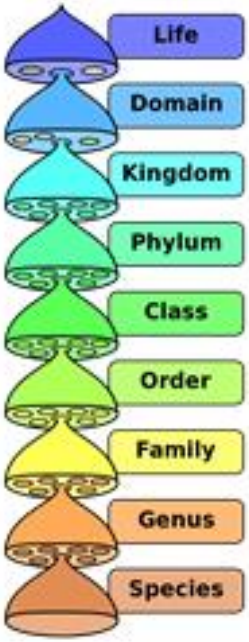
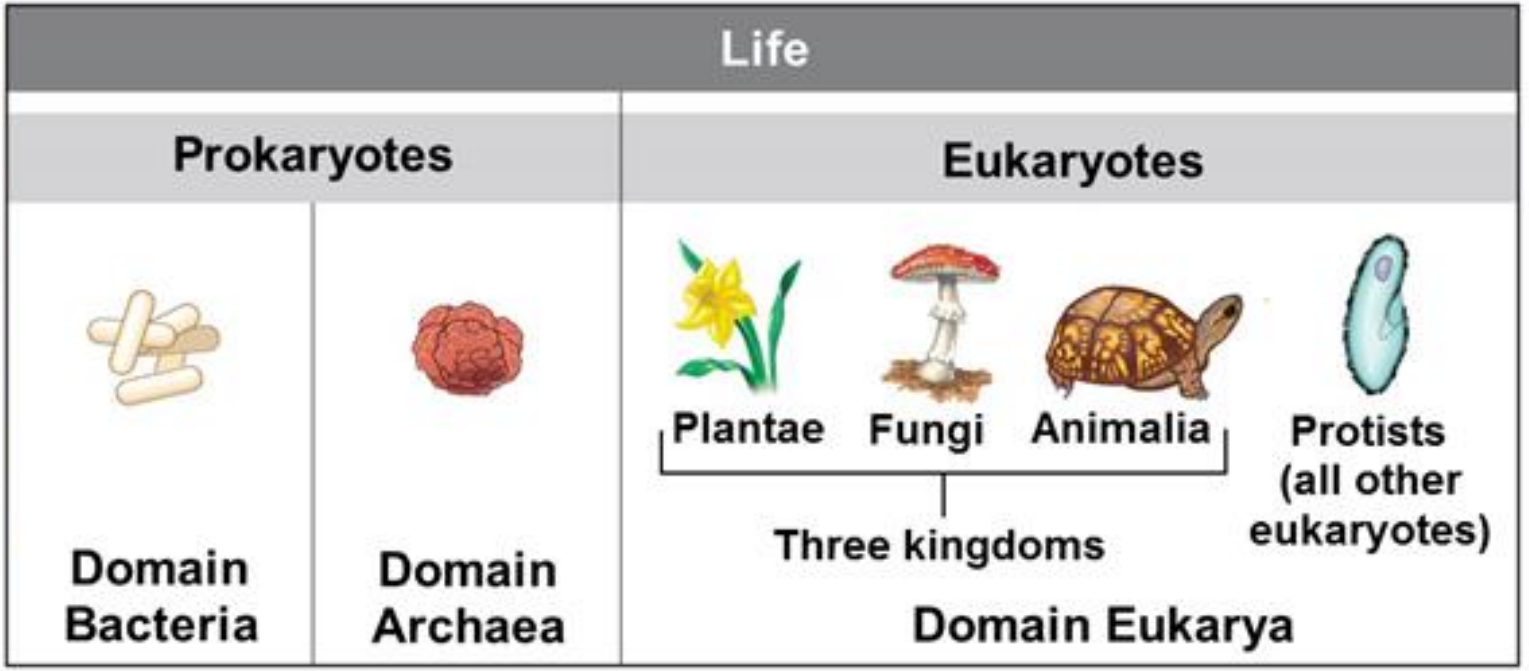
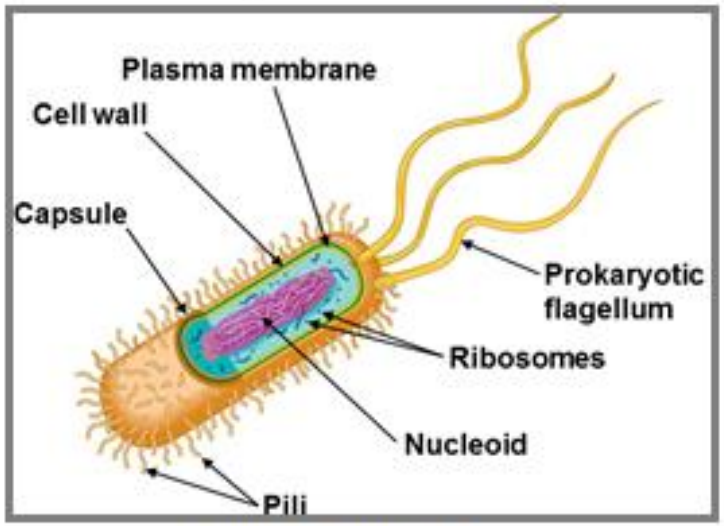
Chapter 6

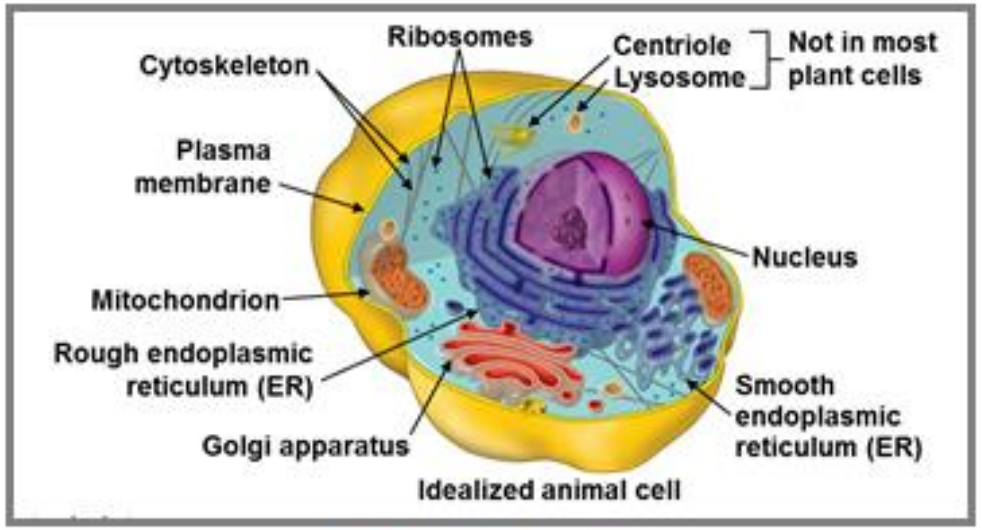
Infection







Prokaryotes

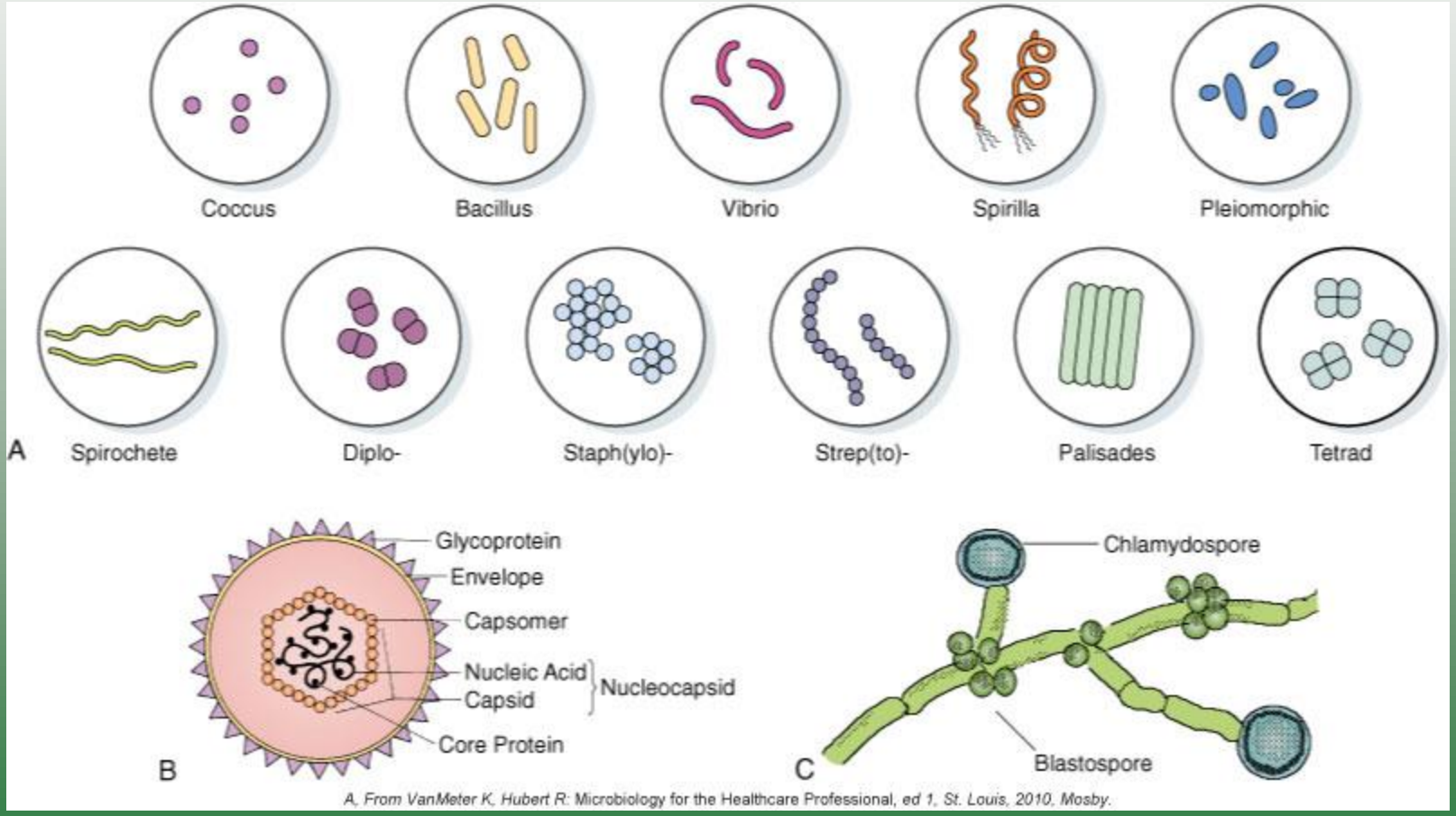


Eukaryotes

Microorganisms

- Small living forms
- Include bacteria, fungi, protozoa, viruses
- Many can grow in artificial culture medium
- Nonpathogenic
  - Usually do not cause disease unless conditions change
  - Part of normal flora
  - Often beneficial
- Pathogens
  - Disease-causing microbes

Types of Microorganisms



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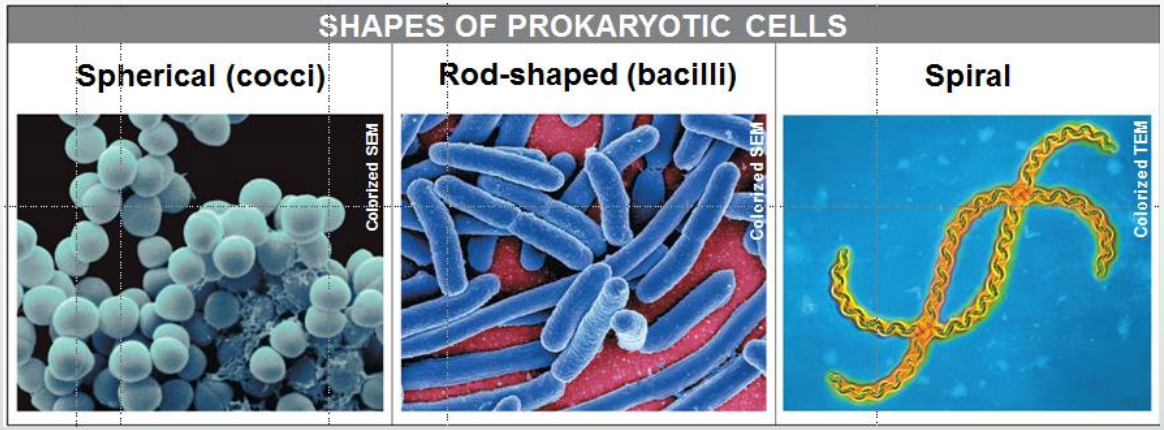
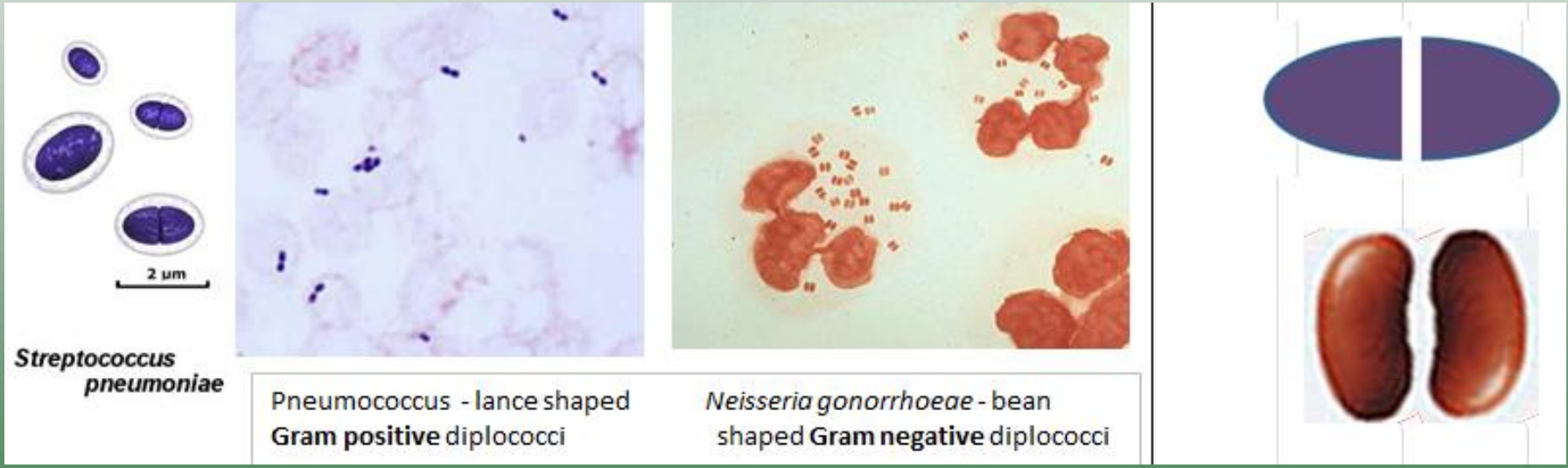




- further defined by their growth requirements

culture no.	ONPG	ADH	LDC	ODC	CIT	H2S	URE	TDA	IND	VP	GEL	GLU	MAN	INO	SOR	RHA	SAC	MEL	AMY	ARA	identification
8101	+	–	+	+	–	–	–	–	+	–	–	+	+	–	+	+	+	+	–	+	*Escherichia coli*

Different kinds of agar in petri dishes are inoculated as a first step.

A series of substrates are inocculated to see which nutriens support the bacterium's growyh. These nutrients include different sugars, amino acids, and other nutrients. Growth results in a color change in the growth medium. The results produce a profile that identifies the species.

Other methods:

- **DNA analysis**

- **MALDI-TOF MS** , an elegant and very fast method in which a bit of a colony is spotted on a plate and mixed with a fluid to prepare it, after which it is vaporized by a laser and the vapor is analyzed to produce an electronic foot print that can be compared with a data base.

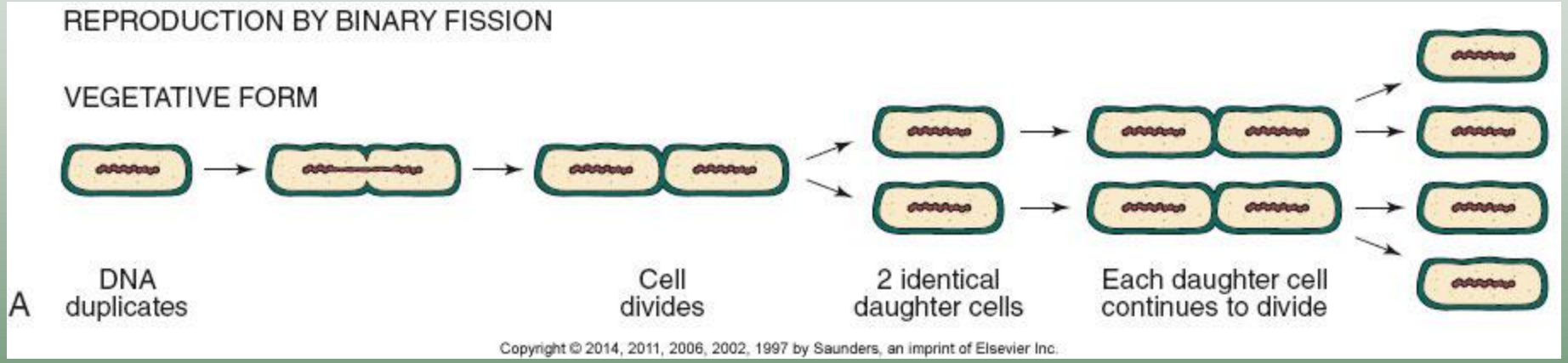
Bruker Corporation Announces **FDA Clearance** to Market the MALDI Biotyper CA System BILLERICA, Mass.--(BUSINESS WIRE)--**Nov. 26, 2013**-- Bruker Corporation (NASDAQ: BRKR) today announced that it has been granted U.S. FDA clearance under Section 510(k) to market its MALDI Biotyper CA System in the United States for the identification of Gram negative bacterial colonies cultured.

- http://www.bruker.com/products/mass-spectrometry-and-separations/maldi-biotyper/overview.html

Bacteria

- Classified as prokaryotes
- No nuclear membrane—no nucleus
- Function metabolically and reproduce
- Divide by binary fission
- Complex cell wall structure
- Do not require living tissues to survive
- Vary in size and shape

Reproduction by Binary Fission



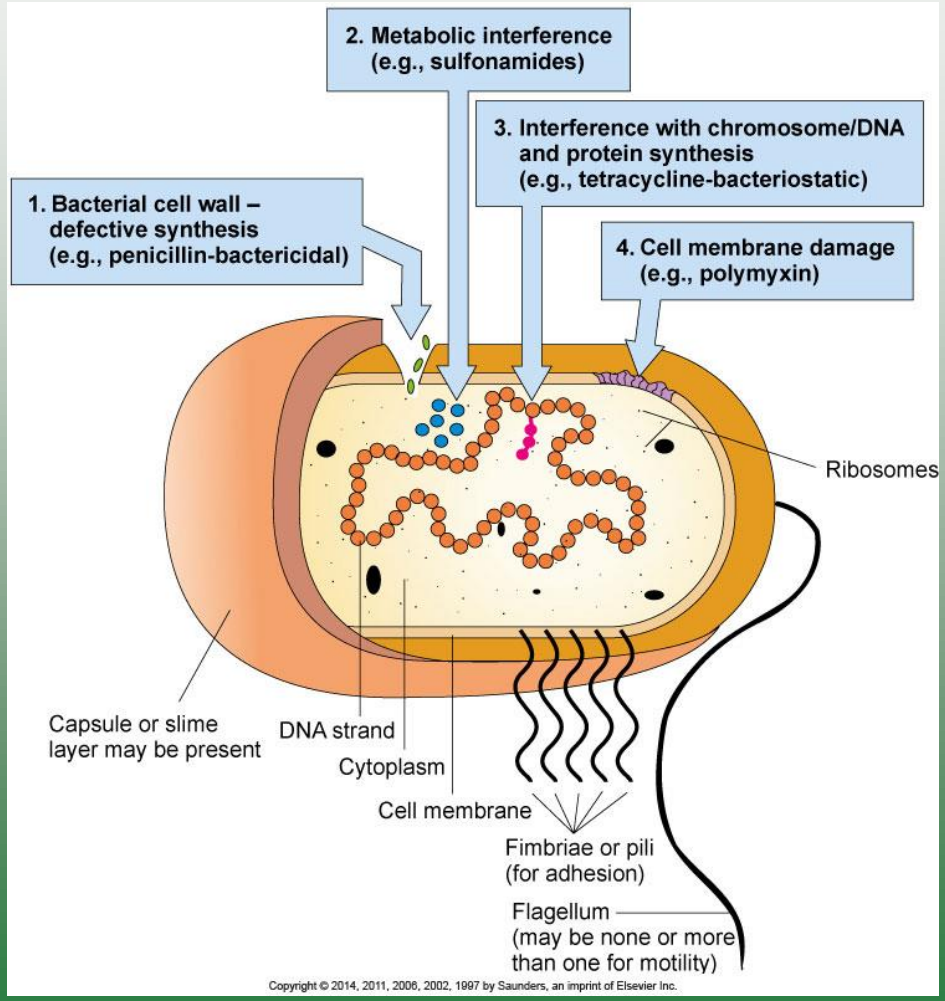
Major Groups of Bacteria

- Bacilli
  - Rod-shaped organisms
- Spirochetes
  - Include spiral forms and *Vibrio* spp.
- Cocci
  - Spherical forms
    - Diplococci
    - Streptococci
    - Staphylococci

Basic Structure of Bacteria

- Rigid cell wall
  - Protects and provides a specific shape
  - Two types that differ in chemical composition:
    - Gram-positive
    - Gram-negative
  - Useful in selecting appropriate antimicrobial therapy
- Cell membrane located inside the bacterial cell wall
  - Selectively permeable

Structure of a Bacterium and Mode of Action of Antimicrobial Drugs



Basic Structure of Bacteria (Cont.)

- External capsule or slime layer
  - Found in some
  - Outside the cell wall
  - Offers additional protection
- Flagellae
  - One or more attached to cell wall
  - Provide motility for some species
- Pili or fimbriae
  - Tiny hairlike structures—found in some bacteria
  - Assist in attachment to tissue
  - Transfer of DNA to another bacterium

- Flagellae Videos

Basic Structure of Bacteria (Cont.)

- Cell membrane
  - Inside the bacterial cell wall
  - Selectively permeable
- Cytoplasm contains:
  - Chromosome
    - One long strand of DNA
  - Ribosomes and RNA
  - Plasmids
    - DNA fragments; nonchromosomal; exchange DNA during conjugation

Basic Structure of Bacteria (Cont.)

- Toxins
  - Exotoxins
    - Usually produced by gram-positive bacteria
  - Endotoxins
    - Present in the cell wall of gram-negative bacteria
    - Released on death of bacterium
    - Vasoactive compounds that can cause septic shock
  - Enzymes
    - Damage tissues and promote spread of infection

Spore Formation

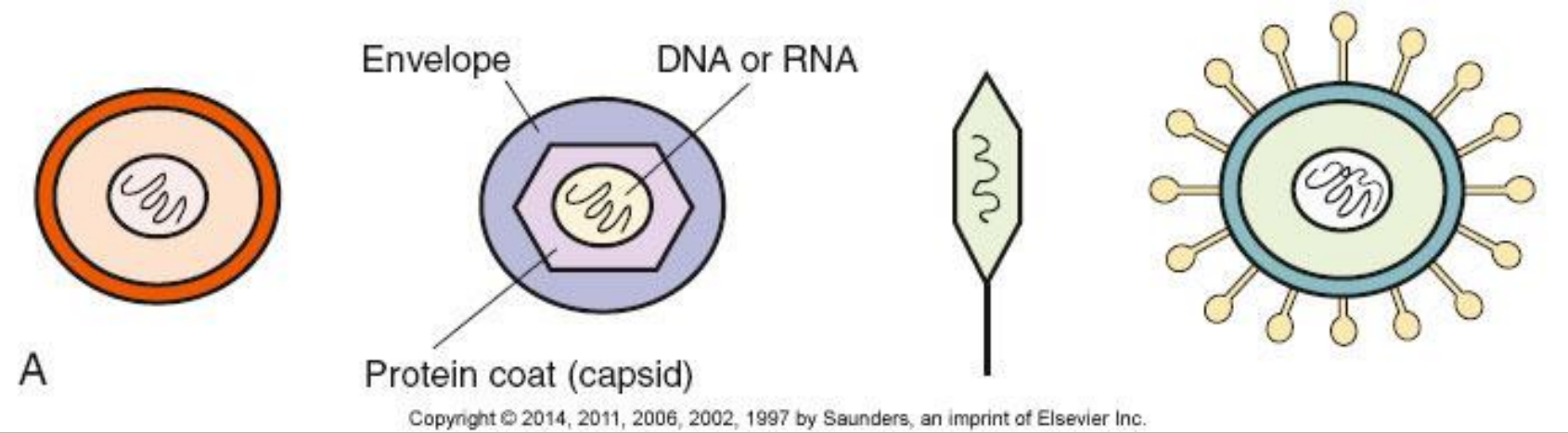
- Spores
  - Formed by several species
  - Dormant-latent form of bacterium
  - Can survive long periods of time in spore state
  - Highly resistant to heat and disinfectants

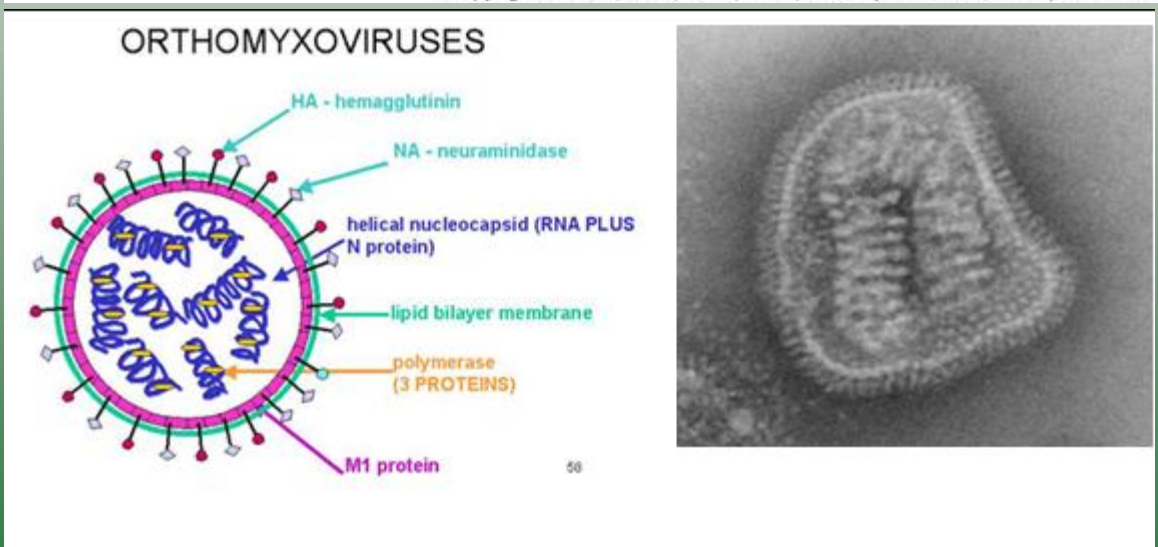
Endospore

Viruses

- Small obligate intercellular parasites
- Protein coat or capsid
- Protein coat comes in various shapes and sizes
  - Can change (mutate) quickly
- Nucleic acid
  - DNA or RNA
  - Classification dependent on nucleic acid present
  - Some RNA-containing viruses contain reverse transcriptase enzyme to convert RNA to DNA.

Different Shapes of Viruses

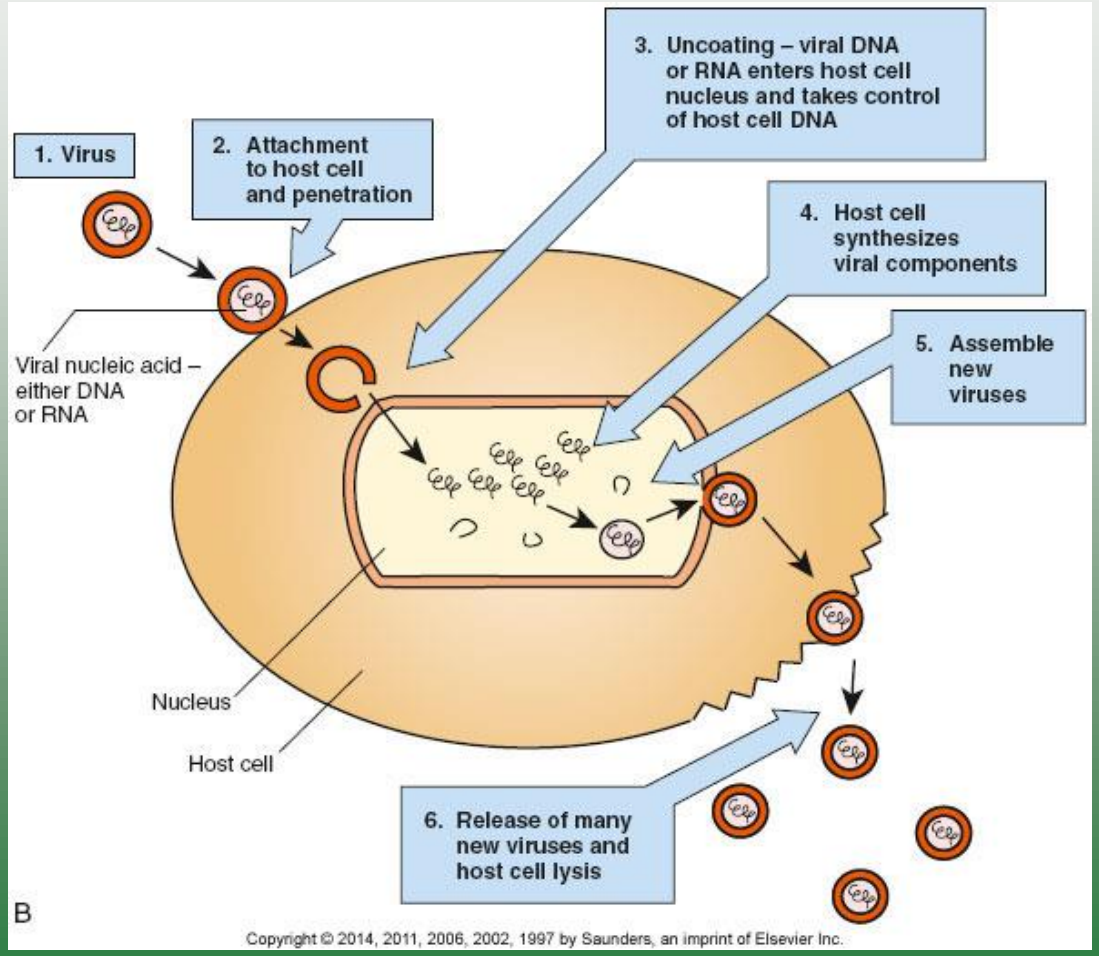




Active Viral Infection

- Virus attaches to host cell.
- Viral genetic material enters the cell.
- Viral DNA or RNA takes control of cell.
- Uses host's cell to synthesize viral proteins and nucleic acids
- New viruses are assembled in cytoplasm of cell.
- Viruses released by lysis of host cell or by budding from host cell membrane

Viral Replication



Latent Viral Infection

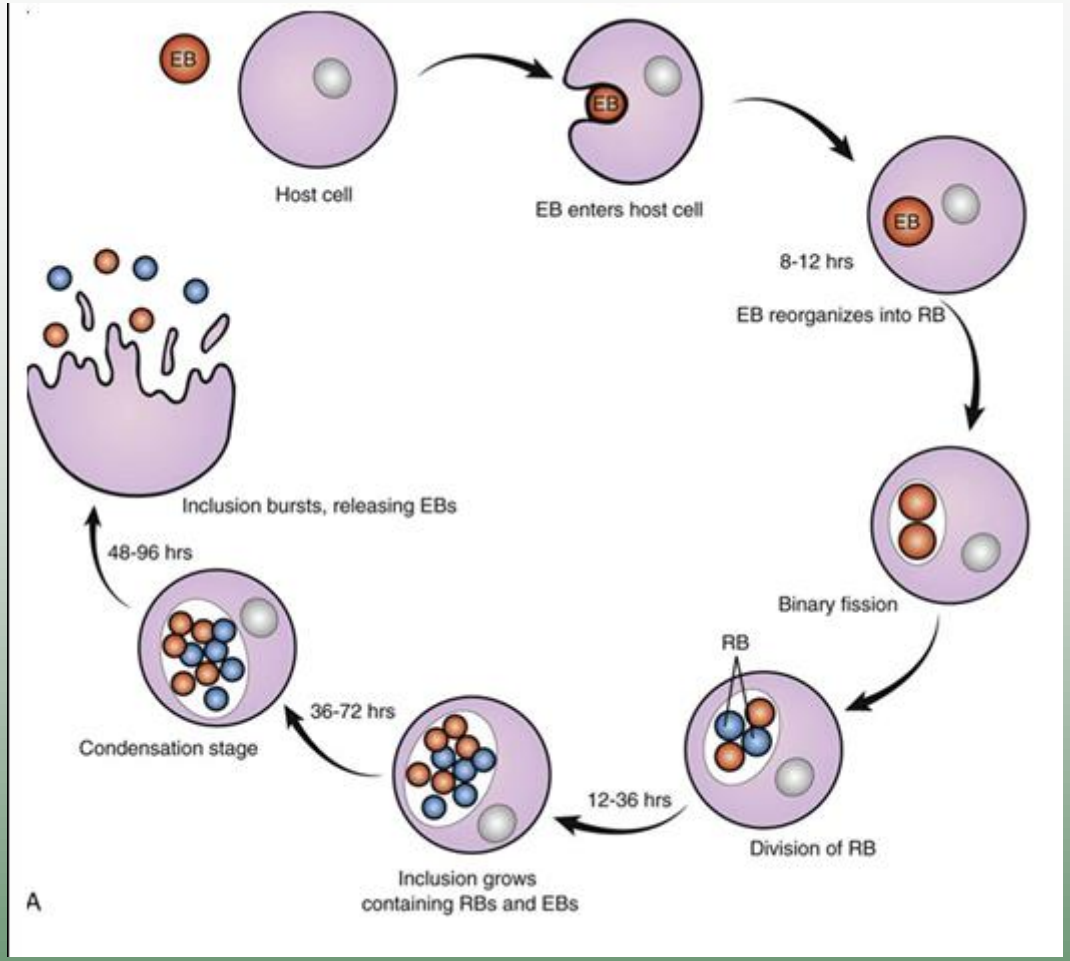
- Virus enters cell as with active infection.
- Viral proteins are produced and Inserted into membrane of the host cell. This may stimulate an immune response and destruction of host cell.
- Virus may reproduce actively if immune system is depressed (e.g., herpesviruses)

Chlamydia, Rickettsiae, Mycoplasmas

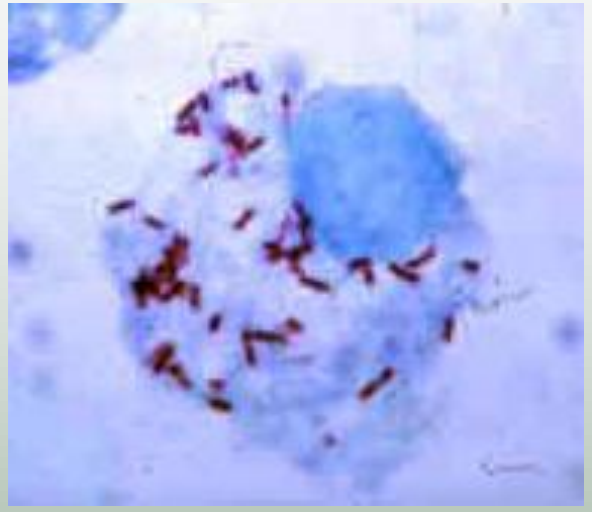
- Obligate intercellular parasites.
- Do not grow on artificial media
- Some similarities with both bacteria and viruses
- Lack some basic components
- Classified as bacteria
- Replicate by binary fission within host cell

Chlamydia, Rickettsiae, Mycoplasmas (Cont.)

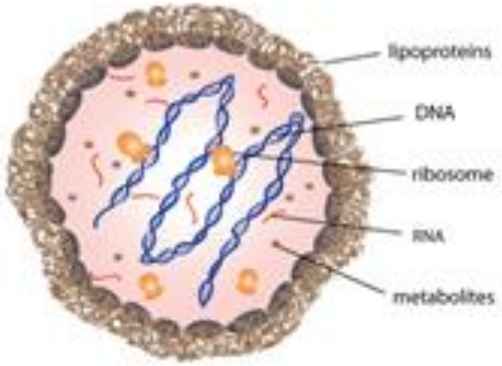
- Chlamydia
  - Common cause of sexually transmitted disease
  - Can result in infertility
- Rickettsiae
  - Gram-negative
  - Transmitted by insect vectors (lice, ticks)
- Mycoplasmas
  - Lack cell wall
  - Cause of atypical type pneumonia

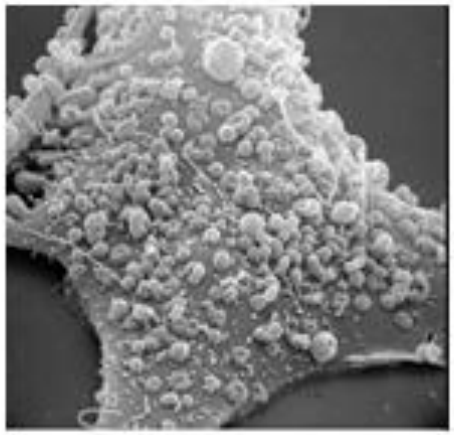


Chlamydiae are considered very primitive forms related to bacteria:
- They exist in two forms. One, the elementary body (EB) is infectious, possessing a cell wall and the ability to bind to epithelial cells. The other form, the reticulate body (RB) is noninfectious, but uses the host cell to make ATP and reproduce as an obligate intracellular organism. After large numbers of new microbes are produced inside the host cells, the new RBs change into EBs, rupturing the host cells' membranes and dispersing to infect more cells.



Rickettsiae are **tiny gram-negative bacteria**





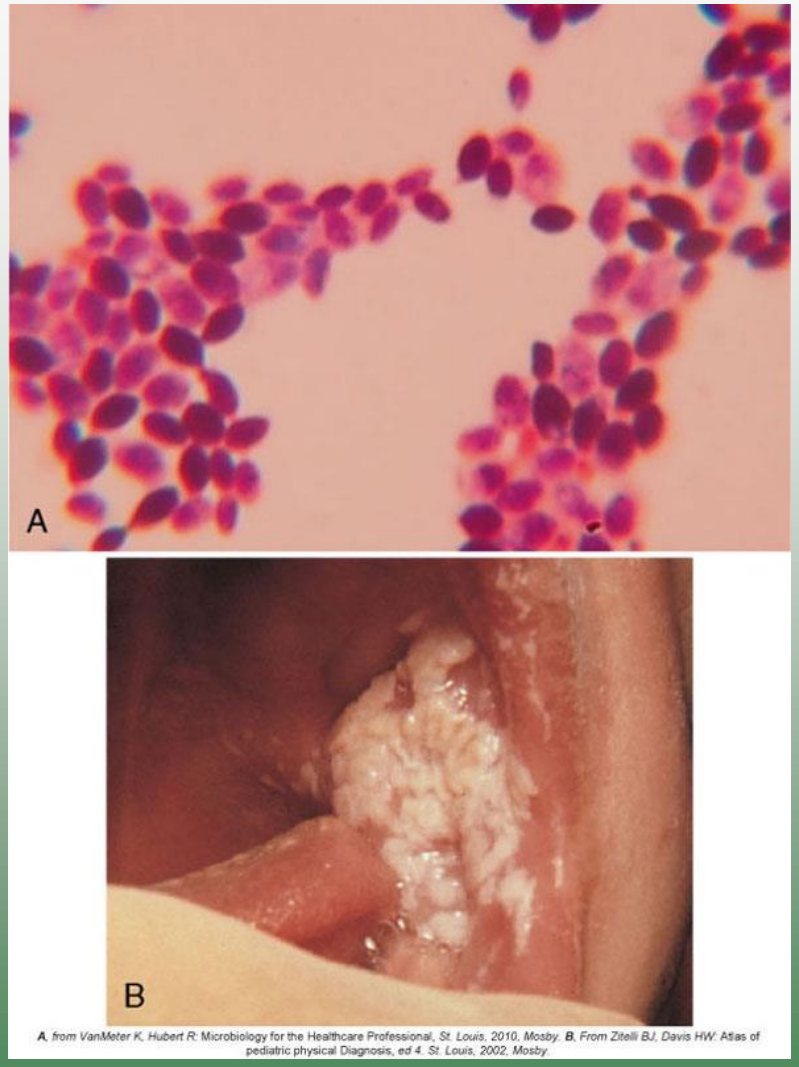
Mycoplasma on the surface of a cell.

Fungi

- Eukaryotic organisms (contain nucleus)
- Found throughout environment
  - On animals, plants, humans, food
- Fungal or mycotic infection
  - From single-celled yeast or multicellular molds
- Only a few are pathogenic.
  - Cause primary infection on skin or mucous membranes but may spread systemically particularly in immunosuppressed individual

Examples of Fungal Diseases

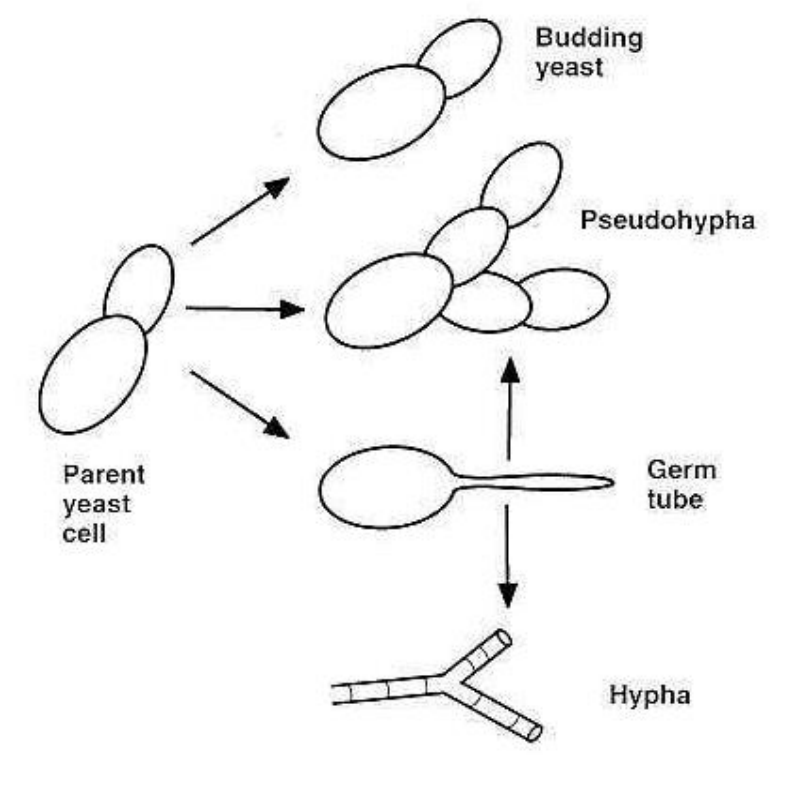
- *Histoplasma* can be inhaled and may infect lungs of a normal person or may spread systemically in an immunocompromized patient.
- *Tinea pedis* (athlete's foot)
- *Candida*: usually harmless, but opportunistic
  - Causative agent of thrush and vaginitis



A, from VanMeter K, Hubert R: Microbiology for the Healthcare Professional, St. Louis, 2010, Mosby. B, From Zitelli BJ, Davis HW: Atlas of pediatric physical Diagnosis, ed 4. St. Louis, 2002, Mosby.

Microscopic appearance of yeast stained with PAS.

Gross appearance of yeast in oral thrush.



Yeast can:

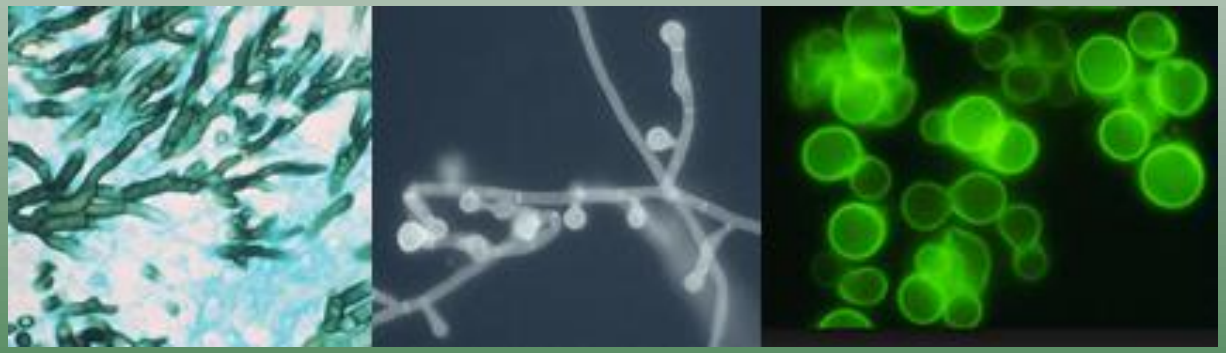
1. Divide and form only yeast (not shown).
2. Bud and make pseudohyphae.
3. Give rise to true hyphae.

Many Techniques to Visualize Fungi

Unstained
Phase Contrast

India Ink
Negative Stain

PAS Stain



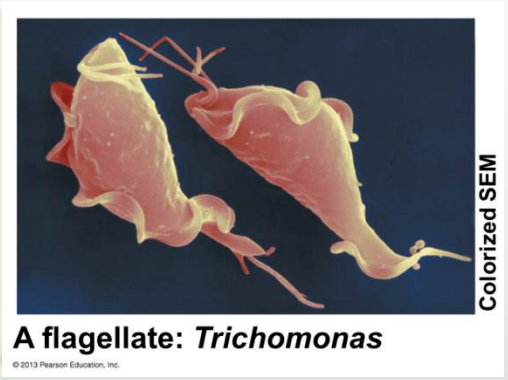
GMS Silver Stain

Calcofluor White
Fluorescent Stain

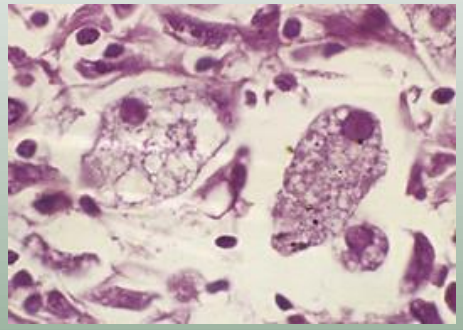
Fluorescent Stain

Protozoa

- Eukaryotic forms
- Unicellular, lack cell wall
- Many live independently, others are obligate parasites
- Pathogens are usually parasites.
- Examples of protozoal diseases:
  - Trichomoniasis
  - Malaria
  - Amebic dysentery

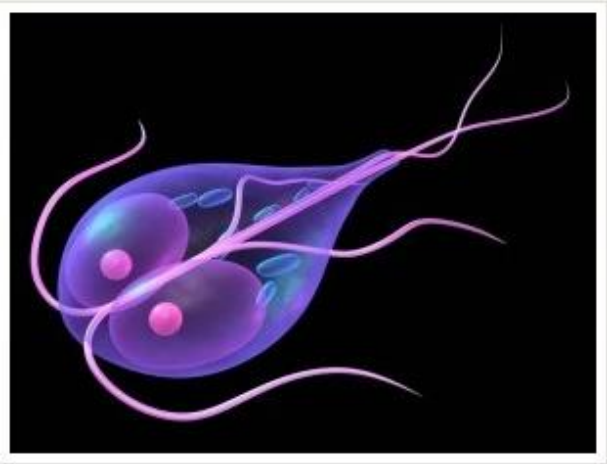


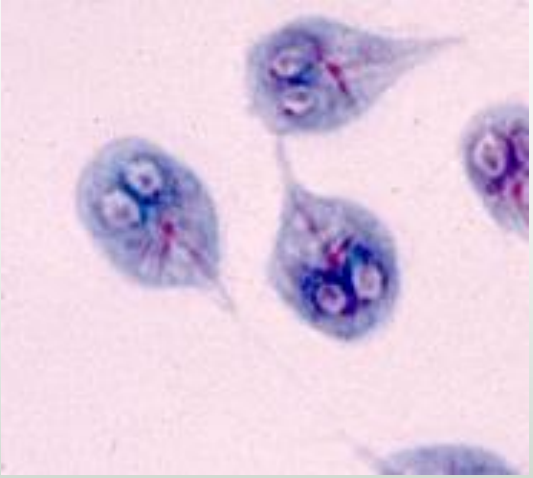
- Trichomonas



- Ameba, Videos

- Plasmodium





Giardia lamblia

Other Agents of Disease

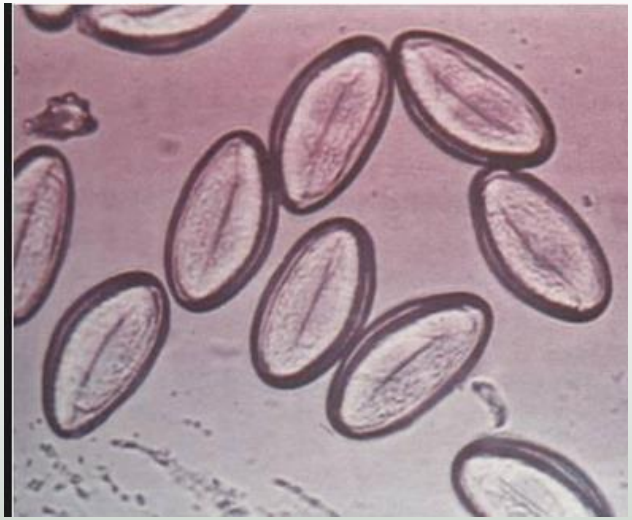
- Helminths (flatworms or roundworms)
  - Are not microorganisms
  - Parasites
  - May be small or up to 1 m in length
  - Life cycle with at least three stages
    - Ovum, larva, adult
  - Enter body through skin or by ingestion, depending on species
  - Infections more commonly found in young children
  - Infection can be life-threatening in an immunosuppressed client.

Helminth Diseases

- Pinworms: ova inhaled in dust in fecally contaminated areas; common in children worldwide
- Hookworms: larvae enter skin from fecally contaminated soil in tropical areas
- Tapeworms: most common form transmitted by larvae in undercooked pork
- *Ascaris*—giant roundworm: ingested with food that has been grown in feces-contaminated soil or prepared with hands that have been in feces-contaminated soil

Other Agents of Disease (Cont.)

- Prions
  - Protein-like agents that change the shape of proteins within host cells
  - Transmitted by contaminated tissues
    - Ingestion of meat
    - Infected blood or donor organs
  - Cause degenerative disease of the nervous system
  - Human prion diseases
    - Creutzfeldt-Jacob disease and variant Creutzfeldt-Jacob disease
    - Both rapidly progressive and fatal



Pinworm *Enterobius Vermicularis*

Tape Worm

Resident Flora

- Many areas of the body have a resident population of mixed microorganisms termed *normal flora.*
  - Skin
  - Nasal cavity
  - Mouth
  - Gut
  - Vagina
  - Urethra

Principles of Infection

- Infection—organism is able to reproduce in or on body's tissues
- Sporadic
  - In a single individual
- Endemic
  - Continuous transmission within a population
- Epidemic
  - Higher than normal transmission or spread to new geographical area
- Pandemic
  - Transmission has occurred on most continents.

Transmission of Infectious Agents

- Transmission from person to person
- Reservoir
  - Source of infection
  - Person with active infection
  - Person who is asymptomatic
- Carrier
  - A person may never develop the disease but still is a carrier.
  - A person with subclinical signs of the disease

Transmission of Infectious Agents: Links in the Infection Chain

- Agent: the microbe causing the infection
- Reservoir:
  - Environmental source such as contaminated soil
  - Infected person or animal
    - Person may carry the agent and show no signs of disease
    - Person or animal may show signs and symptoms of disease

Transmission of Infectious Agents: Links in the Infection Chain (Cont.)

- Portal of exit: means whereby the agent leaves the reservoir
- Mode of transmission: method whereby the agent reaches a new susceptible host
  - Air
  - Water
  - Direct contact
  - Food

Transmission of Infectious Agents: Links in the Infection Chain (Cont.)

- Portal of entry: access to new host
- Susceptible host: susceptibility will depend on:
  - Health status
  - Immunity
  - Age
  - Nutrition

Modes of Transmission

- Direct contact
  - No intermediary
  - Touching infectious lesion, sexual activity
  - Contact with infected blood or bodily secretions
- Indirect contact
  - Involves intermediary object or organism
  - Contaminated hand or food
  - Fomite—inanimate object

Modes of Transmission (Cont.)

- Droplet transmission
  - Respiratory or salivary secretions are expelled from infected individual
- Aerosol transmission
  - Involve small particles from the respiratory tract
  - Suspended in air and can travel farther than droplets
- Vector-borne
  - Insect or animal is an intermediate host

Nosocomial Infections

- Occur in health care facilities
  - Hospitals, nursing homes, physician's offices, dental offices
- 10% to 15% of patients acquire an infection in the hospital because of:
  - Many microbes present
  - Patients with undiagnosed infectious disease
  - Shared environment
  - Treatment that may cause weakened immune system
  - Many health care workers and fomites act as reservoirs.

Host Resistance and Microbial Virulence

BOX 6-1 Host Resistance and Microbial Virulence

Host Resistance	Increased Microbial Virulence
Intact skin and mucous membrane	Production of exotoxins and endotoxins
Body secretions—stomach acid, tears	Production of destructive enzymes
Nonspecific phagocytosis	Spore formation
Effective inflammatory response	Entry of large number of organisms into body
Absence of disease	Presence of bacterial capsule and pili
Effective immune system	
Interferon production (virus)	

Factors That Decrease Host Resistance

- Age (infants and older adults)
- Pregnancy
- Genetic susceptibility
- Immunodeficiency
- Malnutrition
- Chronic disease
- Severe physical or emotional stress
- Inflammation or trauma
- Impaired inflammatory responses

Virulence and Pathogenicity

- Pathogenicity
  - Capability of a microbe to cause disease
- Virulence
  - Degree of pathogenicity
    - Invasive qualities (e.g., motility or enzymes)
    - Toxins
    - Adherence to tissue by pili, fimbriae, specific receptor sites
    - Ability to avoid host defenses

Techniques to Reduce Transmission

- Adequate cleaning of surroundings and clothing
- Sterilization
- Disinfectants
- Antiseptics

Physiology of Infection

- Incubation period
  - Time between entry of organism into the body and appearance of clinical signs of disease
  - Vary considerable with different organisms
- Prodromal period
  - Fatigue, loss of appetite, headache
  - Nonspecific—“coming down with something”
  - More evident in some infections than others
- Acute period
  - Infectious disease develops fully

Means of Disinfection

- Sterilization of equipment by:
  - Chemicals
  - Heat in an autoclave
  - **NOTE:** Equipment must be cleaned prior to sterilization or it will remain contaminated!
- Use of chemicals:
  - Antiseptics are used on the skin and tissues.
  - Disinfectants are used on surfaces or objects.

Patterns of Infection

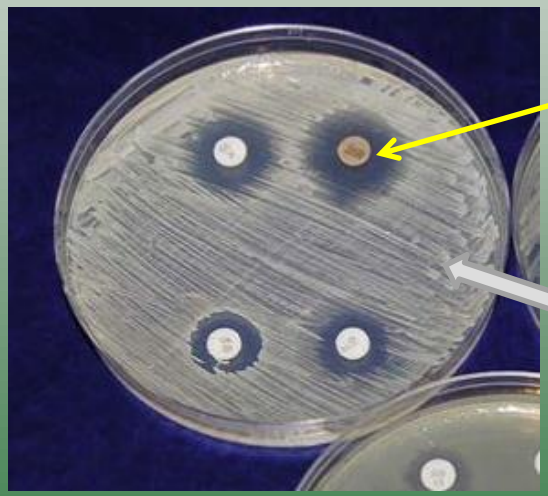
- Local infections
- Focal infections
- Systemic infections
  - Septicemia
  - Bacteremia
  - Toxemia
  - Viremia
- Mixed infections
- Primary infections
- Secondary infections, subclinical infections

Signs and Symptoms of Infection

- Local signs of inflammation
  - Pain, swelling, redness, warmth
    - If bacterial—purulent exudate
    - If viral—serous, clear exudate
- Systemic signs of inflammation
  - Fever may be present.
  - Fatigue and weakness
  - Headache
  - Nausea

Methods of Diagnosis

- Culture and staining techniques
  - Using specific clinical specimens
  - Drug sensitivity tests



Clear zone of no growth around antibiotic disk shows sensitivity of the bacterium to the antibiotic.

Lawn of bacteria

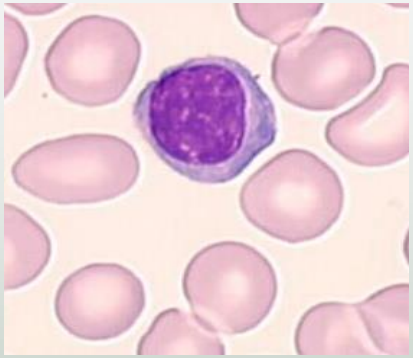
In culture dish

Blood tests

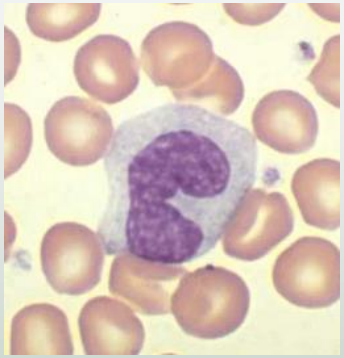
- Variations in numbers of leukocytes
  - Leukocytosis (elevated number of white blood cells, neutrophils, in peripheral blood) often indicates a bacterial infection.
  - Leukopenia (decreased number of white blood cells in peripheral blood) often indicate a viral infection. The percentage of lymphocytes is often increeased.
- Differential count, percent of each white cell type.
- C-reactive protein, acute phase reactant, elevated in inflammation.
- Erythrocyte sedimentation rate (ESR), elevated in inflammation.

White Blood Cell Types seen in Diff

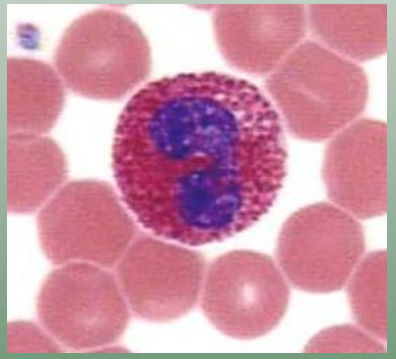
Neutrophil



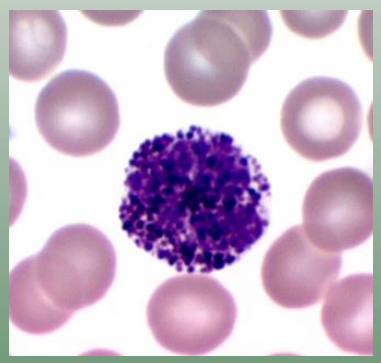
Lymphocyte



Monocyte



Eosinophil



Basophil

Platelet

Diagnostic Tests (Cont.)

- Immunological testing of body fluids
  - Antigen identification
  - Antibody titer

  If a patient has been exposed to or is infected with a given microbe, antibodies against the microbe may be in his circulation and a clue to what is infecting him.

Guidelines for Drug Therapy

- Drugs should be administered and taken as directed.
- Antimicrobial drugs should be taken until prescribed medication is completely used or until new drug is prescribed.
- If symptoms continue without reduction, contact the pharmacist or physician.
- Do not use drugs prescribed for other clients or other infections.
- If drug resistance is known to occur with infection, use multidrug therapy.

Classification of Antimicrobials

- Antibiotic
  - Drugs derived from organisms
- Antimicrobial
  - Antibacterial
  - Antiviral
  - Antifungal
- Bactericidal
  - Drugs destroy organism
- Bacteriostatic
  - Decrease rate of reproduction

Classification of Antimicrobials

- Broad spectrum
  - Effective against both gram-positive and gram-negative organisms
- Narrow spectrum
  - Effective against either gram-positive or gram-negative organisms

Early in an infection, before it is known what organism is operative, a broad spectrum antibiotic will be used.

Narrow spectrum is preferred for less side effects and less disruption of normal flora.

Mode of Action of Antibiotics

- Interfere with bacterial cell wall synthesis
  - Example: penicillin
- Increase permeability of bacterial cell membrane
  - Example: polymyxin
- Interfere with protein synthesis
  - Example: tetracycline
- Interfere with synthesis of essential metabolites
  - Example: sulfonamides

Mode of Action of Antivirals

- Drugs may act by:
  - Blocking entry into host cell
  - Inhibiting gene expression
  - Inhibiting assembly of the virus

- The influenza viruses are classified as RNA viruses of the myxovirus group.

- There are three subgroups of the influenza virus—type A, the most prevalent pathogen, type B, and type C.

- Types A and B cause epidemics and pandemics that tend to occur in cycles. The influenza virus, particularly type A, is difficult to control because it undergoes frequent mutations and engages in antigenic shift.