Microbial Mechanisms of Pathogenicity

I. Entry of a Microorganism into The Host

A. Portals of Entry (Table 1).

1-.Mucous Membranes

.a) Conjunctiva, respiratory, gastrointestinal, and genitourinary tracts

b) Important way is by inhaling droplets of moisture that contain

.microorganisms. Ex.: TB. Respiratory tract very common portal

c) Food, water, and contaminated fingers can introduce microorganisms via gastrointestinal tract

d) Most organisms introduced via the genitourinary tract are done so

.via sexual contact

2-Skin

a) Since most organisms cannot penetrate the skin they do so via cut

bites, injections, surgery, hair follicles, or some fungi can infect the

.skin itself

b) When microorganisms are introduced through the skin it is called

.parenteral route

B. Preferred Portal of Entry - Have to be able to survive and multiply even if are introduced. Example: *Salmonella typhi*

.C. Numbers of Invading Microbes- Need to have a certain dose

Example: Shigella

D. Adherence (Figure .1)

Surface projections on a pathogen called adhesins (ligands) adhere to .

1-complementary receptors on the host cells. Examples

a) *Streptococcus mutans* - Attached to the surface of teeth by

glycocalyx – Forms a biofilm that causes tooth decay.

b) *Treponema pallidum* - Uses tapered end as a hook to attach to host cells - Causes syphilis

c) *Neisseria gonorrhoeae* - Has fimbriae containing adhesins that permit attachment to certain cells in genitourinary tract - Causes .gonorrhea

II. How Bacterial Pathogens Penetrate Host Defenses

A. Capsules

1-Prevent them from being phagocytized, however antibodies can be made by host to capsules which could then be phagocytized :Examples

a*) Klebsiella pneumoniae* - Causes pneumonia

b) *Hemophilus influenza* - Causes pneumonia and meningitis

c) *Streptococcus pneumoniae* - Causes pneumonia

B. Components of the Cell Wall

:1-Proteins facilitate adherence or prevent phagocytosis. Examples .

a) *Streptococcus pyogenes* - M protein - Increases virulence by initiating attachment to epithelial cells

b) *Mycobacterium tuberculosis* - Has a waxy cell wall, so resists .digestion by phagocytes

C. Enzymes

1-Substances that break cells open, dissolve materials between cells, form :or dissolve blood clots, and other functions. Examples

a) Coagulase - Clot the fibrinogen in blood. - Protects the bacterium

from phagocytosis and other host defenses. *Staphylococcus aureus.* Actually report out organisms as coagulase positive or coagulase negative .Staph

b) Hyaluronidase - Hydrolyzes a type of polysaccharide that holds certain cells, particularly connective tissue, together. Responsible for tissue blackening in wound infections. E.g., Strep and Costridium

c) Collagenase - Also breaks down connective tissue, attacks collagen Clostridium perfringens cause of gas gangrene, does this. Allows .bacterium to spread

III. How Bacterial Pathogens Damage Host Cells

A. Direct Damage by Toxins. Two main types: exotoxins and endotoxins. Fig .4

1-Exotoxins - Proteins (mainly enzymatic) that are poisonous that destroy part of the cell (esp. cell membrane- 40%) or inhibit certain metabolic functions (e.g., protein synthesis). Some are the most lethal substances known. Diseases are causes by very minute amounts. Most carried on plasmids or phages. Table .2

a) Cytotoxins - Affect cells

1-Diphtheria Toxin fig.5 - Corynebacterium diphtheria Inhibits protein synthesis in eukaryotes

2-Erythrogenic Toxins - Produced by Streptococcus pyogenes causing scarlet fever. Damage blood capillary plasma membranes under the skin .and produce a red rash.

b) Neurotoxins - Affect nerve cells

1-Botulism Toxin - *Clostridium botulinum* - Acts at neuromuscular junction and prevents transmission of impulses. Causes paralysis in which muscle tone is lacking

2-Tetanus Toxin - *Clostridium tetani* - Reaches central nervous system and binds to nerve cells that control the inhibition of contraction skeletal muscles. Result is uncontrollable muscle contraction

c- Enterotoxins - Affect lining of gastrointestinal tract

1-Vibrio Enterotoxin - *Vibrio cholerae* - Binds to plasma membranes of epithelial cells in small intestine leading to massive fluid and electrolyte loss. Normal muscular contractions are disturbed, leading to severe diarrhea accompanied by vomiting

2-Staphylococcal Enterotoxin - *Staphylococcus aureus*

Affects intestines like vibrio. Also produces another type associated with toxic shock syndrome

d) Membrane Disrupting Toxins

1-Leukocidins - Destroy neutrophils and macrophages Produced by *staphylococci* and *streptococci*

2-Hemolysins - Lyse red blood cells. *Clostridium perfringens* and streptococci

2-**Endotoxins**: lipopolysaccharides (LPS) in cell wall, lipid A portion .

a) Are actually part of the outer portion (lipopolysaccharide) of the

cell wall of gram-negative bacteria. Figure.4b. Exert effect when bacteria die and substances are liberated.

b) All gram-negative endotoxin produce the same symptoms

1-Fever and chills by IL1 release by macrophage (Fig)

2-Stimulate macrophage to release cytokines with symptoms of weakness, generalized aches, clot formation with DIC, and in some cases shock with low BP (TNF damages capillaries) and even death

c) See table .3 for exotoxin and endotoxin comparison

B. Plasmids, Lysogeny, and Pathogenicity

1-Plasmids: Small, circular, double-stranded DNA molecules that are . not connected to the main bacterial chromosome. These molecules are

‹responsible for resistance of some organisms to antibiotics, toxins capsules, and fimbriae - all factors in pathogenicity. (Can pass on resistance to other organisms. Becoming very important in emerging (diseases

2-Bacteriophages inserted into the bacteria change the properties of the cell. New factors such as toxins or capsules can be coded for by the virus's DNA. Ex: diphtheria, staph enterotoxin, botulism, Strep .pneumo .capsule

VI Pathogenic Properties of Nonbacterial Microorganisms

A. Viruses

1-Viral Mechanisms for Evading Host Defenses .

a) Can grow inside cell where immune system can't reach

b) Gain entrance to cell because they have attachment site for receptors on the cell surface

(1)HIV actually attacks the immune system T cells via CD4 receptors

2-Cytopathic Effects (CPE) of Viruses - Table.4 .

a) Stopping of mitosis, lysosome lysis, formation of inclusion bodies aid in ID), cell fusion (syncytium), antigenic changes (triggers) ‹(immune response), chromosomal changes (oncogene, breakage .(and transformation (loss of contact inhibition)

B. Fungi, Protozoa, and Helminths

1-Fungi .

a) Capsules

1-*Cryptococcus neoformans* - India Ink prep to see capsule. Causes meningitis - Capsule resists phagocytosis

b) Proteases

1-*Candida albicans* and *Trichophyton* secrete proteases that allow them to modify host cell membranes so they can attach

c) Toxins: aflatoxin (mutagen), ergot (resembles LSD), amantin

(death angel)

2-Protozoa .

a) Examples

(1):*Plasmodium* - Causes malaria - Invades host cells and reproduces, causes them to rupture

(2):*Toxoplasma* - Enters phagocytic cells and actually growing the phagocytic vacuole

(3):*Giardia lamblia* - Attach to host cells and digest the cells and tissue fluids

(4):*Giardia lamblia* and *Trypanosoma* - Evasion of
immune system. Change surface antigens while growing in the host so the host's antibodies don't kill them

3-**Helminths**

a) *Wucheria bancrofti* - Parasite blocks lymphatic circulation leading

to accumulation of lymph and eventually grotesque swelling of legs

and other body parts (elephantiasis).

.. **Summary of Microbial Mechanisms of Pathogenicity** fig .9