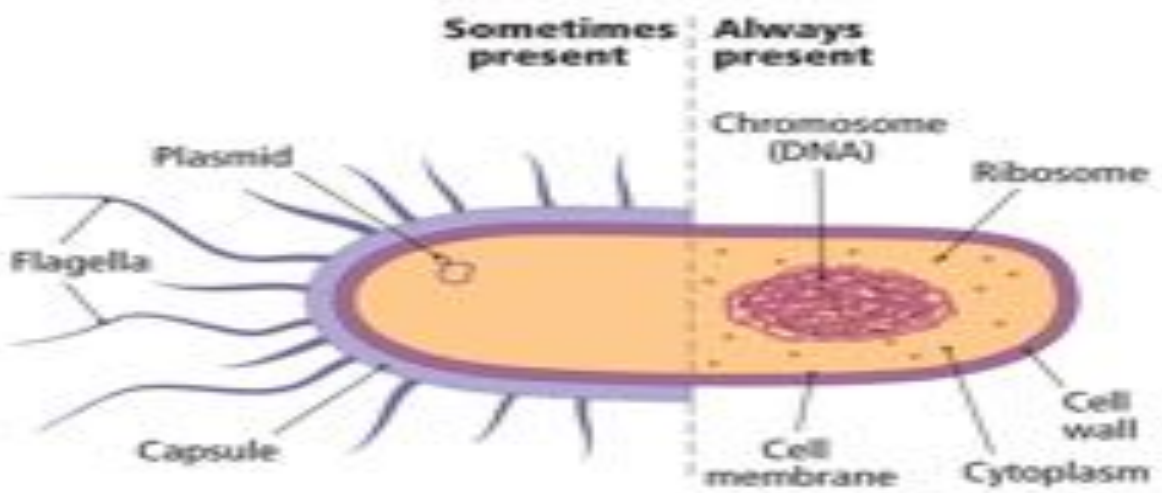
”Poison”

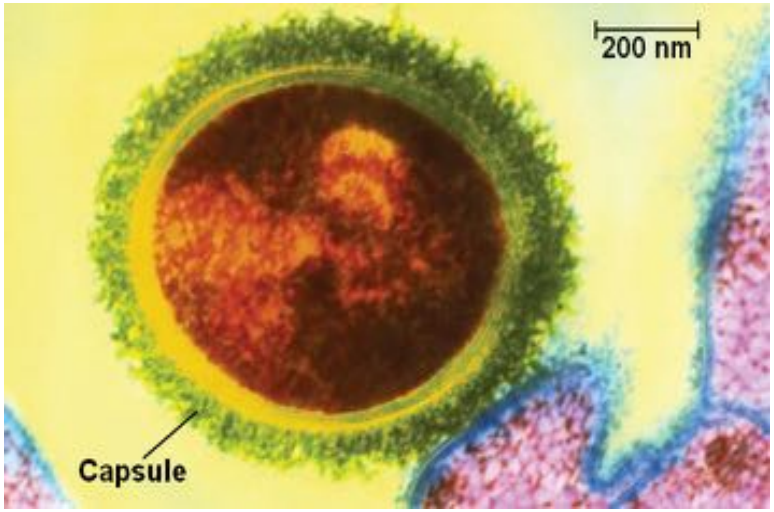
”Weapons”

”Costume, Hide, dig-in….ect”

Virulence factors

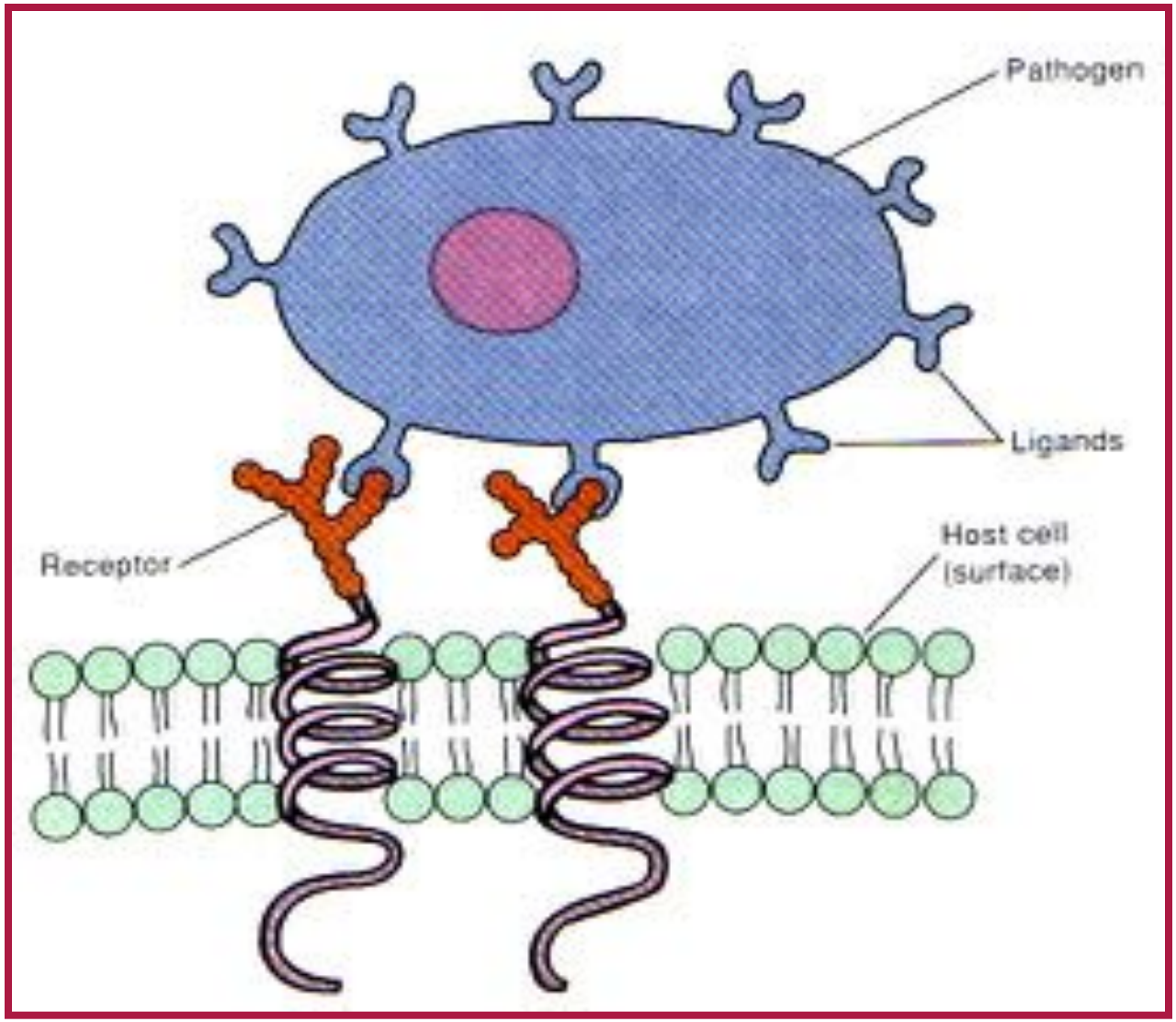
The capsule


Sometimes present
Always present
Chromosome (DNA)
Plasmid
Ribosome
Flagella
Capsule
Cell membrane
Cell wall
Cytoplasm


200 nm
Capsule

Virulence factors

The adherence

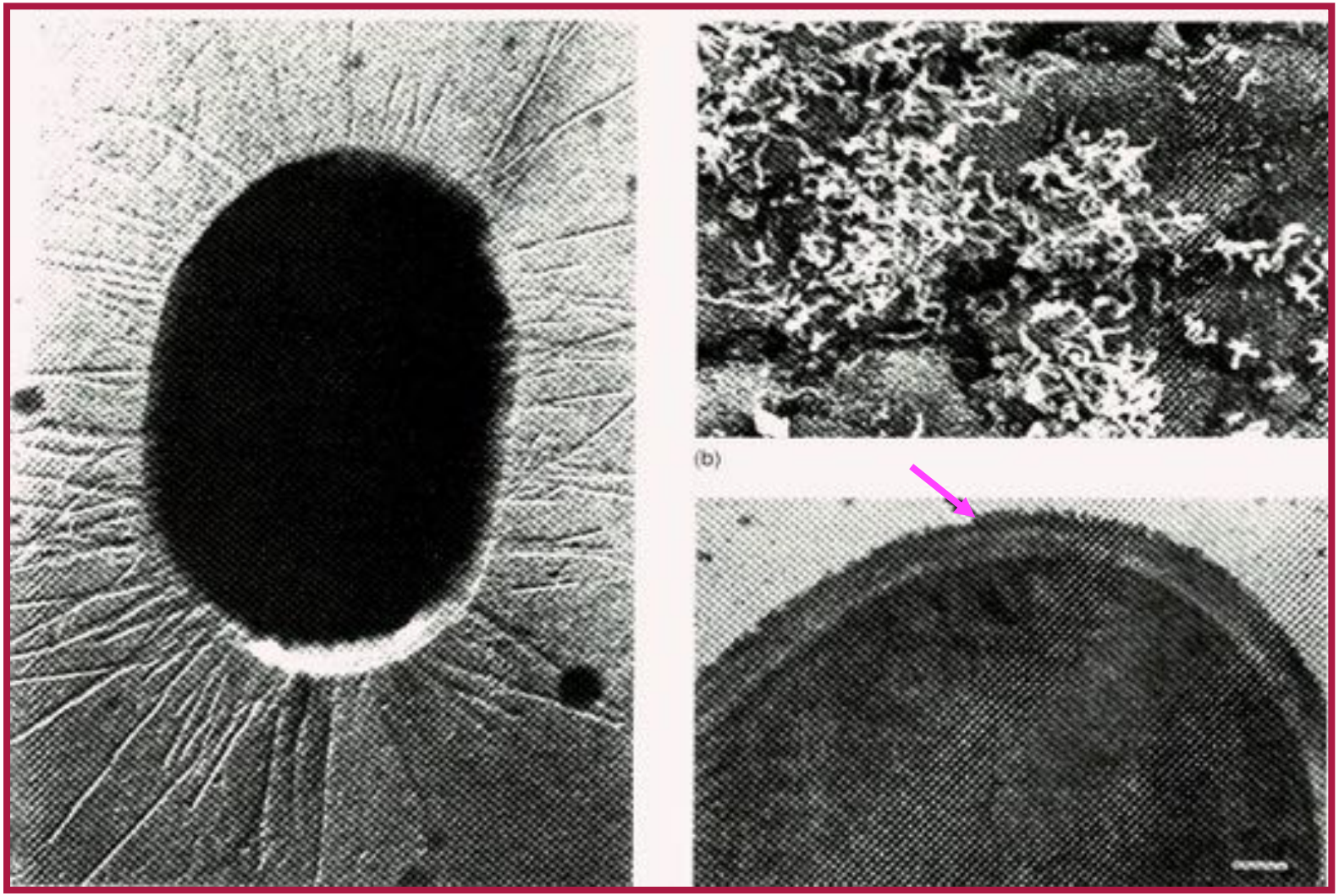


Virulence factors

Adherence factor	Description
Filamentous hemagglutinin	Causes adherence to erythrocytes
Fimbriae	Help attach to bacteria to solid surfaces
Glycocalyx or capsule	Inhibits phagocytosis and aids in adherence
Pili	Bind bacteria together for transfer of genetic material
Slime	Tenacious bacterial film that is less compact than a capsule
Teichoic and lipoteichoic acid	Cell wall components in Gram positive bacteria that aid in adhesion

Virulence factors

Adherence bacteria to cell surfaces



Virulence factors

Invasive properties of pathogenic bacteria

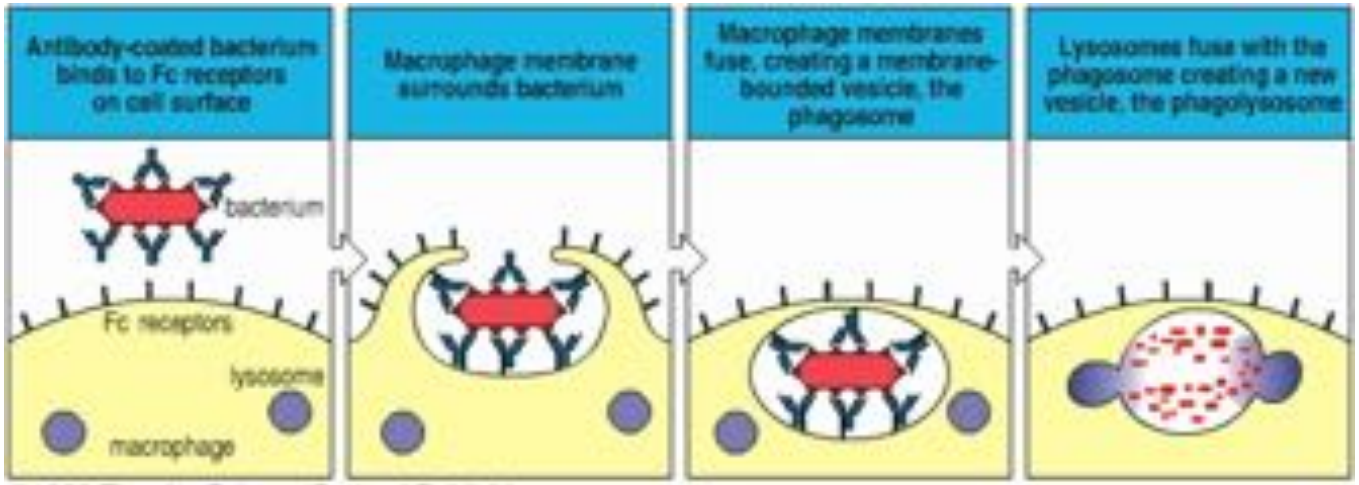
Some virulent microbes are characterized by the ability to penetrate tissues of the infected organism (**invasive properties**).

- immunoglobulin A protease
- leukocidins
- collagenase and hyaluronidase
- protein A

Virulence factors

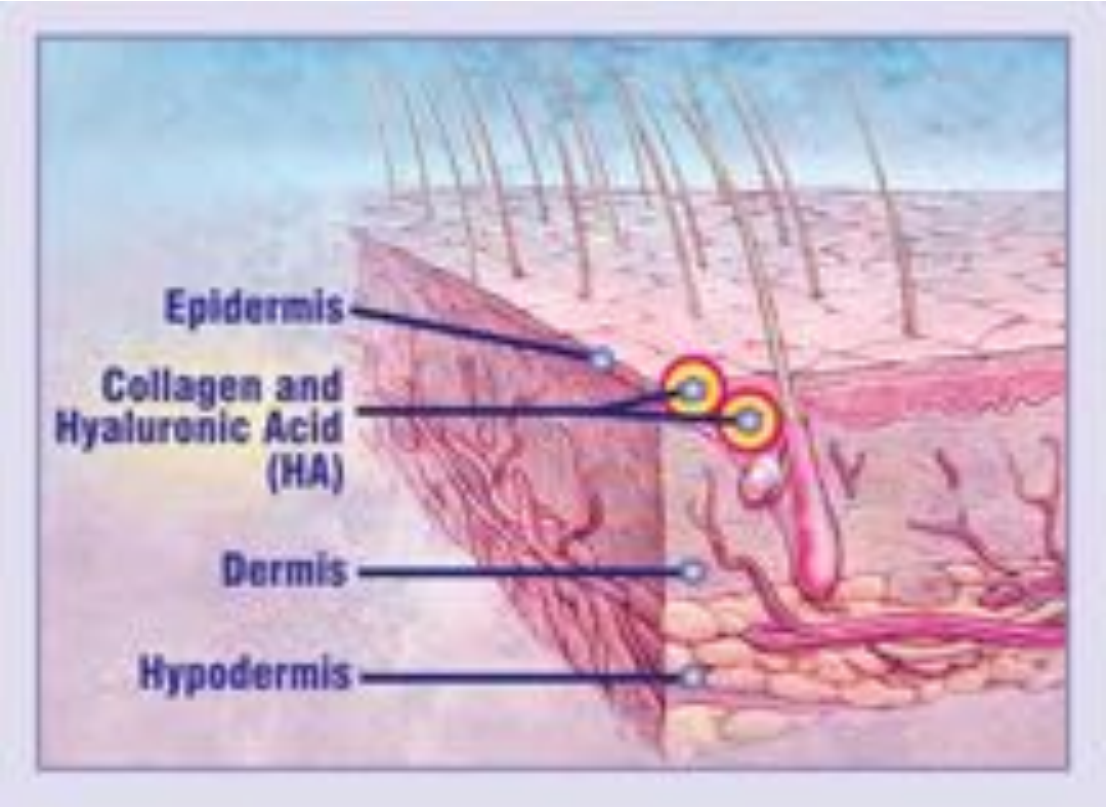
Immunoglobulin A protease degrades IgA, allowing the organism to adhere to mucous membranes, and is produced chiefly by *N. gonorrhoeae, Haemophilus influenzae, and S. pneumoniae.*

Leukocidins can destroy both neutrophilic leukocytes and macrophages. Leukocidins are often associated with *S. aureus*; see later.



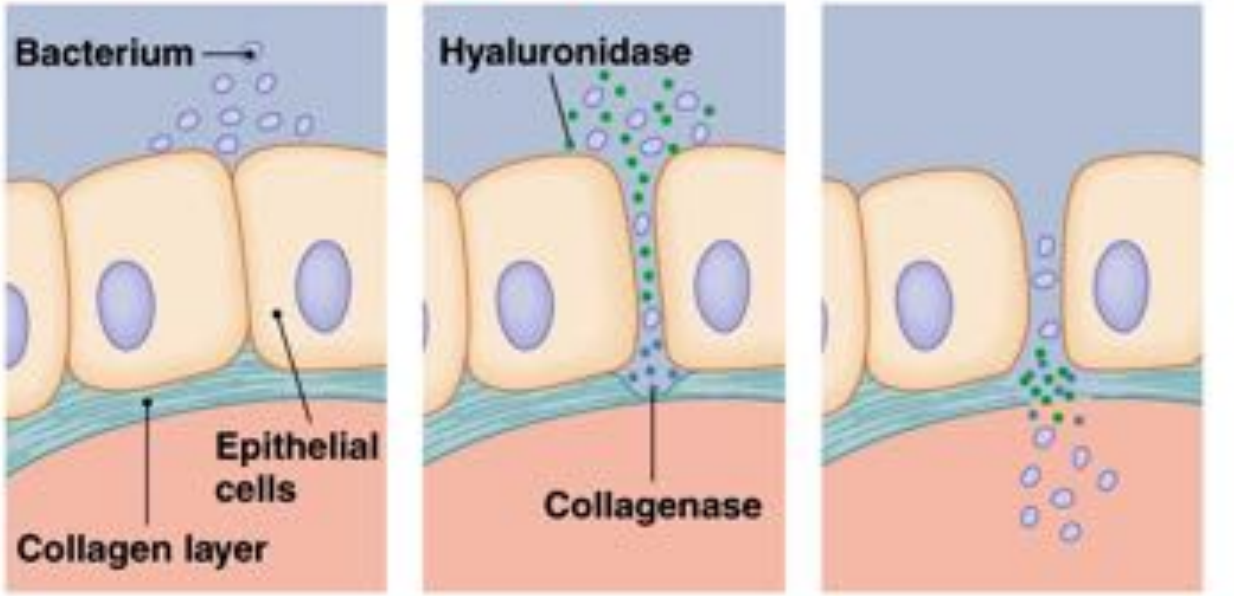
Virulence factors

Collagenase and hyaluronidase degrade collagen and hyaluronic acid, respectively, thereby allowing the bacteria to spread through subcutaneus tissue (*Streptococci, Staphylococci, Clostridium*).



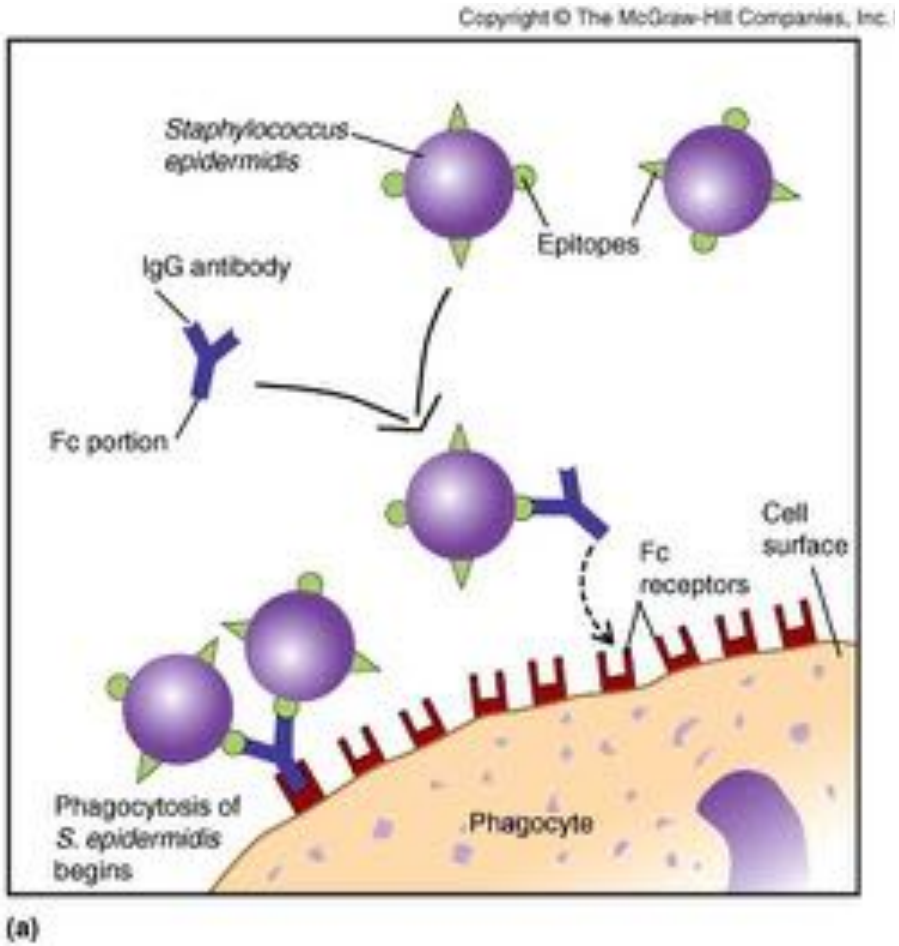
Virulence factors

Collagenase and hyaluronidase degrade collagen and hyaluronic acid, respectively, thereby allowing the bacteria to spread through subcutaneus tissue (*Streptococci, Staphylococci, Clostridium*).



Virulence factors

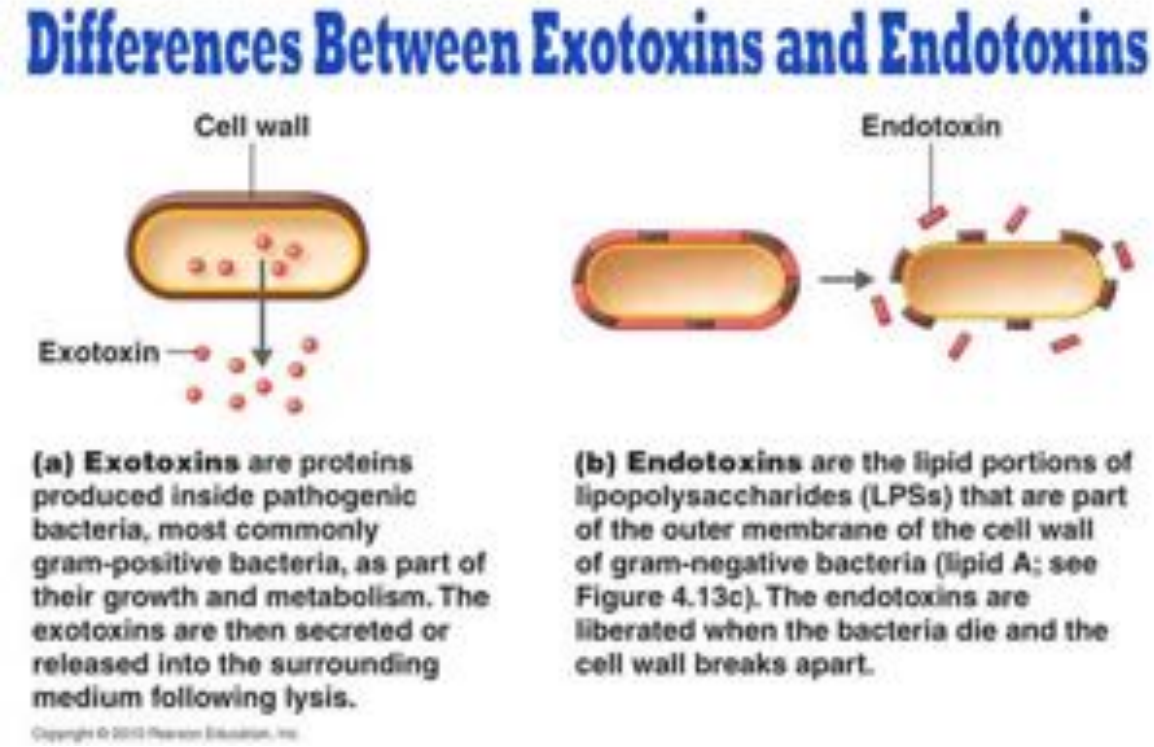
Protein A of *S. aureus* binds to IgG and prevents the activation of complement.



Virulence factors

Toxin production

According to their nature of production, microbial toxins are subdivided into **exotoxins and endotoxins**.



Virulence factors

- Exotoxins easily diffuse from the cell into the surrounding nutrient medium.

- They are characterized by a markedly distinct toxicity, and act on the susceptible organism in very small doses.

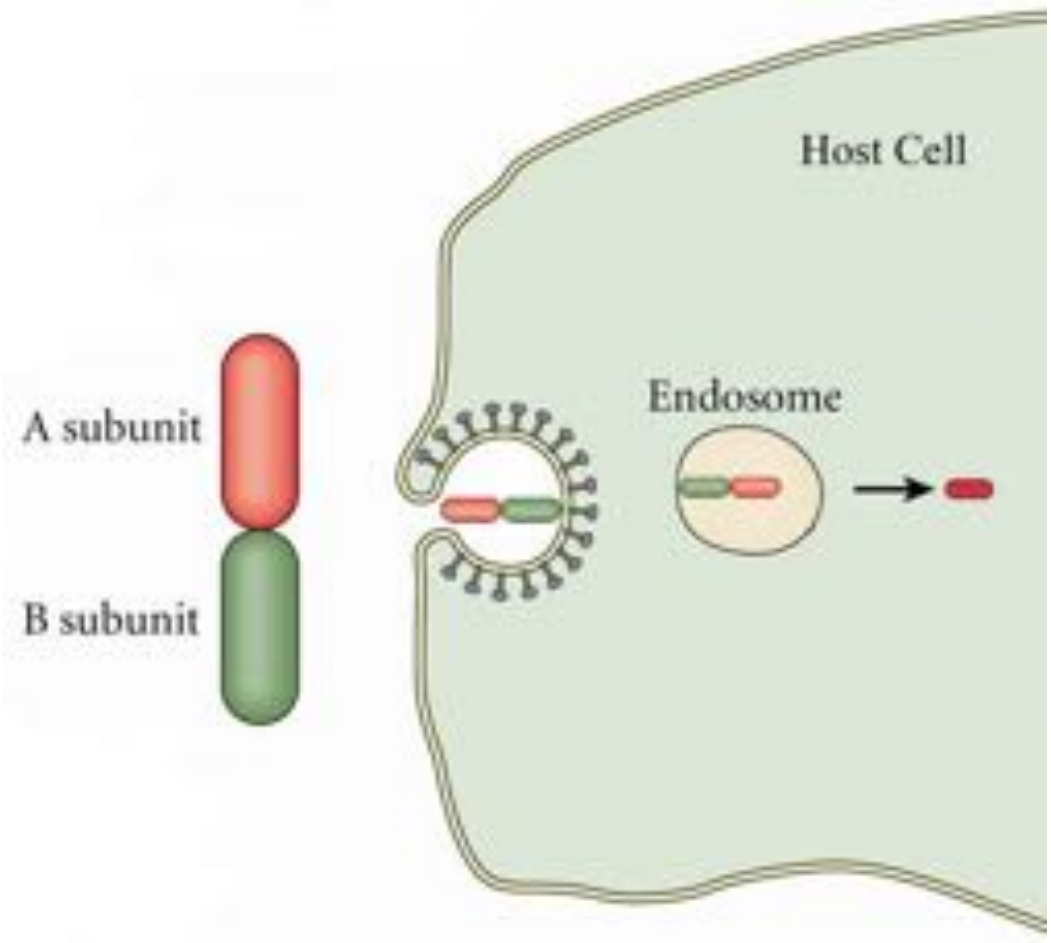
- Exotoxins have the properties of enzymes hydrolysing vitally important components of the cells of tissues and organs.

Virulence factors

Exotoxins exert their effects in a variety of ways

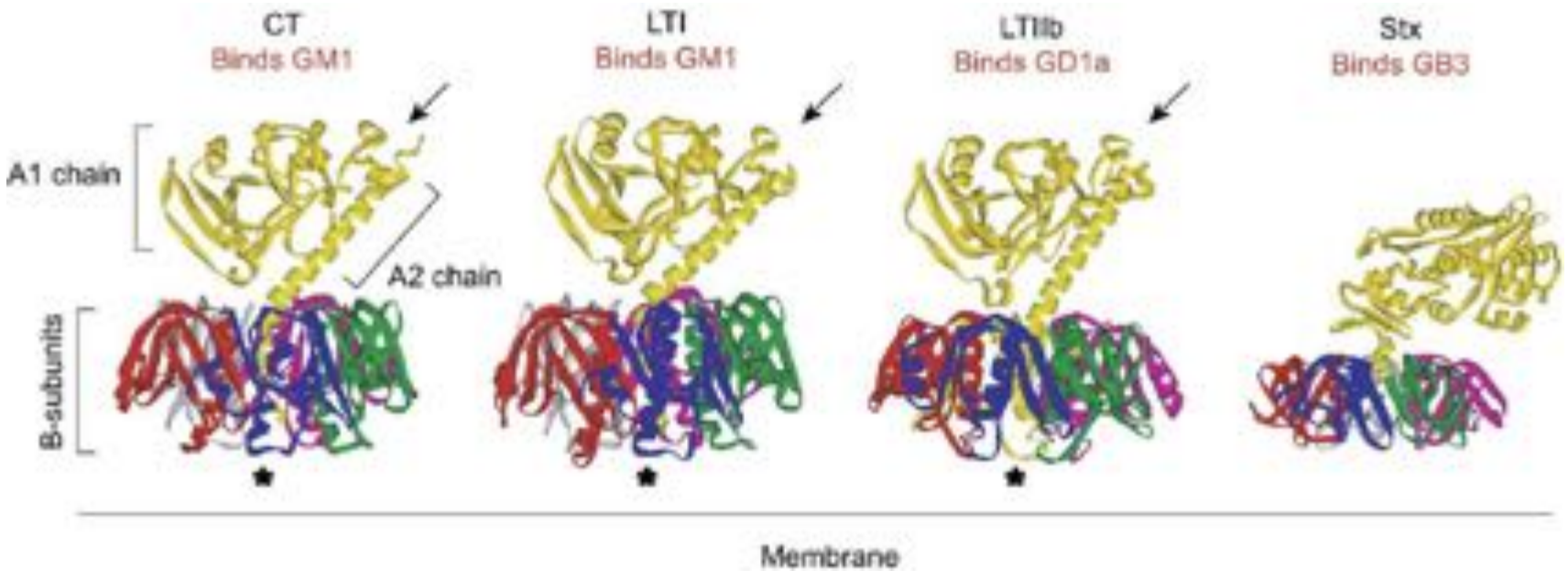
- by inhibition of protein synthesis
- inhibition of nerve synapse function
- disruption of membrane transport
- damage to plasma membranes.

AB toxins



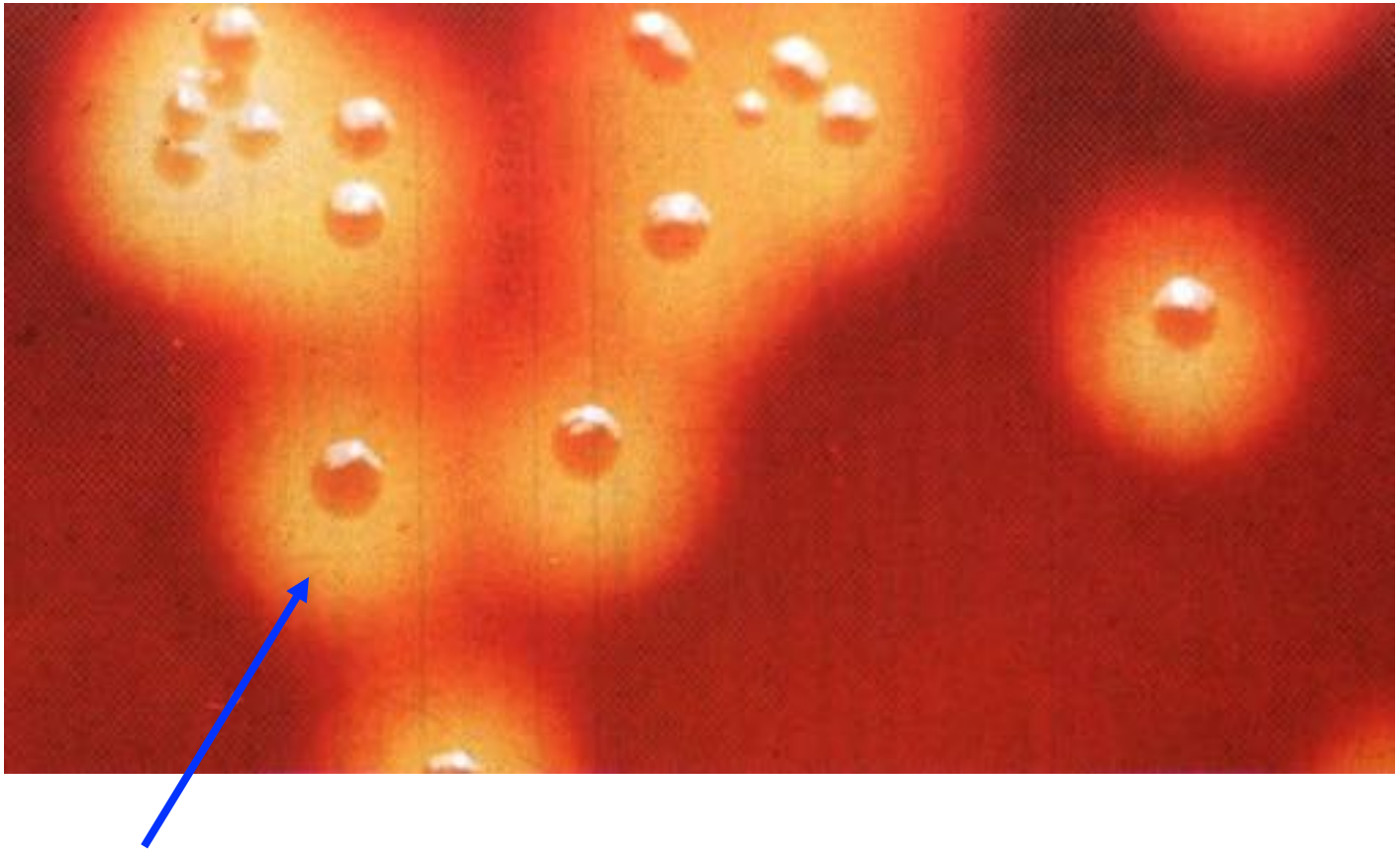
A subunit: Activity
B subunit: Binding

AB_5 toxins



Colera toxin Heat lable toxin I Heat lable toxin IIb Shiga toxin

Virulence factors



Action of the hemolysin on red blood cells

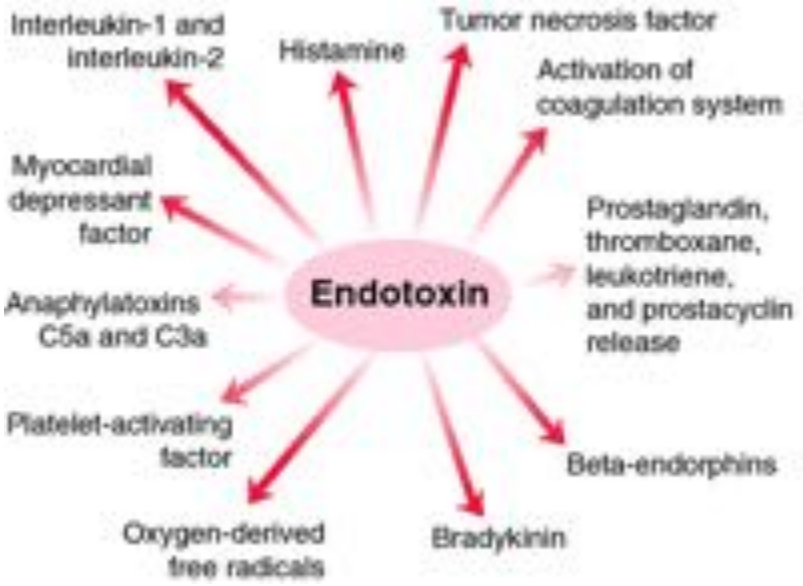
Virulence factors

MICROORGANISM	TOXIN	DISEASE	ACTION
Clostridium botulinum	Several neurotoxins	**Botulism**	Paralysis; blocks neural transmission
Clostridium tetani	Neurotoxin	**Tetanus**	Spastic paralysis; interferes with motor neurons
Corynebacterium diphtheriae	Cytotoxin	**Diphtheria**	Blocks protein synthesis
Bordetella pertussis	Pertussis toxin	**Whooping cough**	Blocks G proteins that are involved in regulation
Streptococcus pyogenes	Hemolysin	**Scarlet fever Food**	Lysis of blood cells
Staphylococcus aureus	Enterotoxin	**Poisoning**	Intestinal inflammation
Aspergillus flavus	Cytotoxin	**Aflatoxicosis**	Blocks transcription of DNA → stopping protein synthesis
Amanita phalloides	Cytotoxin	**Mushroom food poisoning**	Blocks transcription of DNA → stopping protein synthesis

Virulence factors

Endotoxins

- are associated with Gram negative bacteria only
- are more firmly bound with the body of the bacterial cell
- are less toxic and act on the organism in large doses
- their latent period is usually estimated in hours

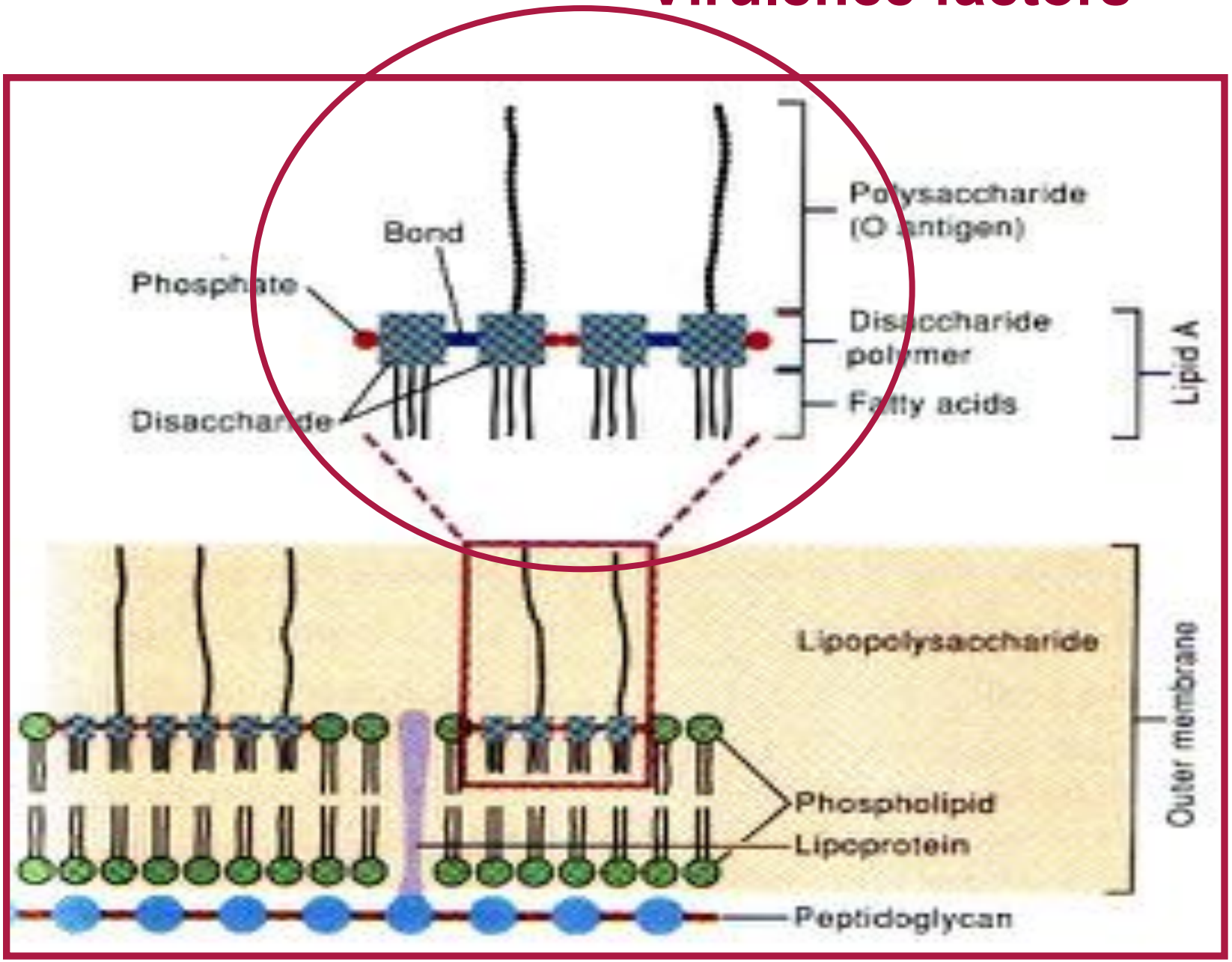


Virulence factors

Endotoxins

- According to chemical structure, endotoxins are related to glucoside-lipid and polysaccharide compounds or phospholipid-protein complexes.
- They are thermostable. Some endotoxins withstand boiling and autoclaving at 120°C for 30 minutes.

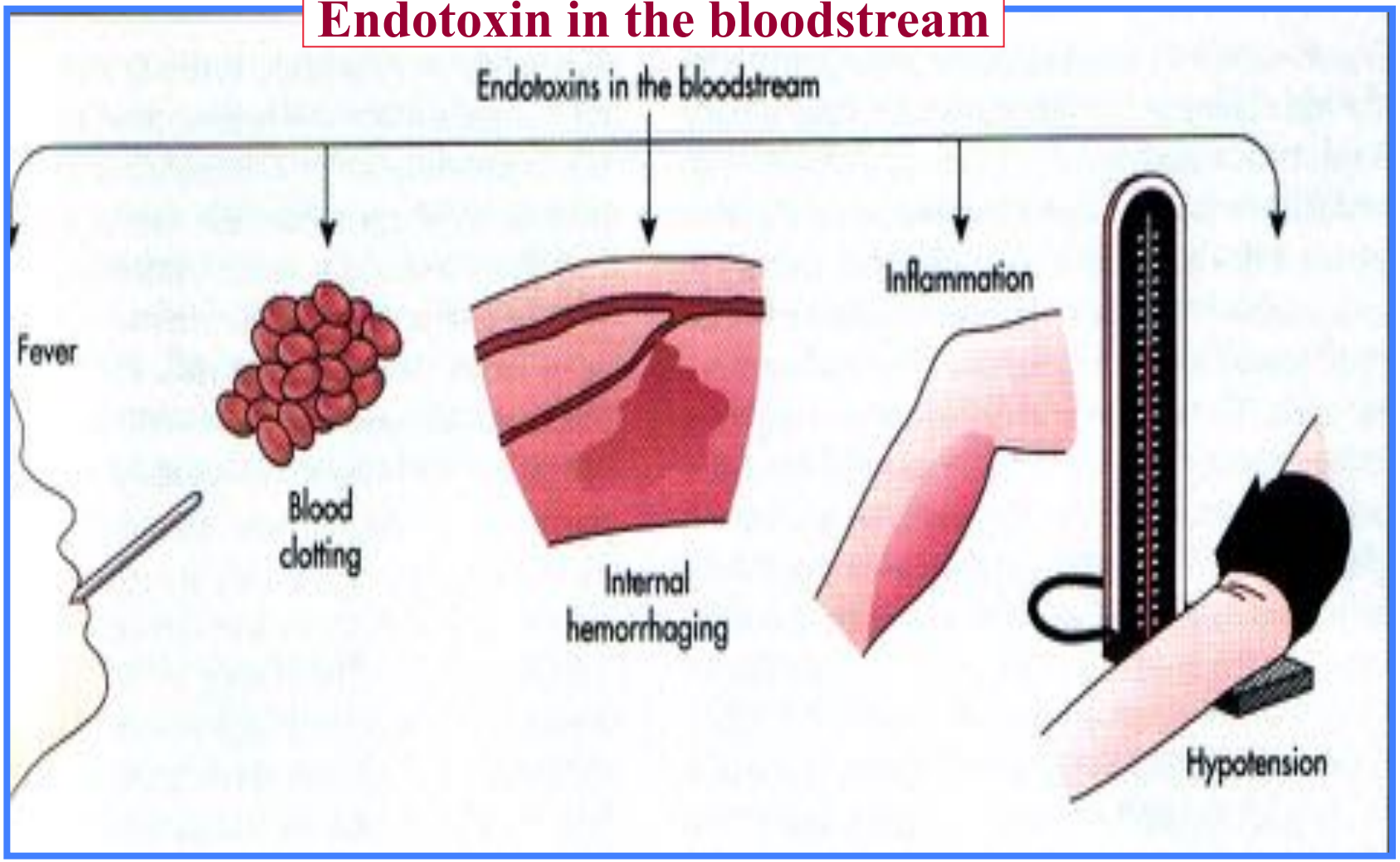
Virulence factors



Virulence factors

Action of the endotoxin

Endotoxin in the bloodstream



Virulence factors

Differences between exotoxins and endotoxins

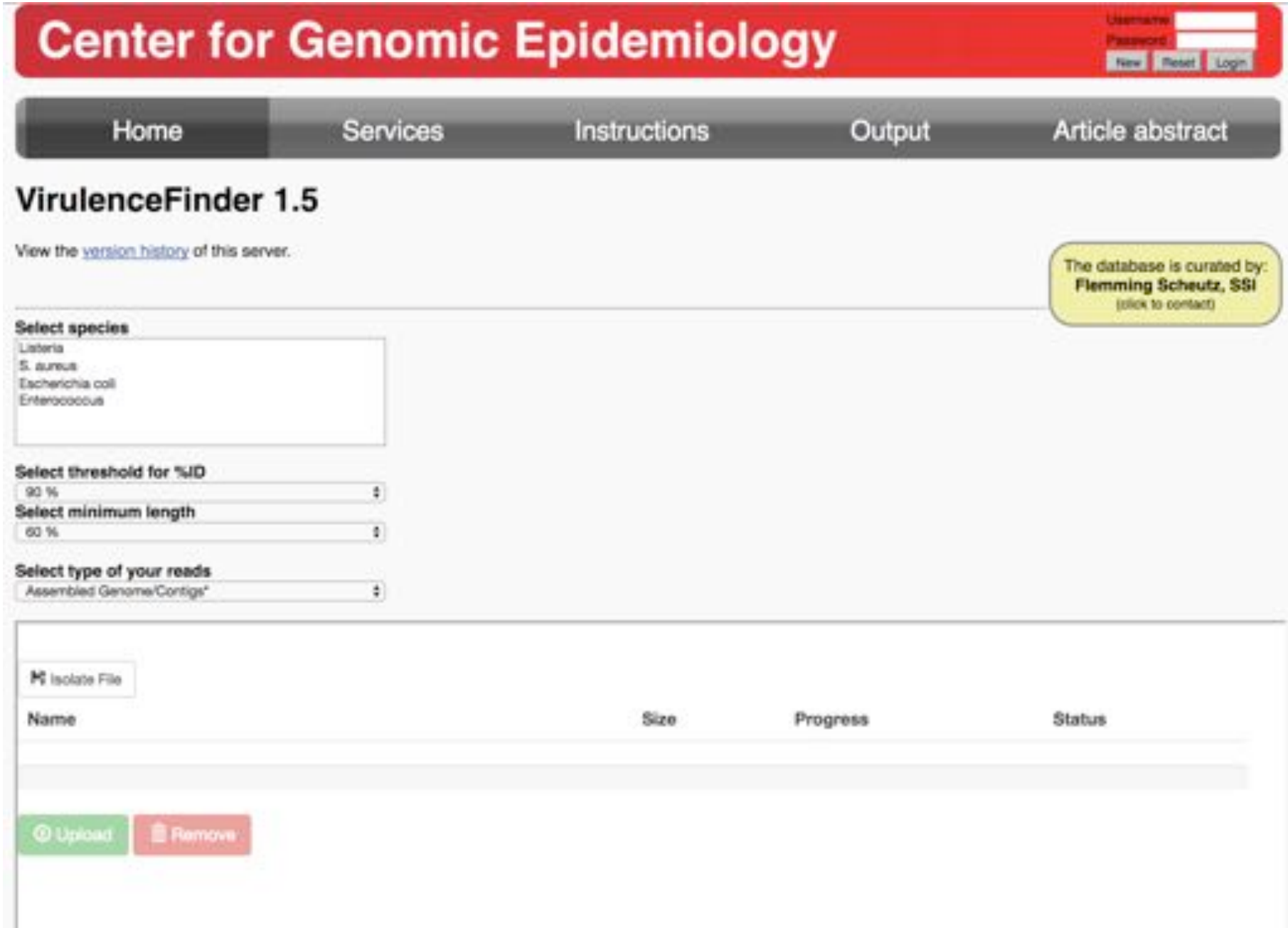
exotoxins	endotoxins
Proteins	Lipopolysaccharides
Heat labile	Heat stable
	
Action often enzymatic	No enzymatic action
Specific pharmacological effect for each exotoxin	Non-specific action of all endotoxins

Bacterial pathogenicity and virulence

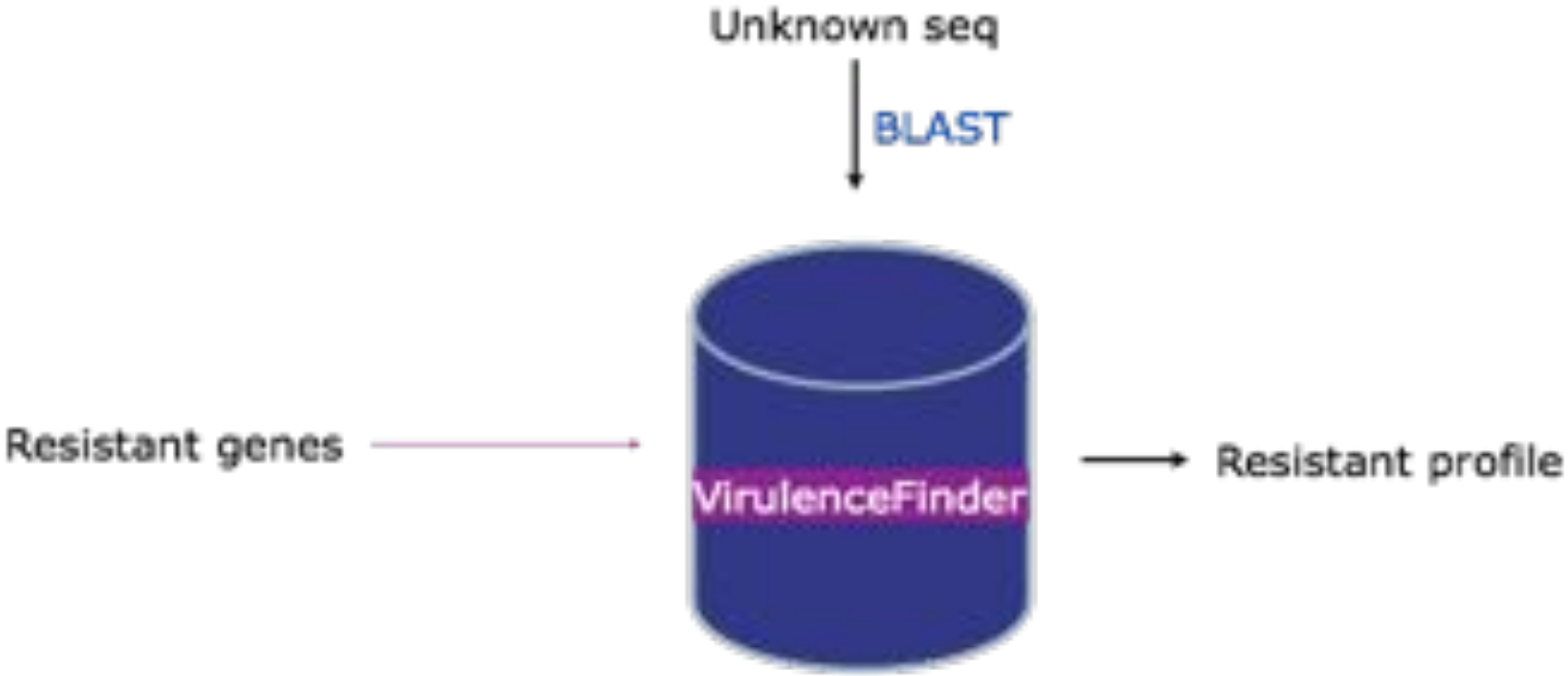
The virulence of pathogenic microorganisms is associated with

- adherence
- invasiveness
- capsule production
- toxin production
- aggressiveness
- interferrence with the immune system

https://cge.cbs.dtu.dk/services/VirulenceFinder/



Virulence Finder – How does it work



VirulenceFinder-1.5 Server - Results

SETTINGS:
Selected %ID threshold: *90.00*

Virulence genes for Escherichia coli						
Virulence factor	**%Identity**	**Query/HSP length**	**Contig**	**Position in contig**	**Protein function**	**Accession number**
agg3B	100.00	441 / 441	Supercontig_1.9	12444..12884	AAF/III minor adhesin. Enterobacteria AfaD invasin protein	AF411067
iha	100.00	2091 / 2091	Supercontig_1.1	12778..14868	Adherence protein	CP003288
agg3A	100.00	501 / 501	Supercontig_1.9	13059..13559	AAF/III major fimbrial subunit	HE603111
sigA	100.00	3858 / 3858	Supercontig_1.2	13971..17828	Shigella IgA-like protease homologue	AE005674
astA	100.00	117 / 117	Supercontig_1.9	14203..14319	EAST-1 heat-stable toxin	AF411067
stx2A	100.00	960 / 960	Supercontig_1.2	1501200..1502159	Shiga toxin 2, subunit A, variant a	AY143336
stx2B	100.00	270 / 270	Supercontig_1.2	1502171..1502440	Shiga toxin 2, subunit B, variant a	AE005174
ORF3	100.00	1029 / 1029	Supercontig_1.9	15211..16239	Isoprenoid Biosynthesis	CU928159
ORF4	99.81	540 / 540	Supercontig_1.9	16243..16782	Putative isopentenyl-diphosphate delta-isomerase	AFRH01000026
aggR	100.00	798 / 798	Supercontig_1.9	19214..20011	AraC transcriptional activator	55989
capU	100.00	1089 / 1089	Supercontig_1.2	201326..202414	Hexosyltransferase homolog	CU928145
gad	100.00	1401 / 1401	Supercontig_1.2	2050426..2051826	Glutamate decarboxylase	CP003297
aap	100.00	351 / 351	Supercontig_1.9	20851..21201	Dispersin, antiaggregation protein	Z32523
aar	100.00	201 / 201	Supercontig_1.9	21932..22132	AggR-activated regulator	SSI_AA784

Questions?