General aspects of bacteriology, bacterial structure and growth

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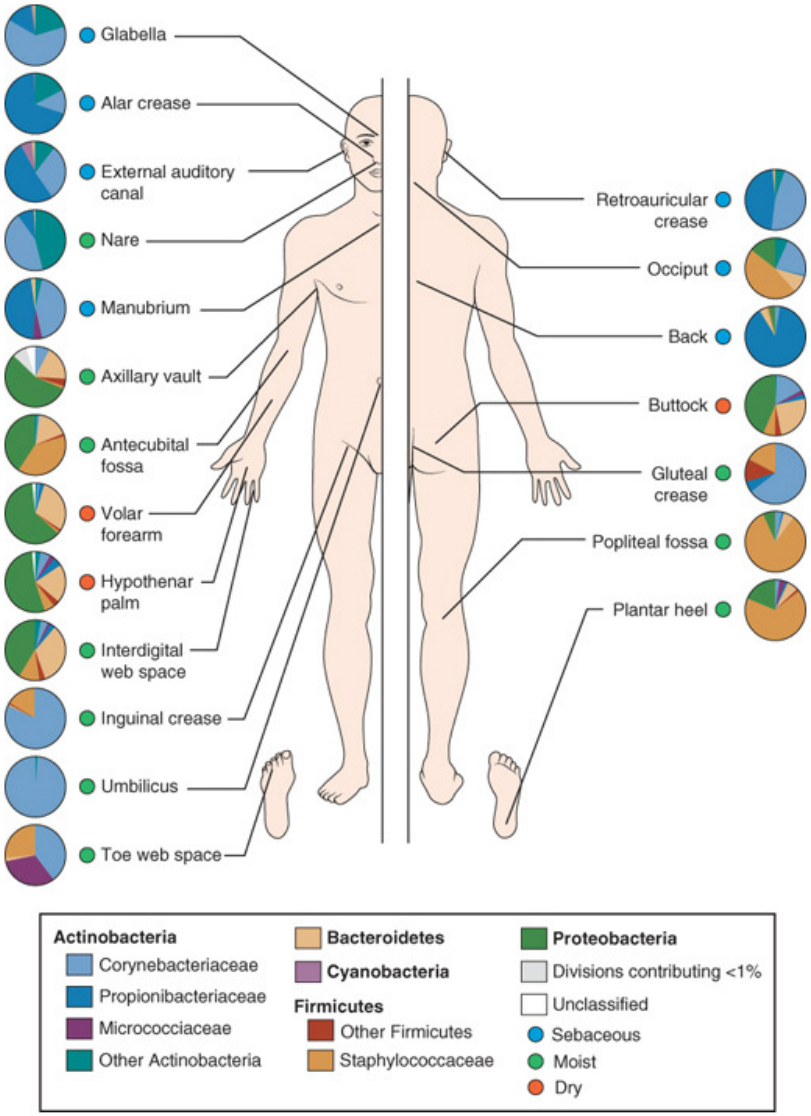
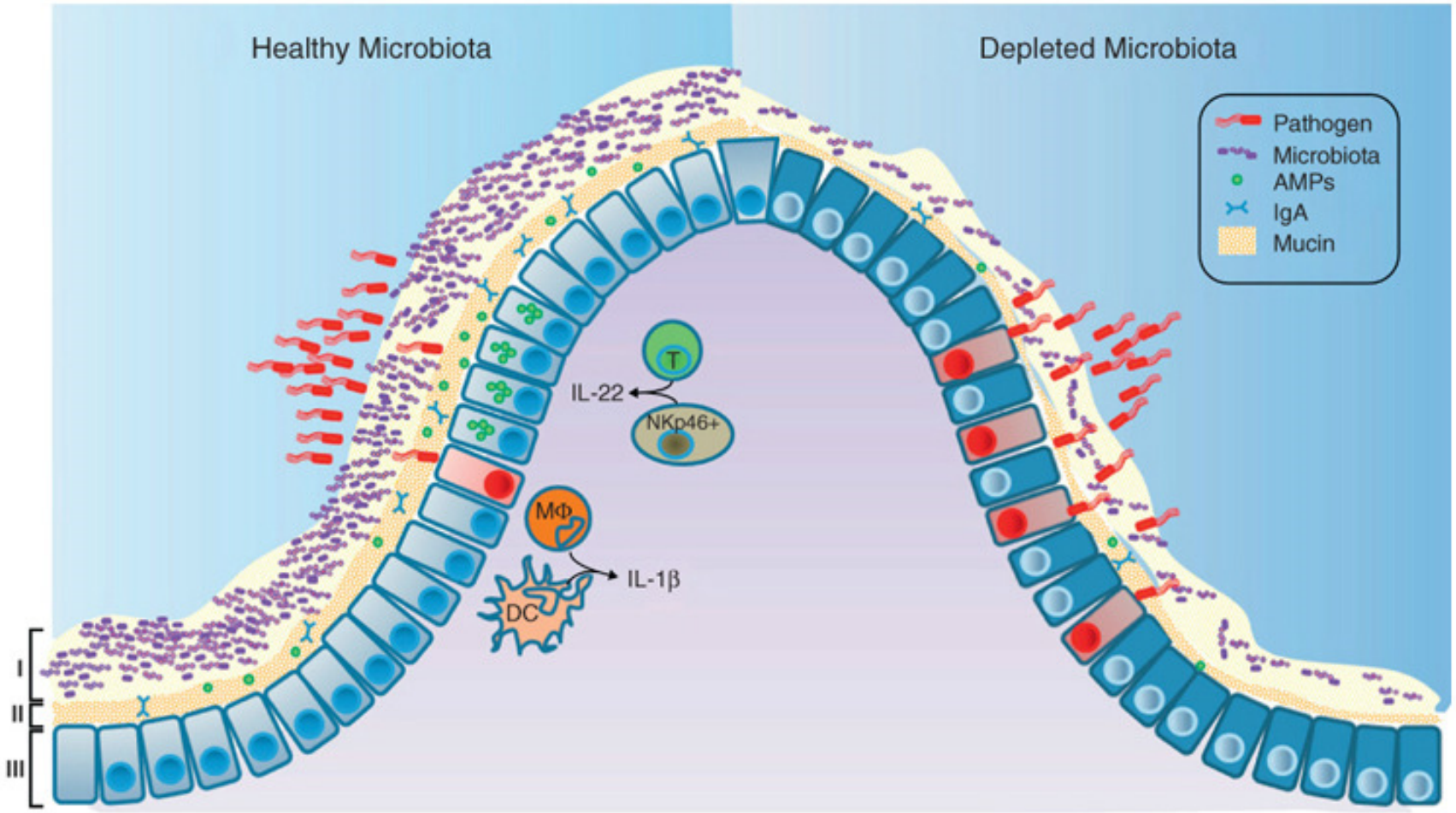
Human Microbiome Project

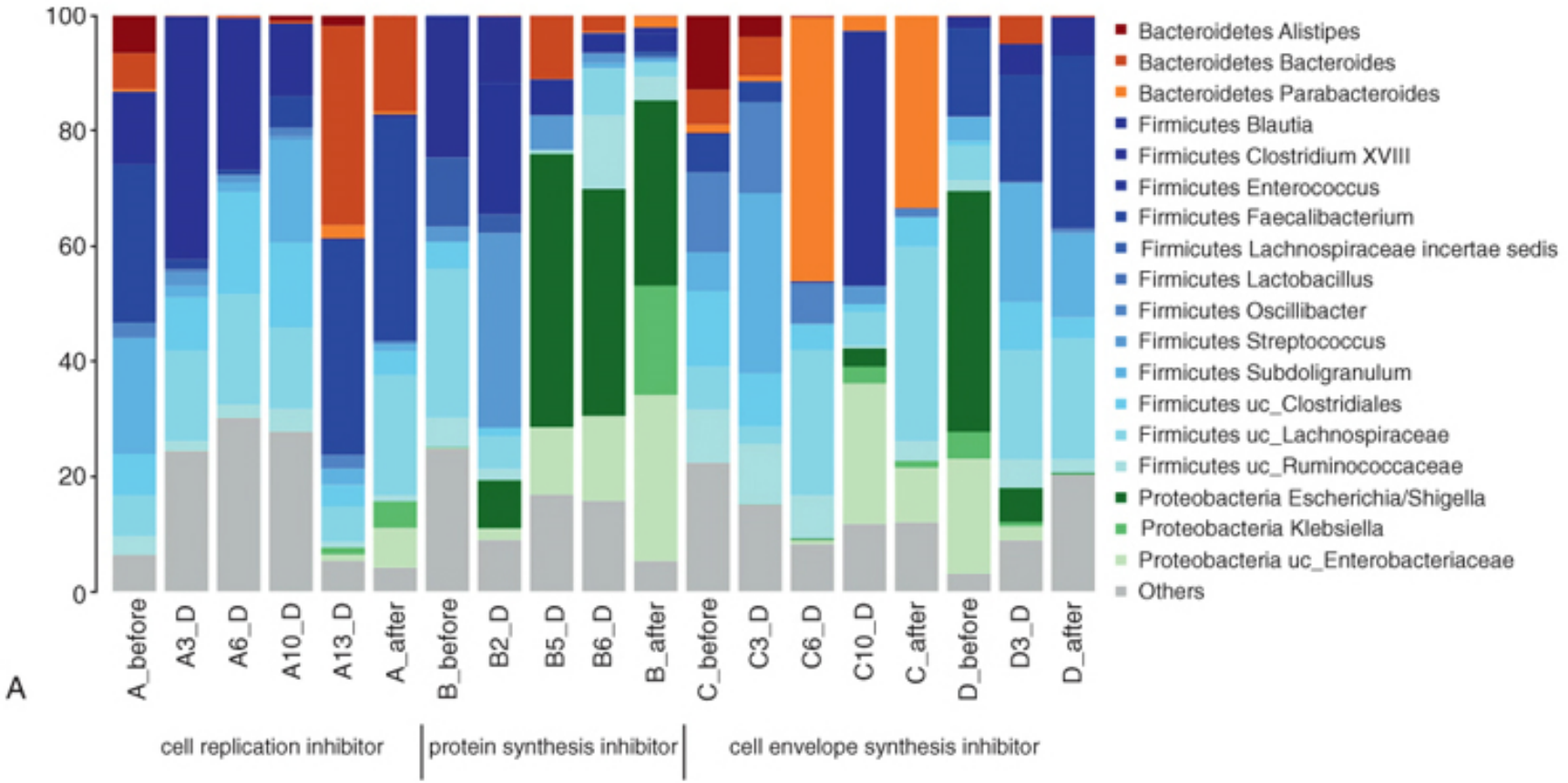


- Providing metabolic function
- Stimulating immunity
- Preventing with unwanted pathogens

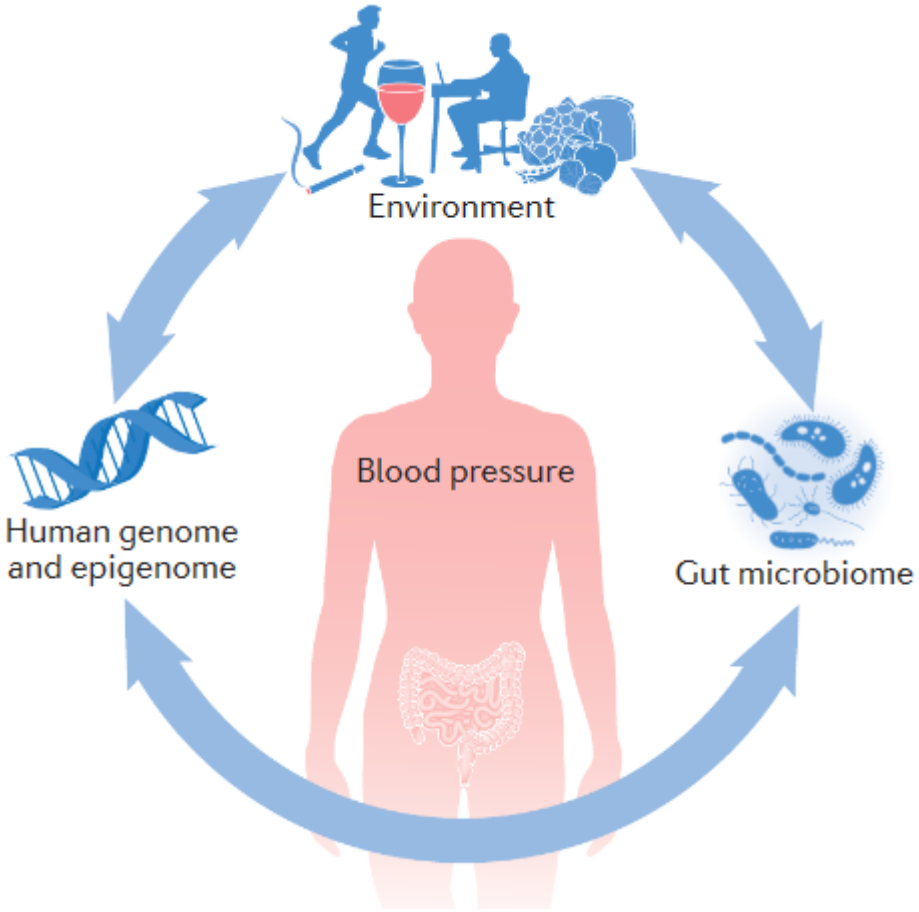
Intestinal microbiota protection against enteric infections



Effect of antibiotics on the gut microbiota

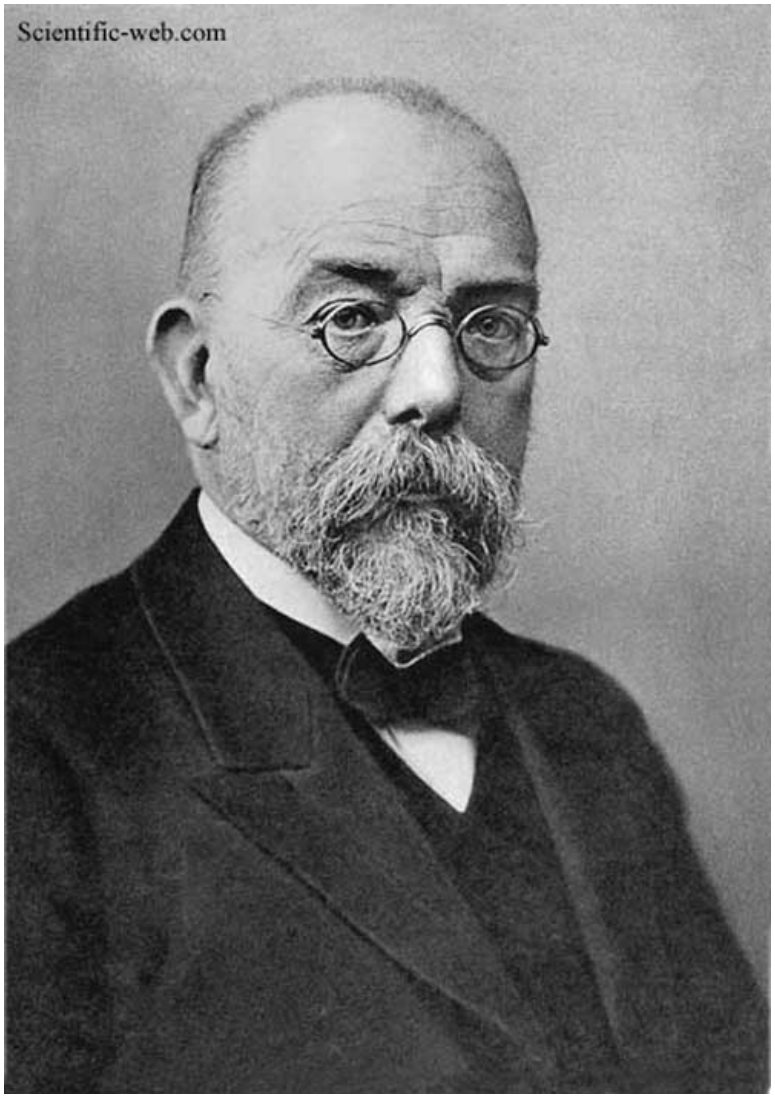


Gut microbiota regulates blood pressure



Nature Reviews Cardiology

Robert Koch



Infectious diseases are caused by microorganisms, each one responsible for a particular disease

Disease caused by a community of organisms rather than a single species of bacteria.

Probiotics and prebiotics

Probiotics are commonly gram-positive bacteria (e.g. *Bifidobacterium*, *Lactobacillus*) and yeasts (e.g. *Saccharomyces*).

Yogurt and Kefir.

Although probiotics are safe dietary supplement, not all probiotics are effective and for all people.

Prebiotics: the use of metabolic supplements promote a healthy microbiota (e.g. fiber, fructo-Oligosaccharide)

Symbiotics: Probiotics + prebiotics

Sterilization

Total destruction of all microbes

Method	Concentration or Level
Physical Sterilants	
Steam under pressure	121° C or 132° C for various time intervals
Filtration	0.22- to 0.45-µm pore size; HEPA filters
Ultraviolet radiation	Variable exposure to 254-nm wavelength
Ionizing radiation	Variable exposure to microwave or gamma radiation
Gas Vapor Sterilants	
Ethylene oxide	450-1200 mg/L at 29° C to 65° C for 2-5 hr
Hydrogen peroxide vapor	30% at 55° C to 60° C
Plasma gas	Highly ionized hydrogen peroxide gas
Chemical Sterilants	
Peracetic acid	0.2%
Glutaraldehyde	2%

Disinfection

Destroy most microbial form

Methods of Disinfection

Method	Concentration (Level of Activity)
Heat	
Moist heat	75° C to 100° C for 30 min (high)
Liquid	
Glutaraldehyde	2%-3.2% (high)
Hydrogen peroxide	3%-25% (high)
Chlorine compounds	100-1000 ppm of free chlorine (high)
Alcohol (ethyl, isopropyl)	70%-95% (intermediate)
Phenolic compounds	0.4%-5.0% (intermediate/low)
Iodophor compounds	30-50 ppm of free iodine/L (intermediate)
Quaternary ammonium compounds	0.4%-1.6% (low)

Antiseptic agents

Reduce the number of microbes

Antiseptic Agents

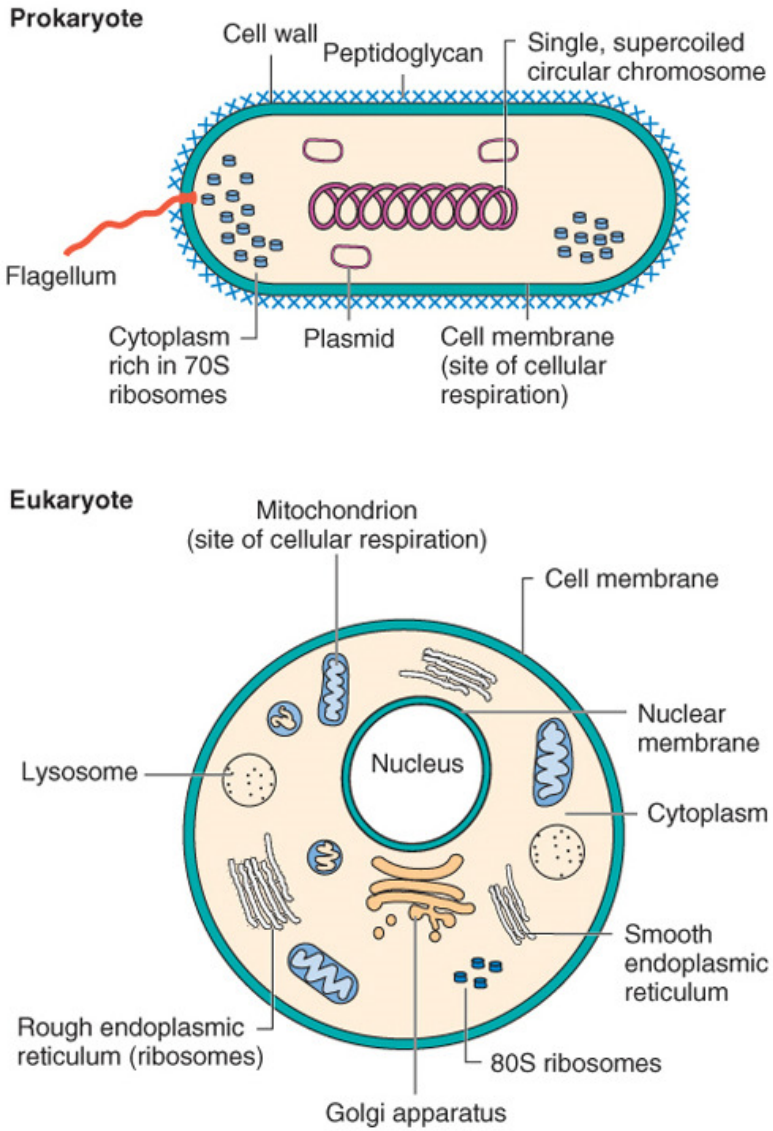
Antiseptic Agent	Concentration
Alcohol (ethyl, isopropyl)	70%-90%
Iodophors	1-2 mg of free iodine/L; 1%-2% available iodine
Chlorhexidine	0.5%-4.0%
Parachlorometaxylenol	0.50%-3.75%
Triclosan	0.3%-2.0%

Properties of disinfectants and antiseptic agents

Germicidal Properties of Disinfectants and Antiseptic Agents

Agents	Bacteria	Mycobacteria	Bacterial Spores	Fungi	Viruses
Disinfectants					
Alcohol	+	+	−	+	+/−
Hydrogen peroxide	+	+	+/−	+	+
Phenolics	+	+	−	+	+/−
Chlorine	+	+	+/−	+	+
Iodophors	+	+/−	−	+	+
Glutaraldehyde	+	+	+	+	+
Quaternary ammonium compounds	+/−	−	−	+/−	+/−
Antiseptic Agents					
Alcohol	+	+	−	+	+
Iodophors	+	+	−	+	+
Chlorhexidine	+	+	−	+	+
Parachlorometaxylenol	+/−	+/−	−	+	+/−
Triclosan	+	+/−	−	+/−	+

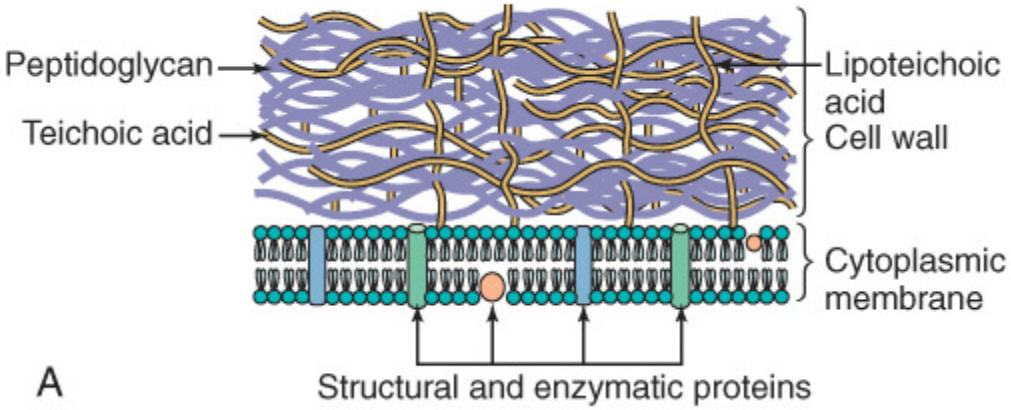
Differences between eukaryotes and prokaryotes

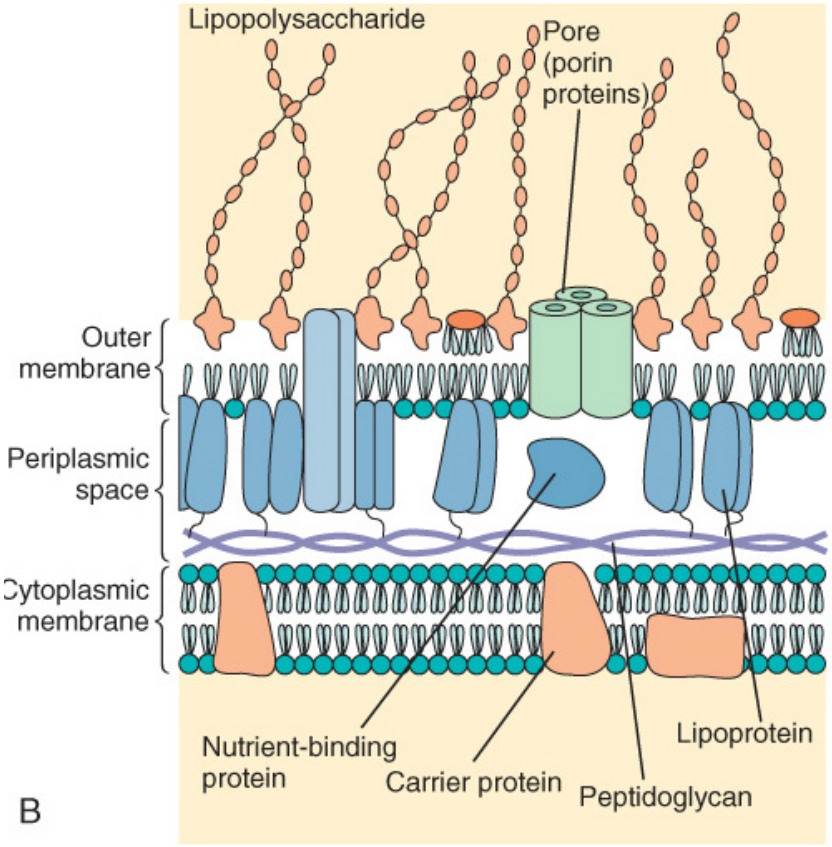


Differences between eukaryotes and prokaryotes

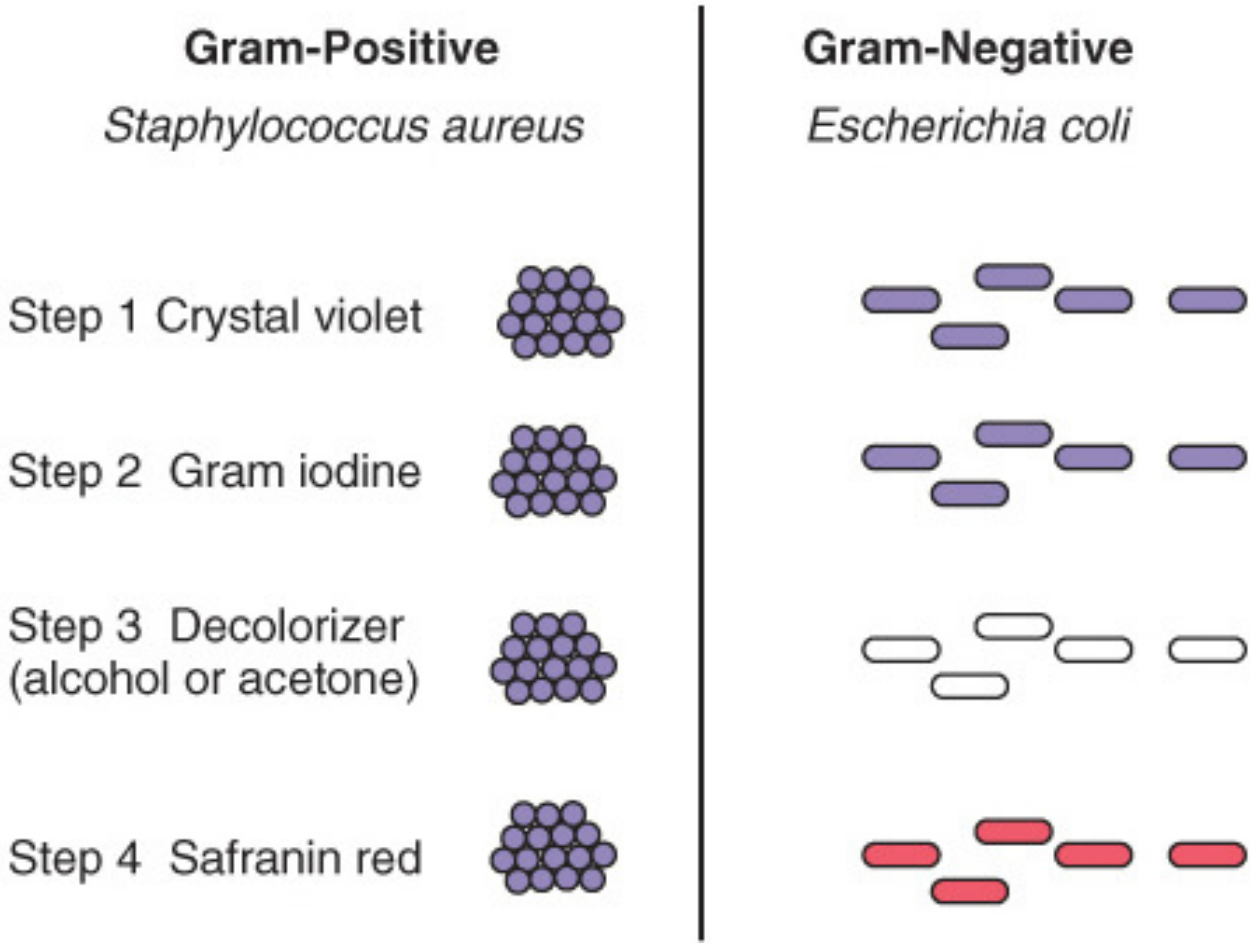
Characteristic	Eukaryote	Prokaryote
Major groups	Algae, fungi, protozoa, plants, animals	Bacteria
Size (approximate)	>5 µm	0.5-3.0 µm
Nuclear Structures		
Nucleus	Classic membrane	No nuclear membrane
Chromosomes	Strands of DNA diploid genome	Single, circular DNA haploid genome
Cytoplasmic Structures		
Mitochondria	Present	Absent
Golgi bodies	Present	Absent
Endoplasmic reticulum	Present	Absent
Ribosomes	80S (60S + 40S)	70S (50S + 30S)
Cytoplasmic membrane	Contains sterols	Does not contain sterols (except mycoplasma)
Cell wall	Present for fungi; otherwise absent	Is a complex structure containing protein, lipids, and peptidoglycans
Reproduction	Sexual and asexual	Asexual (binary fission)
Movement	Complex flagellum, if present	Simple flagellum, if present
Respiration	Via mitochondria	Via cytoplasmic membrane

Bacterial cell walls

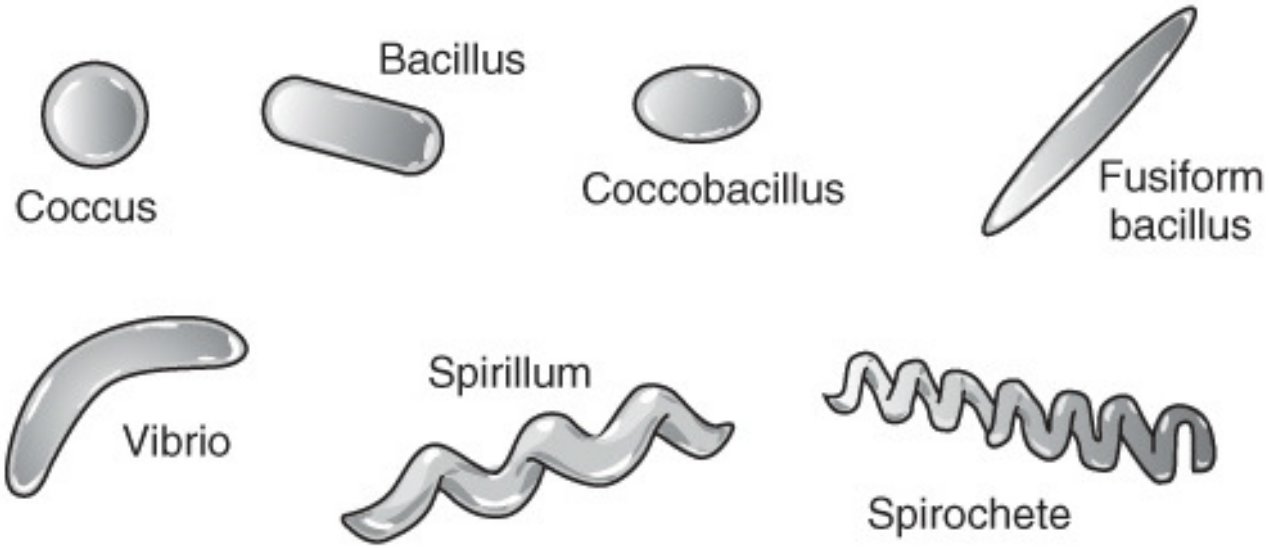




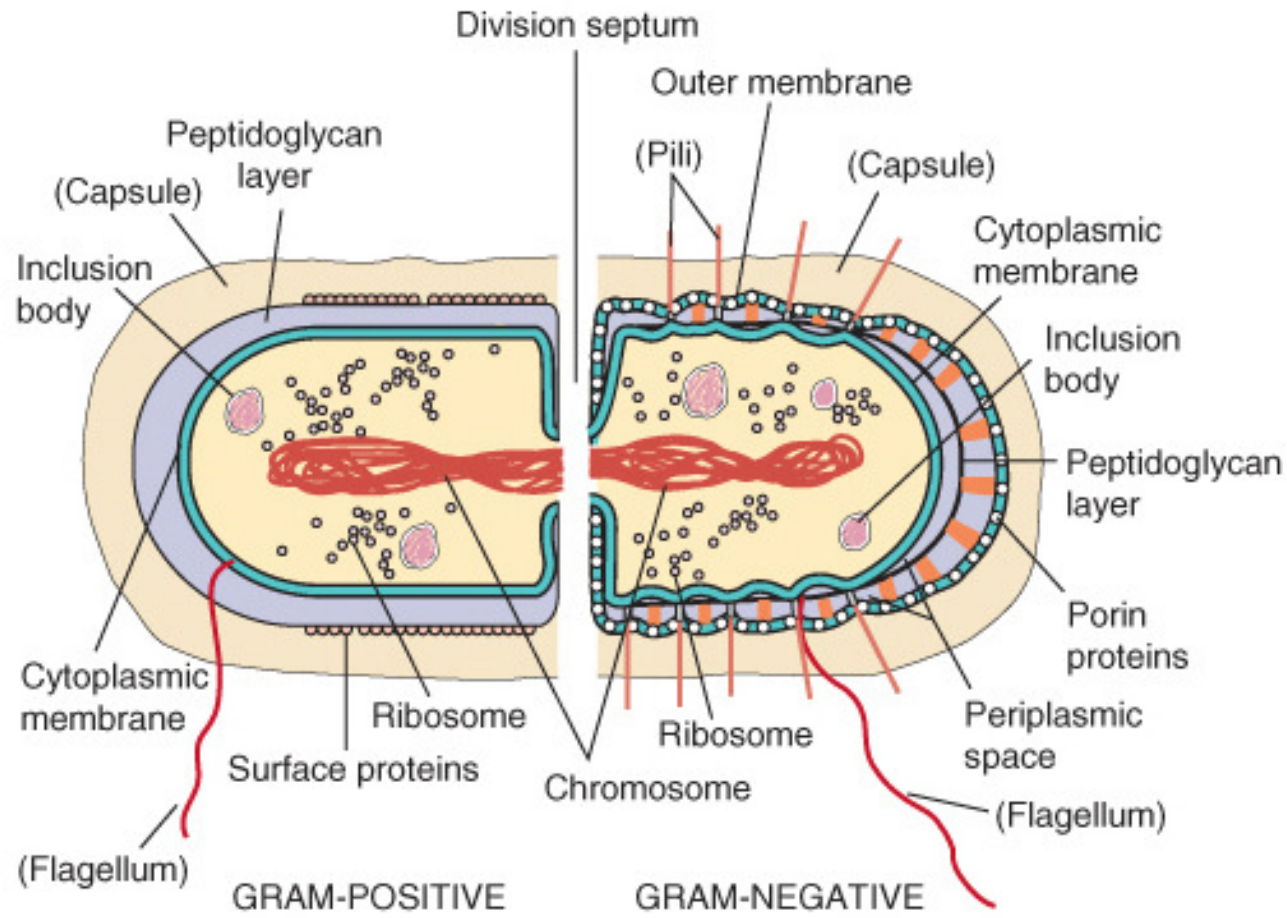
Gram stain


Gram-Positive
Staphylococcus aureus
Gram-Negative
Escherichia coli
Step 1 Crystal violet
Step 2 Gram iodine
Step 3 Decolorizer
(alcohol or acetone)
Step 4 Safranin red

Bacterial morphology



Gram-positive and gram-negative bacteria



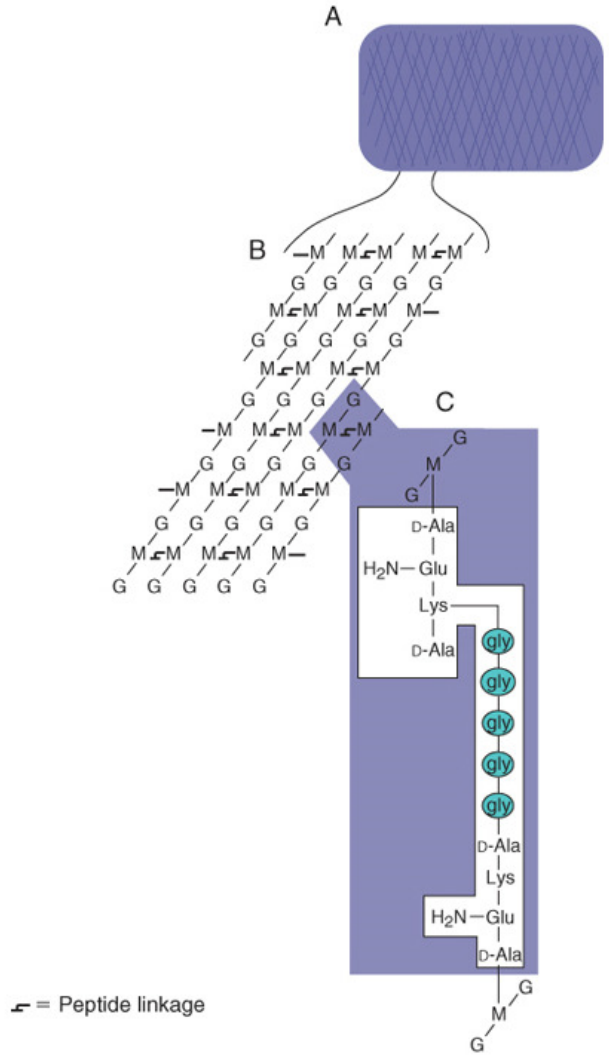
Functions of the bacterial envelope

Function	Component
Structure	
Rigidity	All
Packaging of internal contents	All
Bacterial Functions	
Permeability barrier	Outer membrane or plasma membrane
Metabolite uptake	Membranes and periplasmic transport proteins, porins, permeases
Energy production	Plasma membrane
Motility	Flagella
Mating	Pili
Host Interaction	
Adhesion to host cells	Pili, proteins, teichoic acid
Immune recognition by host	All outer structures and peptidoglycan
Escape from host immune protections	
Antibody Phagocytosis	Protein A Capsule, M protein
Complement	Gram-positive peptidoglycan
Medical Relevance	
Antibiotic targets	Peptidoglycan synthesis, outer membrane
Antibiotic resistance	Outer membrane barrier

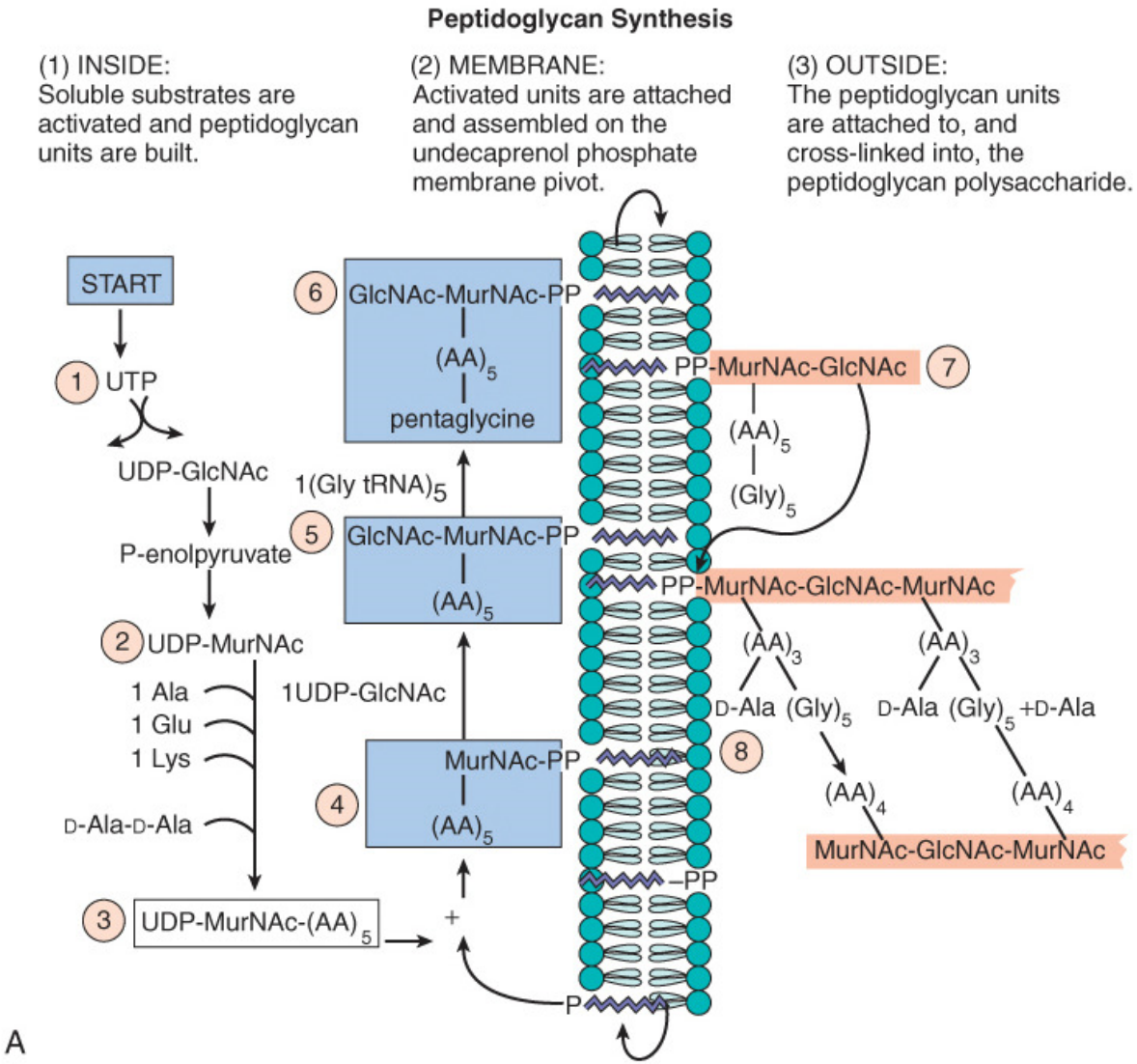
Membrane characteristics of Gram-positive and Gram-negative bacteria

Characteristic	Gram-Positive	Gram-Negative
Outer membrane	–	+
Cell wall	Thick	Thin
Lipopolysaccharide	–	+
Endotoxin	–	+
Teichoic acid	Often present	–
Sporulation	Some strains	–
Capsule	Sometimes present	Sometimes present
Lysozyme	Sensitive	Resistant
Antibacterial activity of penicillin	More susceptible	More resistant
Exotoxin production	Some strains	Some strains

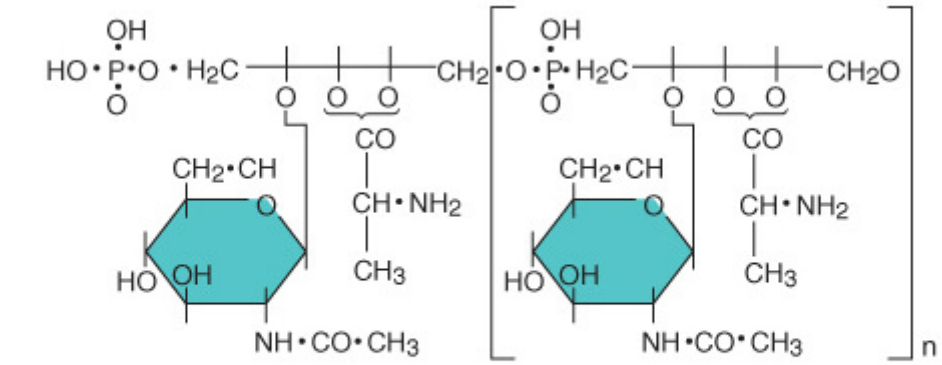
Structure of the peptidoglycan



Peptidoglycan synthesis

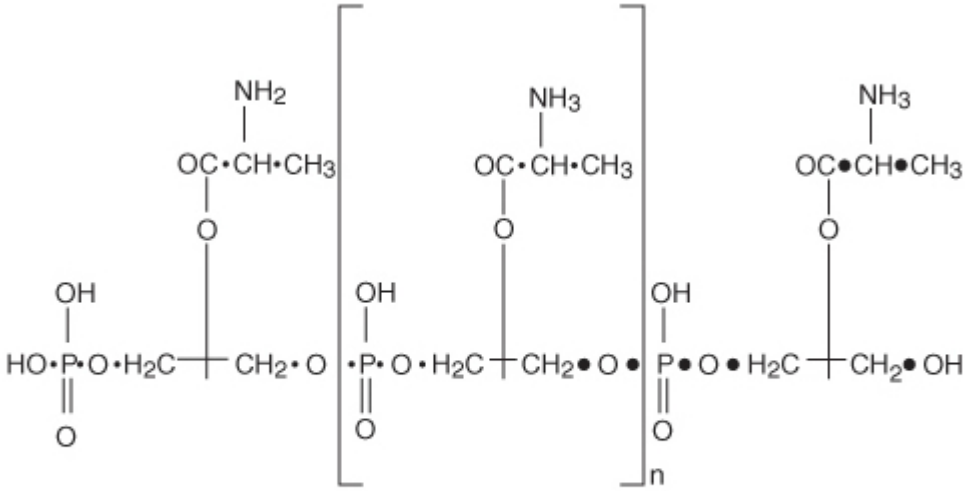


Teichoic acid



Ribitol Teichoic Acid
(*Staphylococcus*)

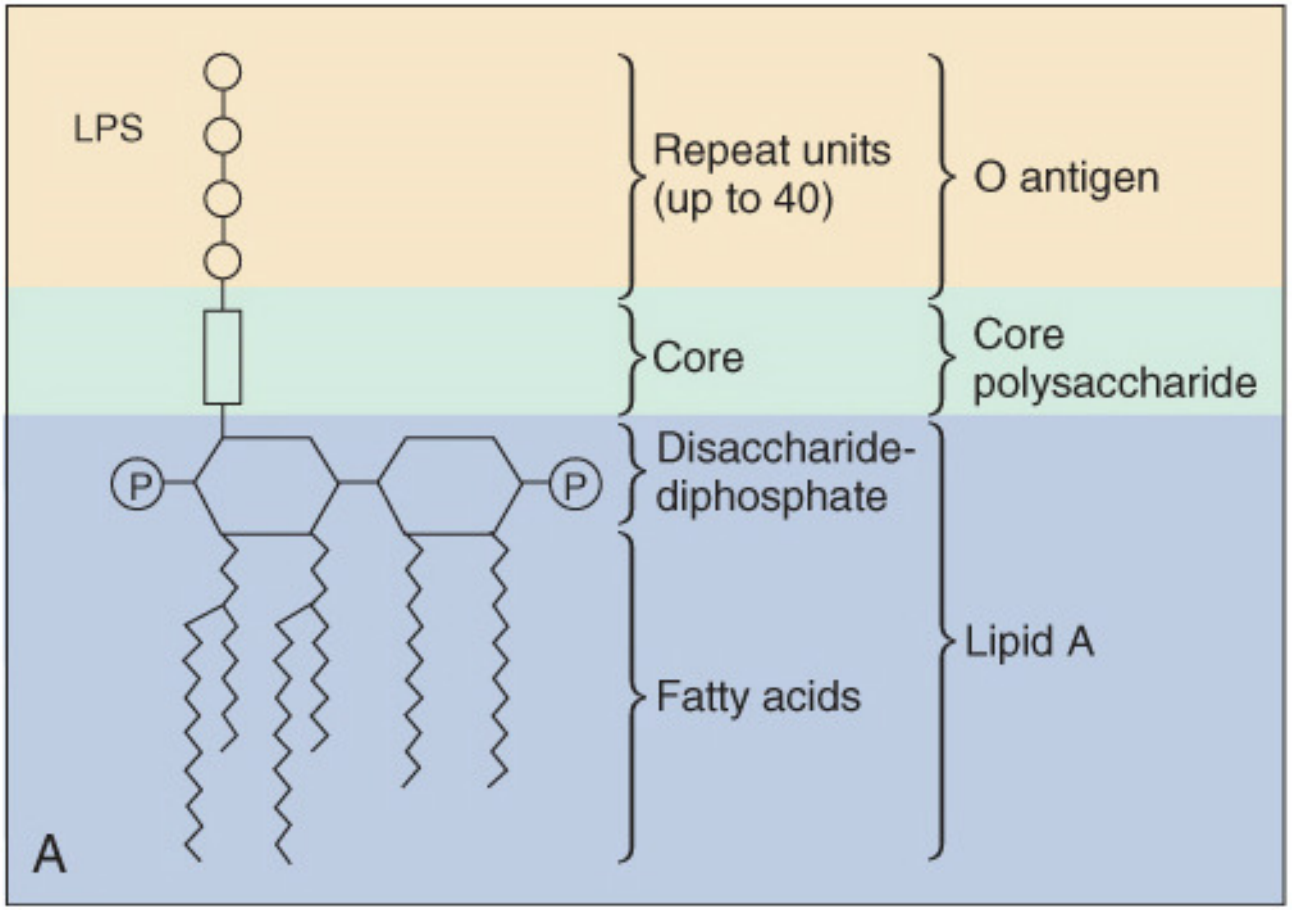
A



Glycerol Teichoic Acid
(*Lactobacillus*)

B

Lipopolysaccharide (LPS)



Lipopolysaccharide (LPS)

Repeat unit: O antigen
Example: (repeated up to 40 times)

Mannose–Abequose
Rhamnose
Galactose

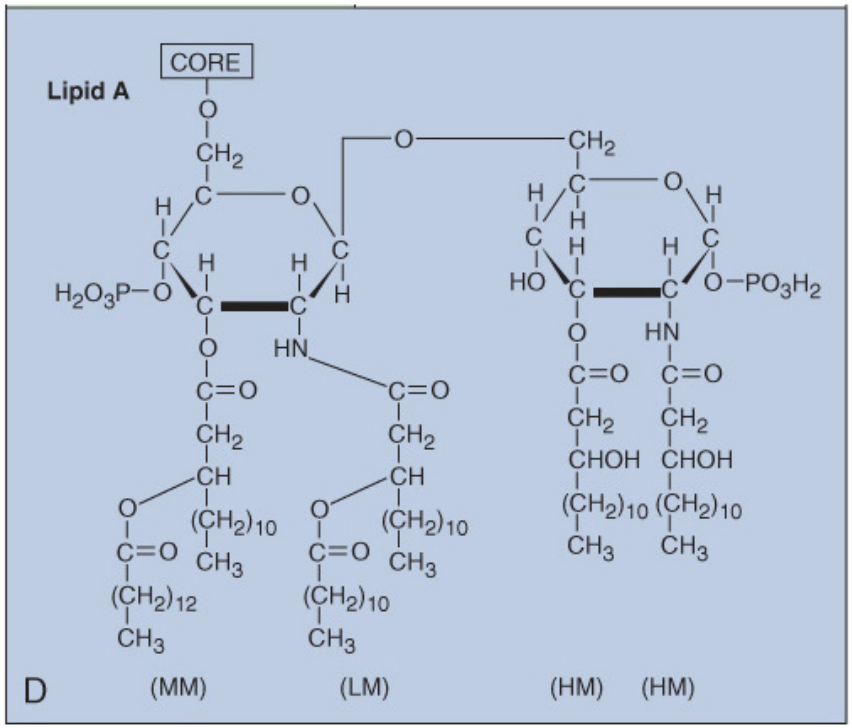
B

Core

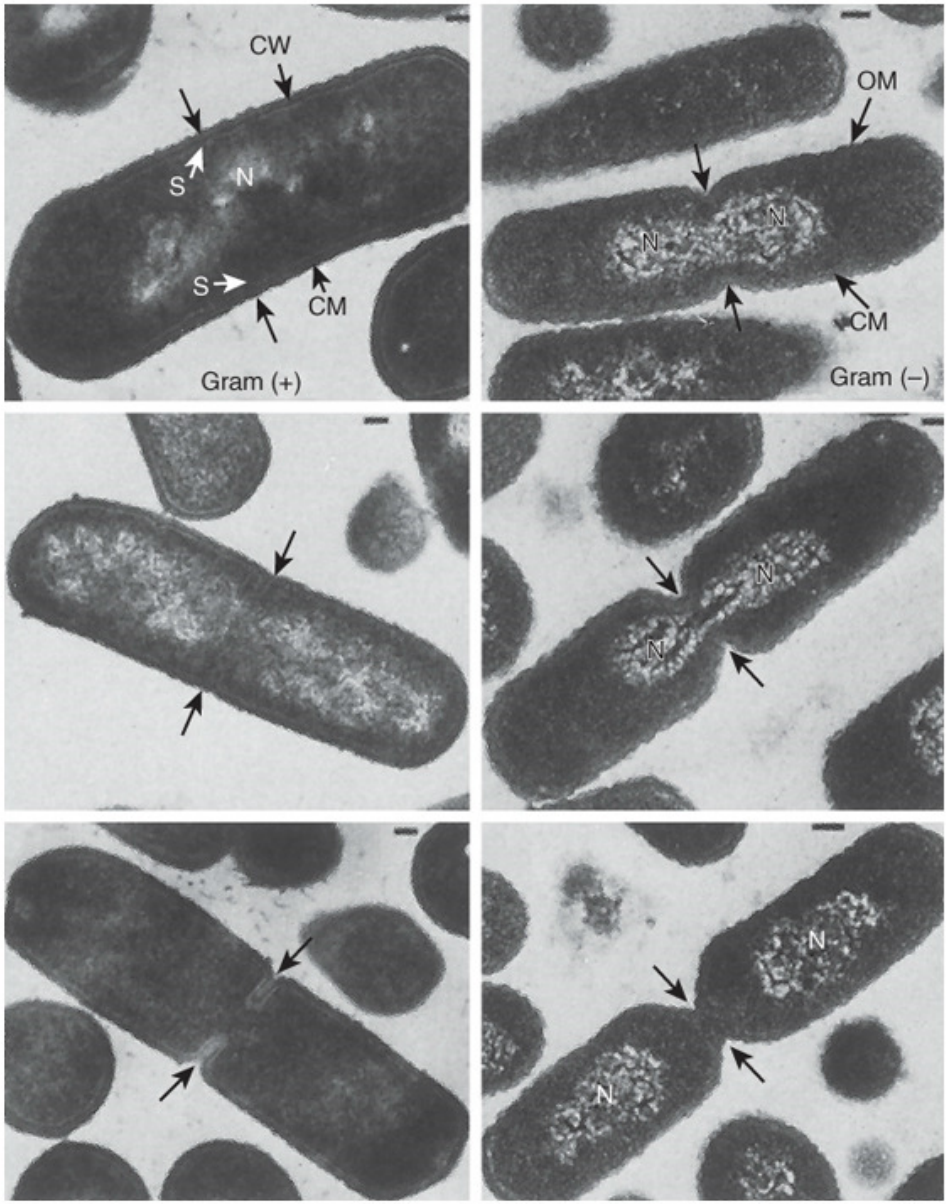
Glu-GlcNAc
Gal
Glu-Gal
Hep
Hep-P-P-Eth·N
KDO
KDO-KDO-P-Eth·N

C

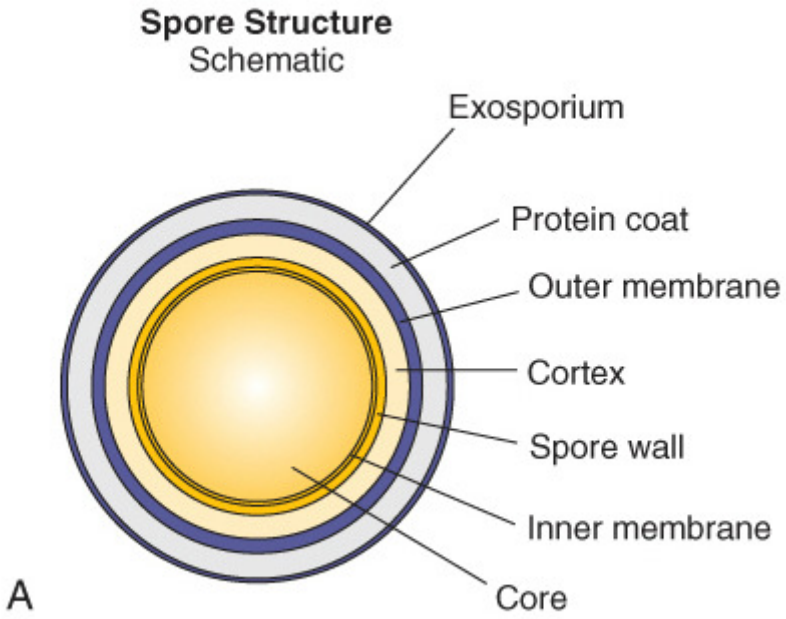
KDO	= Keto-deoxy-octanoate
Hep	= L-Glycero-D-mannoheptose
HM	= Beta-hydroxymyristic acid (C_{14})
LM	= Lauroxymyristic acid
MM	= Myristoxymyristic acid
Eth·N	= Ethanolamine
Glu	= Glucose
GlcNAc	= *N*-Acetyglucosamine
Gal	= Galactose
P	= Phosphate



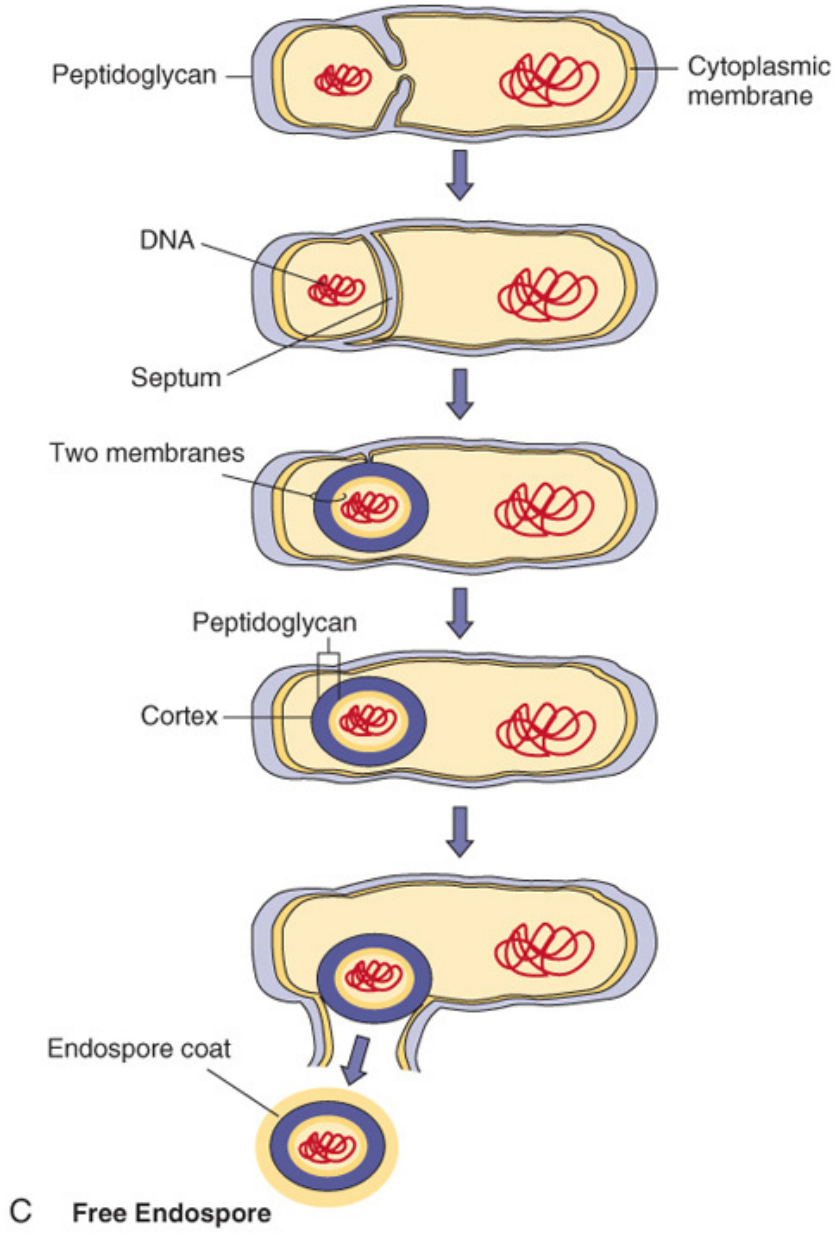
Cell division



Structure of the spore



Sporogenesis



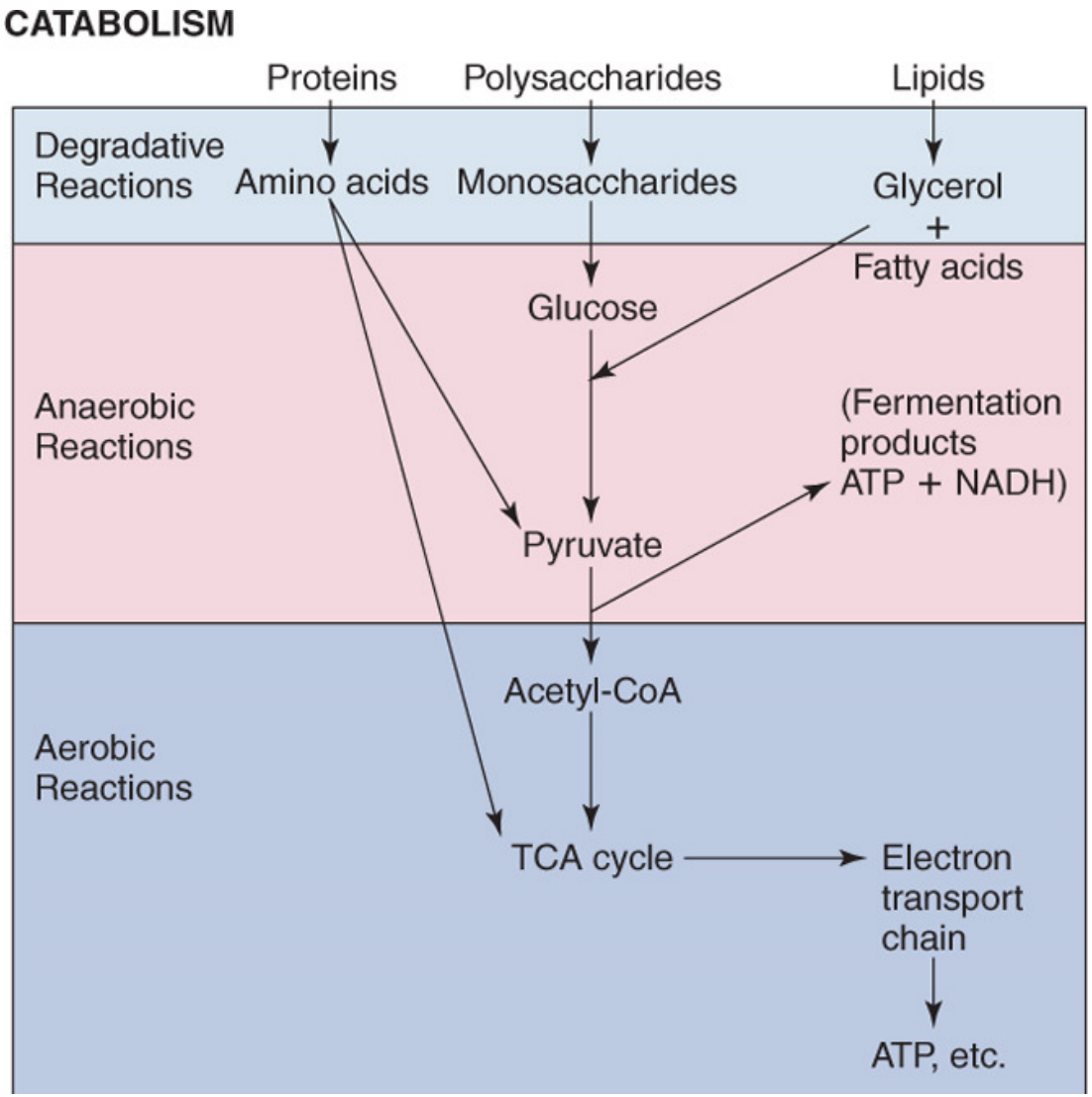
Bacterial metabolism, growth, and genetics

Metabolism and the conversion of energy

- **Biosynthesis**
- **DNA**
- **Transcriptional control**
- **Mutation, repair, and recombination**

- **Obligate anaerobes**
- **Obligate aerobes**
- **Facultative anaerobes**

Catabolism



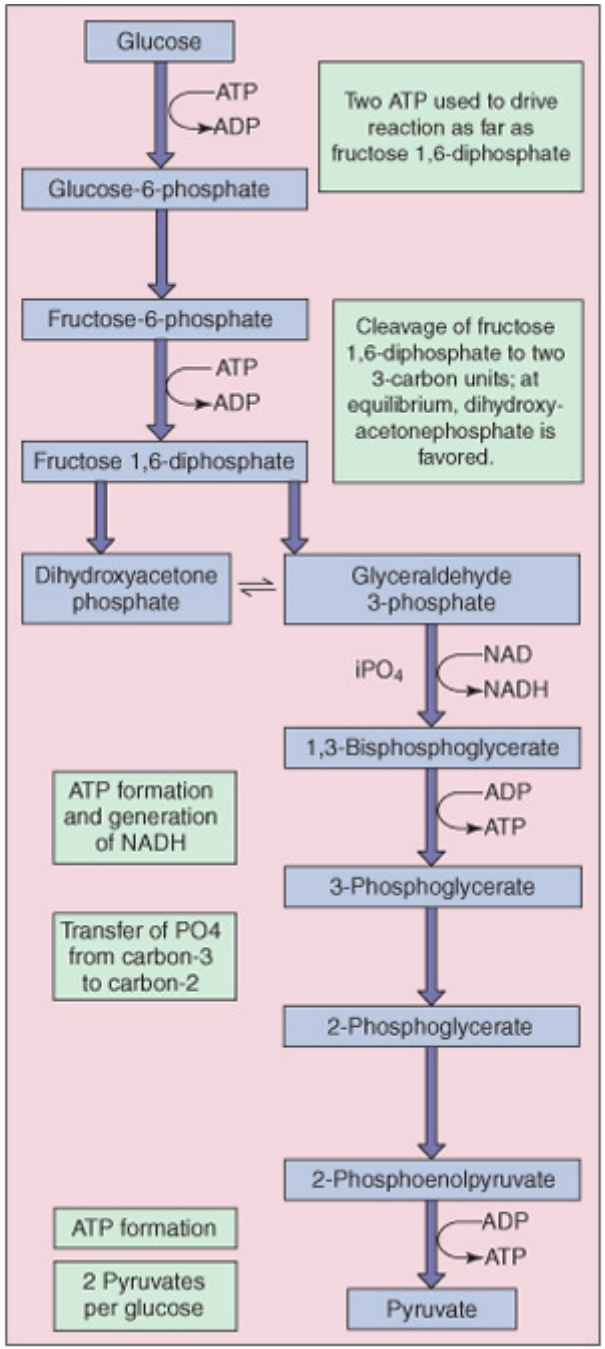
Anabolism

Intermediary metabolism

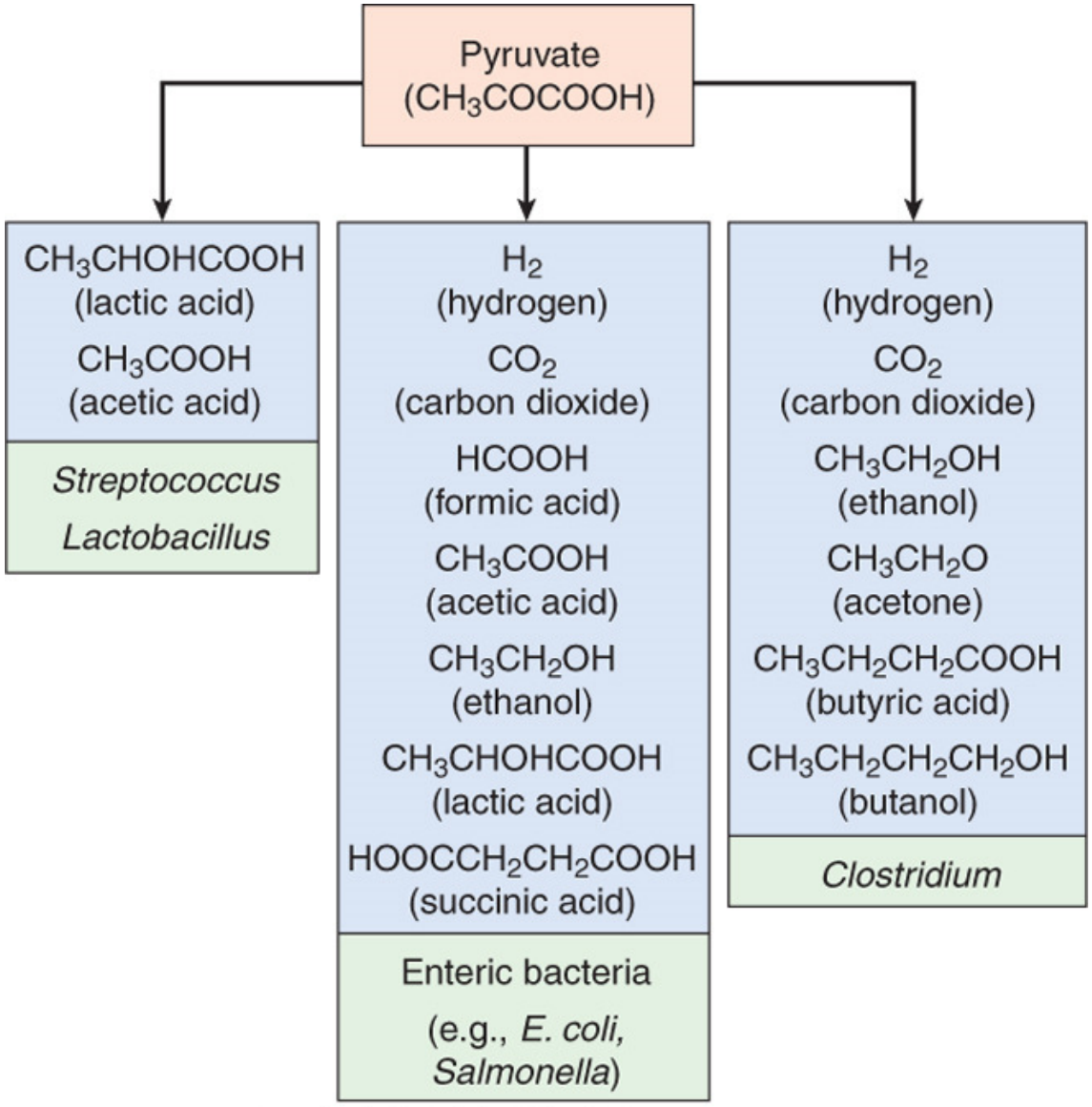
Glycolytic pathway

(Embden-Meyerhof-Parnas pathway)

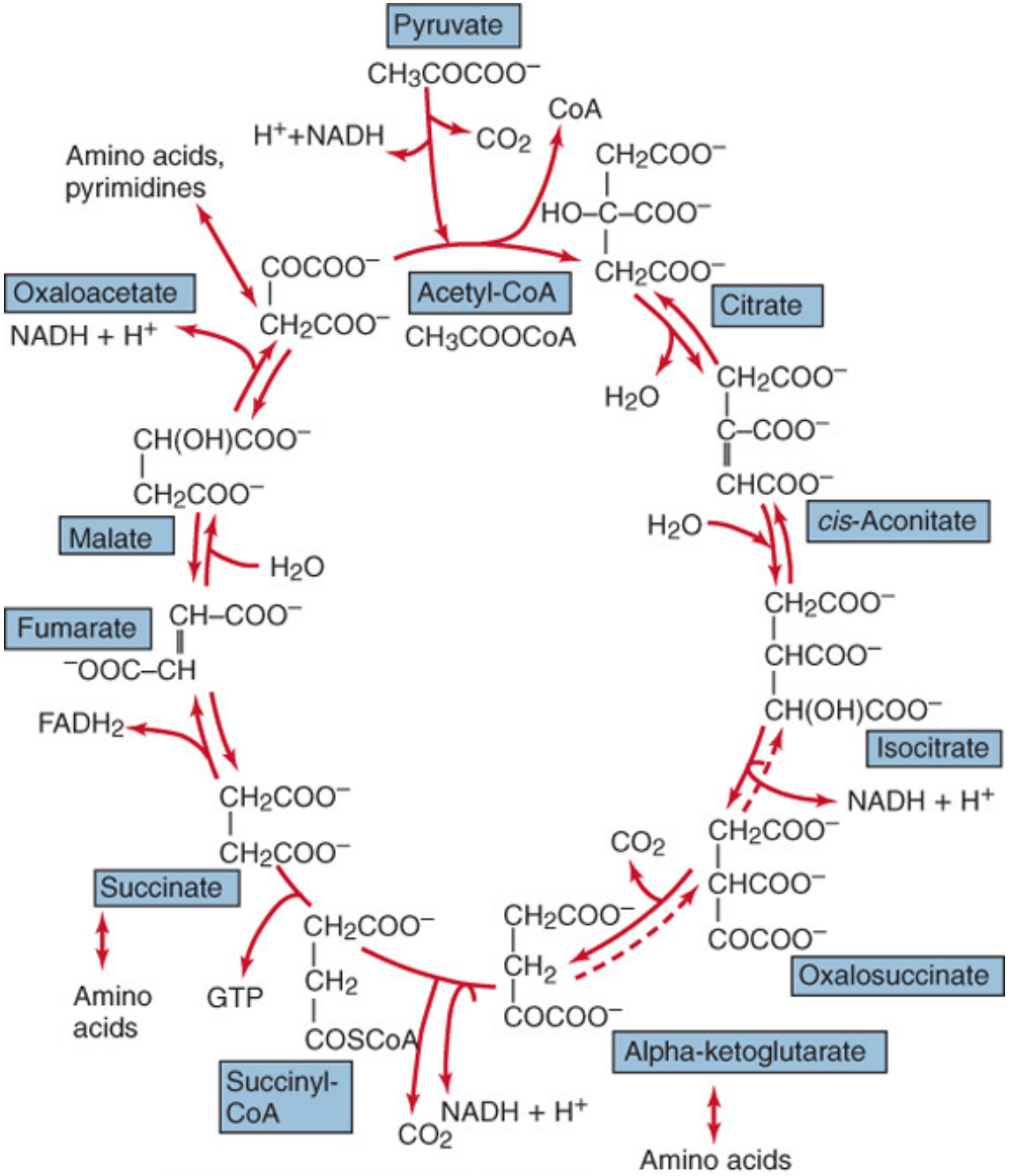
Nicotinamide adenine dinuceotide (NADH)



Fermentation



Tricarboxylic acid (TCA) cycle

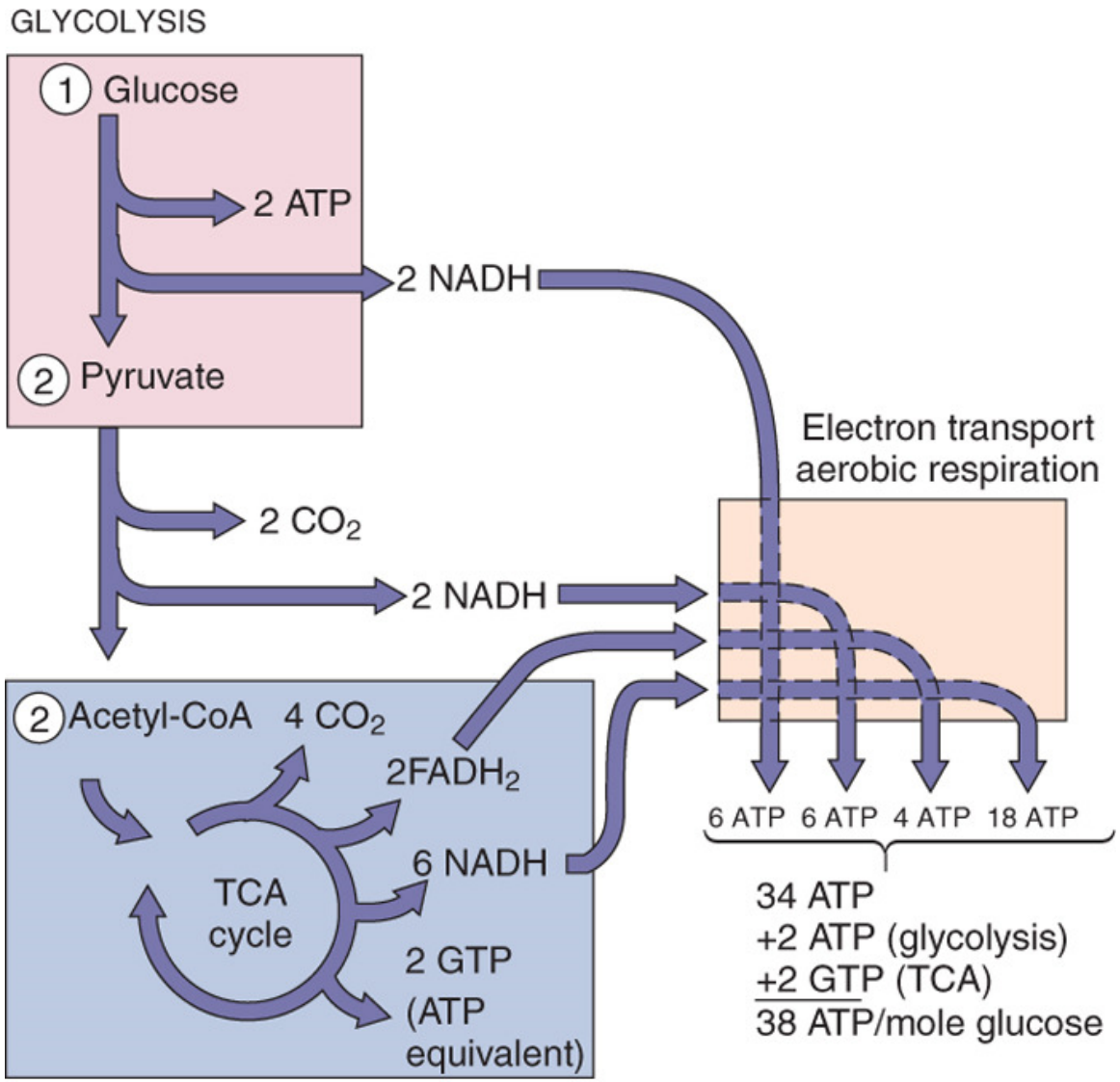


Fermentation an aerobic metabolism

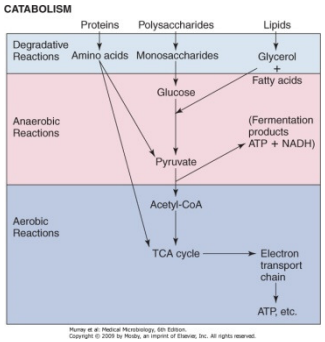
Fermentation: 2 ATP molecules per glucose

Aerobic metabolism with electron transport: 38 ATP per glucose

Aerobic glucose metabolism

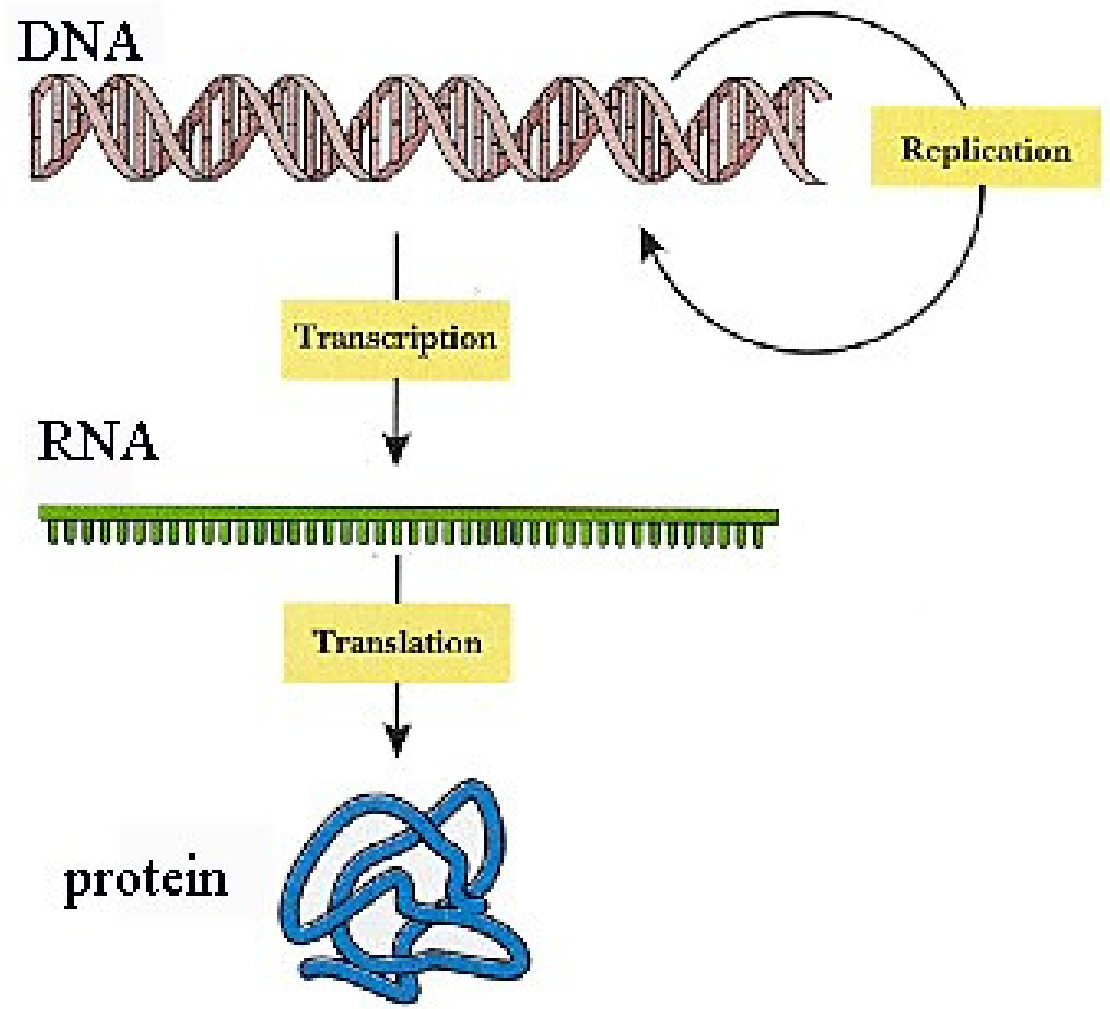


1. **It is the most efficient mechanism for the generation of ATP.**
2. **It serves as the final common pathway for the complete oxidation of amino acids, fatty acids, and carbohydrates.**
3. **It supplies key intermediates for the ultimate synthesis of amino acids, lipids, purines, and pyrimidines.**



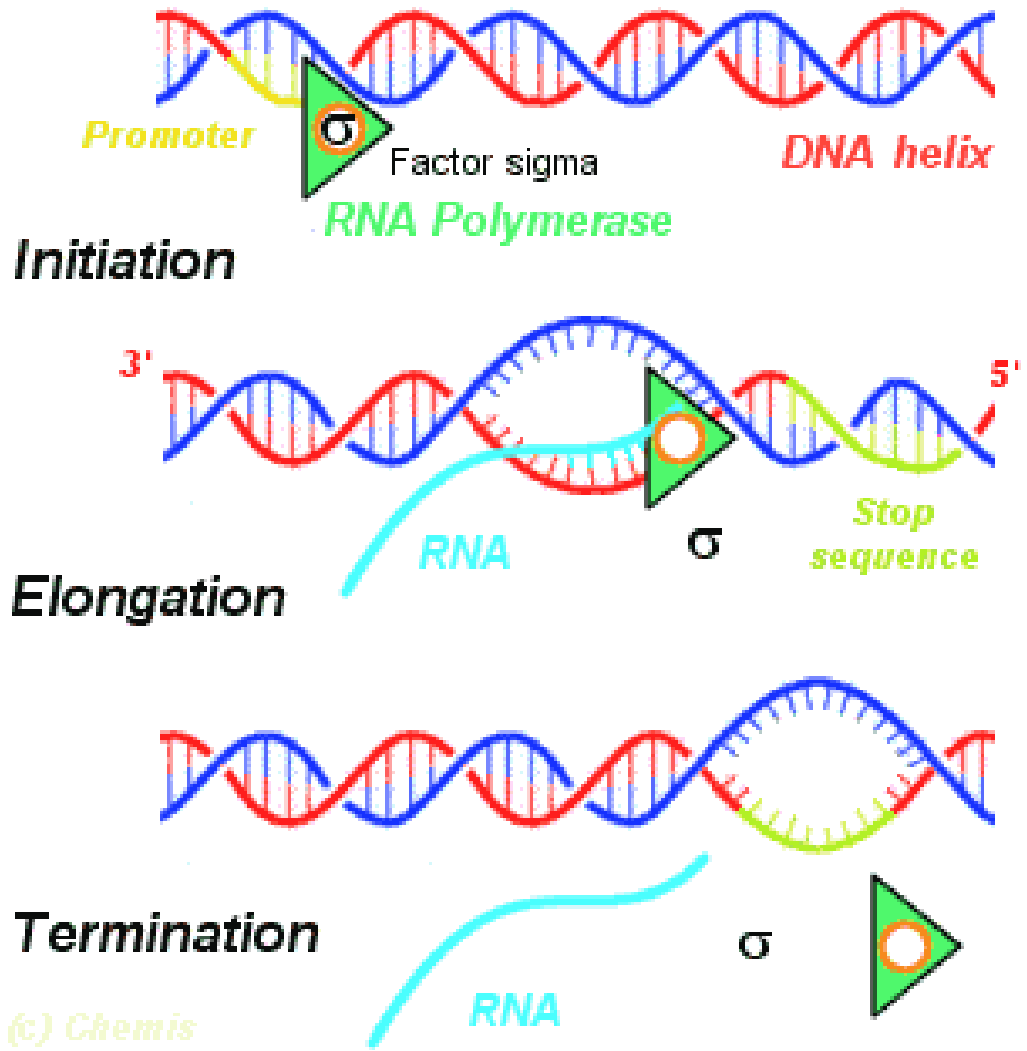
The last two functions make the TCA cycle a so-called amphibolic cycle.

Genes and expression



instruct.westvalley.edu/svenssonCellsandGenes/10MolecularBiology.html

Transcription



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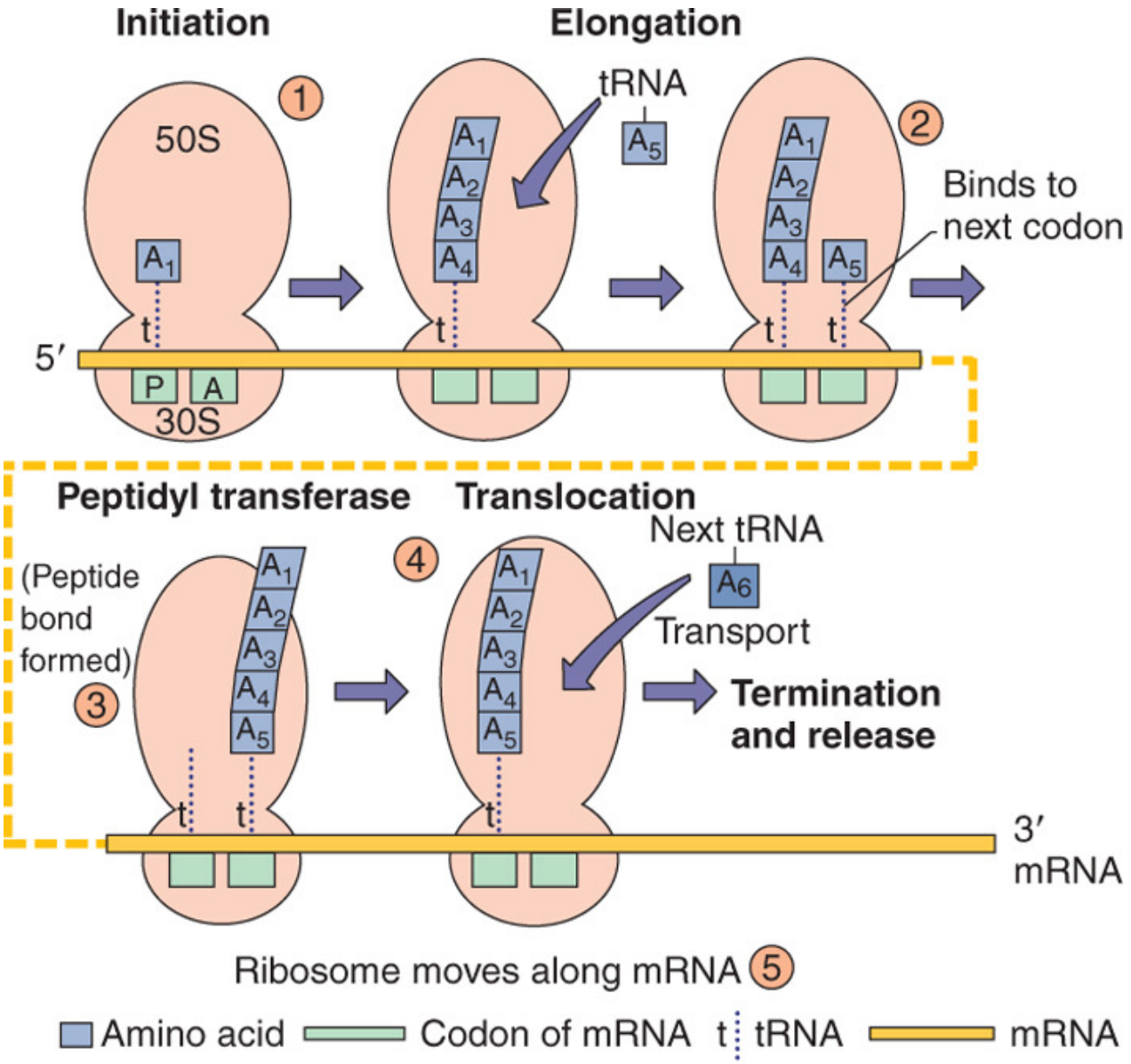
Genetic code

UUU UUC Phe UUA UUG Leu	UCU UCC Ser UCA UCG	UAU UAC Tyr UAA Stop UAG Stop	UGU UGC Cys UGA Stop UGG Trp
CUU CUC Leu CUA CUG	CCU CCC Pro CCA CCG	CAU CAC His CAA CAG Gln	CGU CGC Arg CGA CGG
AUU AUC Ile AUA AUG Met	ACU ACC Thr ACA ACG	AAU AAC Asn AAA AAG Lys	AGU AGC Ser AGA AGG Arg
GUU GUC Val GUA GUG	GCU GCC Ala GCA GCG	GAU GAC Asp GAA GAG Glu	GGU GGC Gly GGA GGG

Bacterial protein synthesis



P: promoter

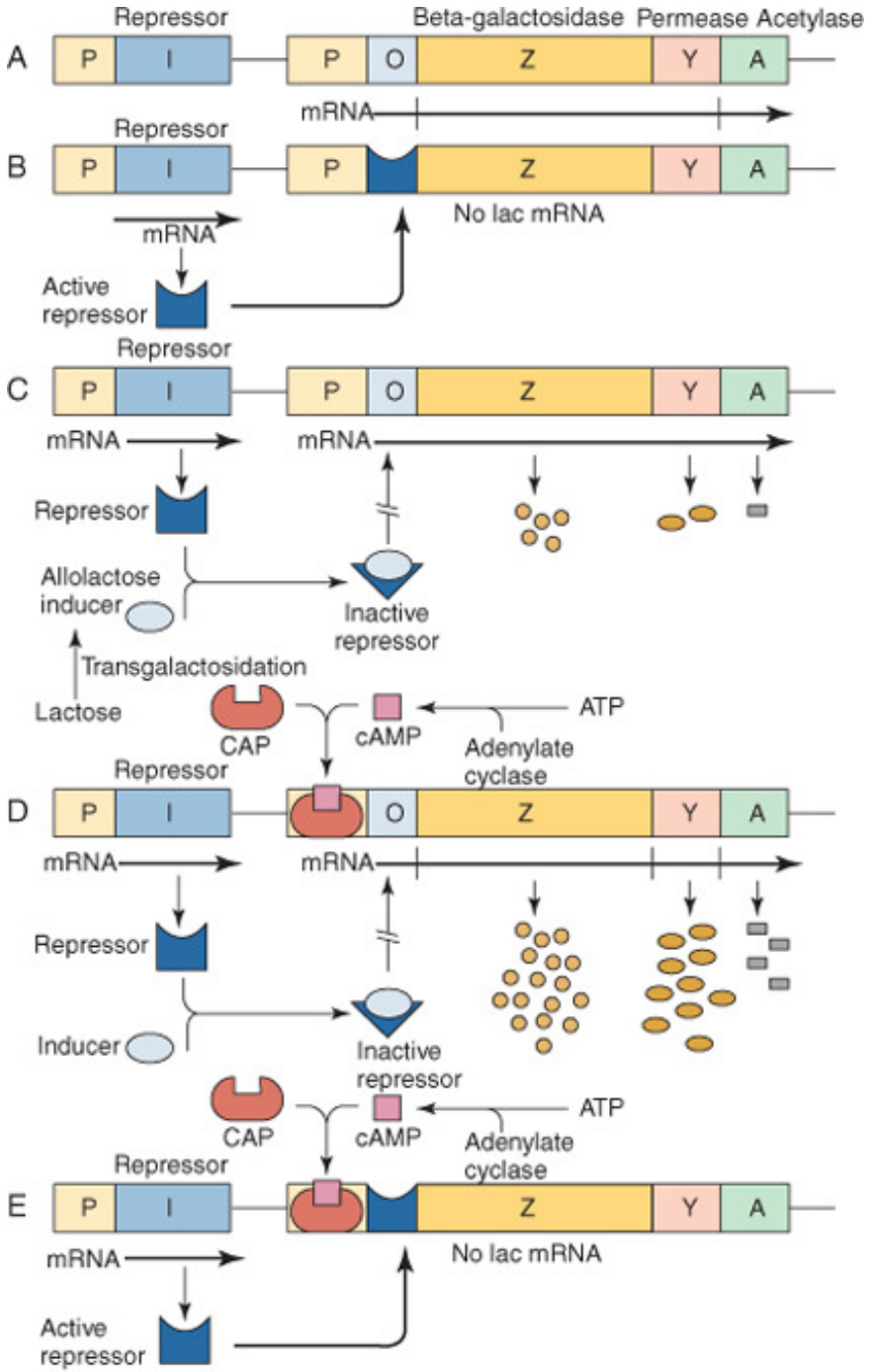
I: Repressor

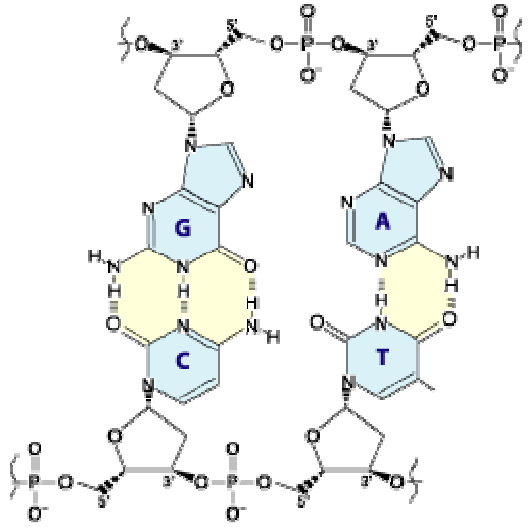
O: Operator

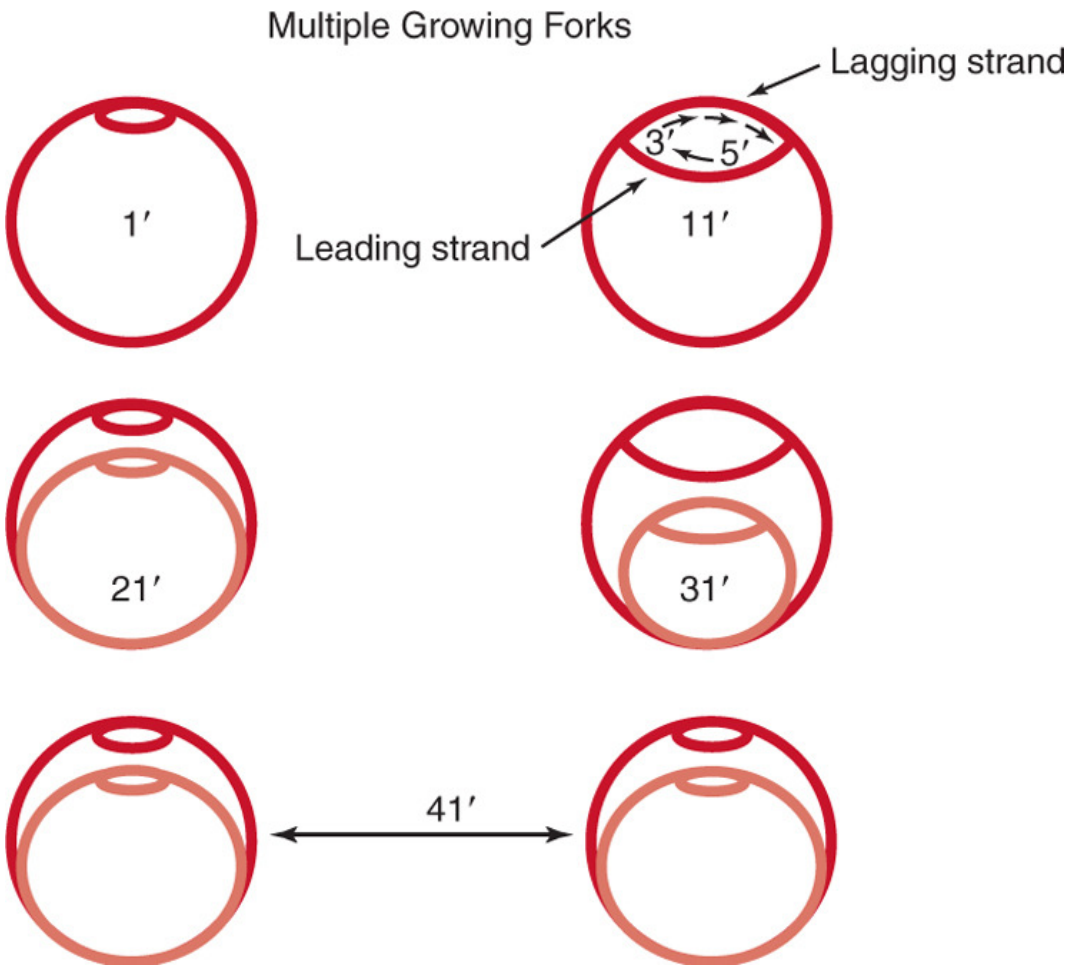
Z:β-galactosidase

Y: permease

A: acetylase







Helicase

Primase

DNA-dependent DNA polymerase

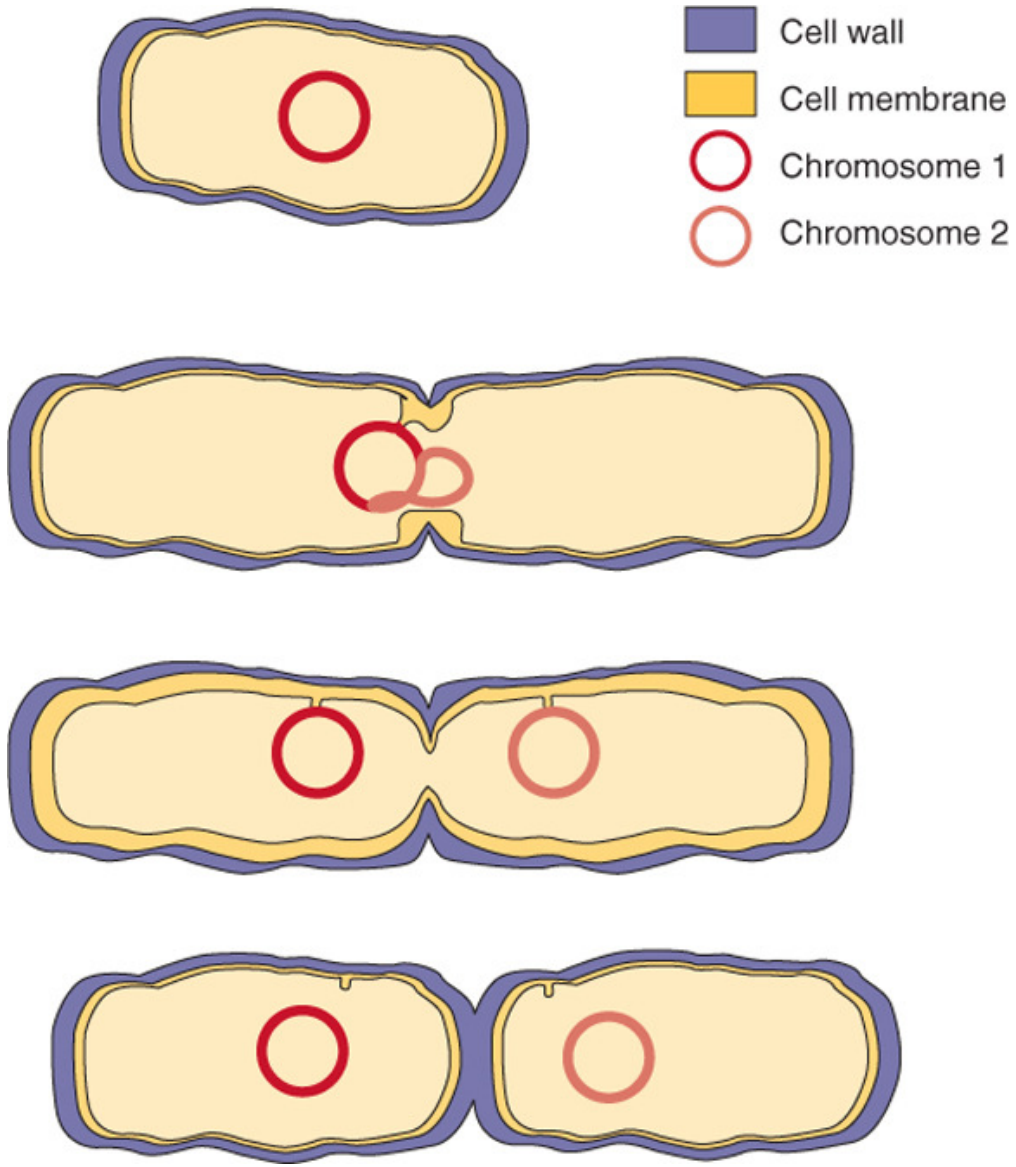
Semiconservatively

5’ to 3’

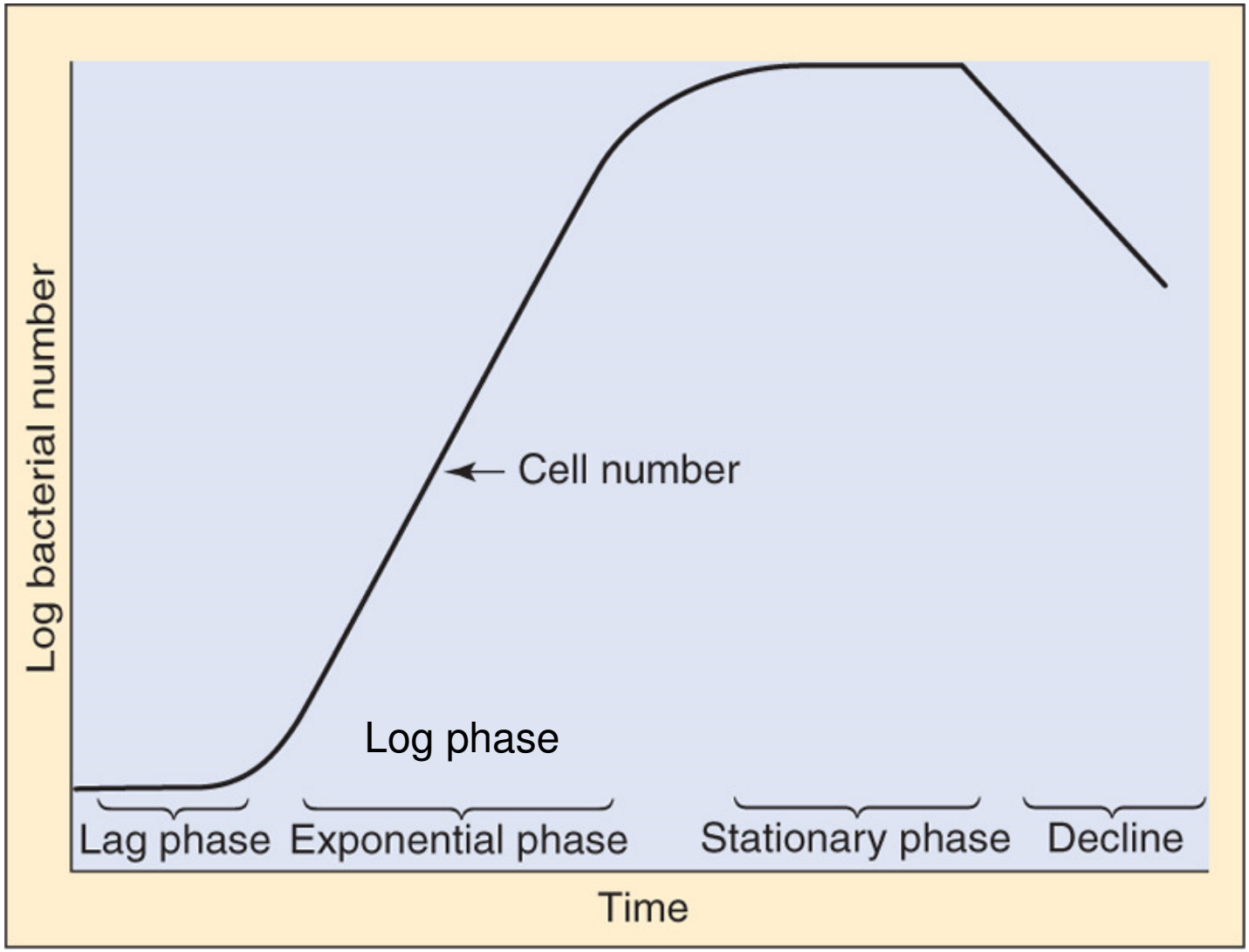
Okazaki fragments

Topoisomerase

Bacterial cell division



Phases of bacterial growth



Transition: one purine is replaced by another purine

Transversion: one purine is replaced by one pyrimidine

Silent mutation: amino acid is not changed

Missense mutation: different amino acid

Conservative mutation: the new amino acid has similar properties

Nonsense mutation: amino acid → stop codon

Frameshift mutation: change in the reading frame

Null mutations: completely destroy gene function

Purine: Adenine (A) Guanine (G)

Pyrimidine: Cytosine (C) Thymine (T) Uracil (U)

Repair mechanisms of DNA

Direct DNA repair

Excision repair

Recombinational repair

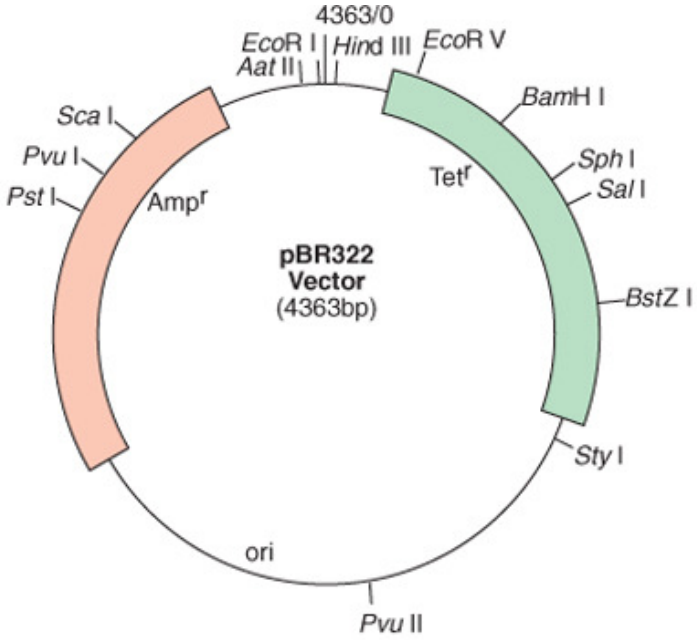
SOS response

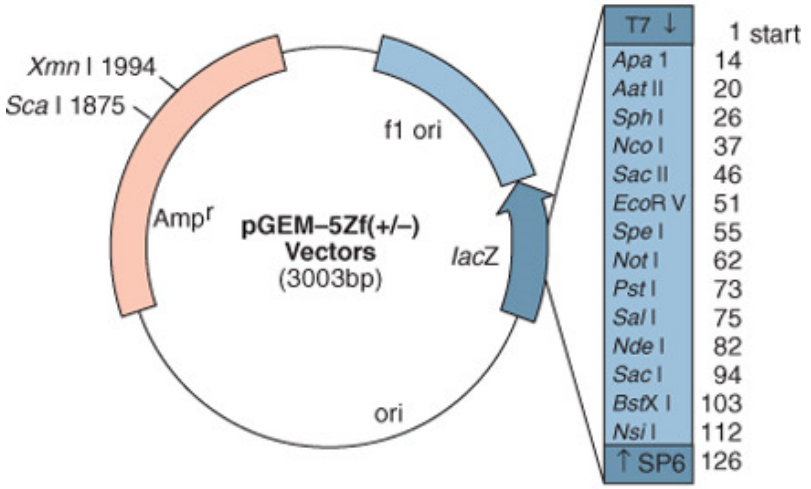
(Error-prone repair)

Plasmid

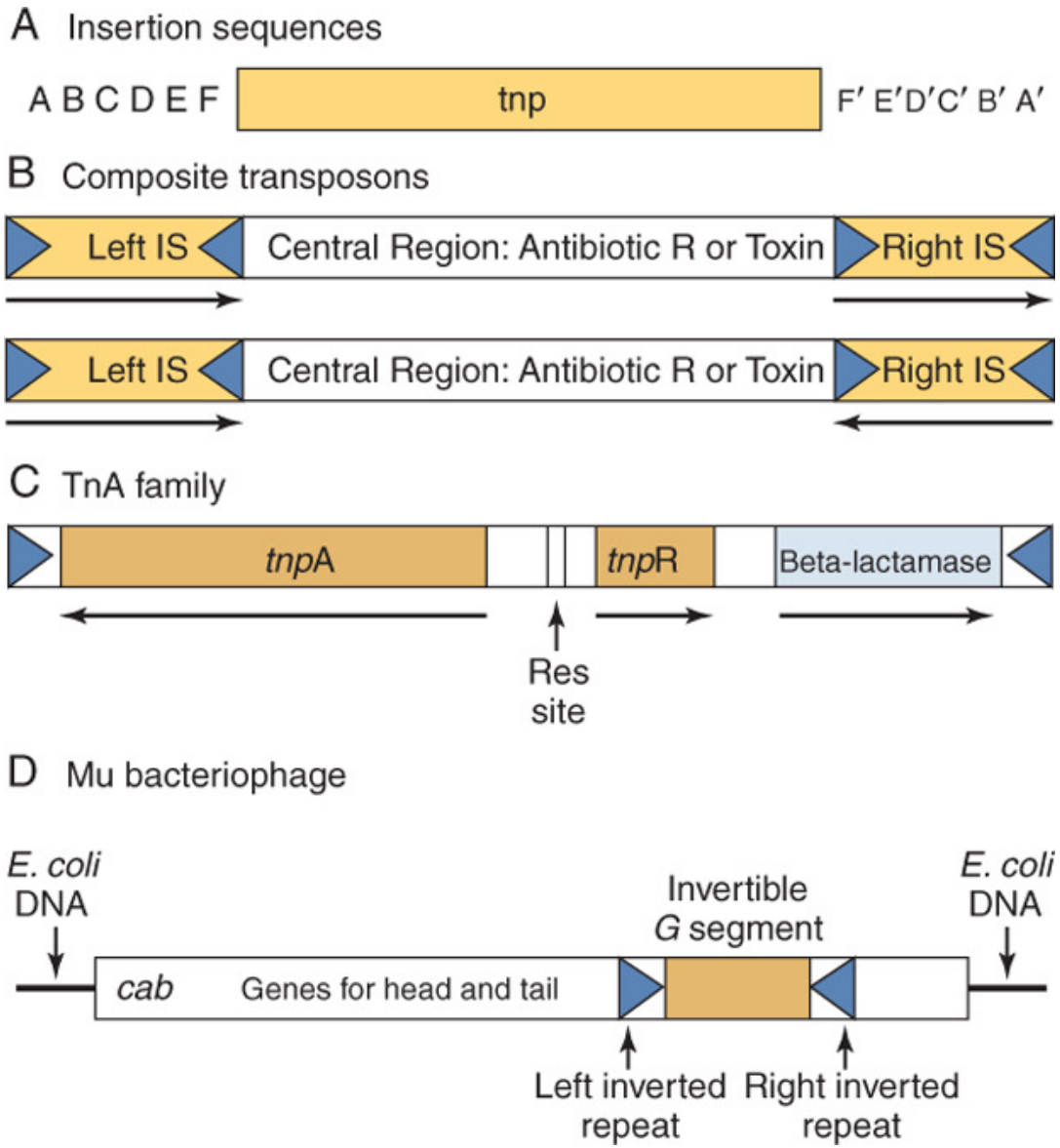
Bacteriophages

Transposons





Transposons

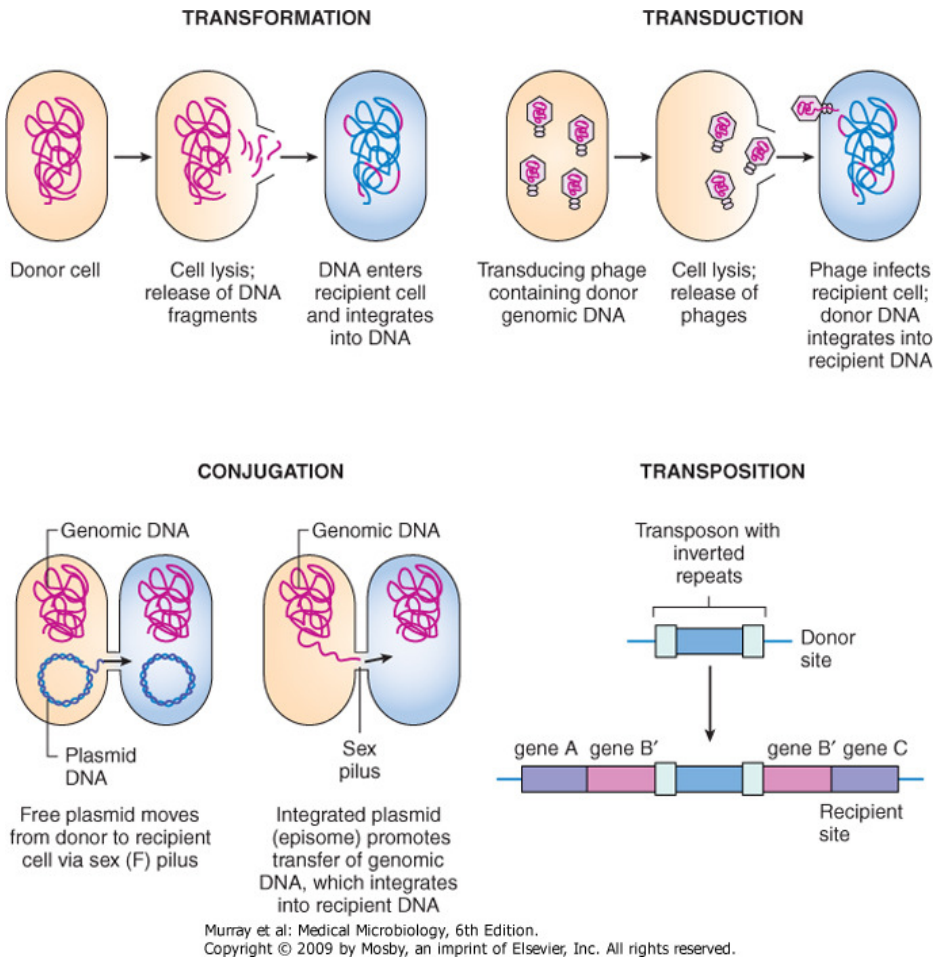


Conjugation

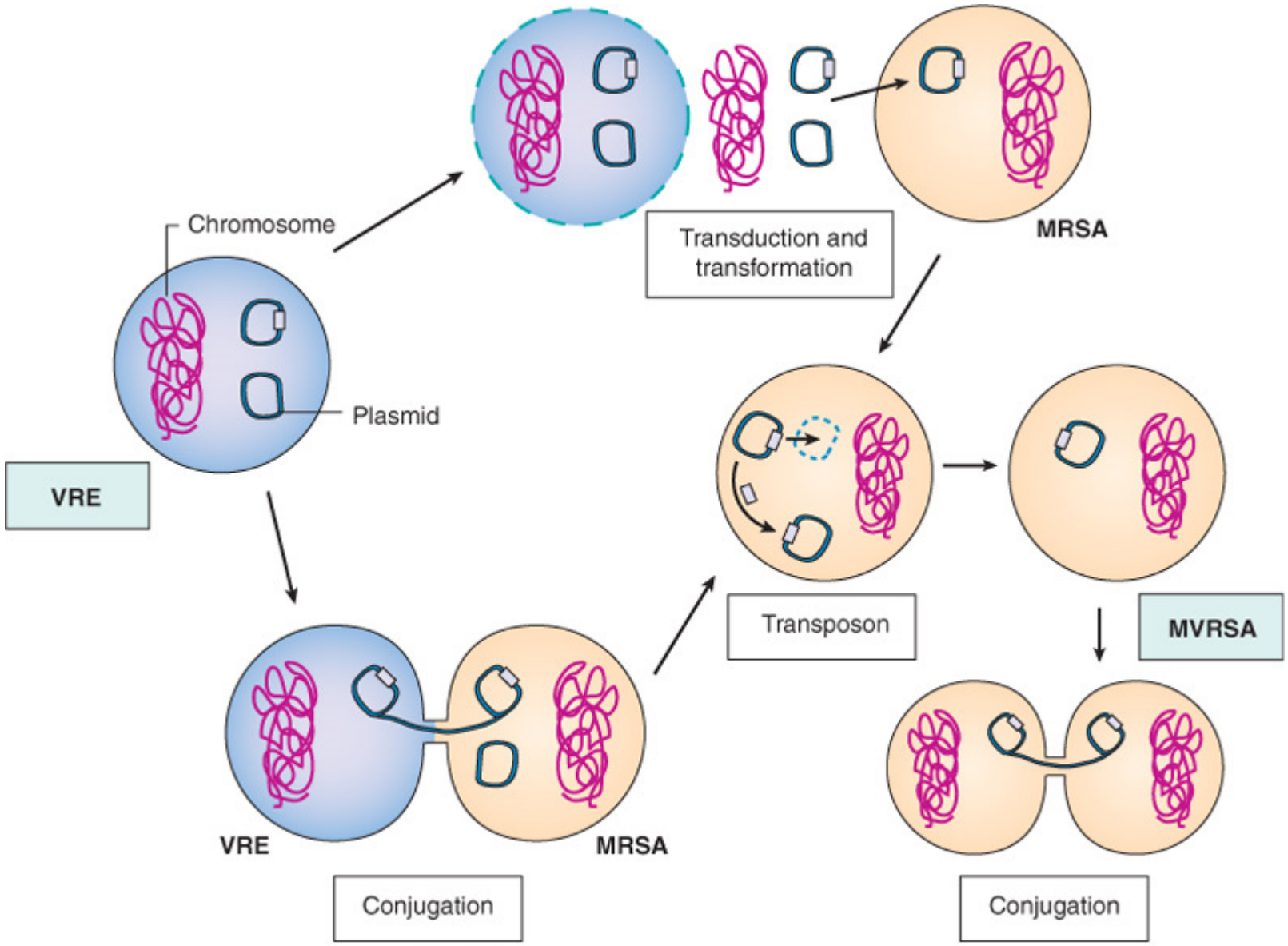
Transformation

Transduction

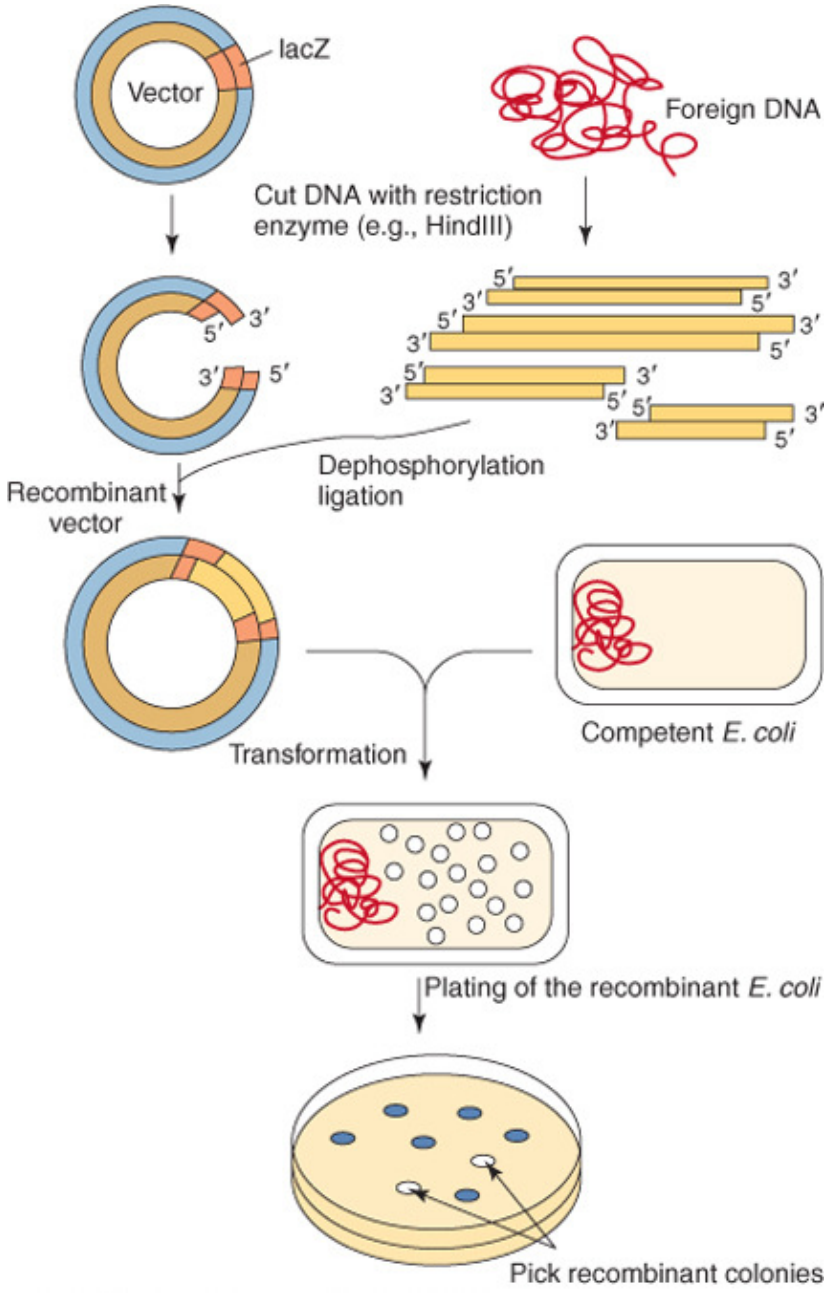
Transposon



Generation of drug-resistant *Staphylococcus aureus* by multiple genetic manipulations



Cloning


Vector
lacZ
Foreign DNA
Cut DNA with restriction enzyme (e.g., HindIII)
5′
3′
Dephosphorylation
ligation
Recombinant vector
Transformation
Competent E. coli
Plating of the recombinant E. coli
Pick recombinant colonies

Viral classification, structure, and replication

Viruses

Definition and Properties of a Virus

Viruses are filterable agents.

Viruses are obligate intracellular parasites.

Viruses cannot make energy or proteins independently of a host cell.

Viral genomes may be RNA or DNA but not both.

Viruses have a naked capsid or an envelope morphology.

Viral components are assembled and do not replicate by “division.”

Viruses

Consequences of Viral Properties

Viruses are not living.

Viruses must be infectious to endure in nature.

Viruses must be able to use host cell processes to produce their components (viral messenger RNA, protein, and identical copies of the genome).

Viruses must encode any required processes not provided by the cell.

Viral components must self-assemble.

Viruses

Means of Classification and Naming of Viruses

Structure: size, morphology, and nucleic acid (e.g., picornavirus [small RNA], togavirus)

Biochemical characteristics: structure and mode of replication

* This is the current means of taxonomic classification of viruses.

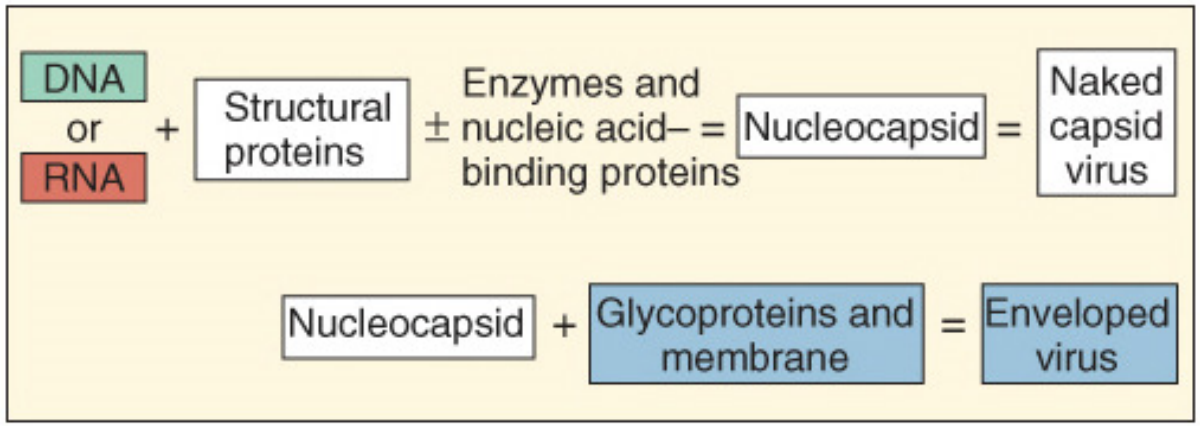
Disease: encephalitis and hepatitis viruses, for example

Means of transmission: arbovirus spread by insects, for example

Host cell (host range): animal (human, mouse, bird), plant, bacteria

Tissue or organ (tropism): adenovirus and enterovirus, for example

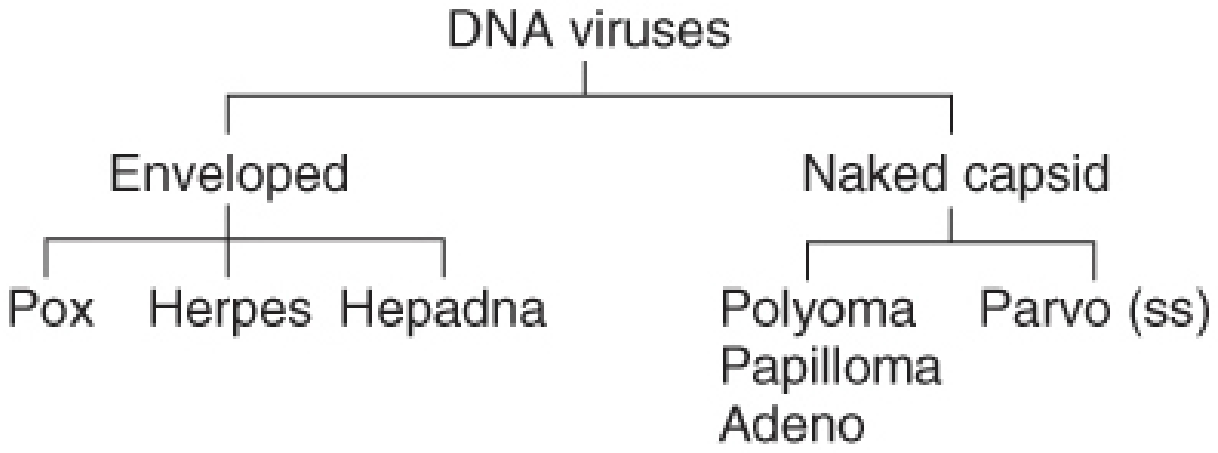
Components of the basic virion



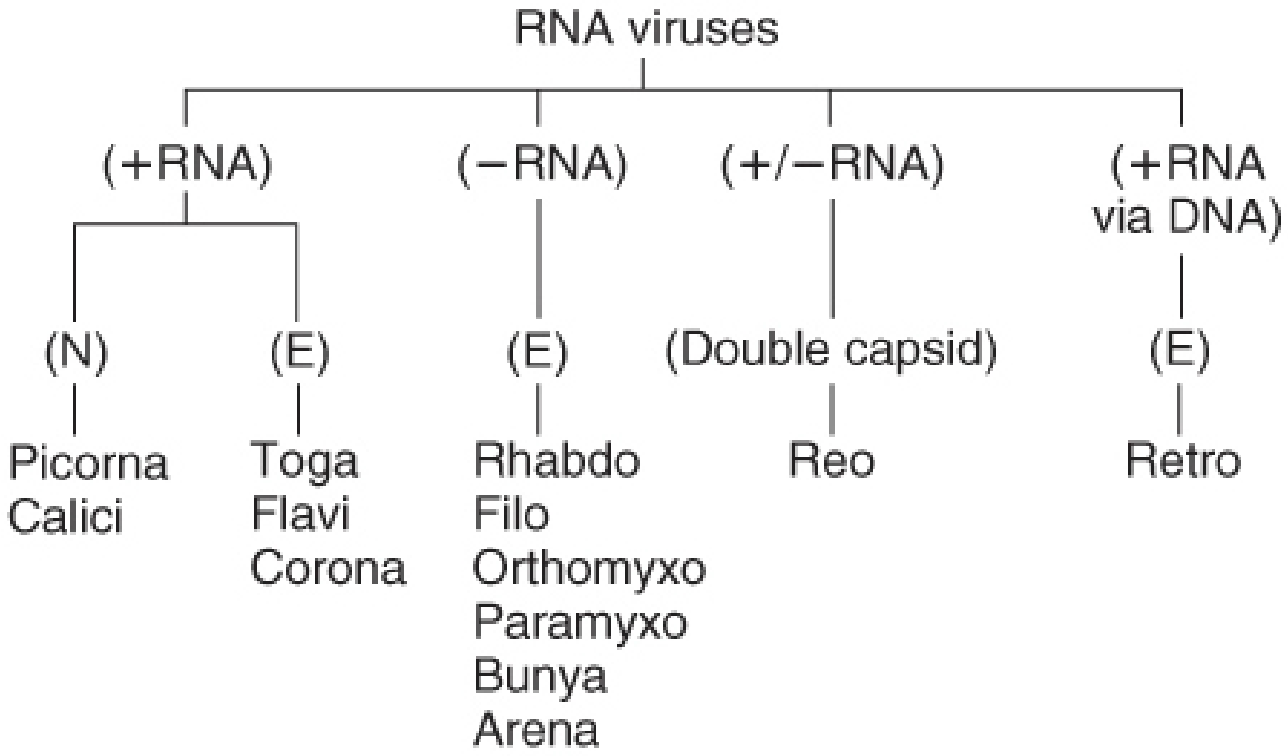
Viruses

Some common causes of disease in humans			
Viruses	DNA viruses	Adenoviruses	Human adenoviruses (e.g., types 3, 4, and 7)
		Herpesviruses	Herpes simplex, varicella zoster, Epstein–Barr virus, cytomegalovirus, HHV8
		Poxviruses	Variola, vaccinia virus
		Parvoviruses	Human parvovirus
		Papovaviruses	Papilloma virus
		Hepadnaviruses	Hepatitis B virus
	RNA viruses	Orthomyxoviruses	Influenza virus
		Paramyxoviruses	Mumps, measles, respiratory syncytial virus
		Coronaviruses	Cold viruses, SARS
		Picornaviruses	Polio, coxsackie, hepatitis A, rhinovirus
		Reoviruses	Rotavirus, reovirus
		Togaviruses	Rubella, arthropod-borne encephalitis
		Flaviviruses	Arthropod-borne viruses, (yellow fever, dengue fever)
		Arenaviruses	Lymphocytic choriomeningitis, Lassa fever
		Rhabdoviruses	Rabies
		Retroviruses	Human T-cell leukemia virus, HIV

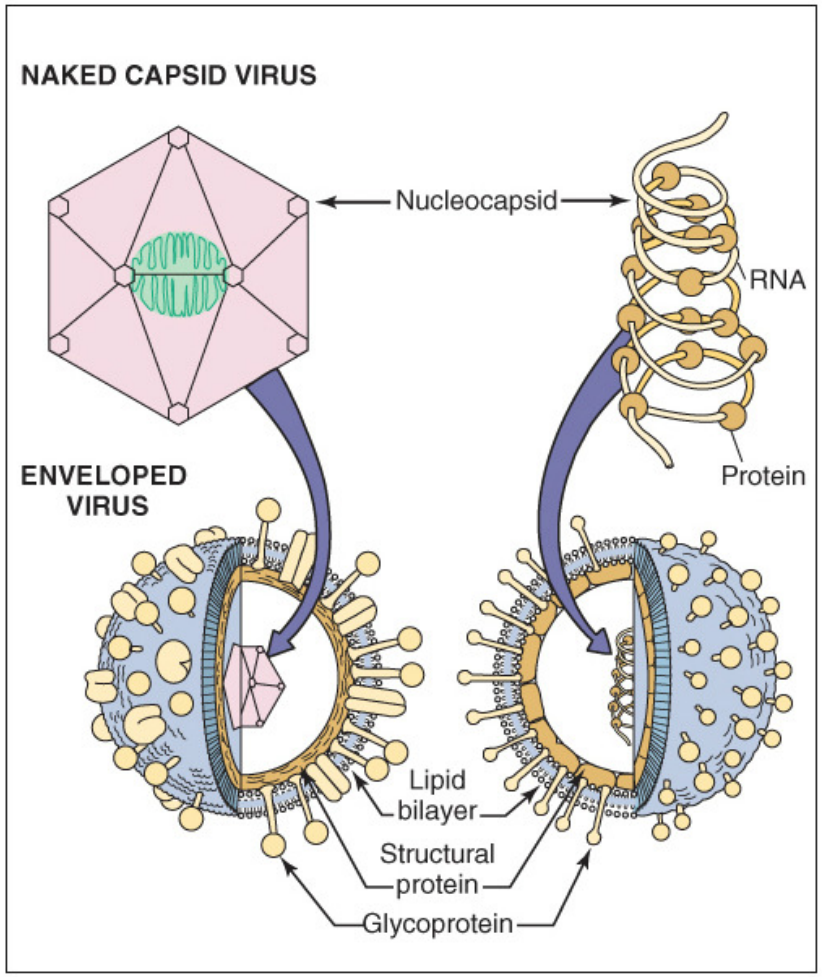
The DNA viruses and their morphology



The RNA viruses, their genome structure, and their morphology



Naked capsid virus and Enveloped virus



Virion structure: Naked capsid

Naked Capsid

Component

- Protein

Properties

* Exceptions exist.

- Is environmentally stable to the followi
  - Temperature
  - Acid
  - Proteases
  - Detergents
  - Drying
- Is released from cell by lysis

Consequences

- Can be spread easily (on fomites, from hand to hand, by dust, by small droplets)
- Can dry out and retain infectivity
- Can survive the adverse conditions of the gut
- Can be resistant to detergents and poor sewage treatment
- Antibody may be sufficient for immunoprotection

Virion structure: Envelope

Envelope

Components

- Membrane
- Lipids
- Proteins
- Glycoproteins

Consequences

- Must stay wet
- Cannot survive the gastrointestinal tract
- Spreads in large droplets, secretions, organ transplants, and blood transfusions

Properties

* Exceptions exist.

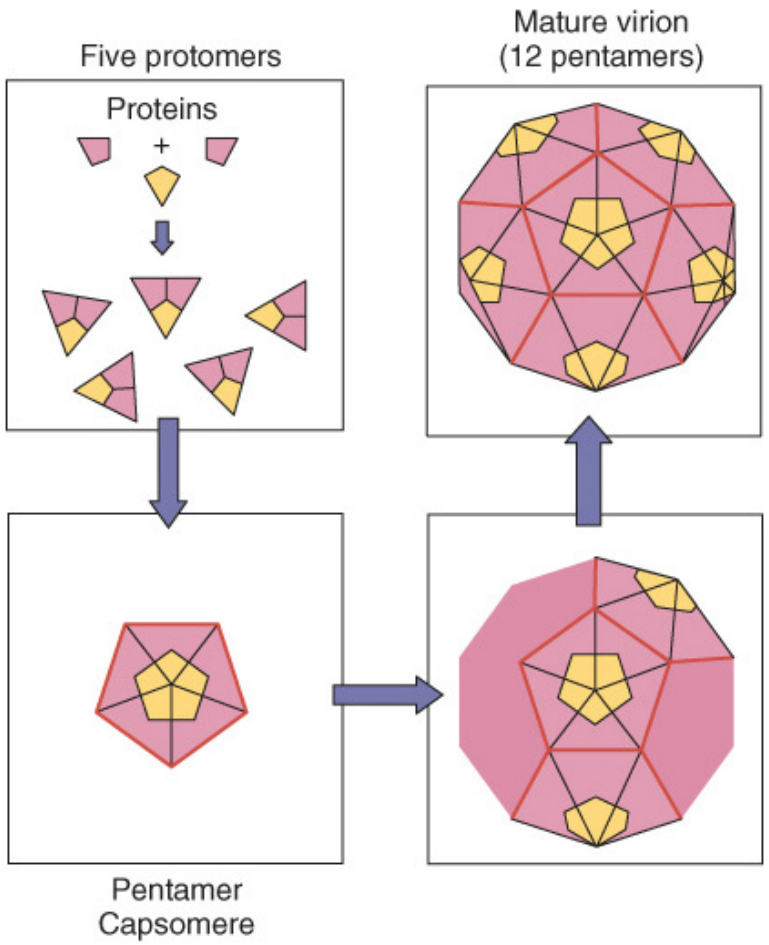
Is environmentally labile—disrupted by the following:

- Acid
- Detergents
- Drying
- Heat

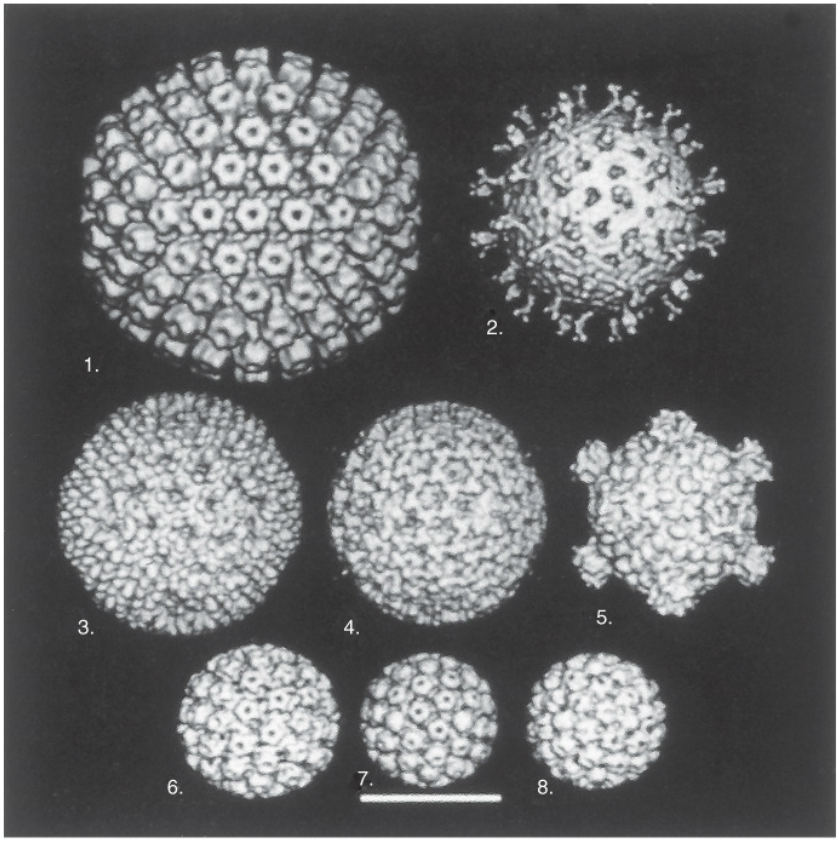
Modifies cell membrane during replication

Is released by budding and cell lysis

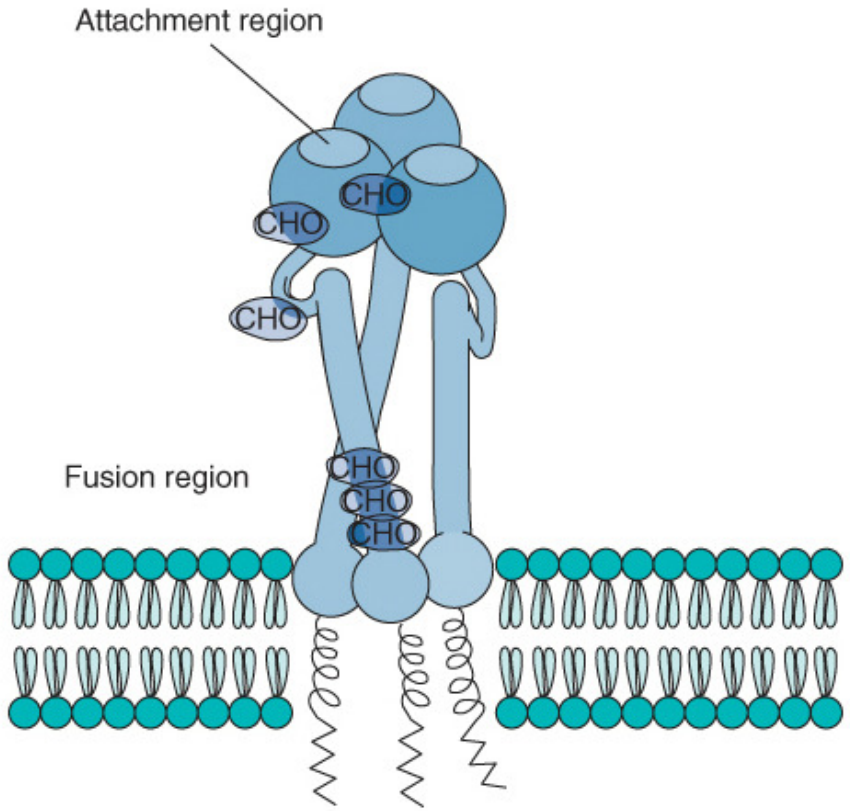
Icosahedral capsid of a picornavirus



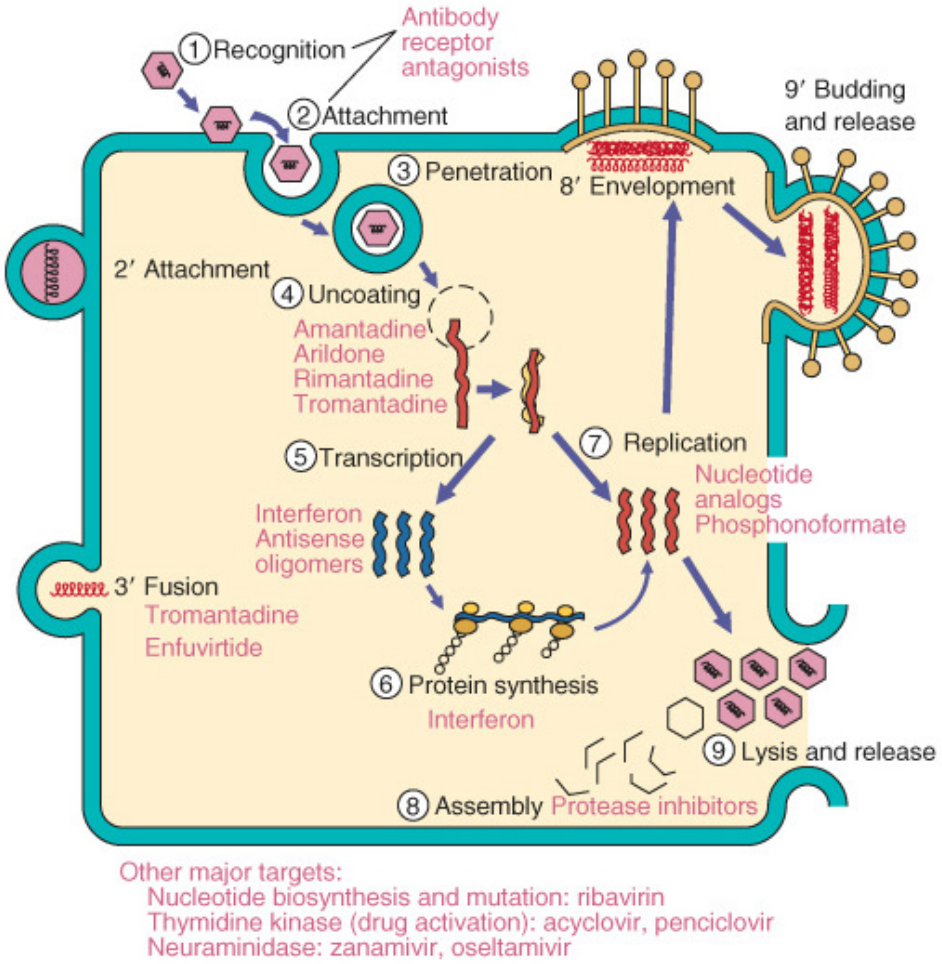
Cryoelectron microscopy and computer-generated 3D image reconstructions of



The hemagglutinin glycoprotein trimer of influenza A virus



Viral replication

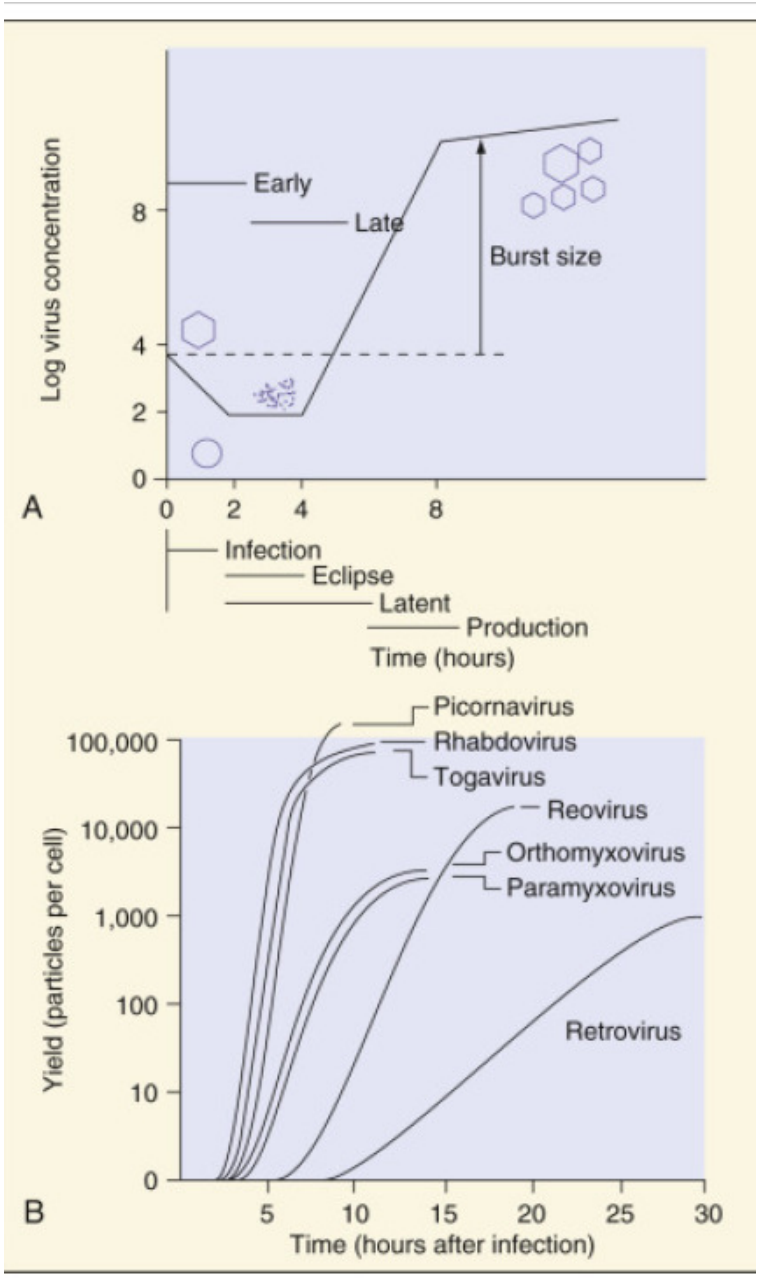


Steps in viral replication

Steps in Viral Replication

1. Recognition of the target cell
2. Attachment
3. Penetration
4. Uncoating
5. Macromolecular synthesis
    a. Early messenger RNA (mRNA) and nonstructural protein synthesis: genes for enzymes and nucleic acid–binding proteins
    b. Replication of genome
    c. Late mRNA and structural protein synthesis
    d. Posttranslational modification of protein
6. Assembly of virus
7. Budding of enveloped viruses
8. Release of virus

Single-cycle growth curve for a virus



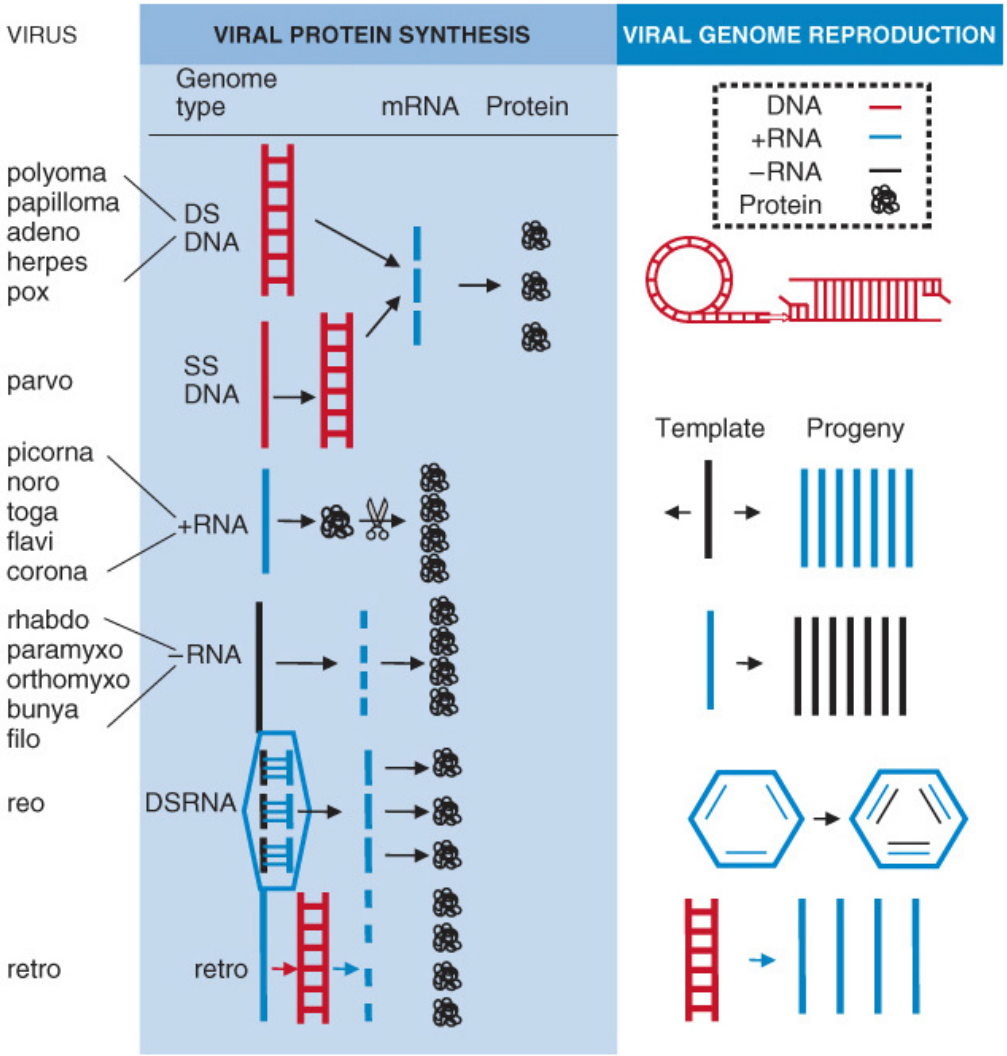
Viral attachment proteins

Virus Family	Virus	Viral Attachment Protein
Picornaviridae	Rhinovirus	VP1-VP2-VP3 complex
Adenoviridae	Adenovirus	Fiber protein
Reoviridae	Reovirus	σ-1
	Rotavirus	VP7
Togaviridae	Semliki Forest virus	E1-E2-E3 complex gp
Rhabdoviridae	Rabies virus	G protein gp
Orthomyxoviridae	Influenza A virus	HA gp
Paramyxoviridae	Measles virus	HA gp
Herpesviridae	Epstein-Barr virus	gp350 and gp220
Retroviridae	Murine leukemia virus	gp70
	Human immunodeficiency virus	gp120

Viral receptors

Virus	Target Cell	Receptor
Epstein-Barr virus	B cell	C3d complement receptor CR2 (CD21)
Human immunodeficiency virus	Helper T cell	CD4 molecule and chemokine coreceptor
Rhinovirus	Epithelial cells	ICAM-1 (immunoglobulin superfamily protein)
Poliovirus	Epithelial cells	Immunoglobulin superfamily protein
Herpes simplex virus	Many cells	Herpesvirus entry mediator (HVEM), nectin-1
Rabies virus	Neuron	Acetylcholine receptor, NCAM
Influenza A virus	Epithelial cells	Sialic acid
B19 parvovirus	Erythroid precursors	Erythrocyte P antigen (globoside)

Viral macromolecular synthesis steps



Mechanisms of viral pathogenesis

Viral disease

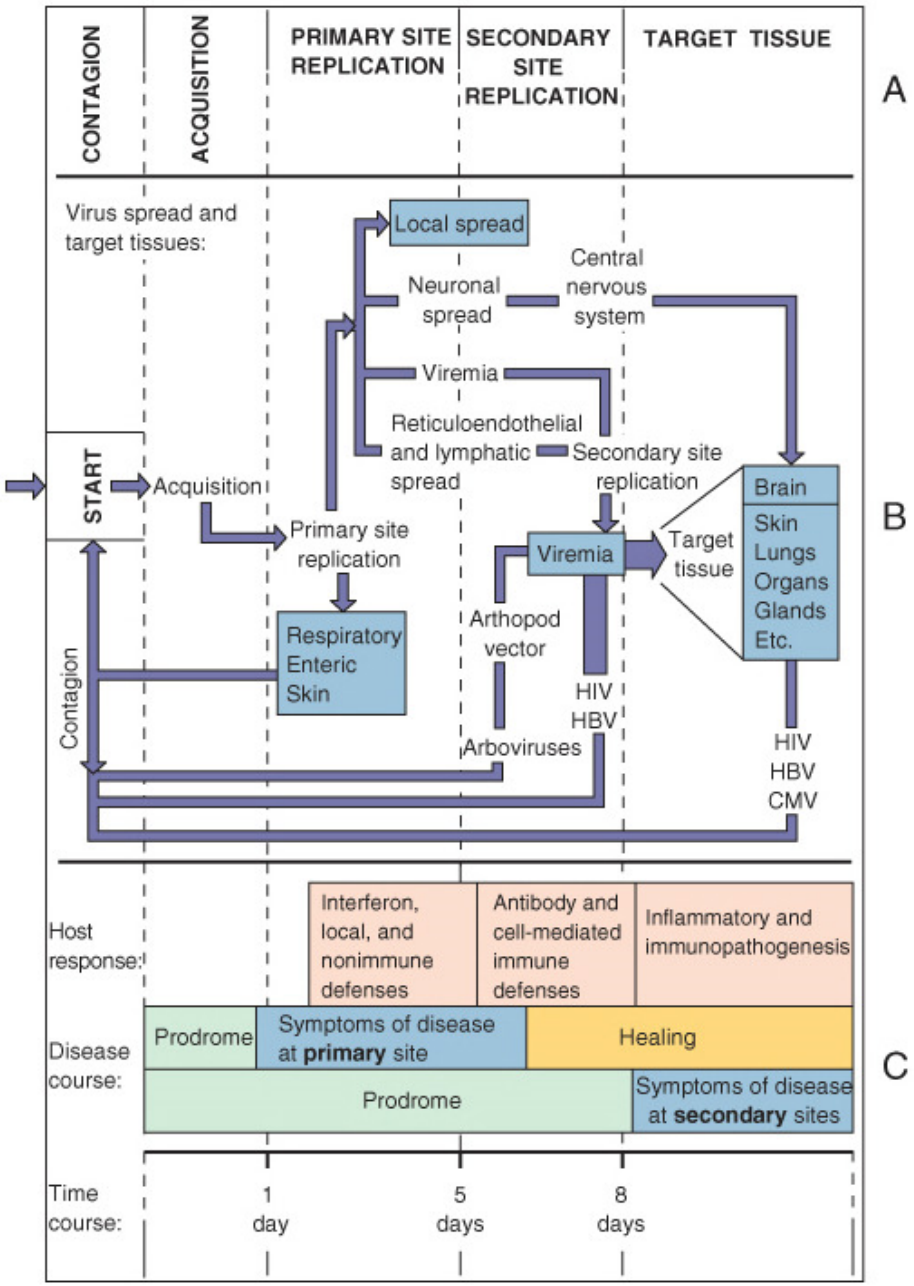
Nature of the Disease

- Target tissue
- Portal of entry of virus
- Access of virus to target tissue
- Tissue tropism of virus
- Permissiveness of cells for viral replication
- Pathogenic activity (strain)

Severity of Disease

- Cytopathic ability of virus
- Immune status (naïve or immunized)
- Competence of the immune system
- Prior immunity to the virus
- Immunopathology
- Virus inoculum size
- Length of time before resolution of infection
- General health of the person
- Nutrition
- Other diseases influencing immune status
- Genetic makeup of the person
- Age

The stages of viral infection



Progression of viral disease

1. **Acquisition** (entry into the body)

2. Initiation of infection at a primary site

3. Activation of innate protections

4. An **incubation period,** when the virus is amplified and may spread to a secondary site

5. Replication in the **target tissue,** which causes the characteristic disease signs

6. **Host responses** that limit and contribute (immunopathogenesis) to the disease

7. Virus production in a tissue that releases the virus to other people for **contagion**

8. **Resolution** or **persistent infection/chronic disease**

Determinants of viral pathogenesis I

Interaction of Virus with Target Tissue

- Access of virus to target tissue
- Stability of virus in the body
  - Temperature and dryness
  - Acid and bile of the gastrointestinal tract
- Ability to cross skin or mucosal epithelial cells (e.g., cross the gastrointestinal tract into the bloodstream)
- Ability to establish viremia
- Ability to spread through the reticuloendothelial system
- Target tissue
  - Specificity of viral attachment proteins
  - Tissue-specific expression of receptors

Determinants of viral pathogenesis II

Cytopathologic Activity of the Virus

- Efficiency of viral replication in the cell
  - Optimum temperature for replication
  - Permissiveness of cell for replication
  - Cytotoxic viral proteins
  - Inhibition of cell's macromolecular synthesis
  - Accumulation of viral proteins and structures (inclusion bodies)
  - Altered cell metabolism (e.g., cell immortalization)

Determinants of viral pathogenesis III

Host Protective Responses

- Antigen-nonspecific antiviral responses
  - Interferon and cytokines
  - Natural killer cells and macrophages
- Antigen-specific immune responses
  - T-cell responses
  - Antibody responses
- Viral mechanisms of escape of immune responses

Immunopathology

- Interferon: flulike systemic symptoms
- T-cell responses: cell killing, inflammation
- Antibody: complement, antibody-dependent cellular cytotoxicity, immune complexes

Types of viral infections at cellular level

Type	Virus Production	Fate of Cell
Abortive	–	No effect
Cytolytic	+	Death
Persistent		
Productive	+	Senescence
Latent	–	No effect
Transforming		
DNA viruses	–	Immortalization
RNA viruses	+	Immortalization

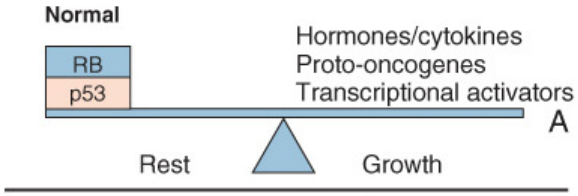
Mechanisms of viral cytopathogenesis I

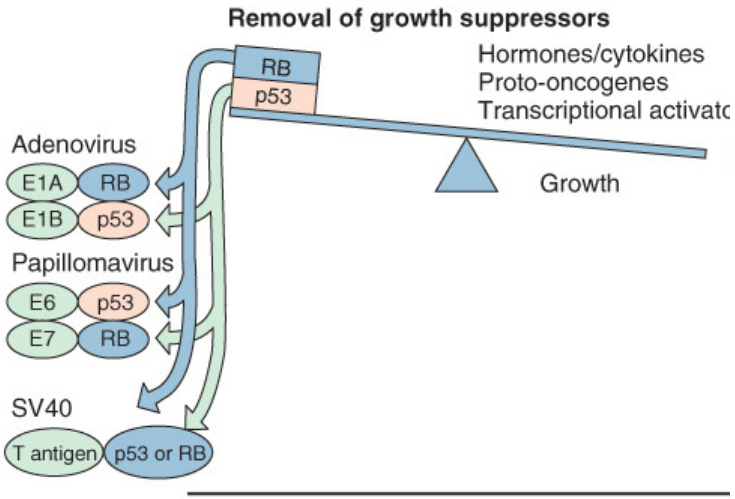
Mechanism	Examples
Inhibition of cellular protein synthesis	Poliovirus, herpes simplex virus (HSV), togaviruses, poxviruses
Inhibition and degradation of cellular DNA	Herpesviruses
Alteration of cell membrane structure	Enveloped viruses
Viral glycoprotein insertion	All enveloped viruses
Syncytia formation	HSV, varicella-zoster virus, paramyxoviruses, human immunodeficiency virus
Disruption of cytoskeleton	Nonenveloped viruses (accumulation), HSV
Permeability	Togaviruses, herpesviruses
Toxicity of virion components	Adenovirus fibers, reovirus NSP4 protein

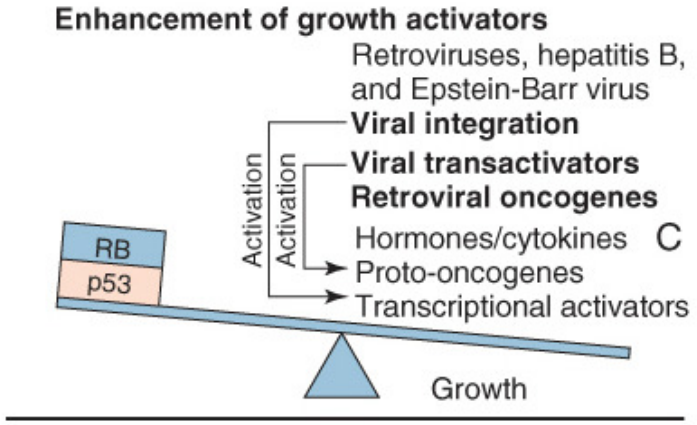
Mechanisms of viral cytopathogenesis II

Inclusion Bodies	Examples
Negri bodies (intracytoplasmic)	Rabies
Intranuclear basophilic (Owl's eye)	Cytomegalovirus (enlarged cells), adenoviruses
Cowdry type A (intranuclear)	HSV, subacute sclerosing panencephalitis (measles) virus
Intracytoplasmic acidophilic	Poxviruses
Perinuclear cytoplasmic acidophilic	Reoviruses

Mechanisms of viral transformation and immortalization







Viral immunopathogenesis

Immunopathogenesis	Immune Mediators	Examples
Flulike symptoms	Interferon, cytokines	Respiratory viruses, arboviruses (viremia-inducing viruses)
Type IV hypersensitivity and inflammation	T cells, macrophages, and polymorphonuclear leukocytes	Enveloped viruses
Immune complex disease	Antibody, complement	Hepatitis B virus, rubella
Hemorrhagic disease	T cell, antibody, complement	Yellow fever, dengue, Lassa fever, Ebola viruses
Postinfection cytolysis	T cells	Enveloped viruses (e.g., postmeasles encephalitis)
Cytokine storm	Antigen-presenting cells, T	Enveloped and other viruses
Immunosuppression	T cells, macrophages, dendritic cells	Human immunodeficiency virus, cytomegalovirus, measles virus, influenza virus

Viral infection

The relative **susceptibility** of a person and the **severity** of the disease depend on the following factors:

1. The mechanism of exposure and site of infection
2. The immune status, age, and general health of the person
3. The viral dose
4. The genetics of the virus and the host

Incubation periods of common viral infections

Disease	Incubation Period (Days) * (hl0000269)
Influenza	1-2
Common cold	1-3
Herpes simplex	2-8
Bronchiolitis, croup	3-5
Acute respiratory disease (adenoviruses)	5-7
Dengue	5-8
Enteroviruses	6-12
Poliomyelitis	5-20
Measles	9-12

Incubation periods of common viral infections

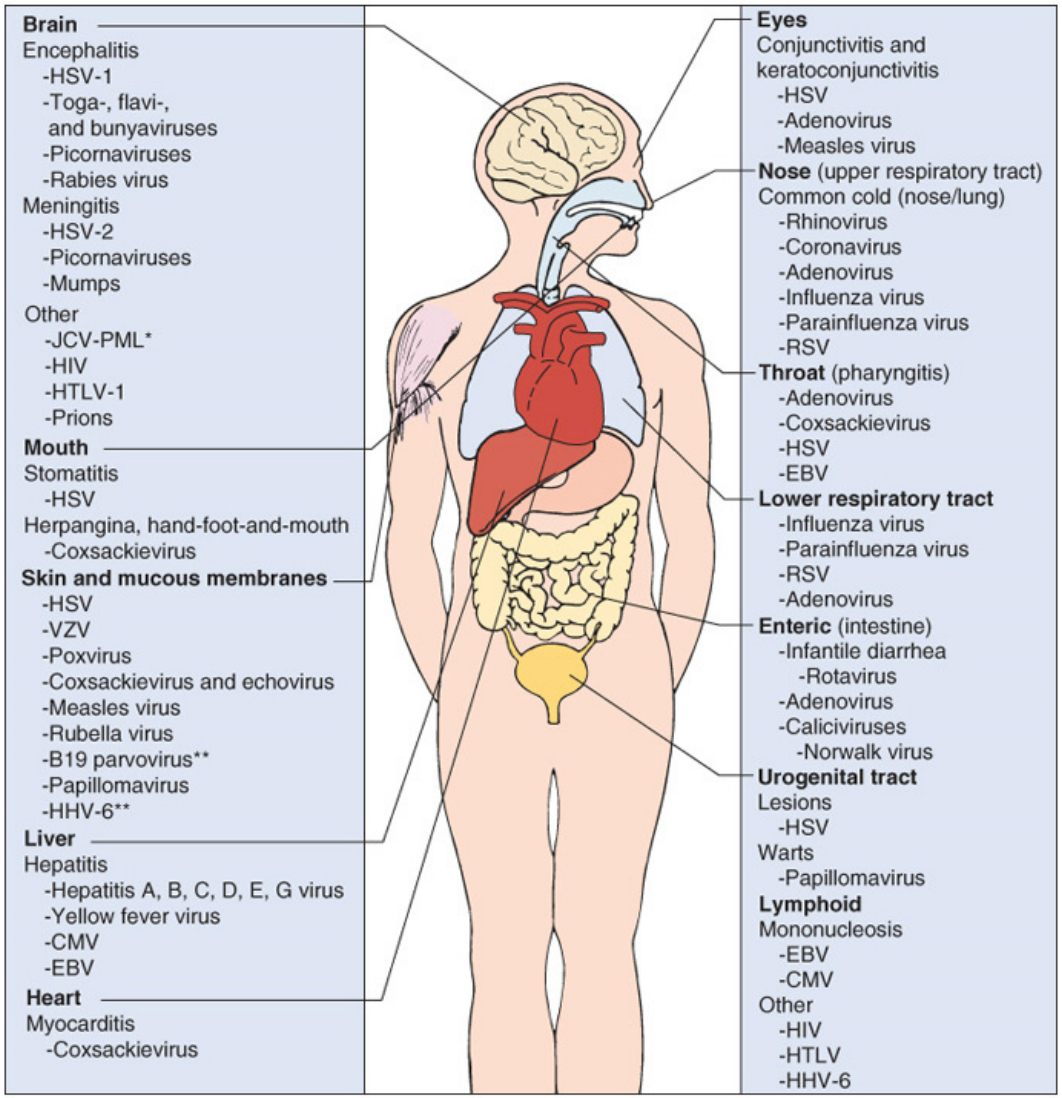
Smallpox	12-14
Chickenpox	13-17
Mumps	16-20
Rubella	17-20
Mononucleosis	30-50
Hepatitis A	15-40
Hepatitis B	50-150
Rabies	30-100+
Papilloma (warts)	50-150
Human immunodeficiency virus	1-15 years
AIDS	1-10 years

Viral transmission

Respiratory transmission	Paramyxoviruses, influenza viruses, picornaviruses, rhinoviruses, varicella-zoster virus, B19 virus
Fecal-oral transmission	Picornaviruses, rotavirus, reovirus, noroviruses, adenovirus
Contact (lesions, fomites)	HSV, rhinoviruses, poxviruses, adenovirus
Zoonoses (animals, insects)	Togaviruses (alpha), flaviviruses, bunyaviruses, orbiviruses, arenaviruses, hantaviruses, rabies virus, influenza A virus, orf (pox)
Transmission via blood	HIV, HTLV-1, HBV, HCV, hepatitis delta virus, cytomegalovirus
Sexual contact	Blood-borne viruses, HSV, human papillomavirus, molluscum contagiosum, HIV, HTLV-1, HBV, HCV
Maternal-neonatal transmission	Rubella virus, cytomegalovirus, B19 virus, echovirus, HSV, varicella-zoster virus, HIV
Genetic	Prions, retroviruses

Role of viruses in disease

Major target tissues of viral disease



Oral and respiratory diseases I

Disease	Etiologic Agent
Common Cold	Rhinovirus * (hl0000119)
	Coronavirus * (hl0000119)
	Influenza viruses
	Parainfluenza viruses
	Respiratory syncytial virus (RSV)
	Metapneumovirus
	Adenovirus
	Enteroviruses

Oral and respiratory diseases II

Pharyngitis	Herpes simplex virus
	Epstein-Barr virus
	Adenovirus * (hl0000119)
	Coxsackievirus A * (hl0000119) (herpangina, hand-foot-and-mouth disease) and other enteroviruses
Croup, Tonsillitis, Laryngitis, and Bronchitis (Children < 2 Years)	Parainfluenza virus 1 * (hl0000119)
	Parainfluenza virus 2
	Influenza virus
	Adenovirus
	Epstein-Barr virus

Oral and respiratory diseases III

Bronchiolitis	RSV * (hl0000119) (infants)
	Metapneumovirus
	Parainfluenza virus 3 * (hl0000119) (infants and children)
	Parainfluenza viruses 1 and 2
Pneumonia	RSV * (hl0000119) (infants)
	Metapneumovirus
	Parainfluenza virus * (hl0000119) (infants)
	Influenza virus * (hl0000119)
	Adenovirus
	Varicella-zoster virus (primary infection of adults or immunocompromised hosts)
	Cytomegalovirus (infection of immunocompromised host)
	Measles

Gastrointestinal viruses

Infants

Rotavirus A * (fn0010)

* Most common causal agents.

Adenovirus 40, 41

Coxsackievirus A24

Infants, Children, and Adults

Norwalk virus * (fn0010)

Calicivirus

Astrovirus

Rotavirus A and B (outbreaks in China)

Reovirus

Viruses transmitted in blood

Hepatitis B, C, G, D

Human immunodeficiency virus

Human T-cell lymphotropic virus 1

Cytomegalovirus

Epstein-Barr virus

West Nile encephalitis virus

Sexually transmitted virus

Human papillomavirus 6, 11, 42

Human papillomavirus 16, 18, 31, 45, and others (high risk for human cervical carcinoma)

Herpes simplex virus (HSV-1 and HSV-2)

Cytomegalovirus

Hepatitis B, C, and D viruses

Human immunodeficiency virus

Human T-cell lymphotropic virus 1

Screening of the blood supply

Human immunodeficiency syndrome

Hepatitis B

Hepatitis C

Human T-cell lymphotropic virus 1 and 2

West Nile encephalitis virus * (fn0025)

Arboviruses and Zoonoses

Virus	Family	Reservoir/Vector
Eastern equine encephalitis	Togaviridae	Birds/ *Aedes* mosquito
Western equine encephalitis	Togaviridae	Birds/ *Culex* mosquito
West Nile encephalitis	Flaviviridae	Birds/ *Culex* mosquito
St. Louis encephalitis	Flaviviridae	Birds/ *Culex* mosquito
Chikungunya	Togaviridae	Birds, mammals/ *Aedes* mosquito
California encephalitis	Bunyaviridae	Small mammals/ *Aedes* mosquito
La Crosse encephalitis	Bunyaviridae	Small mammals/ *Aedes* mosquito
Yellow fever	Flaviviridae	Birds/ *Aedes* mosquito
Dengue	Flaviviridae	Monkeys/ *Aedes* mosquito
Colorado tick fever	Reoviridae	Tick
Lymphocytic choriomeningitis	Arenaviridae	Rodents
Lassa fever	Arenaviridae	Rodents
Sin Nombre hantavirus	Bunyaviridae	Deer mice
Ebola	Filoviridae	Unknown
Rabies	Rhabdoviridae	Bats, foxes, raccoons, etc.
Influenza A	Orthomyxoviridae	Birds, swine, etc.

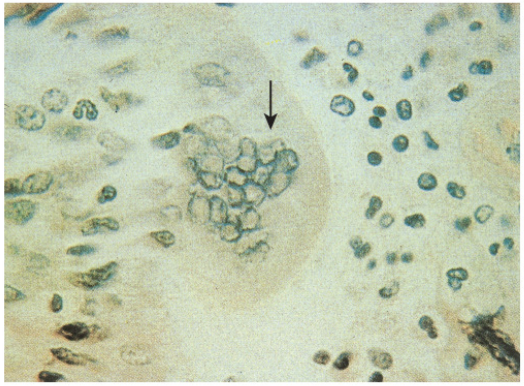
Laboratory diagnosis of viral disease

Laboratory procedures for diagnosing viral infections

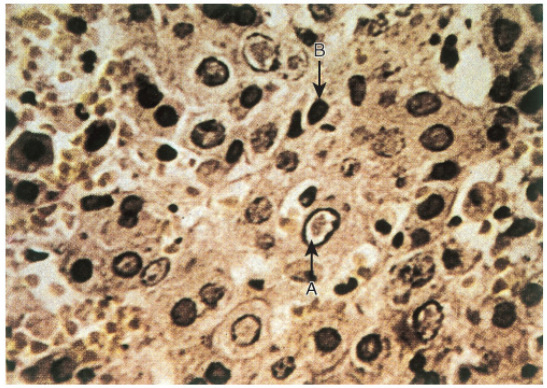
The laboratory methods accomplish the following results:

1. Description of virus-induced **cytopathologic effects (CPEs)** on cells
2. Detection of viral particles
3. Isolation and growth of the virus
4. Detection and analysis of viral components (e.g., proteins [antigens], enzymes, genomes)
5. Evaluation of the patient's immune response to the virus **(serology)**

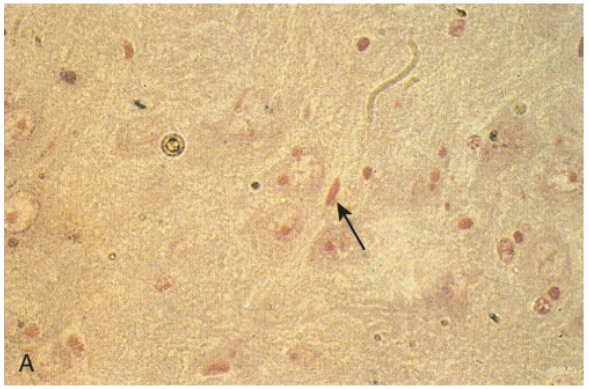
Cytology



Syncytium formation by measles virus

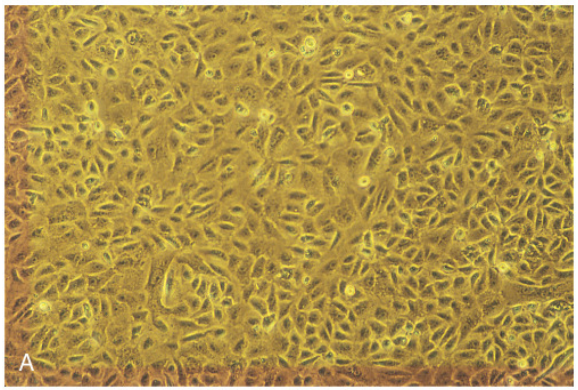


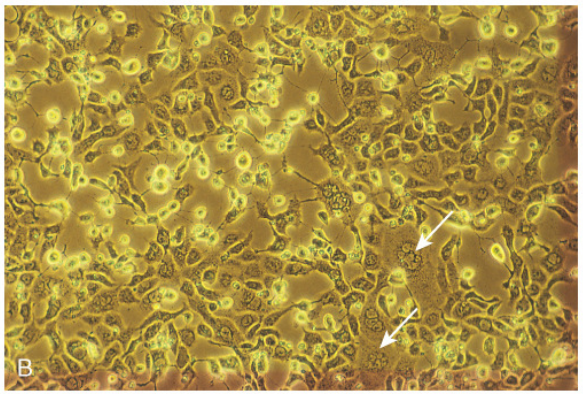
Cytopathologic effect by HSV

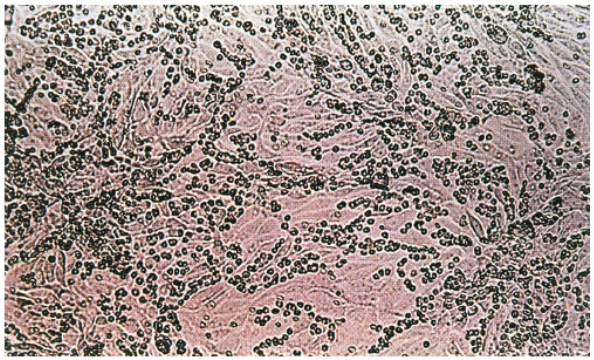


Negri bodies caused by rabies

Viral cytopathologic effects







Systems for propagation of viruses

People

Animals: cows (e.g., Jenner cowpox vaccine), chickens, mice, rats, suckling mice

Embryonated eggs

Organ culture

Tissue culture

- Primary
- Diploid cell line
- Tumor or immortalized cell line

Titer

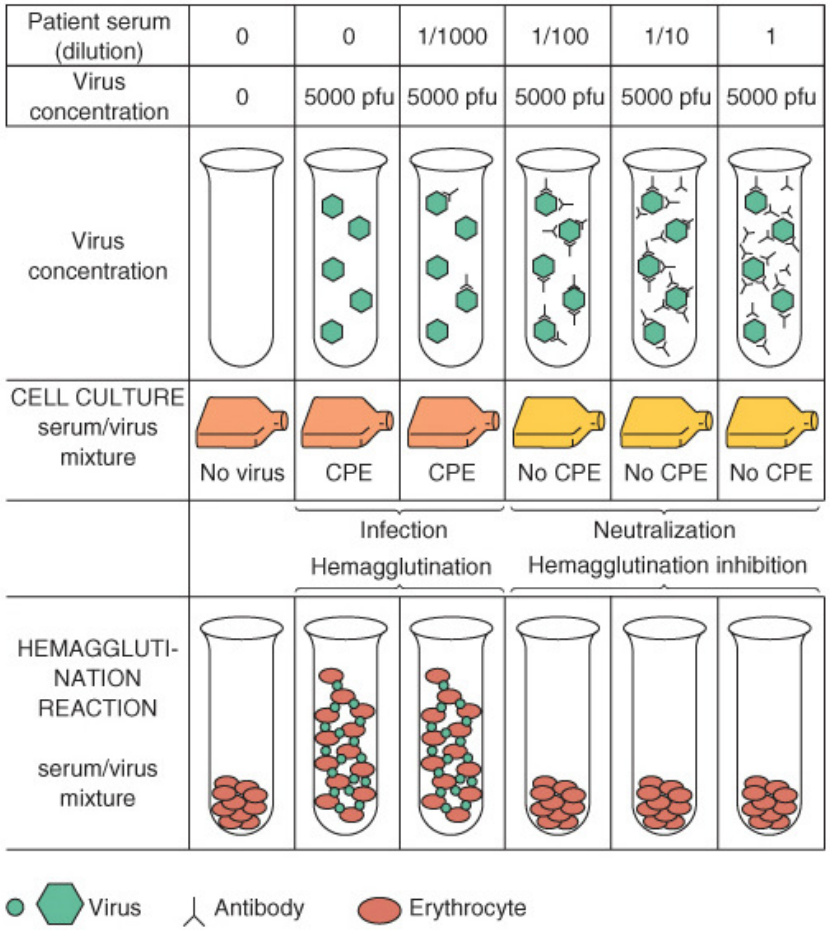
One can quantitate a virus by determining the greatest dilution that retains the following properties **(titer):**

1. **Tissue culture dose (TCD_{50}):** titer of virus that causes cytopathologic effects in half the tissue culture cells

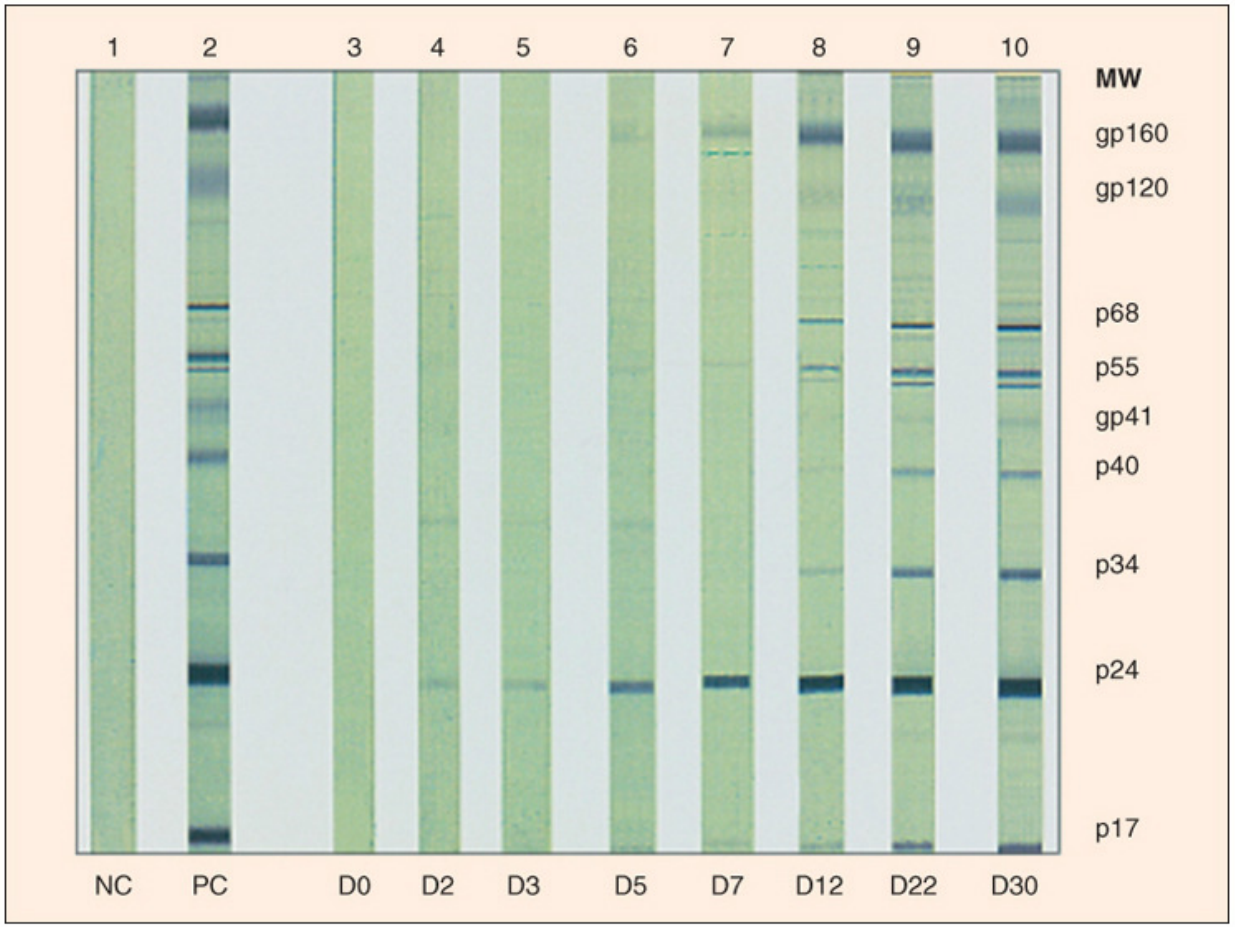
2. **Lethal dose (LD_{50}):** titer of virus that kills 50% of a set of test animals

3. **Infectious dose (ID_{50}):** titer of virus that initiates a detectable symptom, antibody, or other response in 50% of a set of test animals

HA and HI test



Western blot analysis



Antiviral agents and infection control

Viruses treatable with antiviral drugs

Viruses Treatable with Antiviral Drugs

Herpes simplex virus

Varicella-zoster virus

Cytomegalovirus

Human immunodeficiency virus

Influenza A and B viruses

Respiratory syncytial virus

Hepatitis B and C viruses

Papillomavirus

Picornavirus

Examples of targets for antiviral drugs I

Replication Step or Target	Agent	Targeted Virus
Attachment	Peptide analogs of attachment protein	HIV (CCR5 co-receptor antagonist)
	Neutralizing antibodies	Most viruses
	Heparan and dextran sulfate	HIV, HSV
Penetration and uncoating	Amantadine, rimantadine	Influenza A virus
	Tromantadine, docosanol	HSV
	Arildone, disoxaril, pleconaril	Picornaviruses
Transcription	Interferon	HCVs, papillomavirus
	RNA polymerase	HCV
	Antisense oligonucleotides	—

Thank you for your attention!!