A WHOLISTIC VIEW OF HOW DISEASE GETS INTO OUR BODY

Think of yourself as part of nature. You are at the top of the chain, but you are still part of nature. Now, think of group of trees in someone's back yard. Most of the trees are really healthy, but there is one tree that is weak, and it is being attacked by parasites, fungi, and disease.

What would you do to help the little tree survive? First you would clean it up, wipe away all the bugs and moulds. Secondly you would treat the damage, probably the bark, with a formula to help keep the bugs, bacteria or fungus away. And thirdly, you would dig around the soil, giving it some good nutrition to help it grow strong. You watch the little tree, continuing your guard duty keeping away the predators and feeding the tree with healthy supplements around the base of the tree in the soil so it can continue to grow stronger and stronger. Eventually, the tree is strong enough and has enough vital energy to survive on its own, without any intervention from you. Now it is strong, the parasites are not bothering it, it's defences are in place.

We are no different. When we get weak enough, lacking vital energy, our immune defences are compromised. The viruses, bacteria, parasites and fungi are just pathogens doing their job.

Look at them as having a job to take out the weak and sickly.
So if you are being overwhelmed by pathogens of any kind, you can take remedies for different types of pathogens, but don't forget to address your soil - your vital energy (immune system).

Because until you build up your vital inherent health, you are going to be victimized over and over again by attacks on your body in different ways.

Louis Pasteur (1822-1895) gave us pasteurized milk. He was the one that came up with the 'germ theory' that it was germs causing the disease and problems. He found heating things (such as milk) killed off the bacteria. He saved the whole silkworm industry by finding a cure for the pathogens that were attacking the industry. Yet in his last years he admitted he had been wrong in his assumption that the way to overcome the pathogens was to kill them. No, he said, 'the cure is in the 'soil'. Fix the soil and you fix the problem. When the soil or the terrain of our health (our immune system, our vital energy) is weak, then pathogens come in as a natural way of nature.

So watch what you do to your body and how you treat it with the foods you ingest, the chemicals you take into it and what you do to weaken it. If you are serious about remaining on the planet and raising your consciousness, be aware of everything you feed yourself and do to yourself. Don't put poisons into your body.

OUR BODY'S NATURAL DEFENSES

In order for a pathogen (eg. bacteria, virus, parasite) to gain access to the host, the pathogen must pass through a portal of entry. One of the most common portals of entry is the mucous membranes, especially those of the respiratory, gastrointestinal and urogenital tracts.
Another important portal of entry is the skin. Penetration of the skin occurs during a wound or by a hair follicle. When microorganisms penetrate below the skin, the portal of entry is said to be parental route.

Reflexes

- **Cough, gag reflex preventing particles into the lungs**
- **Sneezing expels infectious agents from nasal passage**
- **Swallowing moves potential pathogens to the stomach to be destroyed by acid.**

Intact Skin

- **Sebaceous gland secretions may be inhibitory**

- **Dry surface is not conducive to growth of microbes.**
- **Continuously sloughing epithelial cells carry adherent microbes away.**
- **Sweat removes microorganism through a flushing action and contains**
- **inhibitory substances such as lysozymes enzyme.**

Conjunctiva

- **Flushing action of blinking and tears prevents colonization**
- **Lysozyme enzyme and other antibacterial substances in tears are non-specific effectors.**
- **Lysozyme enzyme hydrolyzes a structural polysaccharide in bacterial cell walls.**

Mucous membrane epithelium

- **Mucous layers entrap micro organisms, which are then swept by ciliary action into the throat to be swallowed.**
- **Lysozyme enzyme in mucous secretions is antibacterial.**
- **Cilia prevent aerosol borne agents from entering lungs.**
- **Epithelial cells may not possess certain receptors necessary for adherence of infectious agents.**
- **Nasal passage provides a barrier to the lungs by airborne particles. Larger particles are stopped by protective barriers while smaller ones can be expired with the next breath.**

Gastrointestinal tract

- **Saliva acts to flush away microbes that have transiently settled on the mucosa.**
- **Lysozyme enzyme in saliva destroys bacteria**
- **Stomach acid and proteolytic enzymes destroy or degrade many infectious agents and destroys enveloped viruses.**
- **Bile secreted by gallbladder is inhibitory to growth of many bacteria.**
- **Normal peristalsis forces organisms to move along GI tract and to be excreted with fecal matter.**
- **Mucosal layer protects epithelial cells.**

Urinary tract

- **Flushing of urine periodically prevents bacterial population buildup.**
- **Acidity of urine is inhibitory to some organisms**
- **Prostatic secretions containing spermine and zinc inhibit growth of some bacterial and are introduced into the urine in males.**

Female vagina

- **Vaginal epithelium is sloughed rapidly and carries with it transient microbes.**
- **Secretions of vaginal tract are acidic, contain antimicrobial substances; they also promote flushing of microorganism from the body.**

OUR NATURAL PROTECTION

The host-parasite relationship may result in an episode of disease. In this case, the body will mount two general forms of defense: non-specific defense and specific defense centered in the immune system.

Non Specific Mechanisms of Defense

The body possesses many mechanisms that impart nonspecific defense. The objectives of these mechanisms are to prevent microorganisms from gaining a foothold in the body and to destroy them if they penetrate to the deeper tissues.

Mechanical barriers.

Mechanical barriers at the portal of entry represent the first line of defense for the body. These

defenses are normally part of the body's anatomy and physiology. The skin is a representative example. The outermost layers of skin consist of compacted, cemented cells, impregnated with the insoluble protein keratin. The thick top layer is impervious to infection and water. In the unbroken state, it usually is not penetrated by pathogens.
The mucous membranes of the urinary, respiratory and digestive tracts are another example. This are moist and permeable, but their fluids, such as tears, mucus and saliva, rid the membrane of irritants. Nasal hairs trap particles in the respiratory tract, and the fluids exert a flushing action. Cilia on the cells sweep and trap particles in the respiratory trace and coughing ejects irritants.

Chemical Defenses

Among the nonspecific chemical defenses of the body are the secretions of lubricating glands. The tears and saliva contain the enzyme lysozyme, which breaks down the peptidoglycan of the cell wall of Gram Positive bacteria. The lactic acid of the vagina imparts defense, and extremely caustic hydrochloric acid of the stomach is a barrier to the intestine. Semen contains the antimicrobial substance spermine that inhibits bacteria in the male urogenital tract.

Genetic Barriers.

The hereditary characteristics of an individual are a deterrent to disease as well. For example, humans suffer HIV infection because their T lymphocytes have the receptor sites for the human immunodeficiency virus. Dogs, cats and other animals are immune to this disease because they do not possess the genes for producing the receptor sites.
Conversely, humans do not suffer canine distemper because humans lack the appropriate receptor sites for the virus that causes the disease.

Inflammation

Inflammation is a nonspecific response to any trauma occurring to tissues. It is accompanied by signs and symptoms that include heat, swelling, redness, pain.
Inflammation mobilizes components of the immune system, sets into motion repair mechanisms and encourages phagocytes to come to the area and destroy any microorganisms present.
Inflammation can be controlled by nervous stimulation and chemical substances called cytokines. These chemical products of tissue cells and blood cells are responsible for many of the actions of inflammation. The loss of fluid leads to a local swelling called edema. In some types of inflammation, phagocytes, accumulate in the whitist mass of cells, bacteria and debris called pus.

Fever

Fever is considered a non-specific defense mechanism because it develops in response to numerous traumas. Fever is initiated by circulating substances called pyrogens, which affect the brain's hypothalamus and cause the latter to raise the temperature. Although excessive fever can be dangerous, fever is believed to have a beneficial role because it retards the growth of temperature-sensitive microorganisms (eg. leprosy bacilli), and it increases the metabolism of body cells while stimulating the immune reaction and the process of phagocytosis.

Interferon.

Interferon is a group of antiviral substances produced by body cells in response to the presence of viruses. Lymphocytes and macrophages produce alpha-interferon, epithelial cells produce beta-interferon, and T-lymphocytes produce gamma-interferon. The interferons do not directly inhibit viruses. Instead, they stimulate adjacent cells to produce substances that inhibit the replication of viruses in those cells. Interferons produced in response to one virus will protect against many other types of viruses and for this reason, interferon is considered a nonspecific form of defense.

Phagocytosis

Phagocytosis is a nonspecific defense mechanism in which various phagocytes engulf and destroy the microorganisms of disease.

Phagocytes. Among the important phagocytes are the circulating white blood cells called neutrophils and monocytes. In the tissues the monocytes are transformed into phagocytic cells called macrophages. The macrophages move through the tissues of the body performing phagocytosis and destroying parasites. they are part of the reticuloendothelial system. Phagocytes also initiate the processes of the immune system.

The process of phagocytosis begins with attachment and ingestion of microbial particles into a bubblelike organelle called a phagosome. Once inside the phagocyte the phagosome containing the microorganism joins with a lysozyme, which contributes enzymes. The fusion of phagosome and lysozyme results in a phagolysosome. Microorganisms are destroyed within minutes, and the microbial debris is eliminated from the cell in the process of egestion. In the immune process, chemical portions of the microorganism called antigenic determinants are displayed on the surface of the phagocyte to stimulate the immune process.

Phagocytosis is enhanced by products of the immune system called antibodies. These protein molecules bind to microorganisms and encourage engulfing by phagocytosis.

The Complement system

The complement system is a series of proteins that circulate in the blood and encourage phagocytosis or otherwise 'complete' the defensive process. Many immune reactions stimulate the complement system.

The complement system operates in a cascade of reactions. In the pathway, certain complement components react with one another and produce new substances that induce other components to react. The results of the myriad reactions are substances that induce other complement components into action. The overall result is a number of substances toxic to microorganisms. The substances encourage phagocytosis or bring about destruction of microbial membranes.

Two general pathways for complement activity exist. The classical pathway operates with the highly specific immune system and is initiated by tumors, cell wall components of bacteria, and various microorganisms. It is sometimes called the properdin pathway because properdin is one of the proteins operating in it. The alternative pathway invokes a slower and less specific method for ridding the body of parasites, particularly Gram-negative bacteria and viruses.

EVADING HOST DEFENSES

Factors contributing to ability of organism to evade or destroy normal host defense mechanisms and multiply:

Production of extracellular matrices that protect organism from host immune mechanisms eg. polysaccharide capsules produced by number of bacteria including S. pneumoniae inhibit phagocytosis by interfering with the ability of leukocytes to attach to the microbe then engulf it.

Ability to induce 'nonprofessional' phagocytic cells to engulf the microbe. Chlamydia trachomatis, the etiologic agent of lymphogranuloma venereum, can be endocytosed only by squamocolumnar junction cells of the human genital tract.

Viruses such as herpes simplex and HIV have the ability to integrate into the host's genome in infected cells, thus remaining latent but potentially active under the right circumstances.

Some organisms including Mycobacterium spp. and many viruses are able to survive intracellularly in macrophages. Several mechanisms promote this ability:

- **Inhibition of lysosomal fusion with the phagosome.**
- **Escape from the phagosome to multiply in the cytoplasm.**
- **Survival and growth in the phagolysosome.**

Numerous microbes produce extracellular substances or otherwise inactivate cellular immune responses.

Hemolysins produced by strep and others directly destroy leukocyte and erythrocyte cell membranes.

Leukotoxins produced by clostridia and others destroy leukocytes.

HIV virus directly infects and destroys T helper cells, thus abrogating an immune response against many infectious agents that require cell mediated immunity for destruction.

Bacteria produce substances that interfere with humoral immune responses.

Gonococci and H. influenzae produce IgA proteases that destroy secretory IgA immunoglobulin.

Proteins on the surface of S. aureus (protein A) bind the Fc portion of antibodies and inhibit specific optimization.

Viruses and some parasites constantly change their surface antigens, thus forcing host to continually produce new specific antibodies.

Some infectious agents do not seem to invoke much of an immune response at all, which allows them time to multiply and cause localized tissue damage. eg. rabiesvirus and Treponema pallidum.

BLOOD - NATURAL DEFENSE:

B Cells and T Cells

Lymphocytes are one of the 5 kinds of white blood cells or leukocytes circulating in the blood.

The most abundant lymphocytes are:
B lymphocytes (called B cells); and
T lymphocytes (called T cells).

B cells are not only produced in the bone marrow, but also mature there.
The precursors of T cells leave the bone marrow and mature in the thymus.

Each B cell and T cell is specific for a particular antigen. Each is able to bind to a particular molecular structure.

Leukocytes

Leukocytes are one of the three cellular types found in the blood.
A normal, healthy adult will have 5000 - 10,000/uL (5-10 x 109/L=5,000,000,000 -10,000,000,000/L) leukocytes in the circulating pool at any given time.
The function of all leukocytes is to provide our body with defenses against foreign invaders.
Each type of leukocyte accomplishes this in a different manner.

Types of Leukocytes:

neutrophils
eosinophils
basophils (nongranulocytes)
monocytes/macrophages
lymphocytes

Functions of Lymphocytes

The acquired (specific) immune system (vs. non-specific, innate) is comprised of the humoral and the cell-mediated immune systems. The lymphocytes found in each system are preprogrammed to respond to a specific antigen. The innate or non-specific immune system involves skin and other mucosal surfaces, inflammatory response, commensal bacteria, and phagocytosis.

The acquired (AKA adaptive or specific) immune system involves two systems:

HUMORAL: humors in medieval physiology were body fluids that determined a person's health and temperament. Humors also were proteins that protected against disease. B lymphocytes are primarily involved with this type of immunity.

CELL MEDIATED: T lymphocytes are responsible for this type of immunity.

B-lymphocytes are responsible for the humoral response. Upon antigenic encounter they transform into plasma cells that produce antibodies specific to the antigen. Production of antibodies is a complex process. Memory B cells are also produced. These memory cells respond more quickly than the initial response to a future encounter with the same antigen. Each activated B cell gives rise to many progeny which together are called a clone of cells because they are all identical.

T-lymphocytes are responsible for the cell-mediated response. After antigenic stimulation they proliferate and differentiate into memory cells and effector cells. There are at least two types of effector cells: helper T-cells (CD4+) and cytotoxic T-cells (CD8+). CD = cluster differentiation markers. They are identifying membrane proteins (antigens). It is the CD4+ lymphocytes to which HIV has an affinity. The normal ratio of CD4+:CD8+ is 2:1. In HIV-infected individuals the ratio decreases and reverses as the AIDS virus invades and destroys the CD4+ cells. The ratio is used to monitor the progress of the disease.

T-helper cells "help" the B-cells produce antibodies by releasing cytokines. They also affect the action of other cells, such as CD8+. CD8+ cells (cytotoxic T-cells) mediate destruction of cells infected with pathogens such as viruses, bacterial, protozoa, or fungi; and are also responsible for rejection in organ transplants. T-helper cells help B-cells produce antibodies and also influence other T-helpers, T-suppressors and cytotoxic T-cells. (T suppressors help keep the immune system in control).

Erythrocytes are also known as red blood cells, erythrocytes, or red corpuscles. Then term erythron refers to all the erythrocytes and their precursors in the blood, bone marrow or at extramedullary sites. Erythrocytes transport oxygen and carbon dioxide between the lungs and all the tissues of the body. A circulating erythrocyte is little more than a container for hemoglobin.

The major function of hemoglobin is the transport of oxygen to the tissues. There are two normal physiologic states of hemoglobin:

- **Oxyhemoglobin - hemoglobin is bound with oxygen, a O2 molecule is associated with each Fe++ molecule (ferrous iron).**
- **Deoxyhemoglobin - hemoglobin is dissociated from oxygen. This is also known as empty hemoglobin.**

Carbon dioxide transport

Carbon dioxide is also transported by hemoglobin. CO_2 transport from tissues can be accomplished by 3 mechanisms, directly and indirectly by erythrocytes and in solution in the plasma. Three-fourths of the CO_2 is transported by indirect erythrocyte transport: CO_2 diffuses into the erythrocytes where it is transformed into carbonic acid ($H_2O + CO_2 = H_2CO_3 = H^+ + HCO_3^-$). Deoxyhemoglobin accepts the H^+ and HCO_3^- (bicarbonate) diffuses back into the plasma. In the lungs HCO_3^- converts back to CO_2 and H_20 and is eliminated via respiration.

BACTERIA

Cellular (usually unicellular) organisms.
Bacteria have complex structure, within containing variety of proteins, nucleic acids, polysaccharides, lipids and their derivatives. Some bacteria are motile, some generate light, but the main activity is reproduction to make new bacteria - and they do it quickly, often dividing 3 times an hour. This requires energy which phototrophs get from sunlight, the chemotrophs (majority of bacteria) get from oxidation of

chemical compounds. The organisms grow (increase in numbers) easily in the presence of air (oxygen), and are described as aerobes.
Many bacteria including some of most important pathogens have a starchy or gelatinous structure around the cell called a capsule; these help protect the cell from phagocytosis by white blood cells. Some bacteria produce a loose network of material usually polysaccharides, outside the cell called extracellular slime or glycocalyz. This enables bacteria to adhere to hard surfaces such as teeth and intravascular devices.

NEEDS:

Oxygen - differ according to the mechanism they use to make energy. Some can only grow in the presence of oxygen and are called obligate aerobes; others are obligate anaerobes and die rapidly if exposed to air. anaerobes are present in large numbers in the human intestines (eg. bacteroides, clostridium) and can cause infection if the intestinal contents contaminate other organs, eg. during surgery. They are infrequently associated with infection in contaminated, traumatic injuries where dead tissue is present, or when a large wound has a poor blood supply and therefore low levels of oxygen. Some species are obligatory aerobes (unable to grow in the absence of free oxygen), but others are facultative anaerobes (able to grow in its absence but often with decreased vigour).
Obligatory anaerobes can't grow if more than a trace of free oxygen is present and in some cases this is because they poison themselves in such circumstances by making peroxides which they can't destroy since they don't possess the enzyme catalase. Micro aerophiles grow best in the presence of a little oxygen.

Many human pathogens and commensals can change the process they use to make energy according to he prevailing conditions and therefore grow either or not with oxygen – these are called facultative anaerobes.

The oxidations on which chemotrophis depend for their energy can be carried out in 3 different ways:

- **aerobic respiration with free oxygen as the final hydrogen acceptor in a chain of oxidation reduction reactions**
- **anaerobic respiration with inorganic compounds (nitrates, sulphates and carbonates) as final hydrogen-acceptors; and**
- **fermentation of a carbohydrates or other organic substance, the hydrogen acceptor being**
  other molecule of the energy source or some other organic molecule. Various organic acids and the gases COs and H2 may be formed as end products of fermentation.
- **Carbon Dioxide is probably necessary in small amounts such as are present in the atmosphere, for the growth of most micro organisms. A higher concentration (5-10%) improves growth of many parasitic species, esp. Neisseria gonorrhea and is usually necessary for the primary isolation of Brucella abortus from pathological materials. Free CO2 can be the sole carbon source for autotrophs.**
- **All bacteria need water, a source of carbon to make the structure of the cell and for energy, nitrogen to make proteins and nucleic acids and various inorganic ions including phosphate, sulphur, calcium and iron to make amino acids and promote enzyme activity.**
- **Some chemotrophic bacteria (called autotrophs) can grow in simple inorganic salt solutions.**
- **At the other end of the scale are the leprosy bacillus and the spirochaete of syphilis, which can't be cultivated in non-living media, and the rickettsiae and viruses, which depend upon their hosts for essential enzymes as well as for raw materials. Among common parasites of man, Escherichia coli can grow in a solution containing glucose, ammonium sulphate and a small range of other inorganic salt. In contrast Haemophilus influenzae has very exacting requirements as well as glucose or other suitable carbohydrate, various minerals and an assortment of amino acids, purines and vitamins - this species must be supplied with nicotinamide adenine dinucleotide or its phosphate as a co-dehydrogenase, and with haemin or some closely related substance as substrate for the synthesis of various respiratory enzymes.**

TEMPERATURES:

Psychrophiles grow best at low temperatures, some below 0oC. They are therefore important in connection with cold storage of food and blood, otherwise aren't relevant to medical microbiology. Thermophiles, found in hot springs, rotting vegetable matter etc. are of no medical importance except as sensitizing agents in 'farmer's lung' etc..

The majority of bacteria including all of those parasitic upon man, are MESOPHILES, with optimal growth temperatures, somewhere between 20 and 40oC. They vary considerable in ranges of temperature over which they will grow. Near all of man's parasites are best suited to temperatures around 37oC - many will multiply at lower temperatures, down to 20oC or less, but few at more than 45oC. Some will grow only within a narrow temperature range eg. Neisseria gonorrheae: 30-39oC.

Unusual among human pathogens is Yersinia pestis, a causative organism of bubonic plague - optimum growth temp is about 27oC related to the fact that multiplication in the proventriculus of the rat-flea is an important stage in its transmission.

Temperature, differs between species. Optimum for human commensals and pathogens is about 37oC; most are only able to multiply very slowly below 10oC. Under moist conditions, most non-sporing bacteria are killed between 50oC and 65oC; spores are destroyed between 100oC and 120oC.

pH:

Most micro organisms of medical importance grow best when it has a slightly alkaline environment. Lactobacilli are among the bacterial flora of the human body that prefer an acid medium of pH 4.0. Doderlein's bacilli which belong to this genus have a protective function in the vagina as they form lactic acid from the glycogen of the mucosa, keeping the vaginal secretion too acid for the growth of most other organisms. The medium devised for the isolation of relatively slow growing fungi makes use of their ability to multiply at a pH value of about 5.4; this is inhibitory to bacteria which would otherwise overgrow them. At the other end of the scale Vibrio cholerae grows best around Ph 8.5.

(pH, each species is different, but most prefer neutral or slightly alkaline pH. Body uses mechanism of adverse pH to discourage potentially harmful bacteria. pH of the vagina usually is between 4 and 5 because of the lactic acid produced by the lactobacilli that live there which discourages growth of other organisms)

REPRODUCTION:

Bacteria carry out different metabolic activities and reproduce by fission. Individual cells: .5 -1 micrometer (or 1,000 of a millimeter).

Cell consists of semi-solid cytoplasm surrounded by cytoplasmic membrane, outside which there is normally a rigid cell wall.

Shape of bacterial cell is determined by its cell wall, which is made of peptidoglycan (network of carbos and aminos).

Cytoplasm (jelly like watery material that fills cells) contains deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Most of the DNA is concentrated in one part of the cell, commonly in the form of a ring or loop, constituting the nucleus.

Bacteria differ from nearly all other cellular organism in that the rigidity of their cell walls is due to a complex of aminosugars and polypeptides known as mucopeptide, of which muramic acid is a component.

Some bacteria form capsules, usually composed of polysaccharide, outside their cell walls; some have fine whip like projections 'flagella' which are organisms of locomotion, some form 'spores', thick walled cells with greatly reduced metabolic activity and greatly increased resistance to adverse conditions.

Bacteria reproduce by binary fission (one cell enlarging, then dividing into 2 approx. equal parts when they reach about twice their size); this division is preceded by simple replication of the nuclear ring, without polarized mitosis that is part of the reproductive
process of most other types of nucleated cell. In the right environment, the cell can divide every 20 minutes. The chromosone contains all the info. necessary for cell division, when it divides, a second copy of the chromosome is made; the cell wall and cytoplasmic membrane grow inwards forming a new cell wall across the inside of the cell and separate the two copies of the chromosome.

Bacteria often carry extra genetic material in the form of small circular pieces of DNA called plasmids. These are replicated and transferred to each cell during binary fission, but they can also replicate independently.

Ineukaryotic organisms, sexual reproduction is used to mix the genetic material from two individuals of the same species and involves the fusion of two cells, one from each individual. Bacteria do not use cell fusion, but have several methods of exchanging fragments of genetic material between cells of the same or different species.

Transformation - fragments of DNA released from damaged bacterial cells can be absorbed into other cells and incorporated into their chromosome, although usually only those of closely related species.

Transduction. Viruses that infect bacterial (bacteriophages) sometimes copy part of the host-cell DNA by mistake, take it out of the cell with the newly constructed viruses and introduce it into the genome of other bacteria that the virus infects.

Conjugation - this special fimbria called a sex pilus extend from one bacterial cell and adheres to another cell. A copy of plasmid DNA in one cell is transferred via the tube into the second cell. Sex pili can be formed between cells of the same species and of different species but, because the genetic information required to make the sex pili and DNA transfer proteins are carried on a plasmid, conjugation can only occur when the cell carries one of these plasmids. Bacteria can have between 1-6 plasmids which often contain genetic information that enable the cell to adhere to tissue, to produce toxins or make enzymes which inactive antimicrobial agents.

TYPES:

Different types of bacteria are defined by two names, the generic name (Staphylococcus) and the specific or species name (aureus).

How to differentiate between bacteria: their shape, surface structure, response to stains, and nutritional requirements.

SHAPES

Shapes of bacteria

- gives clue to their identity:

Basically 3 types:
round/rods/spirals

spherical/round:
- cocci (usually grouped together in clumps eg. streptococci, or in pairs "diplococci')
- repeated division in the same plane produces chains;
- division in 2-3 planes at right angles produces regular packets of 4, 8 or more;
- division without any definite orientation produces irregular clusters.

bacilli or rods:
- elongated cylindrical forms, straight or slightly curved with ends rounded, square, pointed or sometimes swollen to form clubs.

vibrios or comma bacilli:
- resemble bacilli but more curved

spirochaetes (spirals):
- **not very common but include the spirochaetes and Spirilla**
- **corkscrew like spirals**
- **some are tightly coiled (leptospirae)**
- **some have large open coils (borreliae)**

higher bacteria:
- **thought to represent more advanced stage of evolution, resemble fungi in forming branched filaments (eg. actinomycetes)**

Shape is determined by its cell wall which is made of peptidyglycan (carbos & aminos), with varying thickness. Staining helps distinguish

To view bacteria: fix to glass slide by heating, and apply stain. Then examine with oil immersion of the microscope using bright light. Simple stain like methylene blue or carbol fuchsin is used, then can see more of shape, arrangement etc. Some need to be seen with dark ground illumination (dark background) allowing the bacteria to be reflected - usually no stain used but water or oil between slide and condenser to prevent total internal reflection of light within condenser.
Tubercle bacilli can be stained with auramine using sputum and examined microscopically by ultra-violet light.

Flagella - hair like structures that protrude from the surface of the cell and often much longer than the cell itself. They act like a propeller, enabling the cell to move towards nutrients or away from harmful substances. The number and arrangement of flagella varies according to he species although not all bacteria have them and they rarely occur on cocci.

Fimbriae or pili are similar to flagella but thinner and shorter - present on many Gram negative bacteria, enabling the organism to adhere to specific host cells eg. the pili of strains of Escherichia coli responsible for urinary tract infections assist adhesion to epithelial cells in the bladder. Special fimbriae called sex puili are used to join two cells together so that they can exchange genetic information.
Spores - some species of bacteria esp. those of genera bacillus and clostridium, which are a significant cause of infection in humans, develop highly resistant structures called spores which they are exposed to adverse conditions like lack of nutrients or water. The shape (avoid or spherical) and position of the spore within the cell vary between species. Spores are resistant to disinfectants and to high or low temperatures. They may remain viable for many years but when the environmental conditions improve the spores germinate and the bacterial cell inside starts to multiply again.

TOXINS

- **Among the most powerful of known poisons is that produced by Clostridium botulinum, a bacterium that sometimes grows in human or animal foods. It is estimated that one mg of this substance is enough to kill of 20 million mice and the death rate among humans who eat infected food is very high.**
- **Other bacteria like Clostridium tetani and Corynebacterium diphtheriae, produce powerful toxins while growing in the tissues of their hosts. Such poisonous products readily liberated from the living bacteria and diffusing into culture media or host tissues.**
- **EXOTOXINS. With few exceptions they are products by Gram positive bacteria. In general they are proteins and are fairly easily inactivated by heat. Many have been given names corresponding to their effects eg. haemolysins (red cell destroying toxins) and leucocidins (leucocyte destroying toxins) of streptococci and staphylococci and lecithinase of Clostridum welchii (one of the gas gangrene bacilli) which hydrolyses lecithin, a constituent of cell membranes.**
- **ENDOTOXINS do not diffuse out of living cells, but are released when the bacteria die, eg. when they are digested by the leukocytes of a host. These toxins are mainly associated with Gram negative organisms, are complex lipopolysaccharides and relatively heat stable. Their toxic effects which depend little upon the species from which the toxins are derived, are widespread. They include fever, diarrhea and visceral hemorrhages, and may culminate in prostration and death.**
- **Weight for weight, endotoxins are far less potent that the more active of the exotoxins.**

RICKETTSIAE and CHLAMYDIAE

- **Resemble bacteria because they contain RNA and DNA, have muramic acid in their outer coats, reproduce by binary fission and are susceptible to the action of antibacterial drugs that have no effect on viruses.**
- **However, the diameters are only .25-.5m so they are closer in size to viruses than to bacteria, also virus-like in being unable to reproduce except inside the cells of host organisms.**

ANTI BACTERIAL/DISINFECTANTS FOR SKIN:

- **Colloidal silver**
- **Aloe vera gel**
- **Hydrogen Peroxide**
- **Heat**
- **Sunlight**

VIRUSES

- **Some similar in size to rickettsiae and chlamydiae, but most smaller, some smaller than any other known living organisms, too small to be seen with ordinary light microscope unless they aggregate to form inclusion bodies.,**
- **A virus particle is called a virion, not a cell.**
- **At its simplest, as in the viruses of poliomyelitis, this is a mere 25-30nm in diameter (1 nm = a nanometre, a thousandth of a micrometer) and consists of only a nucleic acid core**
- **('nucleoid or genome') and a surrounding protein coat ('capsid')**
- **At the other end of the range, the virions of pox viruses measure about 250 X 300 nm and are chemically and structurally a good deal more complex, but still basically the same plan.**
- **The nucleic acid found in a virus of any given type is either RNA or DNA but not both as in bacteria and other cellular organisms.**
- **Viruses increase in number not by fission, but by replication inside bacterial, plant or animal host cells which they have converted into virus-production units.**

FUNGI

- **Larger than bacteria, usually multicellular.**
- **Thick cell walls are not from mucopeptide as are the bacteria, but from chitin or other components.**
- **The molds grow as tubular branching filaments (hyphae) which become interwoven to form a network (mycelium).**
- **In some families the hyphae are divided into short lengths by cross walls (septa) - these fungi reproduce by forming asexual or sexual spores of various kinds.**
- **Yeasts are oval or pherical cells which commonly reproduce by budding, but may also form sexual spores - these reproductive spores differ in nature and function from bacterial spores).**

PROTOZOA

- **Unicellular organisms, mostly much larger than bacteria which show clear differentiation of their protoplasm into nucleus and cytoplasm.**
- **Their reproductive mechanisms vary from simple binary fission to complex life-cycles involving sexual and asexual phases and the formation of cysts.**

PARASITES

- **May be commensal, symbiotic or pathogenic.**
- **Commensal means 'shares the table' deriving nourishment from its host, but doing nothing in return A NONPAYING GUEST. Many found in secretions of human skin and mucous**
- **membranes.**
- **A symbiont lives in partnership with the host, receiving nourishment and rendering a service in return - APYING GUEST. Such are the nitrogen fixing bacteria of the root nodules of leguminous plants and the vitamin synthesizing bacteria of the human intestine.**
- **A pathogen does harm to its host.**
- **Pathogenicity is an expression fo the host's susceptibility as well as the organism's intrinsic power to cause disease.**

- **The soil is as important as the seed in determining the outcome of infection.**

THE INFECTIOUS PROCESS - HOST FACTORS

- **Innate host Defense Mechanism**
- **1st line of defense, innate or nonspecific host responses must provide an effective barrier that provents microorganism from penetrating, inhibit or destroy invader if it gains access to the tissue and eliminate or neutralize any toxic substances elaborated by the infectious agent. Here is a list of several mechanism available in the immunocompetent host:**

MECHANICAL BARRIERS:

Reflexes

- **Cough, gag reflex preventing particles into the lungs**
- **Sneezing expels infectious agents from nasal passage**
- **Swallowing moves potential pathogens to the stomach to be destroyed by acid.**

Intact Skin

- **Sebaceous gland secretions may be inhibitory**
- **Dry surface is not conducive to growth of microbes.**
- **Continuously sloughing epithelial cells carry adherent microbes away.**
- **Sweat removes microorganism through a flushing action and contains inhibitory substances such as lysozyme.**

Conjunctiva

- **Flushing action of blinking and tears prevents colonization**
- **Lysozyme and other antibacterial substances in tears are non-specific effectors.**
- **Lysozyme hydrolyzes a structural polysaccharide in bacterial cell walls.**

Mucous membrane epithelium

- **Mucous layers entrap micro organism, which are then swept by ciliary action into the throat to be swallowed.**
- **Lysozyme in mucous secretions is antibacterial.**
- **Cilia prevent aerosol borne agents from entering lungs.**
- **Epithelial cells may not possess certain receptors necessary for adherence of infectious agents.**
- **Nasal turbinates provide a barrier to free access into lungs by airborne particles; such particles may impinge and stick to nasal hairs and progress no further. Particles 5 pm in diameter are best able to reach the alveoli; larger ones are stopped by protective barriers while smaller ones may not come to rest and are expired with the next breath.**

Gastrointestinal tract

- **Saliva acts to flush away microbes that have transiently settled on the mucosa.**
- **Lysozyme in saliva destroys bacteria.**
- **Stomach acid and proteolytic enzymes destroy or degrade many infectious agents and destroys enveloped viruses.**
- **Bile secreted by gallbladder is inhibitory to growth of many bacteria.**
- **Normal peristalsis forces organisms to move along GI tract and to be excreted with fecal matter.**
- **Mucosal layer protects epithelial cells.**

Urinary tract

- **Flushing of urine periodically prevents bacterial population buildup.**
  Acidity of urine is inhibitory to some organisms

- **Prostatic secretions containing spermine and zinc inhibit growth of some bacterial and are introduced into the urine in males.**

Female vagina

- **Vaginal epithelium is sloughed rapidly and carries with it transient microbes.**
- **Secretions of vaginal tract are acidic, contain antimicrobial substances; they also promote flushing of microorganism from the body.**

SOLUBLE AND CIRCULATING NON-SPECIFIC EFFECTORS

Complement

Classical pathway of the complement system, comprised of a series of at least 20 proteins and glycoproteins, acts to lyse microbial membranes and releases inflammation enhancing substances. Inasmuch as it is triggered by an antigen antibody complex, initiation of this pathway cannot be considered nonspecific, although the complement effector proteins are nonspecific. The complement cascade can also be activated by the 'properdin' or 'alternate' pathway at the C3 stage.

Alternate pathway:

The alternate pathway can be initiated by the presence of polysaccharides in bacterial or fungal cell walls, including the lipid A of endotoxin. Once initiated, the complement cascade continues from the second stage, resulting in lysis of cell membranes and release of active protein fragments that promote vasodilation, act as chemotactic factors, promote release of histamines, which also increase vascular permeability, and act as opsonins.

Acid and alkaline phosphatases can inactivate herpes viruses.

Interferon-a (IF-sa) proteins are releases by cells once they have been infected by a virus. The interferons protect neighboring cells from viral multiplication by inducing the production of intracellular antiviral proteins. Interferon-a also enhances killer T-cell activity.

Interferon-y (IF-y) activates macrophages to phagocytize an destroy intracellular parasites more effectively; IF-y also interrupts viral replication and promotes T-cell differentiation.

Fibronectin, produced by some macrophages and epithelial cells, may act as a nonspecific opsonin for certain microbes, such as S. aureus which has a natural fibronectin receptor. Inasmuch as fibronectin on cell surfaces may also act to enhance microbial adherence, its effect may not always be beneficial.

METABOLIC OR NATURAL DEFENSES

Body Temperature must be conducive for microbial growth (eg patients with high fevers cannot support infection with T. pallidum)

Specific host cell receptors must be available (eg distemper virus of dogs will not cause disease in humans)

The environment must be suitable; anaerobes cannot thrive in a highly oxygenated tissue, whereas Mycobacterium tuberculosis will not survive in an anaerobic environment.

The nutrional and metabolic state of the host are important factors in development of disease; diabetics in ketoacidosis are particularly vulnerable to yeast and other fungal infections. Low pH and high serum glucose provide a supportive environment.

CELLULAR IMMUNE SYSTEM

T Lymphocytes (T helper cells) enhance antibody production by B lymphocytes.

Cytotoxic T cells can kill virus-infected host cells directly; killing of virus infectd epithelial cells is probably responsible for the various exanthems associated with viral infections.

Natural killer T cells can destroy certain bacteria and attack virus-infected cells.

Many types of cells, including T lymphocytes and monocytic cells, produce cytokines and monokines, respectively.

T suppressor cells also act to subdue the immune response.

B cells can be stimulated by the binding of T-independent antigens, such as LPS and the flagella of some bacteria, to produce specific antibodies, primarily IgM.

ANTIMICROBIAL AGENTS - How to Kill a Microbe

Criteria for a successful antimicrobial agent:

*** displays targeted toxicity (ie to the offending microbe only)**
*** produces no side effects in the host**
*** displays a narrow range of activity (ie doesn't harm normal host flora)**
*** kills the targeted microorganism (bactericidal) rather than merely inhibiting its growth (bacteriostatic)**
*** fails to induce resistance**
*** remains stable in body fluids and retains a long period of activity (half-life)**
*** does not induce an allergic or toxic host response**
*** is soluble in body fluids and tissues.**

Route of Administration:

- **topical, aerosolized, oral, intramuscular, intravenous, in increasing order of systemic effects**
- **intravenous allows high concentration in the blood but the agent may not pass the blood-brain barrier efficiently in some cases.**
- **oral administration may be good for achieving high gut levels of the agent, but systemic levels may not be adequate for treating extra-intestinal sites.**
- **Many agents bind to serum proteins, notably albumin. Only unbound (free) drug is able to exert antimicrobial activity.**
- **When a drug doesn't efficiently cross through capillary walls into he tissues, activity may be less than expected. A highly lipid-soluble agent can more easily cross cell membrane barriers to reach the site of infection. Lipid soluble agents include metronidazole, trimethoprim, and rifampin.**
- **Lipid solubility of the antimicrobial agent: when a drug doesn't efficiently cross through capillary walls into the tissues, activity may be less than expected. A highly lipid soluble agent can more easily cross cell membrane barriers to reach the site of infection. Lipid soluble agents include metronidazole, trimethoprim, and rifampin.**
- **Active transport enzymes in the host: several antimicrobial agents are actively secreted by host metabolic enzymes into urine, bile or other anatomical sites which limits their availability at sites of infection other than those into which the agent is secreted. A second agent to inhibit this transport is sometimes given (eg. probenicid is given to maintain high levels of penicillin after intramuscular injection for treatment of gonorrhea). (in other words, a drug is given so you don't pee out the penicillin)**
- **Some antimicrobial agents may be hydrolyzed or destroyed by the person's own enzymes.**

- **Imipenem is inactivated by a peptidase in the renal tubules, with concomitant loss of activity and nephrotoxicity. This problem has been addressed by administering imipenem with cilastatin, an agent that inhibits the action of the peptidase.**
- **Other agents (drugs) can interfere with the activity of the antimicrobial.**
- **Chemotherapy patients may be already be receiving a hepatoxic agent, adding pyrazinamide**
- **An anti-mycobacterial agent known to be hepatotoxic would be contradicted.**
- **Metronidazole has a disulfiram reaction with alcohol; simultaneous treatment with an alcohol based agent would cause a problem.**
- **Some organisms grow so slowly or are in a protected site and the anti-microbial agent can't effect them.**
- **Staph (staphylococcus) may colonize a prosthetic heart valve or intravenous catheter and surround themselves with 'slim' - a thick glycocalyx layer that inhibits penetration of the person's serum and cellular factors as well as the anti-microbials. Once this is sequestered, the organisms exhibit very decreased metabolic rates not amenable to the action of the antimicrobial agents.**
- **Microbes growing within an abscess are also protected from the antimicrobial agents by their lowered growth.**
- **Some patients develop mycelial fungal infections in lung cavities created as a result of a prior T.B. infection. Fungi growing in such cavities are virtually impossible to treat medically and must be removed surgically.**
- **Bacteria growing in bone matrix during osteomyelitis are notoriously difficult to treat. Herpes virus latent in nerve ganglia can't be reached by any available antiviral agents.**

Could Indigenous bacteria in the body inactivate the Antimicrobial Agent?

There is a theory that says yes that certain indigenous bacteria produce enzymes that hydrolyze antibiotics such as penicillin.

Hospital/Community Susceptibility Patterns

If a resistant strain of the putative infectious agent is prevalent in the community or the hospital, then an antimicrobial must be chosen that will be effective in the face of resistance. For example, in hospitals with numerous strains of methicillin-resistant staph isolated from patients in various units, a new surgical wound infection must be treated empirically with vanocomycin, which is effective against methicillin-resistant staph, until the agent is identified as other than staph or the susceptibility pattern of the isolate is known.
Standard treatment of gonorrhea through the U.S. must be with a more expensive agent such as ceftrizxone that is effective against resistant strains, now that penicillin-resistant gonococci are rampant.

Dosing Schedule

Antimicrobial agent may cost less initially, if it is delivered intravenous every 6 hr, it places difficult demands on the pharmacy and nurses. An equally effective antimicrobial that is slightly more expensive but can be administered every 8 hr will be more cost effective in the long run. Those on numerous chemo regimens must be treated in such a manner as to maximize the therapies and avoid antagonisms between agents.

Toxicities

- **Adverse effects outweigh the benefits in some cases.**
- **Clofazimine used to treat leprosy, is a dye that can cause the skin to become orange-brown.**
- **Chloramphenical used against many anaerobic and gram-negative bacteria can interfere with bone marrow function.**
- **Cephalosporins. most widely used antimicrobial, often contributes to development of antibiotic associated pseudomembranous colitis caused by overgrowth of Clostridium difficle in the bowel.**
- **Aminoglycodes have nephrotroxic and ototoxic effects.**

- **Moxalactam causes bleeding abnormalities.**
- **Those with allergies to penicillin may exhibit reactions to all B-lactam antimicrobial agents.**
- **In severe cases the patient must be temporarily hyposentisized to allow administration of the drug of choice.**
- **Metronidazole has negative effects on a fetus and can't be used to treat Trichomonas.**
- **Tetracycline can discolor developing bones and teeth and interfere with normal development, so not for pregnant women or children under 8 yr old.**
- **Some quinolones can interfere with growth of long bones, use carefully with young children.**

DRUG ANTIBACTERIAL AGENTS

Inhibition of cell wall synthesis
Penicillins, cephalosporins, vancomycin, bacitracin, imipenem, aztreonam

Inhibition of protein synthesis
50S ribosomal subunit
Clindamycin, erythromycin, chloramphenicol
30S ribosomal subunit
Aminoglycosides, tetracyclines

Transcription inhibitors
Rifampin, actimomycin

Protein assembly inhibitor
Griseofulvin

Metabolic analogs
Sulfonamides, 5-fluorocytosine, isoniazid, vidarabine, acyclovir, ribavirin

Inhibitors of cell membrane activities
Colistin, polyenes, imidazoles, possibly amantadine, amphotericin B, ketoconazole

Inhibitors of DNA function
Quinolones, metronidazole, novobiocin, flucytosine

INHIBITION OF CELL WALL SYNTHESIS (Penicillins, Cephalosporins et al)

Penicillins and cephalosporins are members of a broad group of antimicrobial agents called B-lactams. These agents are structurally similar to the terminal peptides that participate in the final stage of cross linking the separate structures of the peptidoglycan bacteria cell wall. Transpeptidases and other enzymes bind the penicillin instead of the peptide side chain, the enzymes become inactive, and cross linkage stops. The enzymes that bind penicillins located in or on the cell membrane are called penicillin binding proteins. Several types are present in all bacteria that are susceptible to the penicillins and cephalosporins.

Once the cell wall structure is no longer stable, bacteria are killed by lysis. Either autolytic enzymes, such as those active in penicillin-mediated killing of Strep Pneumonia or other mechanisms that cause leaky membranes mediate cell lysis and death. Penicillins are considered to be bactericidal.

Penicillin derivatives are achieved by adding or modifying side chains to the structure of the basic B-lactam ring.

Vancomycin is a glycopeptide antimicrobial that prevents the formation of peptidoglycan by binding to cell wall peptide precursors. The agent is active only against gram-positive bacteria.