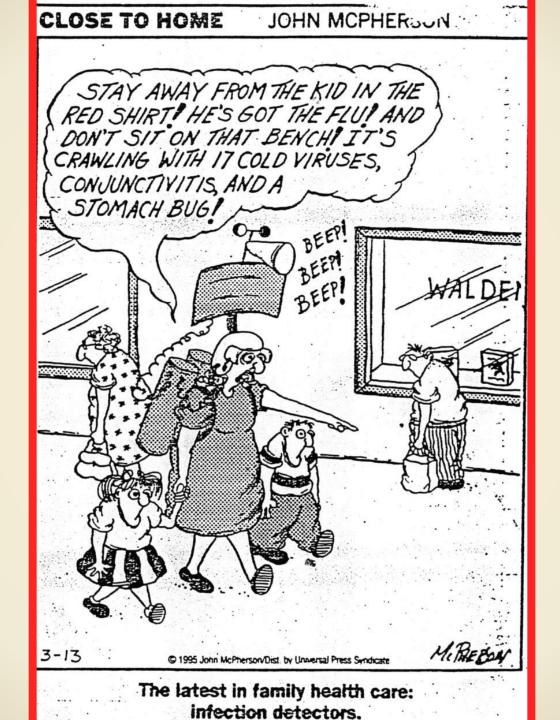
HOST-PARASITE INTERACTIONS

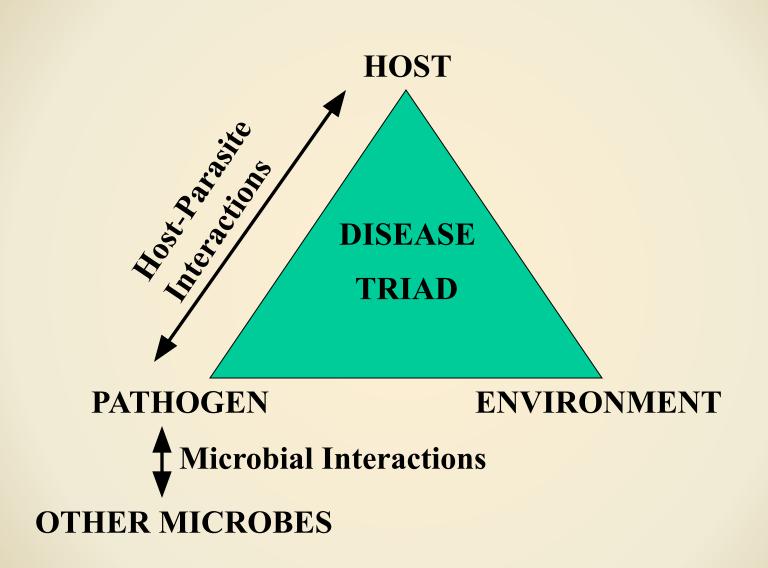


ECOLOGICAL RELATIONSHIPS

Microbial Interactions

Host-Parasite Interactions

Environment



ECOLOGICAL RELATIONSHIPS

SYMBIOSIS: neutral, antagonistic or synergistic relationship between two dissimilar organisms (SYMBIOTES, SYMBIONTS) living in close association with each other;

MUTUALISM (+/+): mutually beneficial relationship between two species

COMMENSALISM (+/0): relationship between two species in which one is benefited and the other is not affected, neither negatively nor positively

PARASITISM (+/-): relationship between two species in which one benefits (**parasite**) from the other (**host**); usually involves detriment to the host

BASIC ECOLOGICAL DEFINITIONS

FLORA; **MICROBIOTA** (Microbiology Definition): microorganisms present in or characteristic of a special location (**FLORA** generically refers to plants; **FAUNA** generically refers to animals)

INDIGENOUS (Resident) MICROBIOTA: microbial flora typically occupying a particular niche; given diversity of environmental conditions, organisms tend to segregate

TRANSIENT FLORA: microbial flora only temporarily occupying a given niche

NICHE (ecological niche): the place of an organism within its community (ecosystem); unique position occupied by a particular species, perceived in terms of actual physical space occupied & function performed within ecosystem

NATURAL MICROBIAL HABITATS

Soil

Water

Air

Animals and Animal Products

MICROBIAL FLORA OF THE NORMAL HUMAN BODY (a.k.a., normal flora)

SKIN RESPIRATORY TRACT

Nose and Nasopharynx; Mouth and Oropharynx EYE (Conjunctivae) and OUTER EAR INTESTINAL TRACT

Stomach and Small Intestine; Large Intestine;
Intestinal Tract of Newborn
Antibiotic Alteration of Flora
Significance of Intestinal Flora

GENITOURINARY TRACT

External Genitalia & Anterior Urethra Vagina BLOOD and TISSUES

NORMALLY STERILE SITES IN THE HUMAN BODY

Colonization of one of these sites generally involves a defect or breach in the natural defenses that creates a portal of entry

Brain; Central nervous system
Blood; Tissues; Organ systems
Sinuses; Inner and Middle Ear
Lower Respiratory Tract: Larynx; Trachea; Bronchioles (bronchi); Lungs; Alveoli
Kidneys; Ureters; Urinary Bladder; Posterior Urethra
Uterus; Endometrium (Inner mucous membrane of uterus); Fallopian Tubes; Cervix and Endocervix

FACTORS CONTROLLING GROWTH OF MICROORGANISMS

1. **NUTRIENT AVAILABILITY:** the accessibility of a necessary resource, substance or compound providing nourishment to maintain life, i.e. capable of conversion to energy and structural building blocks

Fastidious: an organism that has complex nutritional or cultural requirements, making isolation and culture more difficult

MAJOR ESSENTIAL ELEMENTS:

C, O, H, N, S, P, K, Mg, Ca, Fe, Na, Cl **MINOR ESSENTIAL ELEMENTS:** Zn, Mn, Mo, Se, Co, Cu, Ni, W 2. PHYSICO/ENVIRONMENTAL PARAMETERS: WATER ACTIVITY/OSMOTIC PRESSURE:

> Water activity (a_w): represents the available water Osmotic pressure (p): expressed in atmospheres; reflects the concentration of solute in an aqueous solution

OXYGEN: metabolic oxygen requirements; OBLIGATE or FACULTATIVE, ANAEROBIC or AEROBIC, or in between, (MICROAEROPHILIC)

pH: power of hydrogen; a measurement of the amount of hydrogen ion in solution; the logarithm of the reciprocal of the hydrogen ion concentration in an aqueous solution used to express its acidity or alkalinity (0-14)

TEMPERATURE:

Psycrophile (psychrophilic): liking cold temperatures; Optimal growth at 15° to 20°C
Mesophile (mesophilic): liking moderate temperatures; Optimal growth at 20° to 45°C
Thermophile (thermophilic): liking elevated temperatures; Optimal growth at 50° to 70°C

FACTORS CONTROLLING GROWTH OF ORGANISMS (cont.):

3. **COMPETITION:** the simultaneous demand by two or more organisms or species for a necessary, common resource or physical space that is in limited or potentially limited supply, resulting in a struggle for survival

4. **HOST IMMUNE SYSTEM:** the cells and tissues involved in recognizing and attacking foreign substances in the body

ACQUIRING INFECTIOUS AGENTS

PORTAL OF ENTRY/EXIT

INGESTION

INHALATION

DIRECT PENETRATION

Trauma or Surgical Procedure Needlestick Arthropod Bite Sexual Transmission

Transplacental

ACQUIRING INFECTIOUS AGENTS (cont.)

COLONIZATION: the successful occupation of a new habitat by a species not normally found in this niche Adherence (attachment): close association of bacterial cells and host cells generally characterized by receptors on target sites

Adhesin: structure or macromolecule located on the surface of a cell or extracellularly that facilitates adherence of a cell to a surface or to another cell; site of attachment is often a specific receptor and host cell receptors are often sugar moieties (lectin), but the adherence may also be nonspecific

ACQUIRING INFECTIOUS AGENTS (cont.)

INVASION: the entry and spread throughout the cells and/or tissues of the host; specific recognition of receptor sites on target cells enhances pathogenic advantage Invasins (invasive factors): structures or macromolecules that facilitate invasion by a pathogenic microorganism

MULTIPLICATION: the ability of a microorganism to reproduce during an infection; influenced by underlying disease, immunologic status, antibiotic treatment, nutrient availability

TRANSMISSION OF DISEASE

ENTRANCE, COLONIZATION, PENETRATION:

Dependent upon Age, Sex, Nutrition, Immunologic State and General Health of Host, and Bacterial Virulence Factors

VECTOR: a carrier, especially the animal that transfers an infectious agent from one host to another, usually an **ARTHROPOD**

CARRIER (Carrier State): symptomless individual who is host to a pathogenic microorganim with the potential to pass the pathogen to others

NOSOCOMIAL INFECTIONS: an infection acquired in a hospital setting that was not present in the host prior to admission, generally occurring within 72 hours of admission

NOSOCOMIAL INFECTIONS in ACUTE CARE INSTITUTIONS

Infection <u>Site</u>	Percentage of All Nosocomial Infections	Most Common Agents
Urinary Tract	40%	Escherichia coli, Enterococcus, Proteus, Klebsiella, Pseudomonas aeruginosa
Surgical Wound	20%	Staphylococcus aureus, Staphylococcus epidermidis, E. coli
Pulmonary	10%	Klebsiella, Pseudomonas, E. coli, S. aureus
Primary Bacteremia	5% - 10%	<i>S. aureus</i> , <i>S. epidermidis</i> , Gram-negative rods
Others	20% - 25%	S. aureus, E. coli

EPIDEMIOLOGY

EPIDEMIC: disease occuring suddenly in numbers clearly in access of normal expectancy

ENDEMIC: disease present or usually prevalent in a population or geographic area at all times

PANDEMIC: a widespread epidemic distributed or occuring widely throughout a region, country, continent, or globally

Emerging Infectious Diseases

- New diseases and diseases with increasing incidences are called emerging infectious diseases (EIDs).
- EIDs can result from the use of antibiotics and pesticides, climatic changes, travel, the lack of vaccination, and insufficient case reporting.
- The CDC, NIH, and WHO are responsible for surveillance and responses to emerging infectious diseases.

Tuberculosis SARS [*]		Venezuelan Equine
Encephalitis		
Hepatitis C	AIDS	Enterohemorrhagic <i>E.</i>
Coli		
Malaria	Lassa Fever	S.American Hemorrhagic
Fevers		
Influenza		Hantavirus

PATHOGENICITY vs. VIRULENCE

PATHOGENICITY: the quality of **producing disease** or the ability to produce pathologic changes or disease

VIRULENCE: a measure of pathogenicity; a measurement of the degree of disease-producing ability of a microorganism as indicated by the severity of the disease produced; commonly ascertained by measuring the **dosage** required to caused a specific degree of pathogenicity; one general standard is the LD_{50} (lethal dose 50%)

PATHOGENICITY vs. VIRULENCE (Definitons)

DOSAGE: the number of pathogenic microorganisms entering the host

LD₅₀ = the number of microorganisms required to cause lethality (death) in 50% of the test host

TRUE PATHOGEN: any microorganism capable of causing disease; an infecting agent

OPPORTUNISTIC PATHOGEN: a usually harmless microorganism that becomes pathogenic under favorable conditions causing an **opportunistic infection**

INFECTION vs. DISEASE

INFECTION: the **colonization** and/or **invasion** and **multiplication** of pathogenic microrganisms in the host with or without the manifestation of **disease**

DISEASE: an **abnormal condition** of body function(s) or structure that is considered to be harmful to the affected individual (host); any deviation from or interruption of the normal structure or function of any part, organ, or system of the body

INFECTION vs. DISEASE (Definitons)

BENIGN: a non-life or non-health threating condition

MALIGNANT: a disease tending to become progressively worse (**MORBIDITY** = illness) and potentially result in death (**MORTALITY** = death)

CONTAGIOUS: capable of being transmitted from one host to another; **communicable**; **infectious**

INFECTIOUS DOSE: number of pathogenic organisms required to cause disease in a given host

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Four criteria that were established by Robert Koch to identify the causative agent of a particular disease, these include:

1. the microorganism (pathogen) must be **present** in all cases of the disease

2. the pathogen can be **isolated** from the diseased host **and grown in pure culture**

3. the pathogen from the pure culture must cause the **same disease when inoculated** into a healthy, susceptible laboratory animal

4. the pathogen must be **reisolated** from the new host and **shown to be the same** as the originally inoculated pathogen

Bacterial Virulence Mechanisms Adherence (Colonization) Invasion **Degradative enzymes Exotoxins** Endotoxin Induction of excess inflammation Evasion of phagocytic & immune clearance Byproducts of growth (gas, acid) Superantigen Resistance to antibiotics

MICROBIAL PATHOGENICITY VIRULENCE FACTORS

COLONIZATION FACTORS: specific recognition of

receptor sites on target cells enhances pathogenic advantage

1. CAPSULE: nonspecific attachment

2. SURFACE RECEPTORS/TARGET SITES:

Receptors on both bacteria (adhesins) and host (target)

Examples include:

i) fimbriae (formerly known as pili) of *Enterobacteriaceae*ii) *Chlamydia* binds host N-acetyl-D-glucosamine which is a cell surface lectin (polysaccharide target receptor)
iii) Protein adhesin of *Mycoplasma* located in specialized
tip structure; adheres to sialic acid-containing cell receptors

MICROBIAL PATHOGEN

Staphylococcus aureus Staphylococcus spp. Group A Streptococcus Streptococcus pneumoniae Escherichia coli

Other Enterobacteriaceae Neisseria gonorrhoeae Treponema pallidum Chlamydia spp. Mycoplasma pneumoniae Vibrio cholerae **ADHESIN**

RECEPTOR

Lipoteichoic acid Unknown Slime layer Unknown LTA-M protein complex Fibronectin N-acetylhexosamine-gal Protein Type 1 fimbriae D-Mannose CFA 1 fimbriae GM ganglioside P blood grp glycolipid P fimbriae D-Mannose Type 1 fimbriae Fimbriae GD₁ ganglioside P₁, P₂, P₃ Fibronectin Cell surface lectin N-acetylglucosamine Protein P1 Sialic acid Type 4 pili Fucose and mannose

VIRULENCE FACTORS (cont.)

INVASIVE FACTORS (invasins): enable a pathogenic microorganism to enter and spread throughout the tissues of the host body; specific recognition of receptor sites on target cells enhances pathogenic advantage

DEGRADATIVE ENZYMES: a class of protein capable of catalytic reactions; bacterial and host enzymes both play roles in the disease process

VIRULENCE FACTORS (cont.)

TOXIGENICITY: the ability of a microorganism to cause disease as determined by the **toxin** it produces which partly determines its virulence

1. **ENDOTOXIN:** a complex bacterial toxin that is composed of protein, lipid, and polysaccharide (LPS) which is released only upon lysis of the cell

2. **EXOTOXINS:** a potent toxic substance formed and secreted by species of certain bacteria

BASIC EFFECTS of ENDOTOXIN

FEVER: any elevation of body temperature above normal

LEUKOPENIA/LEUKOCYTOSIS: abnormal reduction in number of leukocytes in blood, (<5000/mm³) / abnormally large number of leukocytes in blood, as during hemorrhage, infection, inflammation, or fever (<212,000mm³)

METABOLIC EFFECTS : pathogenic organisms can affect any of the body systems with disruptions in metabolic processes, e.g.,hypotension, hypoglycemia, etc.

RELEASE OF LYMPHOCYTE FACTORS: agranular leukocyte concentrated in lymphoid tissue; active in immunological responses, including production of antibodies **CELLULAR DEATH:**

SEPTIC SHOCK: associated with overwhelming infection resulting in vascular system failure with sequestration of large volumes of blood in capillaries and veins; activation of the complement and kinin systems and the release of histamines,

prostaglandins, and other mediators may be involved

DISSEMINATED INTRAVASCULAR COAGULATION (DIC): disorder characterized by a reduction in the elements involved in blood coagulation due to their utilization in widespread blood clotting within the vessels; late stages marked by profuse hemorrhaging

ORGAN NECROSIS: the sum of morphological changes indicative of cell death and caused by the progressive degradative action of enzymes

EXOTOXINS

TWO-COMPONENT (BIPARTITE) A-B TOXINS with INTRACELLULAR TARGETS: conform to general structural model; usually one component is a binding domain (B subunit) associated with absorption to target cell surface and transfer of active component across cell membrane, the second component is an enzymatic or active domain (A subunit) that enzymatically disrupts cell function

BACTERIAL CYTOLYSINS (a.k.a. Cytotoxins) with CELL MEMBRANE TARGETS: hemolysis, tissue necrosis, may be lethal when administered intravenously

EXAMPLES of BIPARTITE A-B TOXINS with INTRACELLULAR TARGETS

- Diphtheria toxin ADP-ribosylation inhibits cell protein synthesis by catalyzing transfer of ADP- ribose from NAD (nicotinimamide adenine nucleotide) to EF-2 (elongation factor- 2)
- Pseudomonas aeruginosa toxin similar action as DT
- Cholera toxin A-subunit catalyzes ADP-ribosylation of the B-subunit of the stimulatory guanine nucleotide protein Gs; profound life-threatening diarrhea with profuse outpouring of fluids and electrolytes
- Enterotoxigenic Escherichia coli (ETEC) heat-labile enterotoxin - similar or identical to cholera toxin
- Tetanus neurotoxin less well understood; binding domain binds to neuroreceptor gangliosides, releases inhibitory impulses with trismus
- Botulinum neurotoxin among most potent of all biological toxins; binding domain binds to neuroreceptor gangliosides, inhibits release of acetylcholine at myoneural junction resulting in fatal paralysis

BACTERIAL CYTOLYSINS with CELL MEMBRANE TARGETS

Three Major Types:

1. Hydrolyze membrane phospholipids (phospholipases);

e.g., Clostridium, Staphylococcus

2. **Thiol-activated** cytolysins (**oxygen-labile**) alter membrane permeability by binding to cholesterol; e.g., *Streptococcus, Clostridium*

3. **Detergent-like activity** on cell membranes; e.g., *Staphylococcus*, rapid rate of lysis

ENDOTOXINS

- 1 Integral part of cell wall
- 2.Endotoxin is LPS;
 - lipid A is toxic
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 Released from the cell before or after lysis
 Protein

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MICROBIAL PATHOGENICITY (cont.) RESISTANCE TO HOST DEFENSES

ENCAPSULATION and ANTIGENIC MIMICRY, MASKING or SHIFT

CAPSULE, GLYCOCALYX or SLIME LAYER

Polysachharide capsules Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae, etc.Polypeptide capsule of Bacillus anthracis

EVASION or **INCAPACITATION** of **PHAGOCYTOSIS** and/or **IMMUNE CLEARANCE**

PHAGOCYTOSIS INHIBITORS: mechanisms enabling an invading microorganism to resist being engulfed, ingested, and or lysed by phagocytes/ phagolysosomes
RESISTANCE to HUMORAL FACTORS
RESISTANCE to CELLULAR FACTORS

MICROBIAL PATHOGENICITY (cont.) DAMAGE TO HOST

DIRECT DAMAGE

(Tissue Damage from Disease Process):

Toxins Enzymes

INDIRECT DAMAGE

(Tissue Reactions from Immunopathological Response): Damage Resulting from Vigorous Host Immune Response (a.k.a, immunopathogenesis; autoimmune hypersensitivy)

Hypersensitivity Reactions (Types I - IV)

HOST RESISTANCE

The degree to which a host can limit the effects of an infection, ranging from:

- TOLERANCE in which symptoms are suppressed or unusually large doses of a drug, toxin, or protein are able to be endured
- HYPERSENSITIVITY in which only a few cells surrounding the infected cell(s) are affected or an increased susceptibility to an antigen, such as an allergic reaction to a previous exposure to an antigen, the extreme case being anaphylactic shock
- IMMUNITY in which the microorganisms do not multiply due to any one or a combination of host immune factors or the biological condition by which a body is capable of resisting or overcoming an infection or disease

HYPERSENSITIVITY REACTIONS

TYPE I: ANAPHYLACTIC REACTION (ANAPHYLAXIS, ANAPHYLACTIC SHOCK): a life-

threatening immediate hypersensitivity reaction to a previously encountered antigen, characterized by respiratory distress, vascular collapse, and shock; allergy or atopic diseases

TYPE II: CYTOTOXIC REACTION: a specific

destructive action against certain cells by an invading agent; humorally mediated, autoimmune diseases, cytotoxic diseases, antibody diseases

TYPE III: IMMUNE COMPLEX REACTION: serum sickness diseases

TYPE IV: CELL-MEDIATED IMMUNE RESPONSE:

delayed-type hypersensitivity, cell- mediated cytotoxic diseases, granulomatous diseases

- **Type I Hypersensitivity Reactions:**
 - **DAnaphylactic Reaction** (Anaphylaxis;
 - Anaphylactic shock)
 - •IgE-mediated: Cross-linking of cell-bound IgE antibodies by antigen with degranulation of mast cells or basophils
 - •Life-threatening immediate hypersensitivity reaction to a previously encountered antigen, characterized by respiratory distress, vascular collapse, and shock

Allergy or atopic diseases

 Atopy: hereditary hypersensitivity to common environmental antigens

Type II Hypersensitivity Reactions:

- **Humorally-Mediated Autoimmune Diseases**
 - Interaction of cross-reactive antibody with host cell surface antigen; Autoantibodies and immune complexes
 - **Cytotoxic reaction** (antibody-mediated) (ADCC): Specific destructive action against certain cells presenting antigens from an invading agent

♦Type III Hypersensitivity Reactions:

Immune Complex Reaction

- **Antibody-mediated**
- Deposition of circulating immune complexes in small vessels with complement activation causing damage to vessels
- **Serum sickness diseases**

Type IV Hypersensitivity Reactions: Cell-Mediated Immune Response

- IT cells sensitized to "self" antigens secrete lymphokines that either do direct damage to host cells (e.g., TNF) or indirect damage enhancing the inflammatory response
- Delayed-type hypersensitivity (TB test) (CD4+
 mediated)
- **Cell-mediated cytotoxic diseases** (CD8+ mediated) **Granulomatous disease**

HOST DEFENSE MECHANISMS

EXTERNAL (PRIMARY): Physical barrier of gross surface area; e.g., skin, respiratory tract, gastrointestinal tract, genitourinary tract

Mechanical and Physical Factors: sweat, fatty acids, pH, indigenous competitive flora (microbial antagonism), peristalsis, hair, cilia, urinary flushing, mucus, [tears, nasal secretions, saliva (lysozyme)], semen (spermine), mucosal secretory antibody (IgA predominant)

INTERNAL (SECONDARY): When an infecting parasite succeeds in penetrating the skin or mucuos membranes, cellular defense mechanisms include local macrophages and blood-borne phagocytic cells. Mononuclear phagocytes (monocytes and macrophages) and polymorphonuclear leukocytes (PMNs) are the most important phagocytic cells targeting bacterial infections.

MONONUCLEAR PHAGOCYTE SYSTEM (formerly Reticular Endothelial System): total pool of monocytes and cells derived from monocytes; predominantly macrophages (phagocytic cells)

OTHER:

NON-SPECIFIC: oxygen metabolites (superoxide anion radical, hydrogen peroxide, hydroxyl radicals, halide radicals), kinin forming system related to **clotting**

HOST-GENERATED PROTEINS: complex array of humoral and cellular mediators; e.g., lysosomal enzymes, lipid mediators, prostaglandins, histamine, heat-shock proteins (stress proteins)

CELLULAR IMMUNE RESPONSE: any immune response directed at the cellular level; includes **INFLAMMATION** and **PHAGOCYTOSIS** processes

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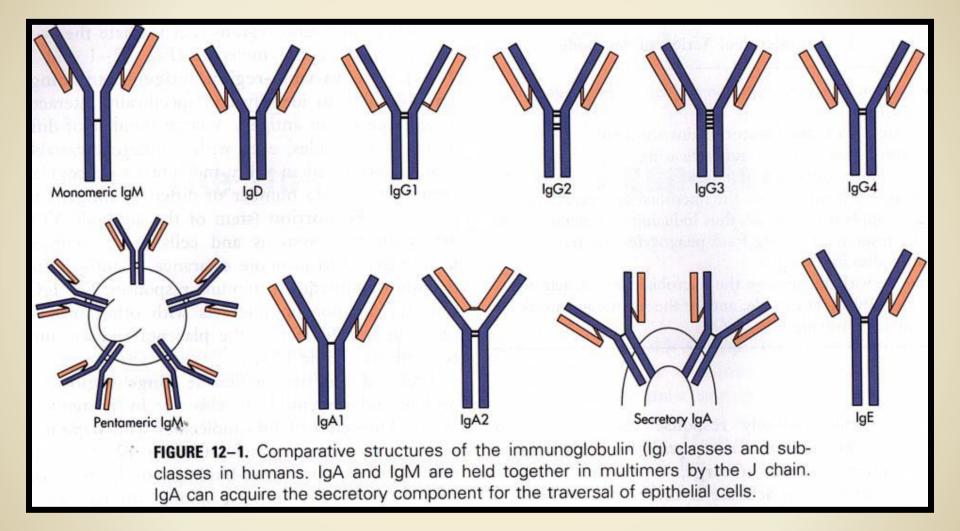
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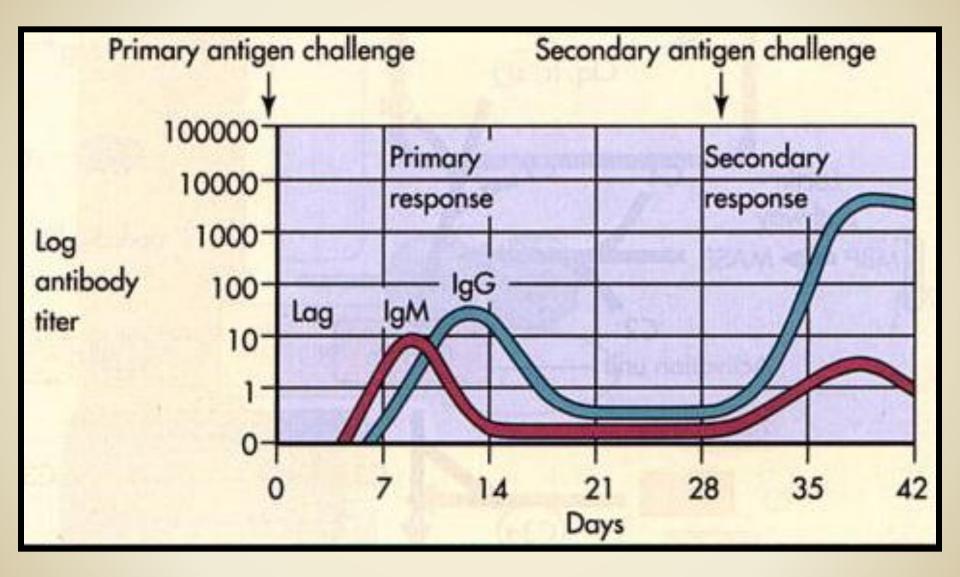
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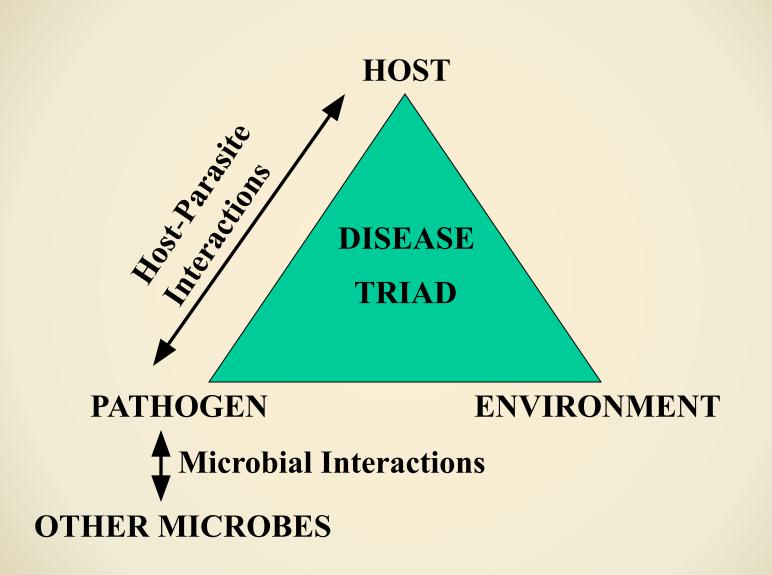
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REVIEW





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