Microbial Pathogenicity and Diseases

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Lec. ٢

Prevention of Host Defenses

- **Prevention of Host Defenses:-**

- Some pathogenic bacteria are inherently able to resist the bactericidal components of host tissues. For example, the poly-D-glutamate capsule of Bacillus anthracis protects the organisms against cell lysis by cationic proteins in sera or in phagocytes. The outer membrane of Gram-negative bacteria is a formidable permeability barrier that is not easily penetrated by hydrophobic compounds such as bile salts which are harmful to the bacteria. Pathogenic mycobacteria have a waxy cell wall that resists attack or digestion by most tissue bactericides. And intact lipopolysaccharides (LPS) of Gram-negative pathogens may protect the cells from complement-mediated lysis or the action of lysozyme.

Enzymes (exoenzymes):- The microbes produce many enzymes to prevent host defenses are-

Coagulases: clot fibrin in blood to create protective barrier against host defenses.

Kinases: dissolve clots (fibrinolysis) to allow escape from isolated wounds e.g.Streptokinase (*Streptococcus pyogenes*) Staphylokinase (*Staphylococcus aureus*)

Hyaluronidase: Hydrolyzes hyaluronic acid (‘glue’ that holds together connective tissues and epithelium barriers) allowing deeper invasion e.g. *Clostridium* species: allows them to cause gangrene (tissue necrosis).

Collagenase: breaks down collagen (fibrous part of connective tissue) for invasion into muscles and organs e.g. Clostridium species

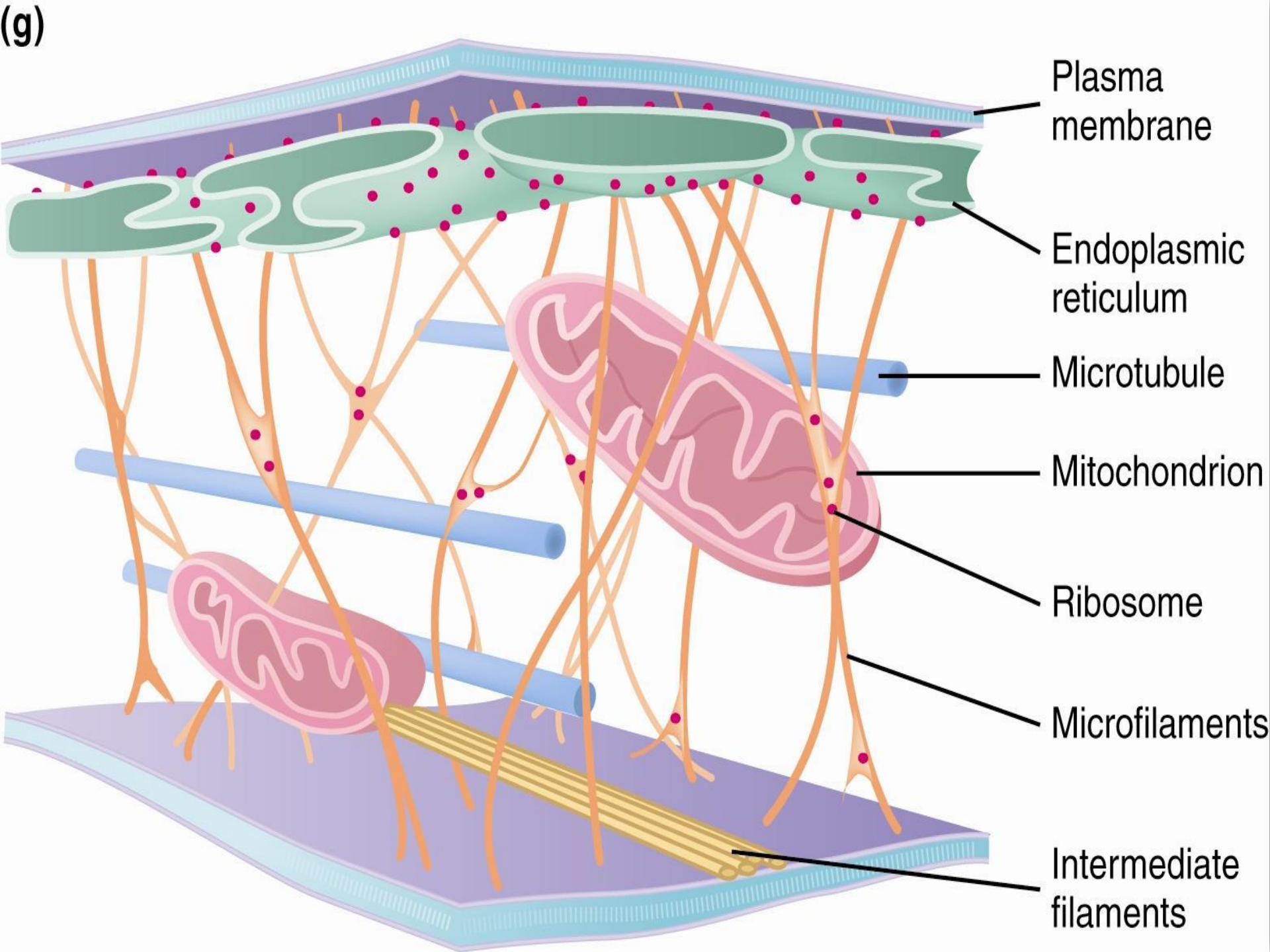
IgA proteases: destroy host IgA antibodies found in mucous secretions to allow adherence and passage at mucus membranes e.g. Neisseria species that infect CNS.

Antigenic Variation

There are many pathogens which alter its surface antigens to escape attack by antibodies and immune cells e.g. *Neisseria gonorrhoeae* has many variety of Opa gene, which can alter one is being expressed e.g. influenza virus constant genetic recombination between flu viruses always new spike proteins.

Penetration into Host Cytoskeleton

Many a time the pathogen penetrates into host cytoskeleton and use actin of host cell to penetrate and move within the cells of host. The invasins a surface proteins produced by bacteria to control actin e.g. *Salmonella rearrange* actin to cause the cell membrane to wrap around the microbe and take it into the cell (endocytosis) allows *Salmonella* to penetrate intestinal epithelium e.g. *Shigella* and *Listeria* trigger endocytosis.


(g)
Plasma membrane
Endoplasmic reticulum
Microtubule
Mitochondrion
Ribosome
Microfilaments
Intermediate filaments

Damage to Host Cells-

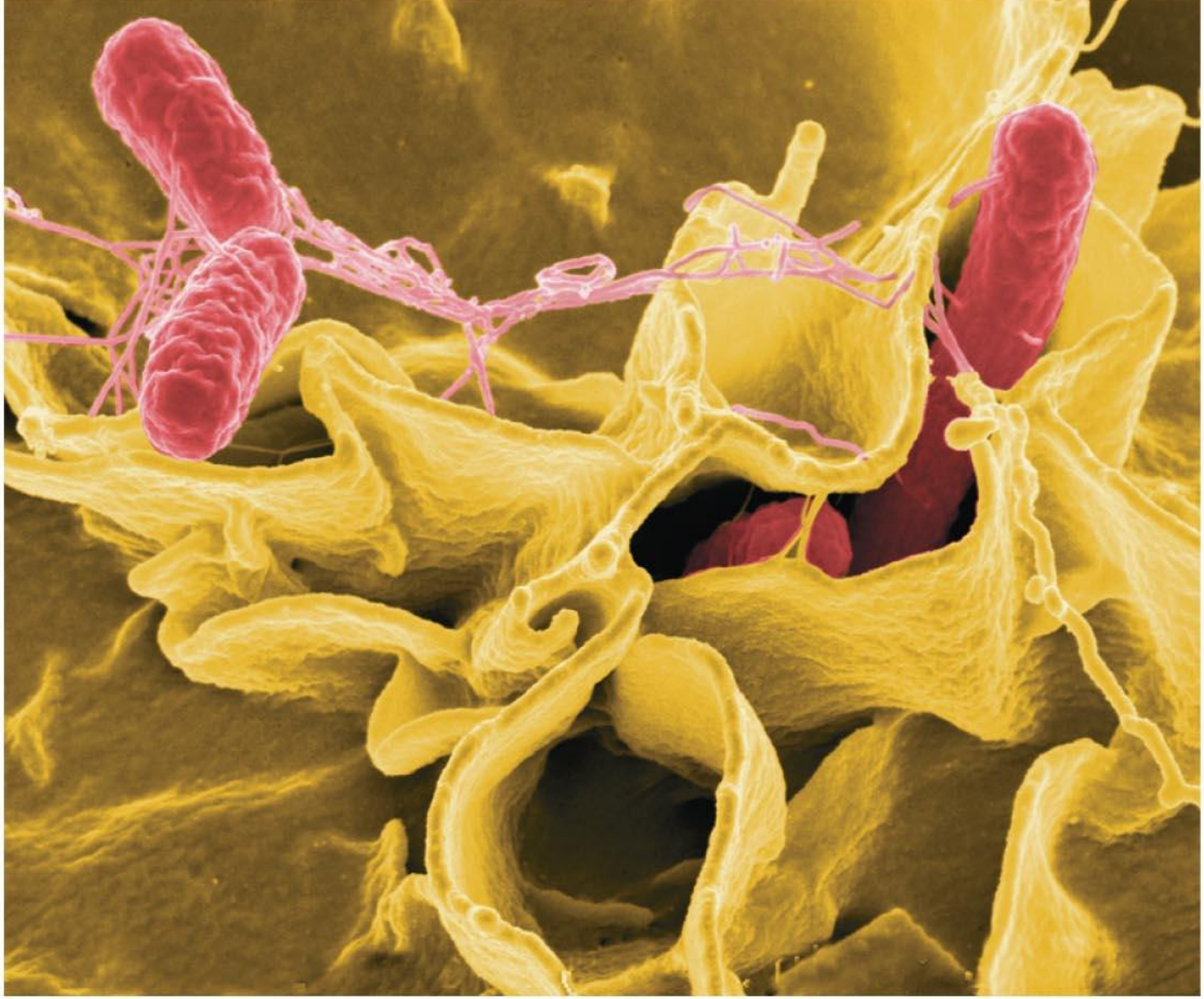
The damages to the host cell can be direct or indirect. The direct damages are: -

Tissue damage, cell components and metabolic by-products, toxins and enzymes.

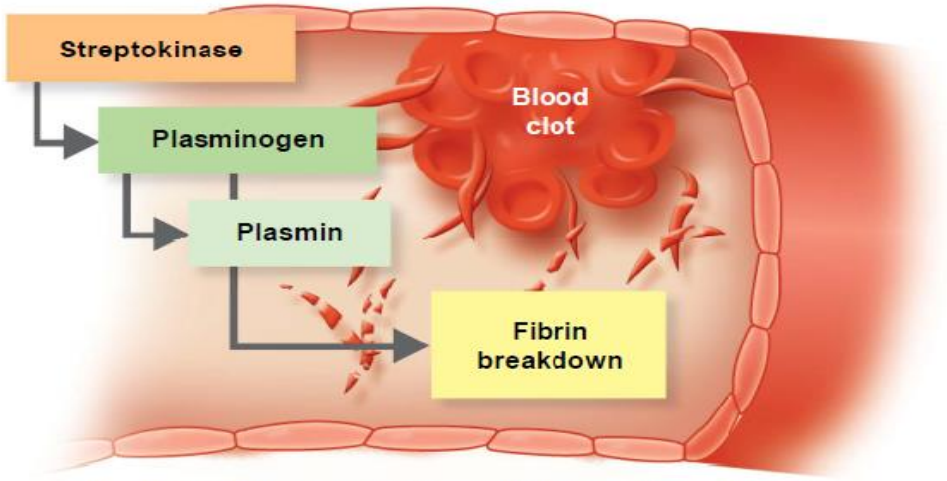
Organ necrosis: - Sum of morphological changes indicative of cell death and caused by the progressive degradative action of cellular components, metabolic by-products, enzymes and/or toxins.

Metabolic Effects: Pathogenic organisms can affect any of the body systems with disruptions in metabolic processes.

Indirect Damage: Damage to host from excessive or chronic immune response (immunopathogenesis).

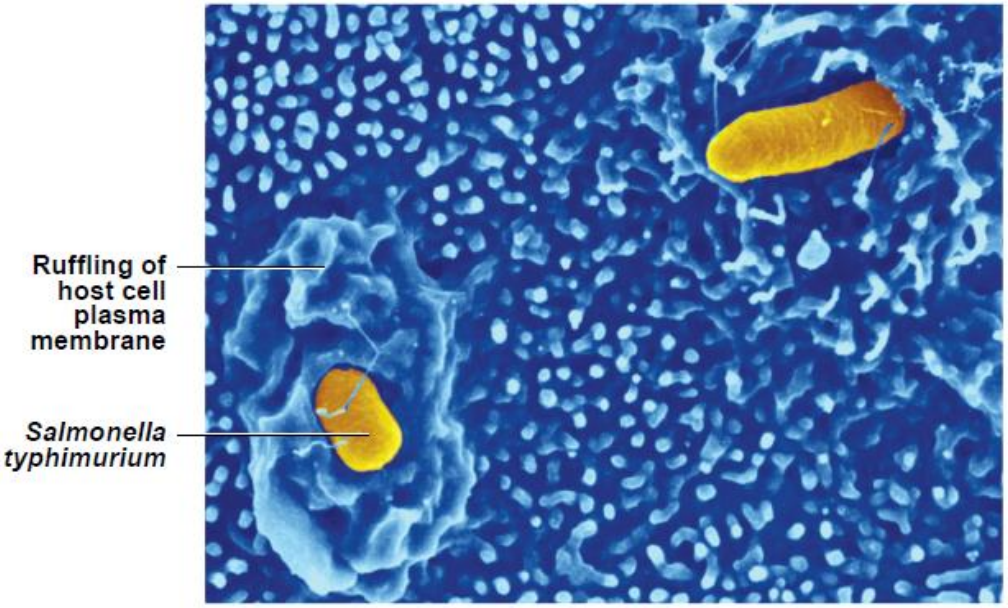

SEM
1.5 μm

Mechanism of streptokinase



Streptokinase breaks down plasminogen (precursor to plasmin) to produce plasmin – an enzyme which breaks apart blood clots

Salmonella entering intestinal epithelial cells as a result of ruffling.



Production of Toxins

Toxins are poisonous substance produced by microbes tend to cause widespread damage/disease in host may be necessary for virulence

Toxins- •Toxin Substances that contribute to pathogenicity

•Fatel, fever, cardiovascular disturbance, diarrhea, shock, inhibit protein synthesis, destroy blood cells, blood vessels, causing spasms

•Toxigenicity Ability to produce a toxin

•Toxemia Presence of toxin the host's blood

•Toxoid Inactivated toxin used in a vaccine

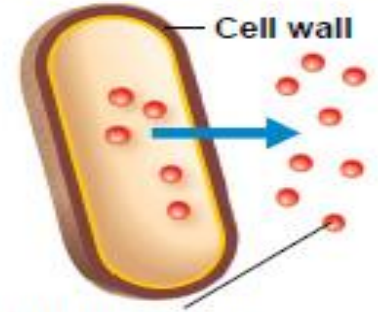
•Antitoxin Antibodies against a specific toxin by Toxoid.

- **There are two types of toxins produced by bacteria.**

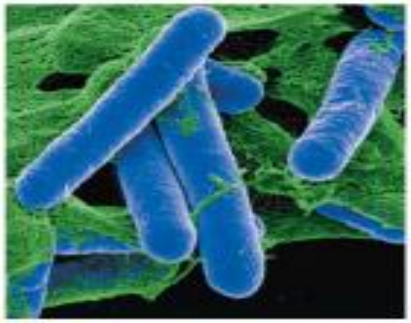
Exotoxins and Endotoxins Mechanisms of Action

exotoxins

Exotoxins are proteins produced inside pathogenic bacteria, most commonly gram-positive bacteria, as part of their growth and metabolism. The exotoxins are then secreted into the surrounding medium during log phase.



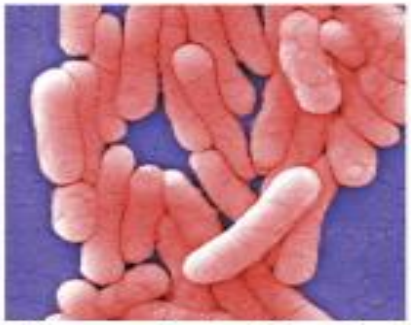
Exotoxin: toxic substances released outside the cell



Clostridium botulinum, an example of a gram-positive bacterium that produces exotoxins

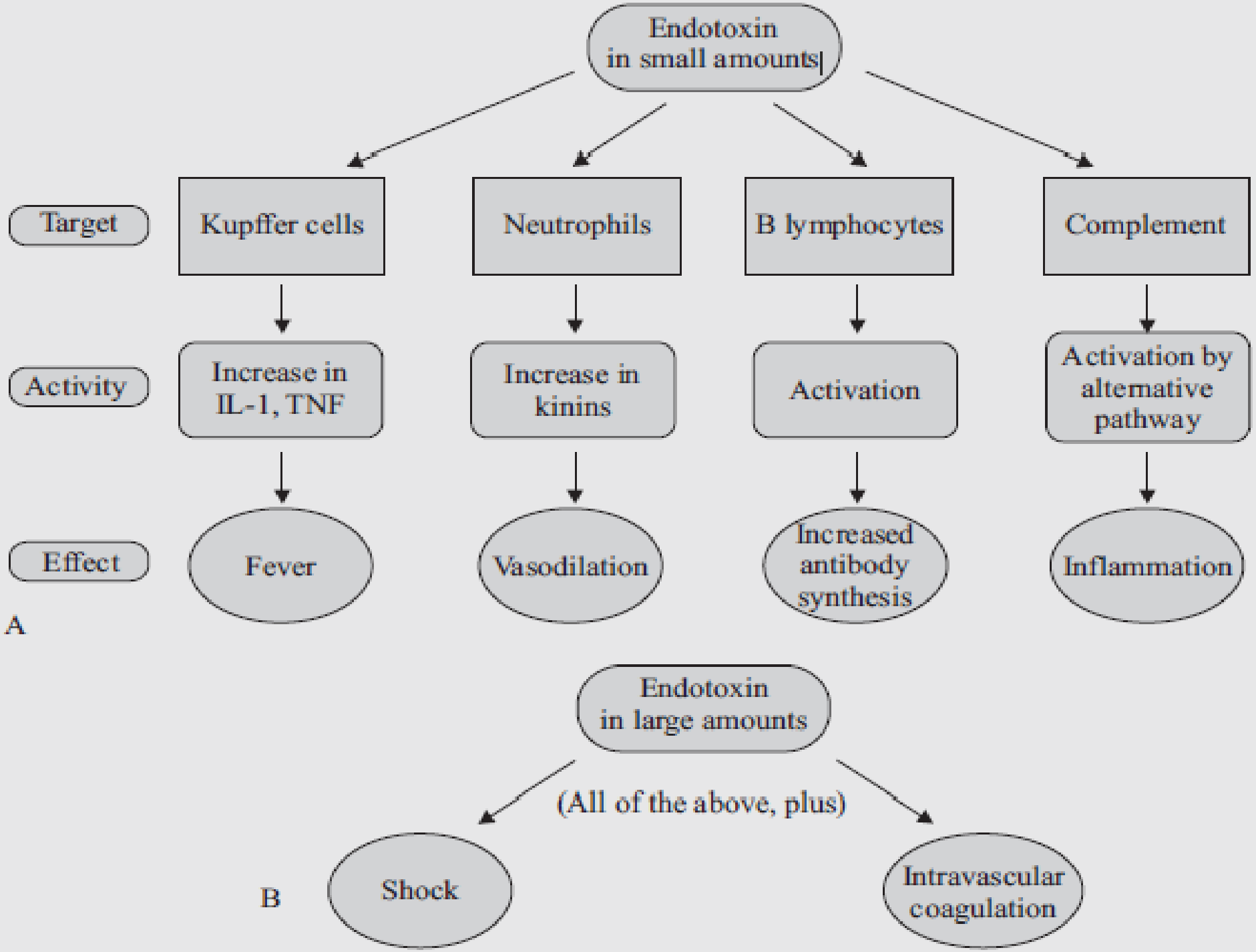
endotoxins

Endotoxins are the lipid portions of lipopolysaccharides (LPS) that are part of the outer membrane of the cell wall of gram-negative bacteria (lipid A; see Figure 4.13c). The endotoxins are liberated when the bacteria die and the cell wall breaks apart.



Salmonella typhimurium, an example of a gram-negative bacterium that produces endotoxins

Endotoxins: toxins composed of lipids that are part of the cell membrane


Endotoxin in small amounts
Target
Kupffer cells
Neutrophils
B lymphocytes
Complement
Activity
Increase in IL-1, TNF
Increase in kinins
Activation
Activation by alternative pathway
Effect
Fever
Vasodilation
Increased antibody synthesis
Inflammation
A
Endotoxin in large amounts
(All of the above, plus)
B
Shock
Intravascular coagulation

Pathogenic Properties of Virus

Viruses have mechanisms to evade host defenses viruses grow inside host cells to hide from immune defense.

Kill immune cells e.g. HIV – TH Cells.

Cytopathic effects: - The visible effects of viral infection on host cell. Some effects will kill the cell and some will just change the cells.

Viruses stop DNA, RNA and/or protein synthesis e.g. Herpes virus block mitosis.

Lysosomal autolysis of host cells e.g. Influenza: bronchiolar epithelium.

Production of inclusion bodies (visible viral parts inside the cell) can identify a particular virus e.g. Rabies virus: Negri bodies.

Syncytium formation (neighboring cells fuse together) e.g. Varicella Zoster virus.

Change in cell function e.g. Measles, production of interferons by host cell (triggers host immune response), induce antigenic changes on host cell surface (triggers destruction of infected cell by host immune response).

Induce chromosomal changes, cell transformation: may activate or deliver oncogenes resulting in loss of contact inhibition (cancer) e.g. *Papilloma* virus.

Eukaryotic Pathogens

Fungi

They produce toxins causing allergies or disease e.g. -chronic sinusitis (black molds).

Stachybotrys: headaches, vomiting, mental disturbance.

Invasive systemic mycosis in immune compromised patients e.g. *Candida.*

Mushrooms: mycotoxins may be hallucinogenic or deadly.

Protozoa:

They can grow inside host cells causing lysis e.g. Malaria (*Plasmodium*)

They use host cells as food source and produce wastes that cause disease.

Algae: - It produces neurotoxin substances e.g. shellfish poisoning a causative microbe and a disease.

Steps involved in the pathogenesis of the bacteria:

١. Transmission ٢. Colonization ٣. Adhesion ٤. Invasion ٥. Survival in the host ٦. Tissue Injury

number of pathogenic bacteria, however, adherence to the mucosal surface represents only the first stage of the invasion of tissues. Examples of organisms that are able to invade and survive within host cells include *Mycobacteria*, *Salmonella, Shigella* and others. The initial phase of cellular invasion involves penetration of the mammalian cell membrane and many intracellular pathogens use normal phagocytic entry mechanisms to gain access. Inside the cell, they become surrounded by host cell-derived membrane vesicles. Many intracellular pathogens escape from these vesicles into the cell cytoplasm where they multiply rapidly before spreading to adjacent cells and repeating the process of invasion. The availability of specific receptors on host cells defines the type of host cells.

Virulence determinants

Both primary and opportunistic pathogens possess **virulence determinants or aggressins** that **facilitate pathogenesis**. Possession of a single virulence determinant is rarely sufficient to allow the initiation of infection and production of pathology. Many bacteria possess several virulence determinants, all of which play some part at various stages of the disease process. In addition, not all strains of a particular bacterial species are equally pathogenic. For example, although six separate serotypes of encapsulated *Haemophilus influenzae* are recognized, serious infection is almost exclusively associated with isolates of serotype b (hence Hib vaccine). Moreover, even within serotype b isolates, ٨٠% of serious infections are caused by six out of > ١٠٠ clonal types.

Different strains of a pathogenic species may cause distinct types of infection, each associated with possession of a particular complement of virulence determinants. Different strains of *E. coli,* for example, cause several distinct gastrointestinal diseases, urinary tract infections, septicemia, meningitis and arange of other minor infections.

Many pathogens produce an impressive armoury of virulence determinants; however, their **expression is coordinated or regulated** by several nutritionaland environmental factors. Among virulence regulators are the availability of Nutrition (e.g. iron), oxygen, suitable temperature or other growth requirements. Importantly, differences in virulence between similar organisms may be due to additional cryptic phenotypic or genotypic variations. For example, some virulence factors are only expressed when indirect contact with host cells.

Virulence genes can move between bacteria via special genetic vehicles e.g. plasmids, bacteriophage and transposons. The horizontally transferred virulence factors (e.g. toxins) may or may not transform the recipient bacteria into betteradapted or more virulent pathogens.

SURVIVAL IN THE HOST

- Many bacterial pathogens are able to resist the cytotoxic action of plasma and other body fluids involving antibody and complement (classical pathway) or complement alone (alternate pathway) or lysozyme. Killing of extracellular pathogens largely occurs within phagocytes after opsonization (by antibody and/ or complement) and phagocytosis. Circumvention of phagocytosis by extracellular pathogens is thus a major survival mechanism. Capsules (many pathogens), protein A (*S. aureus*) and M protein (*S. pyogenes*) function in this regard.

End