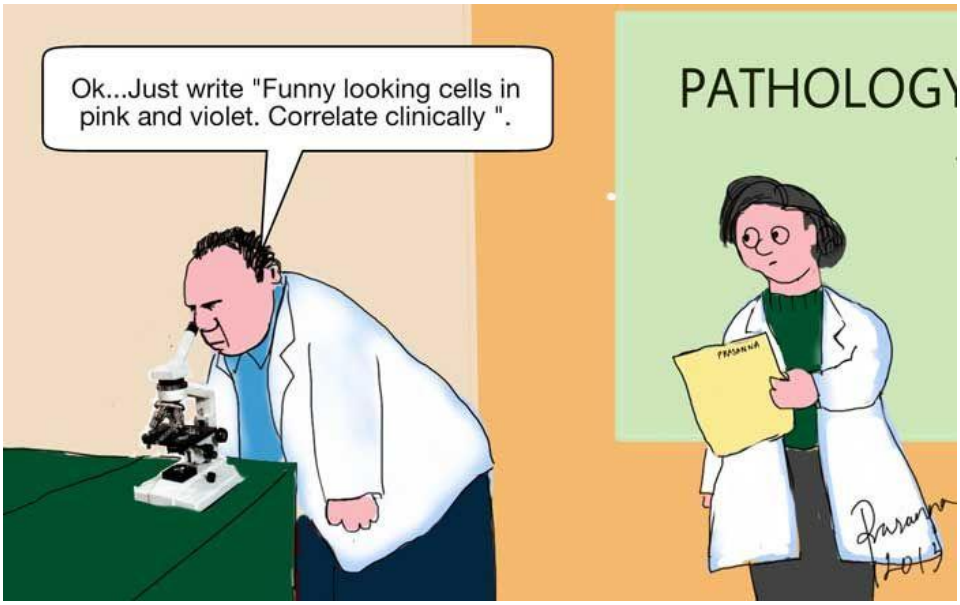
PATHOLOGY & MICROBIOLOGY SUPPLEMENTS

NISHTAR MEDICAL UNIVERSITY MULTAN

ALI RAZA CHAUDARY (N67)

www.facebook.com/humanfountainsarc


Ok...Just write "Funny looking cells in pink and violet. Correlate clinically ".
PATHOLOGY

REFERENCES

PATHOLOGY & MICROBIOLOGY

1. Robbins Basic Pathology by Kumar, Abbas and Astar, 10th Ed. (MEDIUM ROBBINS)
2. Medical Microbiology and Immunology by Levinson and Jawetz, 15th Ed., Mc Graw-Hill.
3. www.medfools.com

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HOW TO DO?

TOPIC	WHERE TO DO?
CELL INJURY	Medium Robbins Unit 2
INFLAMMATION	Medium Robbins Unit 3
TISSUE REPAIR	Medium Robbins Unit 3 & 1
HEMODYNAMICS	Medium Robbins Unit 4
IMMUNOLOGY	Levinson Microbiology Part VII
NEOPLASIA	Medium Robbins Unit 6
GENETICS	Kaplan Pathology Unit 6
VIROLOGY	Kaplan Microbiology Unit 4
BACTERIOLOGY	Levinson Microbiology Part I & II
PARASITOLOGY	Levinson Microbiology Part VI
MYCOLOGY	Levinson Microbiology Part V

CELL INJURY

IMPORTANT DIFFERENCES

TABLE 1.1. Differences between metaplasia and dysplasia

Features	Metaplasia	Dysplasia
Definition	Replacement of one adult epithelial or mesenchymal cell type by another	Disordered cellular development characterized by (a) Loss of orientation of cells with respect to one another (b) Lack of uniformity of individual cells
Types	Squamous, columnar (epithelial) and osseous, cartilaginous (mesenchymal)	Epithelial only
Cellular pleomorphism	Mature cellular development; no pleomorphism	Disordered cellular development due to aberrant/delayed maturation or differentiation; pleomorphism present
Natural history	Reversible on withdrawal of stimulus	May regress on withdrawal of inciting stimulus or progress to higher grades of dysplasia or carcinoma in situ

TABLE 1.2. Differences between reversible and irreversible cell injury

Features	Reversible injury	Irreversible injury
Definition	If the structural and functional changes, induced by an injurious stimulus, *can* revert to normal on removal of the same, it is called reversible injury	If the structural and functional changes, induced by an injurious stimulus, *cannot* be reversed even after removal of the same, it is called irreversible injury
Cell membrane		
(a) Blebbing, blunting, distortion	Present	Present; more prominent than reversible injury
(b) Defect	Absent	Present
Endoplasmic reticulum	Shows swelling only	Shows swelling and lysis
Ribosomes	Dispersed	Dispersed and destroyed
Lysosomes	Autophagy of organelles by lysosomes, no rupture	Rupture of lysosomes and autolysis of cell
Mitochondria	Swelling, small densities present	Swelling, large densities present
Nucleus	Clumping of nuclear chromatin	Pyknosis, karyolysis or karyorrhexis
Calcification	Absent	Dystrophic calcification may be seen

TABLE 1.3. Differences between autolysis and necrosis

Features	Autolysis	Necrosis
Definition	Self-digestion of cells by enzymes liberated from its own lysosomes	Spectrum of morphologic changes that follow cell death in living tissue, resulting from the progressive degradative action of enzymes on lethally injured cells
Reaction	• In *living tissue*, inflammatory cells may be present • In *post-mortem* cases, there is complete absence of inflammatory cells	• Presence of inflammatory cells • Does not occur post-mortem
Calcification	Absent	Dystrophic calcification may be present

TABLE 1.4. Differences between coagulative and liquefactive necrosis

Features	Coagulative necrosis	Liquefactive necrosis
Cause	Hypoxic/ischaemic injury in all tissues except in brain, eg, myocardial, renal or placental infarction	• Bacterial and fungal infections • Hypoxic injury in brain
Tissue architecture	Tissue architecture is preserved; the basic outline of cell is intact, although cytoplasmic and nuclear details are lost	Both cell outline and intracellular details are lost; tissue architecture is not preserved
Pathogenesis	Due to intracellular acidosis, structural as well as enzymatic proteins are denatured and proteolysis is blocked; dead cells are removed by fragmentation and phagocytosis	Hydrolytic enzymes from bacteria and fungi as well as inflammatory cells cause complete digestion of dead cells and formation of pus (lysis)
Morphology	Conversion of cells into acidophilic, coagulated, anucleate units	No cellular outline/tissue architecture recognized

TABLE 1.5. Differences between coagulative and caseous necrosis

Features	Coagulative necrosis	Caseous necrosis
Cause	Hypoxia	Tuberculous infection of lymph nodes, lungs, skin, etc.
Pathogenesis	Due to intracellular acidosis, structural as well as enzymatic proteins are denatured and proteolysis is blocked	Delayed hypersensitivity reaction to *mycobacterial* capsular antigens
Gross	Affected tissue is firm in texture	Cheesy white appearance
Tissue architecture	Preserved	Completely obliterated

TABLE 1.6. Differences between dry and wet gangrene

Features	Dry gangrene	Wet gangrene
Cause	Mainly arterial occlusion (coagulative necrosis)	More in venous occlusion; obstruction invariably followed by secondary bacterial infection (liquefactive necrosis)
Distribution	Limbs	More common in bowel
Gross appearance	Organ is dry, shrunken and black	Moist, soft, swollen
Line of demarcation	Present at junction between healthy and gangrenous parts	Not clear
Putrefaction	Limited (no infection and less blood supply)	Marked
Presence of bacteria	Absent, little or no septicaemia	Overwhelming septicaemia present
Prognosis	Better	Poor

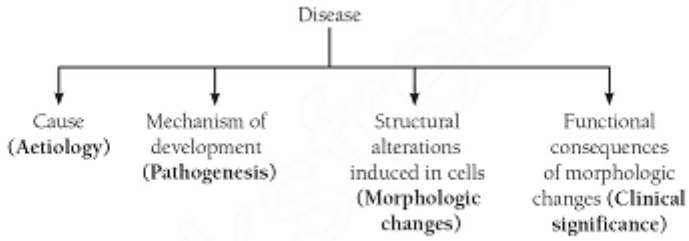
TABLE 1.7. Differences between apoptosis and necrosis

Features	Apoptosis	Necrosis
Definition	Programmed and coordinated cell death, which eliminates unwanted/harmful cells or removes cells damaged beyond repair	Spectrum of morphologic changes that follow cell death in living tissue, largely resulting from the progressive degradative action of enzymes on lethally injured cells
Causes	May be physiological or pathological	Always pathological, eg, hypoxia, toxins
Involves	Single or small groups of cells	Large groups of cells
Inflammation	Absent	Present
Cellular change	Cell shrinkage	Cell swelling
Cell membrane	Bleb formation	Membrane disruption
Nucleus	Chromatin condensation followed by fragmentation	Nuclear pyknosis, karyolysis and karyorrhexis
Removal of cell	Phagocytosis of apoptotic bodies by macrophages	Enzymatic digestion or phagocytosis of cell debris by macrophages
Lysosomes/other organelles	Intact	Hydrolytic enzyme release due to rupture
Mechanism	Genetically coordinated	Due to ATP depletion, free radicals, mitochondrial damage, etc.
Agarose gel electrophoresis	Stepladder DNA pattern	Diffuse DNA pattern

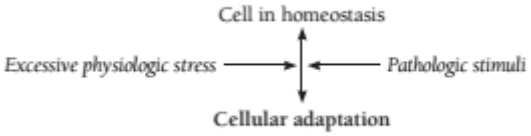
TABLE 1.8. Differences between dystrophic and metastatic calcification

Features	Dystrophic calcification	Metastatic calcification
Definition	Deposits of calcium salts in dead and degenerated tissue	Deposits of calcium salts in viable tissue
Calcium metabolism	Normal	Deranged
Serum calcium level	Normal	Increased
Sites of deposition	Necrosis, infarcts, thrombi, haematomas, dead parasites, old scars, atheromas	Blood vessels, kidneys, lungs and gastric mucosa

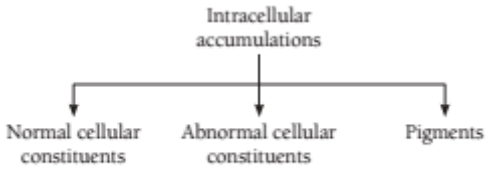
IMPORTANT FLOWCHARTS



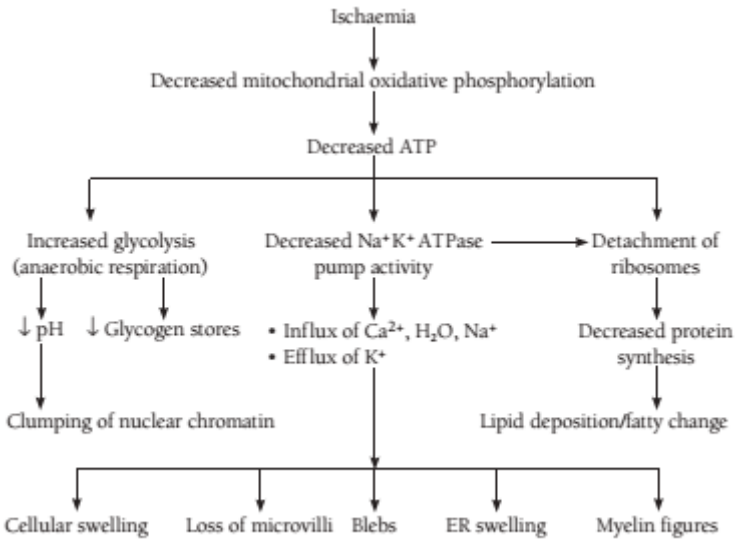
FLOWCHART 1.1. Different aspects that form the core of pathologic basis of disease.



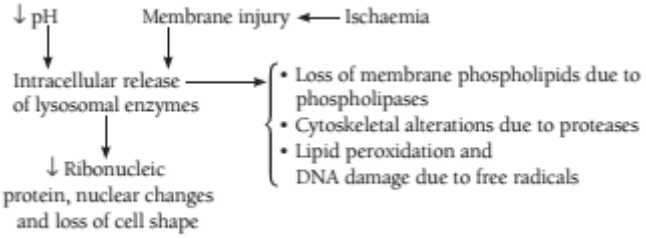
FLOWCHART 1.2. Cellular adaptation.



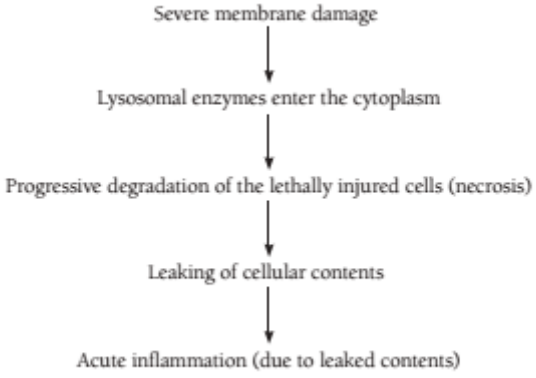
FLOWCHART 1.3. Intracellular accumulations.



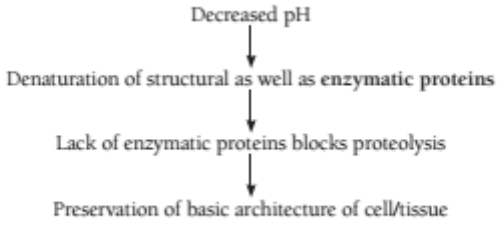
FLOWCHART 1.4. Sequence of events in reversible injury.



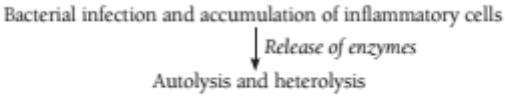
FLOWCHART 1.5. Sequence of events in irreversible injury.



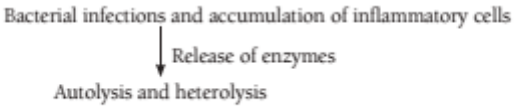
FLOWCHART 1.6. Sequence of events in cellular necrosis.



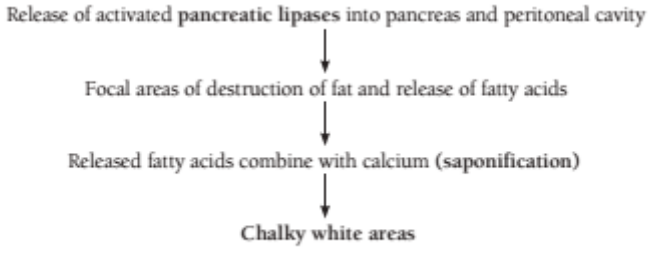
FLOWCHART 1.7. Mechanism of evolution of coagulative necrosis.



FLOWCHART 1.8. Mechanism of evolution of liquefactive necrosis.



FLOWCHART 1.9. Mechanism of evolution of gangrenous necrosis.



FLOWCHART 1.10. Mechanism of evolution of enzymatic fat necrosis.

Extracellular signals
- *Injuries*: radiation, toxins and free radicals
- *Withdrawal of growth factors, hormones or cytokines*
- *Receptor–ligand interactions* (Fas–Fas ligand, TNF–TNF receptor)

↓

Act on intracellular regulatory molecules

OR

Directly affect targets within the cell (eg, physicochemical agents like heat, radiation, viruses and xenobiotics and glucocorticoids directly bind to nuclear receptors)

Binding of Fas L to Fas (receptor–ligand interactions)

↓

Three or more molecules of Fas are brought together

↓

The cytoplasmic domain of three Fas molecules forms a binding site for an adapter protein FADD (Fas-associated death domain)

↓

FADD binds inactive Caspase-8

↓

Activation of Caspase-8 and initiation of caspase cascade

FLOWCHART 1.11. Extrinsic/death receptor-initiated pathway.

Activation of BCL-2 sensor proteins (BAD, BIM, Puma, Noxa) by cell injury

↓

Activation of proapoptotic proteins (BAX and BAK) which form oligomers that insert into mitochondrial membrane

↙ ↘

Formation of pores in **inner mitochondrial membrane**

↓

- Decreased membrane potential
- Mitochondrial swelling

→ Release of **cytochrome** C and other proapoptotic factors into cytosol

Increased permeability of **outer mitochondrial membrane**

↓

↓

Cytochrome C binds to *Apaf-1

(**Apaf-1* is *apoptosis activating factor*)

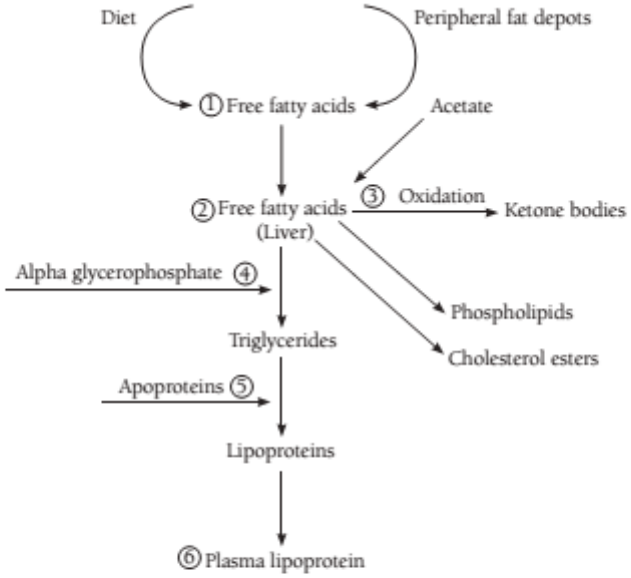
↓

Formation of cytochrome C–Apaf-1 complex ('apoptosome')

↓

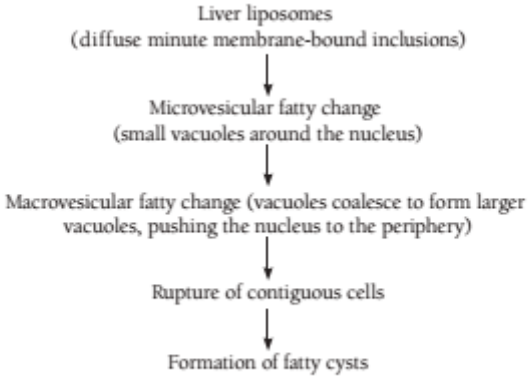
Activation of initiator caspase-9

FLOWCHART 1.12. Intrinsic/mitochondrial pathway.

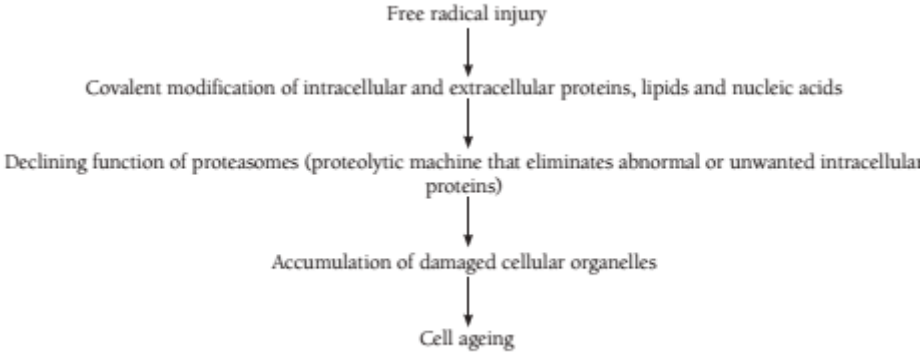


FLOWCHART 1.13. Mechanism of development of fatty liver.

1. Excessive entry of free fatty acids into the liver (starvation, toxins, diabetes mellitus, anoxia).
2. Increased synthesis of free fatty acids in the liver (obesity, alcohol abuse).
3. Decreased oxidation of fatty acids into ketones (anoxia, starvation).
4. Increased esterification of fatty acids into triglycerides (alcohol).
5. Decreased synthesis of apoproteins (CCL4 toxicity, protein energy malnutrition).
6. Defective excretion of lipoproteins.



FLOWCHART 1.14. Sequence of events in the evolution of fatty liver.



FLOWCHART 1.15. Exogenous influences in cellular ageing.

INFLAMMATION

IMPORTANT DIFFERENCES

TABLE 2.1. Comparison between acute and chronic inflammation

Feature	Acute	Chronic
Causative agents	Physical (heat, radiation and mechanical trauma) Chemical agents (organic and inorganic poisons) Infectious agents (bacteria, viruses and parasites) Immunological agents (hypersensitivity reactions)	Persistent acute inflammation due to nondegradable pathogens Persistent foreign bodies Autoimmune reactions
Major cells involved	Mainly neutrophils; also eosinophils and basophils	Mononuclear cells (monocytes, macrophages, lymphocytes, plasma cells) and fibroblasts
Primary mediators	Vasoactive amines, eicosanoids	Interferon gamma (IFN-γ) and other cytokines, growth factors, reactive oxygen species, and hydrolytic enzymes
Onset	Immediate/rapid	Insidious/delayed
Duration	Few days	Up to many months or years
Outcomes	Resolution, fibrosis and chronic inflammation	Tissue destruction and scarring
Cardinal signs and systemic manifestations	1. Pain (dolour)	Absence of any cardinal signs
	2. Heat (calor)	Patient is asymptomatic or presents with low-grade fever, lethargy, loss of appetite and weight loss
	3. Redness (rubor) 4. Swelling (tumour) 5. Loss of function (functio leasa)	Patient may also present with high-grade fever
Oedema	Present	Absent
Angiogenesis	Absent	Present
Tissue destruction	Absent	Present
Attempts at repair	Absent	Present
Fibrosis	Absent	Present

TABLE 2.2. Differences between granulation tissue and granuloma

Features	Granulation tissue	Granuloma
Component of	Healing and repair	Chronic inflammation; occurs due to delayed hypersensitivity response
Definition	Tissue composed of newly formed blood vessels (**angiogenesis**), proliferating fibroblasts and chronic inflammatory cells	Microscopic aggregation of macrophages that are transformed into epithelium like (**epithelioid cells**) surrounded by a collar of mononuclear cells (**lymphocytes and plasma cells**) Older granulomas have an enclosing **rim of fibroblasts and connective tissue**
Giant cells	Not seen	Epithelioid cells fuse to form '**Langhans giant cells**' 40–50 microns in size with 20 or more nuclei arranged peripherally
Remodelling (maturation and reorganization of fibrous tissue)	Seen	Not seen
Growth factors	Angiogenic and fibrogenic growth factors involved, eg, PDGF, FGF, TNF and VEGF	Involvement of cytokines like IL-1, IL-12 and γIFN

IMPORTANT FLOWCHARTS

Immediate transient vasoconstriction of arterioles
↓ *Histamine, prostaglandins, PAF, kinins and NO*
Persistent progressive vasodilatation of arterioles
↓
Opening of new capillary beds (local heat and redness)
↓
Increased blood volume in microcirculation elevating the hydrostatic pressure
↓
Transudation of fluid into the extracellular space
↓ *Further injury*
Histamine, leukotrienes, PAF, kinins
Increased vascular permeability and escape of exudate into the interstitium
(hallmark of acute inflammation)
↓
Stasis
↓
Leucocytic margination or peripheral orientation of WBCs along the endothelial surface
(neutrophils stick to the endothelium and migrate through vascular wall into the interstitial tissue. RBCs are smaller, move faster and are oriented centrally)

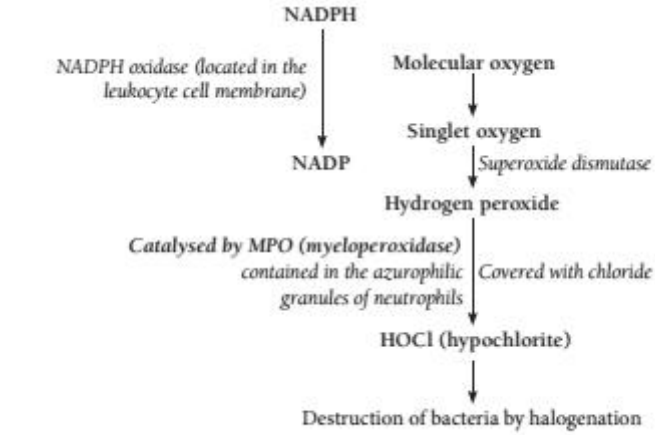
FLOWCHART 2.1. Vascular events in acute inflammation.

Normal axial flow
(RBCs confined to a central column with WBCs oriented peripherally as the latter are heavier)
↓ *Inflammation leading to stasis*
Margination and pavementing of WBCs
↓
Adhesion
↓
Emigration and diapedesis

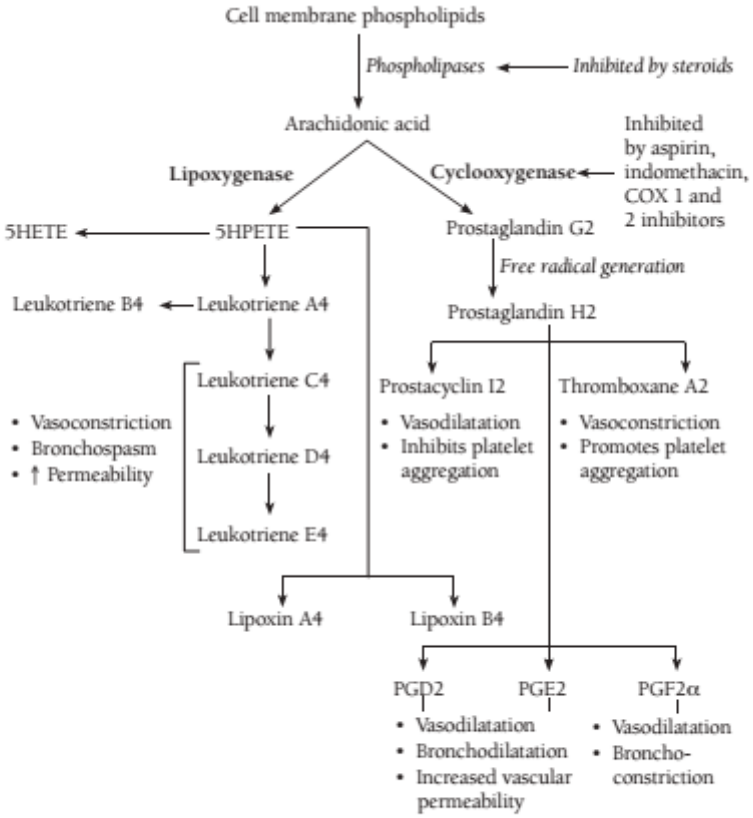
FLOWCHART 2.2. Sequence of cellular events in acute inflammation.

Binding of chemoattractants to **specific transmembrane G protein–coupled receptors (GPCRs) on the surface of leukocytes**
↓
Recruitment of G protein due to signals from GPCRs
↓
Activation of **phospholipase C (PLC), phosphoinositol 3 kinase (PI3K) and protein tyrosine kinases (effector molecules)**
↓
PLC + PI3K act on **membrane phospholipids**
↓
Generation of **lipid second messengers**
↓
↑ Cytosolic calcium
↓
Activation of **GTPases and numerous kinases**
↓
Polymerization of actin
↓
Locomotion

FLOWCHART 2.3. Mechanism of chemotaxis.

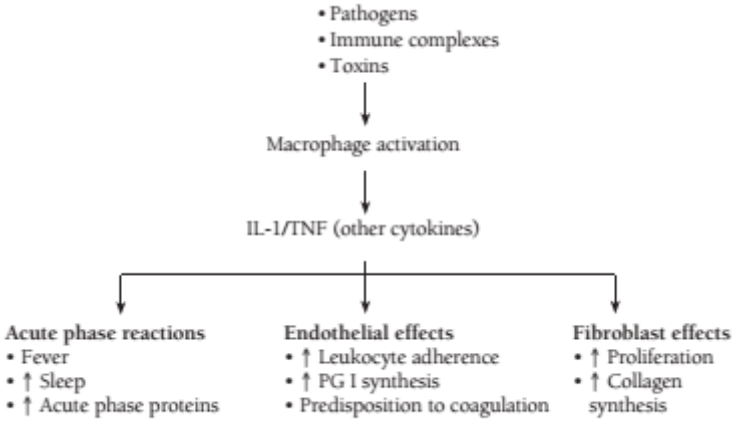


FLOWCHART 2.4. Mechanism of killing by MPO–H_2O_2–halide system.

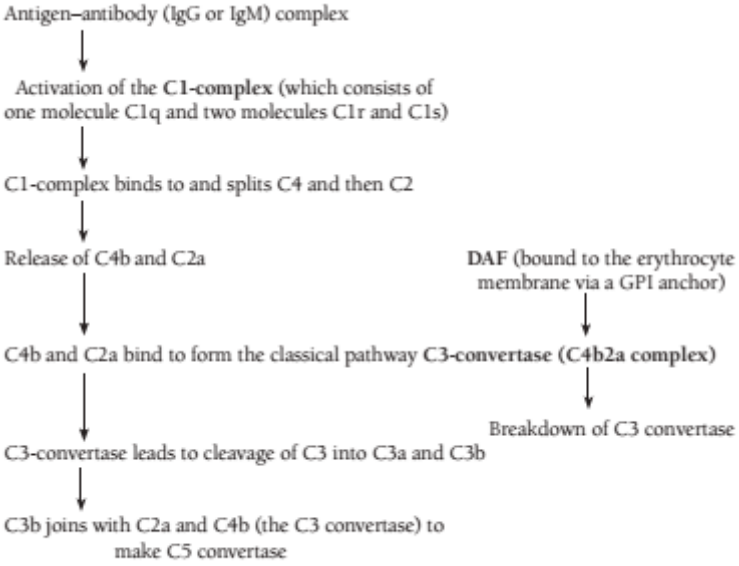


HETE – Hydroxyeicosatetraenoic acid
HPETE – Hydroperoxyeicosatetraenoic acid

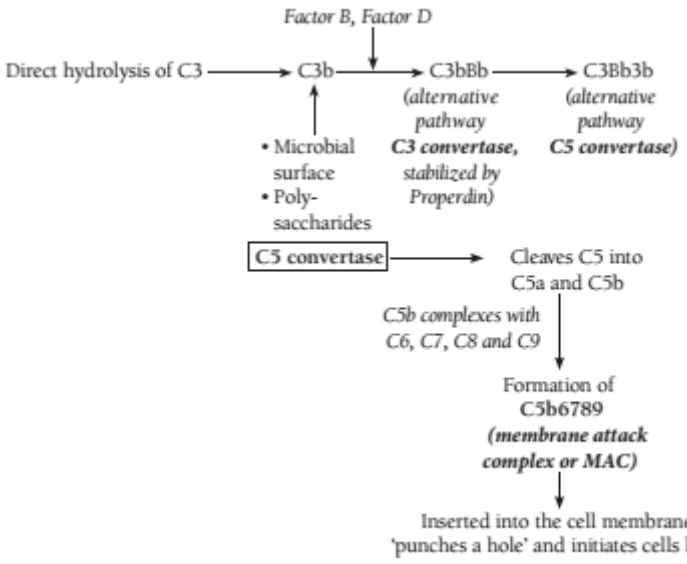
FLOWCHART 2.5. Generation of arachidonic acid metabolites and their role in inflammation.



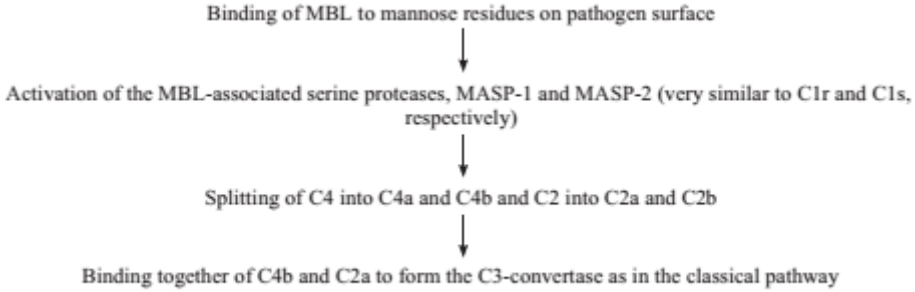
FLOWCHART 2.6. Major effects of IL-1 and TNF in inflammation.



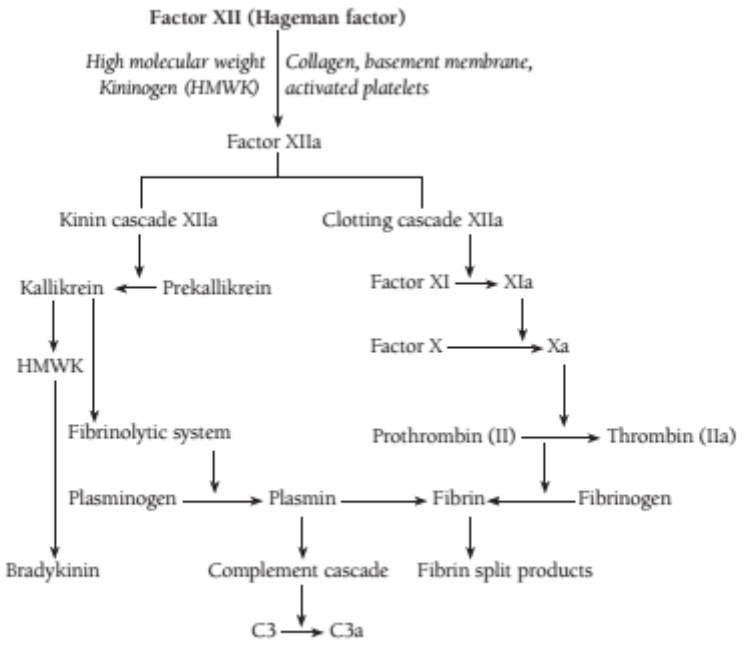
FLOWCHART 2.7. Classical pathway of complement activation.



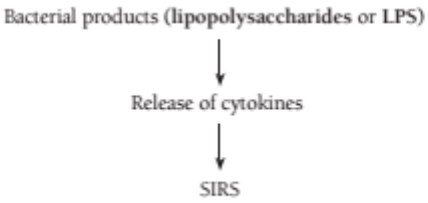
FLOWCHART 2.8. Alternative pathway of complement activation.



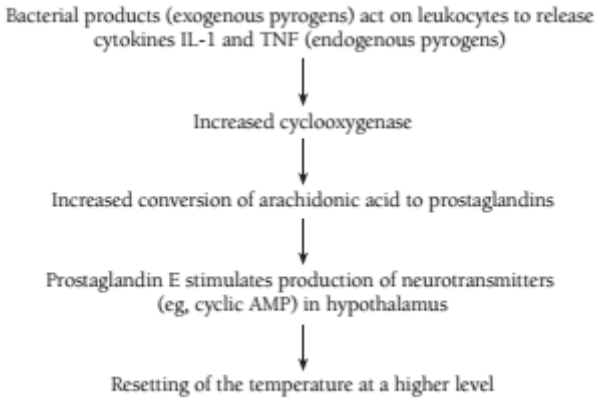
FLOWCHART 2.9. Complement activation by MBL–MASP pathway.



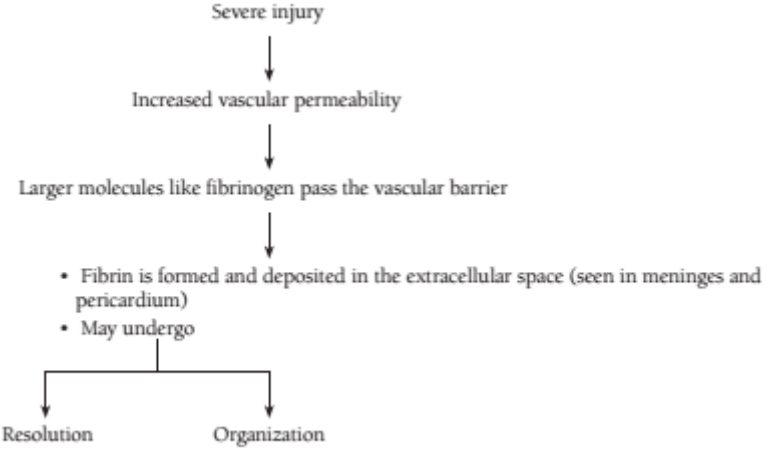
FLOWCHART 2.10. Interrelationship of four plasma-derived systems (Hageman factor XII of the clotting system plays a key role in the interaction of these systems).



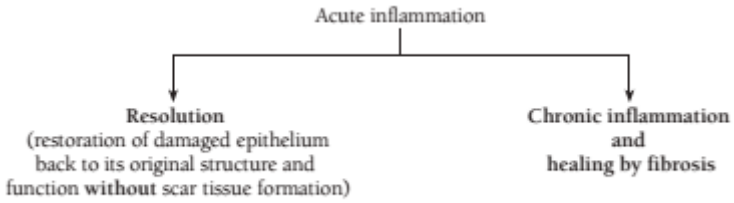
FLOWCHART 2.11. Systemic inflammatory response syndrome.



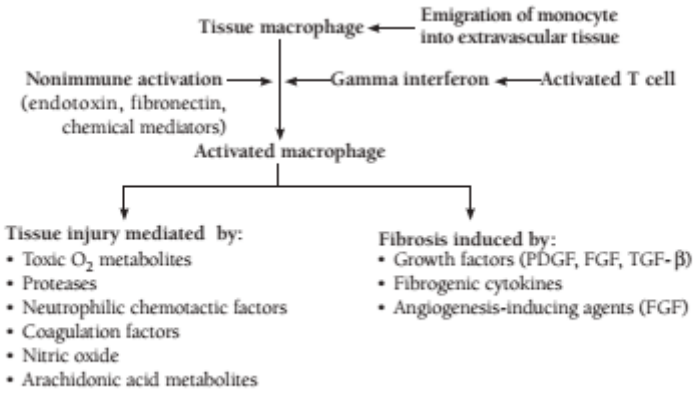
FLOWCHART 2.12. Mechanism of development of fever in SIRS.



FLOWCHART 2.13. Pathogenesis and outcomes of fibrinous inflammation.



FLOWCHART 2.14. Outcomes of acute inflammation.



FLOWCHART 2.15. Interactions of macrophages with lymphocytes in chronic inflammation.

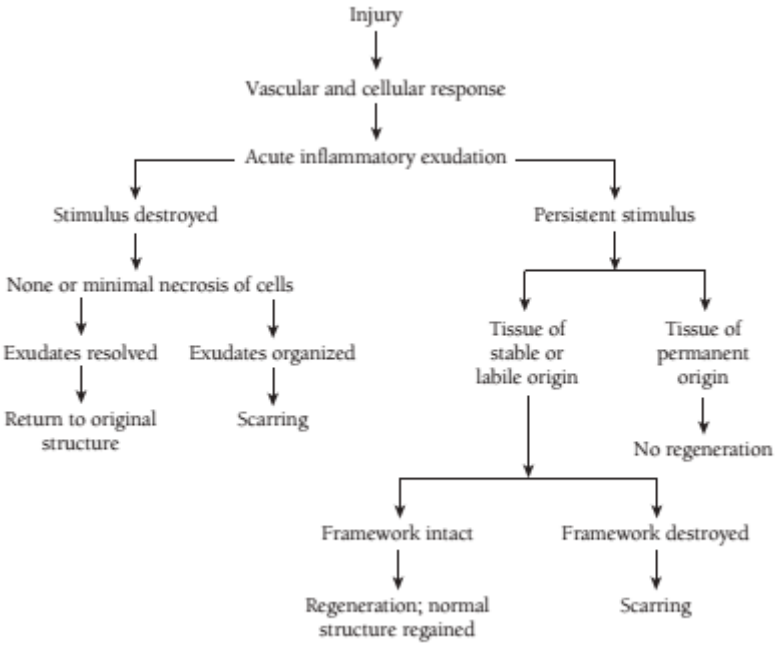
TISSUE REPAIR

IMPORTANT DIFFERENCES

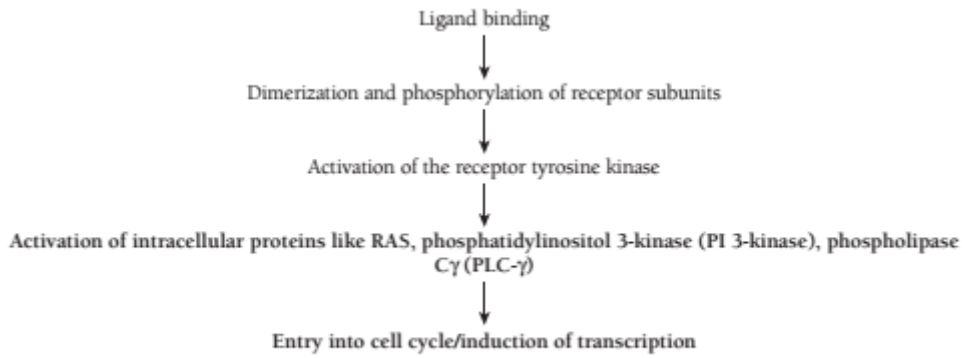
TABLE 3.2. Differences between healing by primary and secondary intention

Features	Healing by primary intention	Healing by secondary intention
Nature of wound	Seen in incised wounds with well opposed edges (clean and uninfected wound)	Seen in large, open, infected wounds with separated edges; associated with extensive loss of cells
Amount of fibrin and blood	Filled with moderate amount of fibrin and blood	Filled with a large blood clot and necrotic debris and exudate
Inflammatory reaction	Less intense	More intense
Amount of granulation tissue	Less granulation tissue	Extensive granulation tissue
Wound contraction	Wound contraction is not seen	Wound contraction is seen
Complications	Less common	More common

IMPORTANT FLOWCHARTS



FLOWCHART 3.1. Pathways of reparative response following injury.



FLOWCHART 3.2. Signal transduction mediated by receptors with intrinsic tyrosine kinase activity.

Signalling initiated by ligand binding and conformational change in receptors

↓

Receptors associate with intracellular G proteins that contain GDP

↓

Exchange of GTP with GDP resulting in activation of the proteins

↓

Activation of cyclic AMP and inositol 1,4,5 triphosphate, which releases calcium from endoplasmic reticulum

FLOWCHART 3.3. Signal transduction mediated by seven transmembrane G protein–coupled receptors.

Activation of receptors on endothelial cells in pre-existing vessels by angiogenic growth factors

↓

Release of endothelial proteases that degrade the basement membrane to allow endothelial cells to escape from the original (parent) vessel wall into the surrounding matrix

↓

Migration of endothelial cells towards area of angiogenic stimulus

↓

Proliferation of endothelial cells behind the migrating cells

↓

Remodelling of endothelial cells into capillary tubes

↓

Recruitment of pericytes and smooth muscle cells to form mature vessels

FLOWCHART 3.4. Steps in angiogenesis.

Wound

↓

- Filled with blood clot and inflammatory cells
- Neutrophils appear at the margin of the wound

} Day 1

↓

- Neutrophils largely replaced by macrophages
- Granulation tissue formation begins and infiltrates the incision space
- Collagen fibres form at the margins of the incision and are laid down vertically
- Thickening of the epithelial layer due to epithelial cell proliferation and migration of epithelial cells along incised margins

} Day 3

↓

- Incisional space is filled with granulation tissue
- Neovascularization is at its peak
- Collagen fibres become abundant and bridge the incisional gap
- Epidermis regains its normal thickness
- Differentiation of surface cells yields mature epidermal architecture

} Day 5

↓

- Continued accumulation of collagen and proliferation of fibroblasts
- Regression of vessels and blanching

} Day 7

↓

- Scar tissue formation by the end of the first month
- Gradual gain in tensile strength overtime

FLOWCHART 3.5. Steps in healing by primary intention.

HEMODYNAMICS

IMPORTANT DIFFERENCES

TABLE 4.1. Differences between exudate and transudate

Features	Exudate	Transudate
Definition	Oedema associated with increased vascular permeability	Filtrate of blood or plasma; no increase in vascular permeability observed
Nature	Inflammatory oedema	Noninflammatory oedema
Protein content	1. High (more than 4 g/dl) 2. Has high fibrinogen and tendency to coagulate	1. Low (less than 3 g/dl) 2. Mainly albumin, low fibrinogen
Specific gravity	High (more than 1.018)	Low (less than 1.015)
pH	>7.3	<7.3
LDH	High Fluid LDH/serum LDH ratio is >0.6	Low Fluid LDH/serum LDH ratio is <0.6
Cells	Highly cellular; rich in polymorphs	Few, mainly mesothelial cells
Example	Pus seen in pyogenic infections	Fluid in congestive cardiac failure

TABLE 4.2. Contrasting features of cardiac and renal oedema

Features	Cardiac oedema	Renal oedema
Causes	CHF and right-sided heart failure	Nephritic and nephrotic syndrome/acute tubular injury/necrosis
Mechanism	Decreased cardiac output	Hypoalbuminemia and decreased plasma oncotic pressure
Clinical	• Dependent oedema, the distribution of which changes with posture • Mainly pedal or sacral; later generalized	First observed around face, eyes, ankle and genitalia
Serum albumin	Normal	Decreased
Proteinuria	Absent	Present

TABLE 4.3. Differences between hyperaemia and congestion

Features	Hyperaemia	Congestion
Definition	Characterized by increased blood flow due to *arteriolar dilatation*	Characterized by blood pooling due to impaired outflow/drainage from tissue
Nature of process	Active	Passive
Appearance	Red	Bluish-red/cyanosed
Type of blood	Oxygenated	Deoxygenated; tissue hypoxia present
Oedema	Absent	Present
Examples	Menopausal flush, muscular exercise, high-grade fever, etc.	Local: portal venous obstruction in cirrhosis of liver; systemic: right-sided heart failure

TABLE 4.4. Coagulation factors

I	Fibrinogen
II	Prothrombin
V	Proaccelerin
VII	Proconvertin
VIII	Anti-haemophilic factor
IX	Christmas factor
X	Stuart-Prower factor
XI	Plasma Thromboplastin antecedent
XII	Hageman factor
XIII	Fibrin stabilizing factor

Prekallikrein: Fletcher factor
HMW kininogen: Fitzgerald factor

TABLE 4.5. Differences between arterial and venous thrombi

Features	Arterial thrombi	Venous thrombi
Sites	Common in coronary, cerebral, iliac and femoral arteries (vessels with active blood flow)	Superficial varicose veins and deep veins of leg, eg, femoral and iliac veins (vessels with less active blood flow)
Pathogenesis	Due to endothelial injury (as in atherosclerosis or turbulent blood flow)	Due to venous stasis
Progression	Grows in a retrograde direction from point of attachment	Extends in the direction of blood flow
Occlusion	Do not occlude lumen completely	Invariably occlusive
Gross	Grey-white, friable, prominent lines of Zahn	Dark red with fibrin strands; lines of Zahn less prominent or absent
Microscopy	Lines of Zahn show paler layers of fibrin and platelets alternating with darker layers of RBCs	Constituted by more of RBCs and less of fibrin
Complications	Ischaemia/infarction of vital organs	Embolism, oedema, ulceration

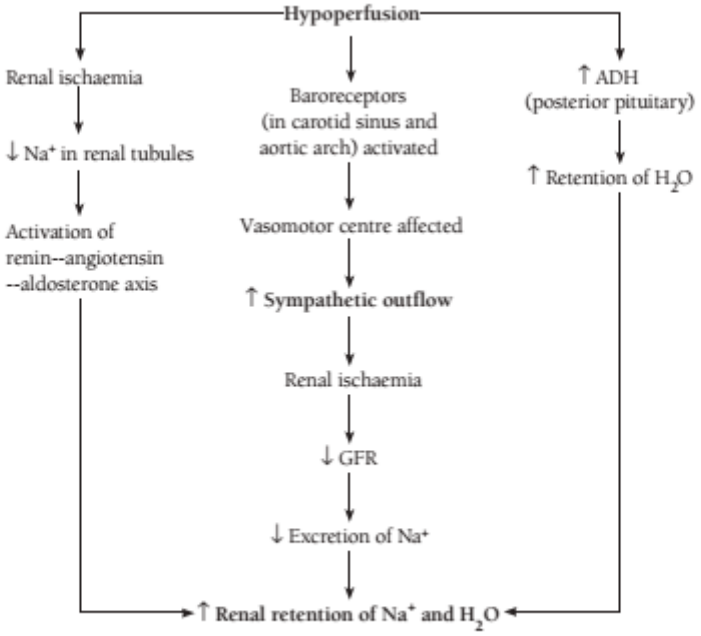
TABLE 4.6. Differences between antemortem and post-mortem clot

Features	Antemortem clots/thrombi	Post-mortem clots
Origin	Formed as part of normal haemostasis or pathological derangement of clotting pathway in a living person	Form in a dead person due to sedimentation and settling down of blood components
Gross	• Dry, granular, firm and friable • **Lines of Zahn** are prominent in arterial thrombi	• Gelatinous, soft and rubbery • Dark red, dependent portion of the clot is called **currant jelly** and yellow supernatant, free of red cells is called **chicken fat**
Shape	Do not form a cast of the vessel	Take the shape of the vessel or its bifurcation forms a cast of the vessel
Attachment to vessel wall	Present; strong	Very weak
Location	Anywhere in the body	In dependent parts of the body

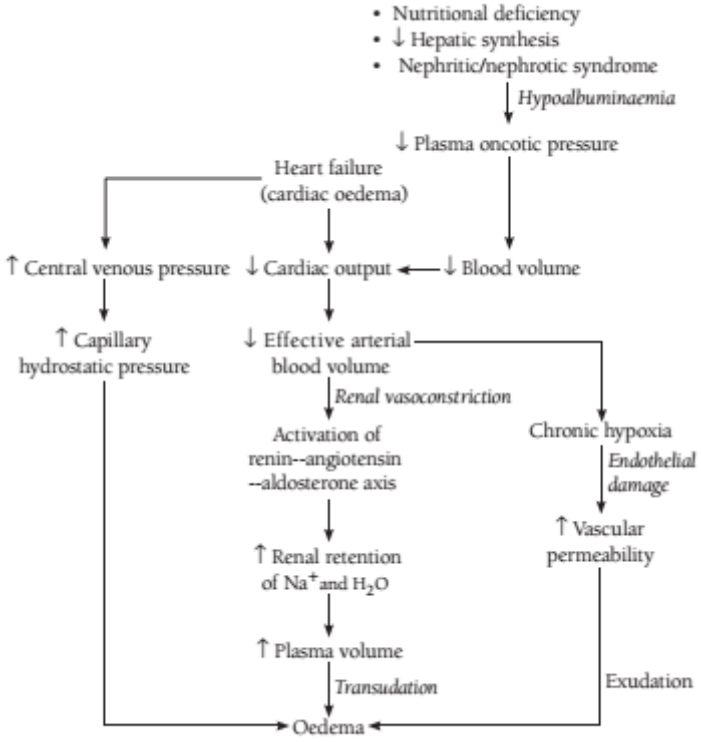
TABLE 4.7. Differences between red/haemorrhagic and white/pale/anaemic infarcts

Features	Red infarct	White infarct
Organs involved	Spongy organs like lung and gastrointestinal tract	Solid organs, like heart, spleen and kidney
Cause	*Venous occlusion* Seen • In loose tissues that allow collection of blood or tissues with dual blood supply (lungs, GIT). Haemorrhage seeps into such an infarct when flow is re-established. • In tissues that were previously congested due to sluggish venous outflow • When blood flow is re-established in a site with previous arterial occlusion, eg, after coronary angioplasty	*Arterial obstruction* Seen in solid organs where the solidity of the tissue prevents haemorrhage that can seep through from adjoining capillaries and tissues with end arterial circulation
Morphology	Congested and red due to haemorrhage; turns brown and firm with time but never appears pale. Hemosiderin-laden macrophages are present in large numbers.	Becomes progressively pale
Margins	Not sharply defined	Sharply defined
Oedema	Present	Absent

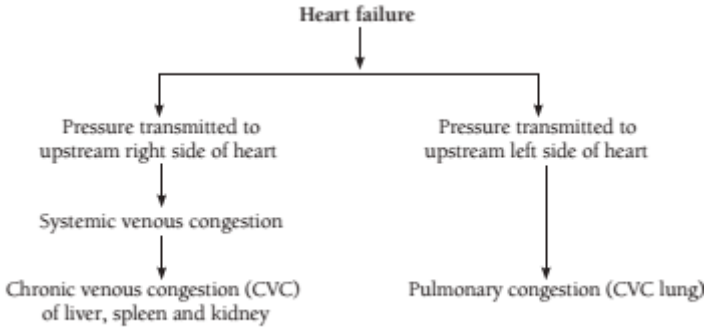
IMPORTANT FLOWCHARTS



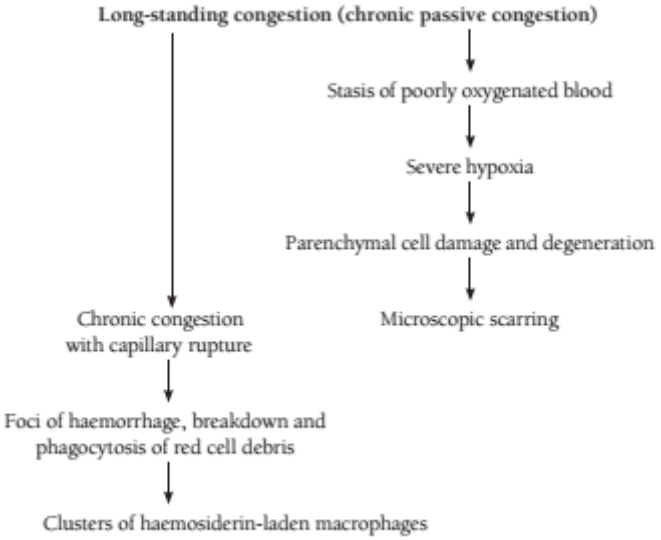
FLOWCHART 4.1. Normal regulatory mechanisms responsible for maintaining sodium and water balance.



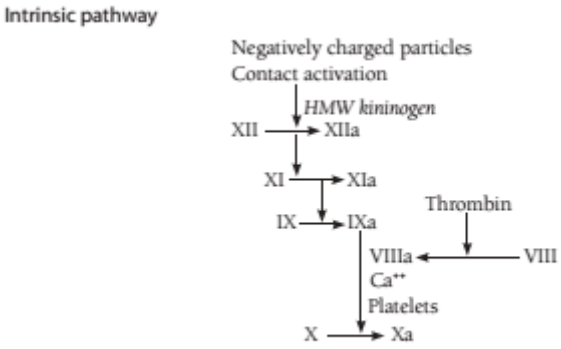
FLOWCHART 4.2. Pathogenesis of oedema.



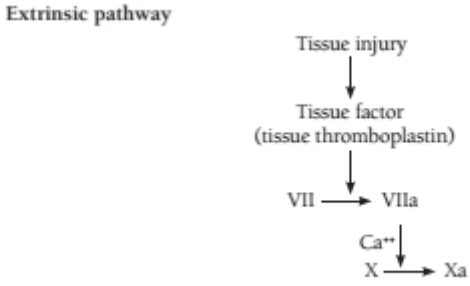
FLOWCHART 4.3A. Pathogenesis of chronic venous congestion.



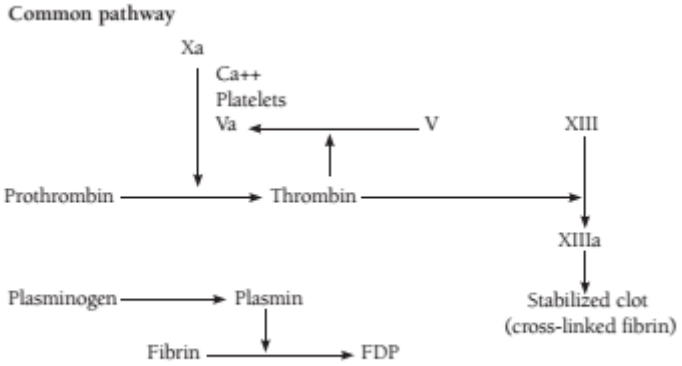
FLOWCHART 4.3B. Outcomes of chronic congestion.



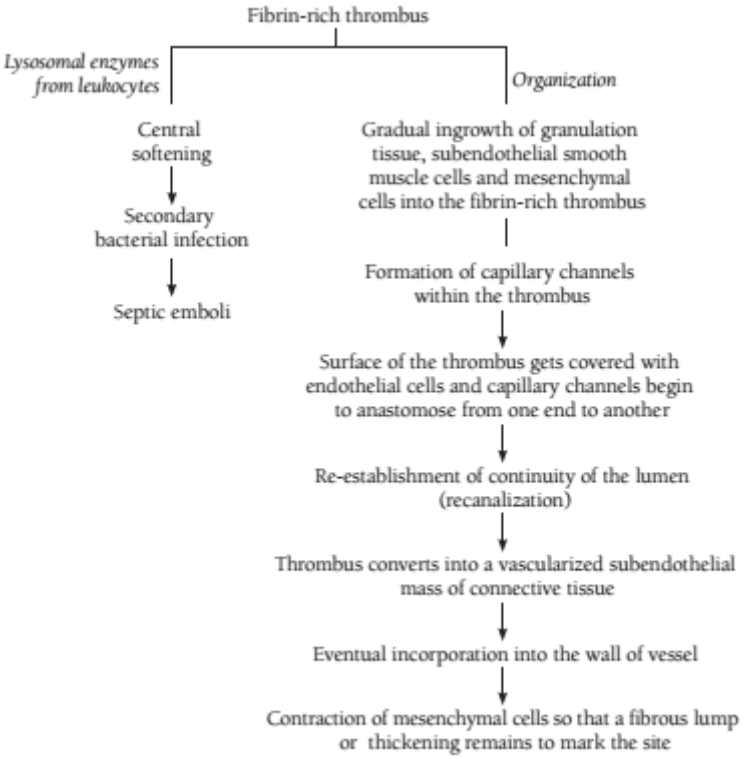
FLOWCHART 4.4. Intrinsic pathway of coagulation.



FLOWCHART 4.5. Extrinsic pathways of coagulation.

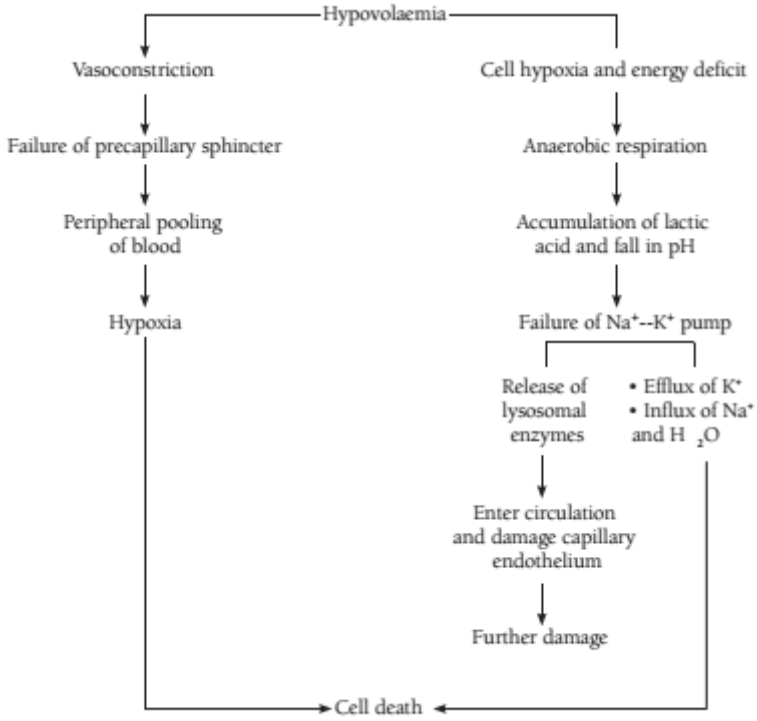


FLOWCHART 4.6. Common pathways of coagulation.

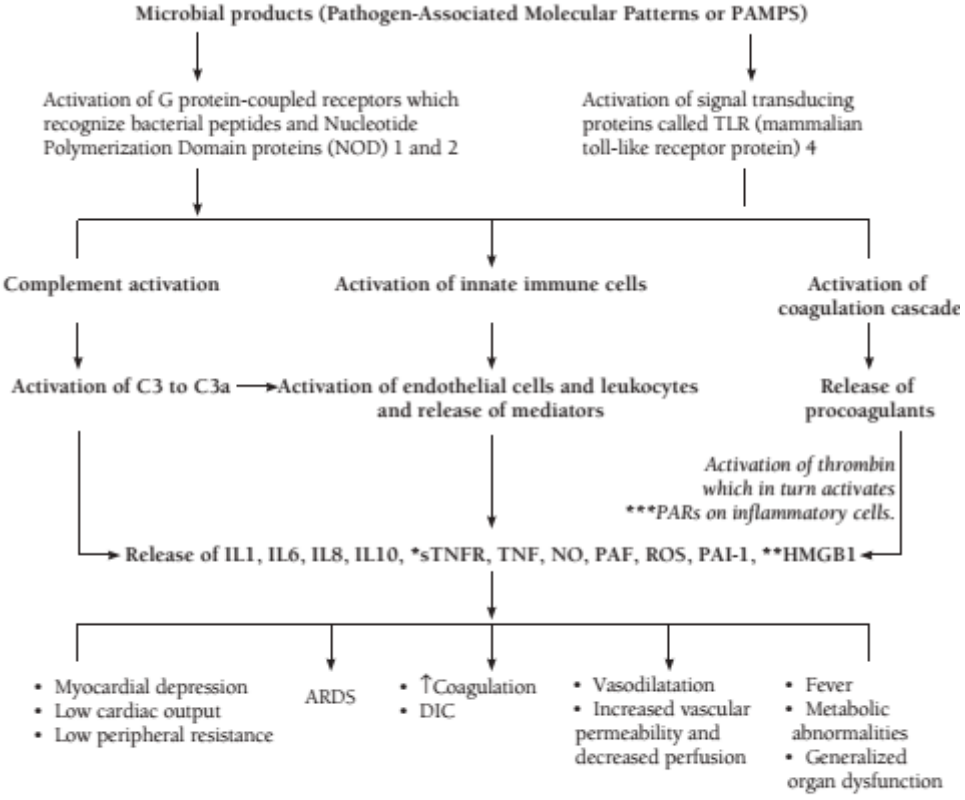


FLOWCHART 4.7. Sequence of events in evolution of a thrombus.

FLOWCHART 4.8. Biochemical basis of cellular injury in fat embolism.



FLOWCHART 4.9. Pathogenesis of hypovolaemic shock.



*sTNFR—Soluble TNF receptor
**HMGB1—High mobility group box 1 protein
***PARs—Protease-activated receptors

FLOWCHART 4.10. Pathogenesis of septic shock.

IMMUNOLOGY

IMPORTANT DIFFERENCES

TABLE 5.1. Differences between T lymphocytes and B lymphocytes

Features	T cell	B cell
Origin	Stem cells in bone marrow → thymus	Stem cells in bone marrow → secondary lymphoid organs
Life span	• Blasts: several days • Small T cells: months to years	• Blasts: several days • Small B cells: <1 month
Location		
(i) Lymph node	Para/deep cortex	Germinal centre, superficial cortex
(ii) Spleen	Periarteriolar sheath	Germinal centre, red pulp
(iii) Peyer's patches	Perifollicular zone	Follicular centre
Percentage population in		
(i) Blood	80%	20%
(ii) Bone marrow	Rare	Numerous
(iii) Lymph node	85%	15%
Surface markers		
(i) TCR Ag receptor	Present	Absent
(ii) Surface Ig	Absent	Present
(iii) Fc receptor	Absent	Present
(iv) Complement receptor	Absent	Present
(v) CD markers	• T (helper): CD4,3,7,2 • T (suppressor): CD8,3,7,2	CD19,21,23
Functions	(i) CMI via cytotoxic T cells (ii) Delayed hypersensitivity via CD4+ T cells	(i) Precursors of plasma cells (ii) Contribute to humoral immunity by synthesizing specific antibodies (Igs)

TABLE 5.3. Differences between MHC class I and class II

Features	MHC I	MHC II
Location	Present on all nucleated cells and platelets	Found on antigen-presenting cells–macrophages, dendritic cells and activated T and B cells
Constituted by	Alpha chains (α1, α2, α3) and β2 microglobulin	Alpha chains (α1, α2) and beta chains (β1, β2)
Genes coding region	HLA-A, HLA-B, HLA-C	HLA-D (DP, DQ, DR)
Antigen presentation in association with	CD8+ T cells	CD4+ T cells
Functions	Graft rejection, lysis of virus-infected cells and tumour cells	Graft-versus-host response and immunologic reactions involving CD4+ T cells

TABLE 5.4. Subsets of helper T cells

Features	T_H 1 cells	T_H 2 cells	T_H 17 cells
Cytokines that induce this subset	IFN-γ and IL-12	IL-4	TGF-β, IL-6, IL-1 and IL-23
Cytokines produced by this subset	IFN-γ	IL-4, 5 and 13	IL-17 and IL-22
Function	Responsible for delayed hypersensitivity, macrophage activation and synthesis of IgG; they provide defence against intracellular microbes.	Responsible for synthesis of other classes of antibodies including IgE; they provide defence against helminthic parasites.	Release IL17, which is a powerful recruiter of neutrophils and monocytes and is important in defence against extracellular bacteria and fungi.
Role in disease	Autoimmune and chronic inflammatory diseases	Allergies	Autoimmune and chronic inflammatory diseases

TABLE 5.5. Differences between helper and suppressor T cells

Features	Helper/inducer T cells	Suppressor/cytotoxic T lymphocytes
Type	• CD4-positive • CD8-negative	• CD8-positive • CD4-negative
Percentage of peripheral T cells	60%	30%
Antigen recognition in association with	HLA class II	HLA class I
Functions	Release lymphokines and activate macrophages and B cells, responsible for delayed hypersensitivity	Cytotoxicity mediated by pore formation and release of granzymes. Also Fas/FasL-dependent killing
Subsets	Two subsets, TH1 and TH2	No subsets

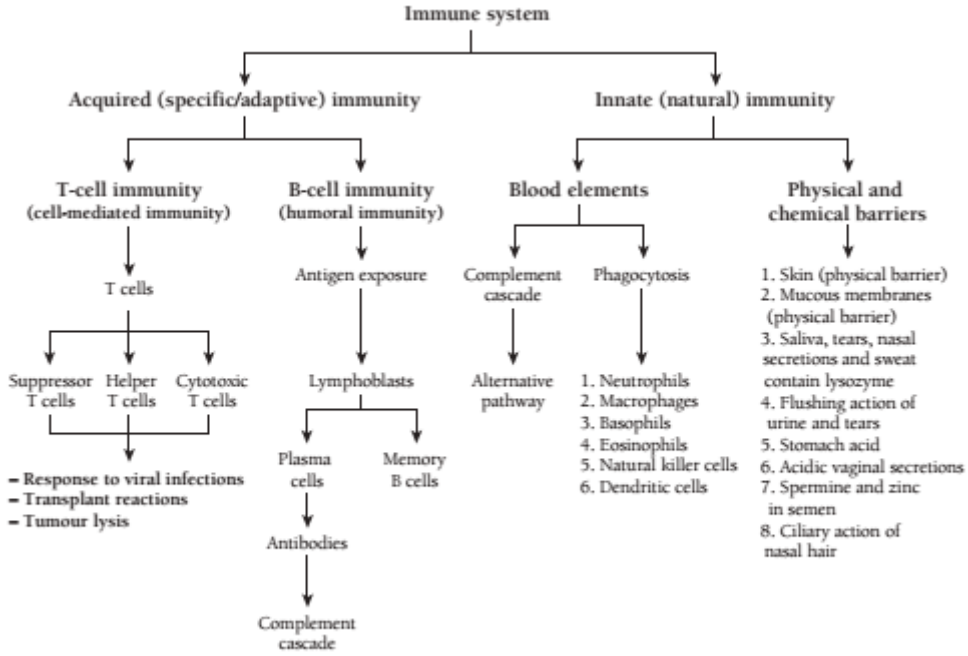
TABLE 5.6. Differences between types I, II, III and IV hypersensitivity

Features	Type I	Type II	Type III	Type IV
Reaction type	Anaphylactic	Cytotoxic	• Serum sickness • Arthus reaction	Delayed hypersensitivity
Cells involved	Mast cells, basophils, eosinophils, neutrophils, monocytes, CD4+ T cells, B cells	Nonsensitized macrophages, NK cells, neutrophils, eosinophils, B cells	Neutrophils, B cells	CD4+ T cells, macrophages, CD8+ T cells
Antibody type	IgE	IgG, IgM	IgG, IgM	None
Chemical mediators	IL-3, 4, 5; vasoactive amines	Complement system	Complement system	Lymphokines, IL-12, IL-2, INF-γ, TGF-β, TNF-α
Antigen presentation by APC	Required	Not required	Required	Required
Pre-sensitization	Required	Not required	Required	Required
Pathogenesis	Formation of IgE and immediate release of mediators to recruit inflammatory cells inducing inflammatory changes	Opsonization and phagocytosis, ADCC, antireceptor antibody type	Formation and deposition of Ag–Ab complexes → activates complement system → neutrophils recruited → release of lysosomal enzymes and other toxic agents	• Sensitized T- lymphocytes mediate release of lymphokines • T cell-mediated cytolysis
Time for onset	Minutes	Hours to days	Hours to days	Hours to days
Examples	Allergic bronchial asthma	Transfusion haemolytic reactions	Glomerulonephritis, rheumatoid arthritis	Transplant rejection

TABLE 5.7. Differences between central and peripheral tolerance

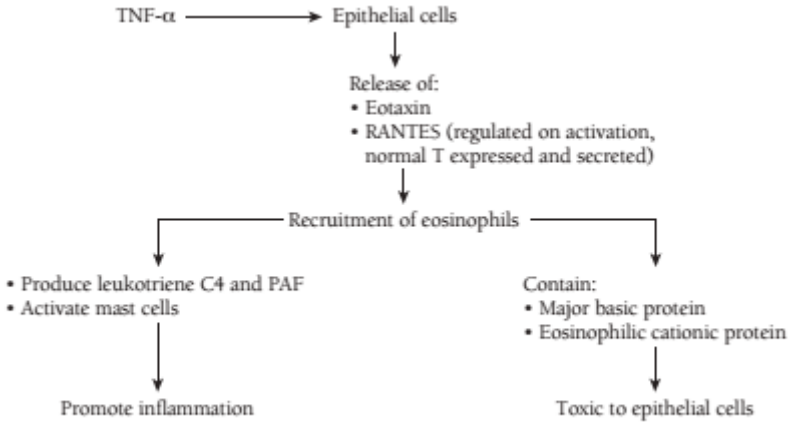
Features	Central tolerance	Peripheral tolerance
Origin	Thymus/bone marrow	Peripheral tissue
Mechanism	Clonal deletion of self-T/B cells	Clonal deletion, clonal anergy, peripheral suppression by T cells
Role in autoimmune diseases	Failure may not result in autoimmune diseases	Failure usually results in autoimmune diseases

IMPORTANT FLOWCHARTS

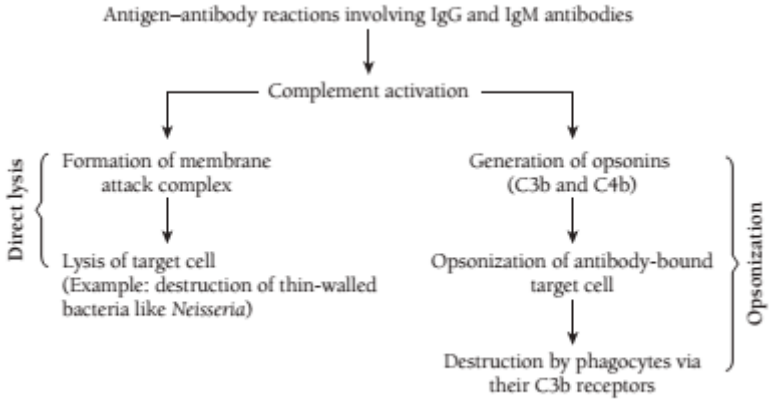


FLOWCHART 5.1. Types of immune responses.

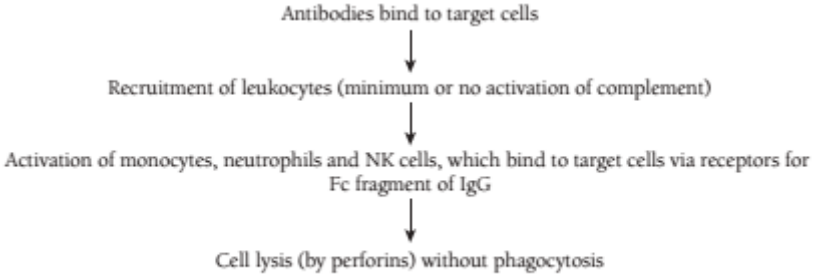
FLOWCHART 5.2. Mechanism underlying type I hypersensitivity.



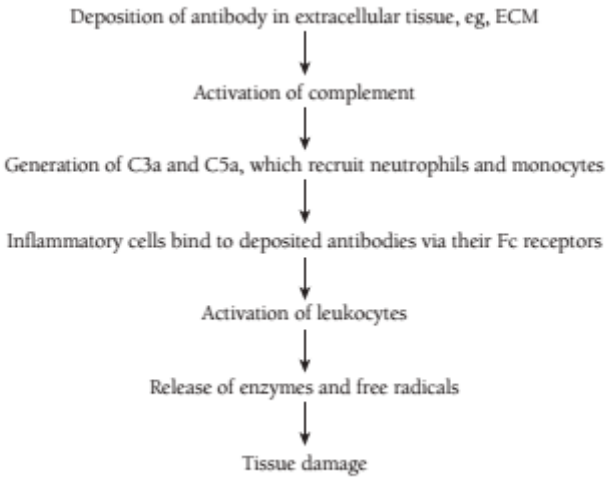
FLOWCHART 5.3. Role of eosinophils in type I hypersensitivity.



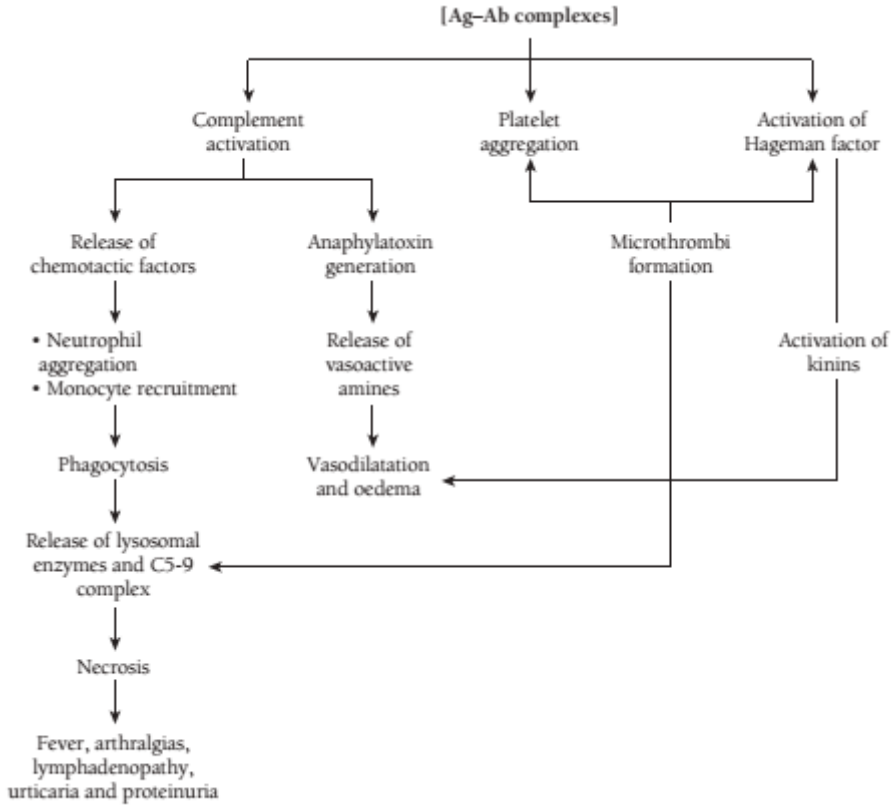
FLOWCHART 5.4. Steps in opsonization and phagocytosis.



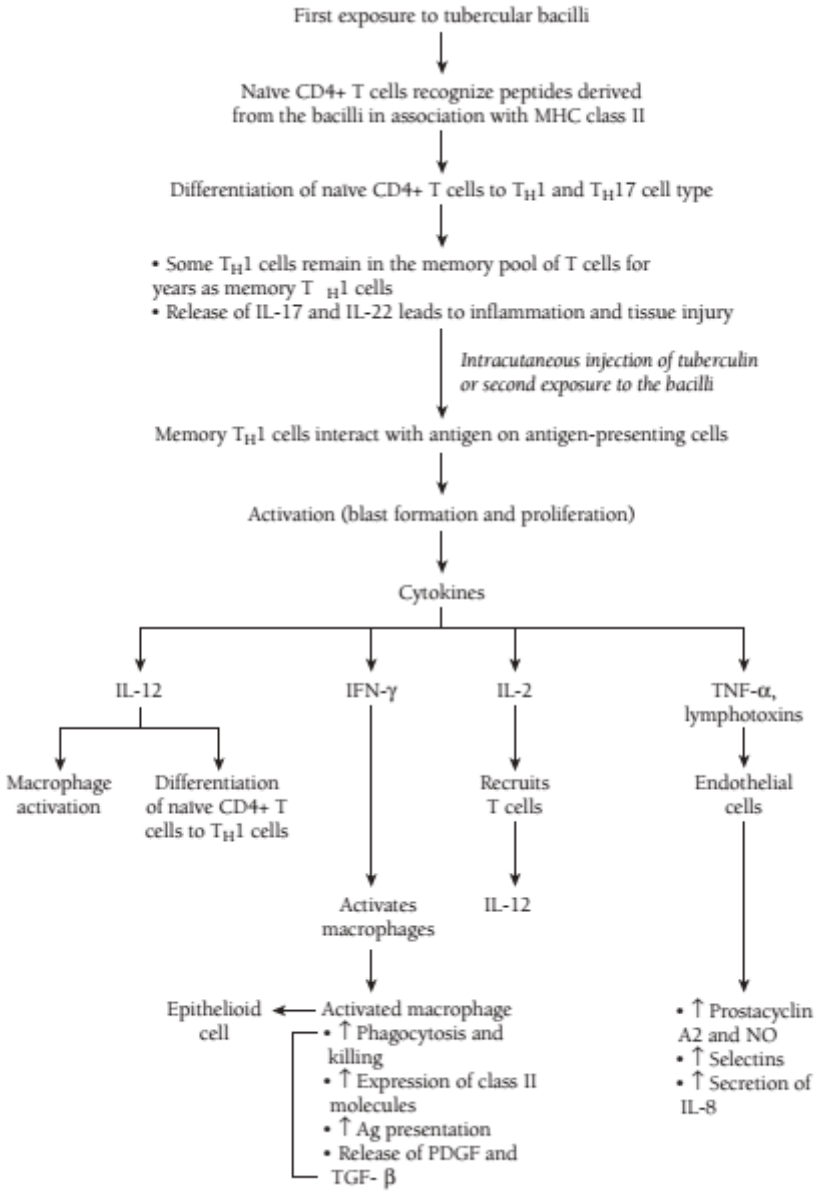
FLOWCHART 5.5. ADCC.



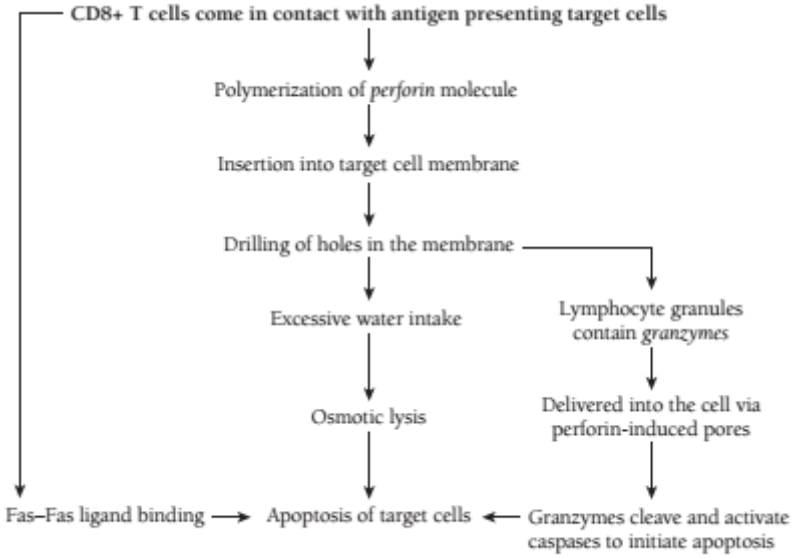
FLOWCHART 5.6. Complement and Fc receptor-mediated inflammation.



FLOWCHART 5.7. Mechanism of immune complex-mediated tissue injury.



FLOWCHART 5.8. Sequence of events in development of DTH.



FLOWCHART 5.9. T cell-mediated cytotoxicity/cytolysis.

NEOPLASIA

IMPORTANT DIFFERENCES

TABLE 6.1. Differences between a hamartoma and a neoplasm

Features	Hamartoma	Neoplasm
Definition	Disorganized focal overgrowth of mature tissue indigenous to a particular site	Abnormal, excessive, unregulated, autonomous proliferation of cells
Behaviour	Always benign	May be benign or malignant
Degree of differentiation	Well-differentiated cells, which completely resemble normal counterparts	Vary from well-differentiated to poorly differentiated anaplastic lesions
Clonality	Polyclonal	Monoclonal
Examples	Vascular hamartoma	Squamous cell carcinoma

TABLE 6.2. Differences between dysplasia and anaplasia

Features	Dysplasia	Anaplasia
Definition	Lack of uniformity of individual cells with architectural distortion	Lack of morphological and functional differentiation of cells
Behaviour	A potentially precancerous condition, which may or may not progress to cancer	Anaplasia is usually a hallmark of malignant transformation
Tissue involved	Mainly epithelium	Both epithelium and mesenchyme
Cellular pleomorphism and nuclear atypia	Present, but usually low grade	High grade
Mitotic figures	Present, usually not atypical	Abnormal and atypical figures may be seen (tripolar, quadripolar and multipolar spindles)
Tumour giant cells	Absent	Present

TABLE 6.4. Contrasting features of benign and malignant tumours

Features	Benign	Malignant
Gross features		
Boundaries	Encapsulated/well circumscribed	Ill circumscribed/unencapsulated
Size	Usually small	Usually large
Secondary changes	Less frequent	More frequent
Surrounding tissue	Compressed	Invaded
Microscopic features		
Pattern	Resembles tissue of origin	Poor resemblance to tissue of origin
Polarity	Retained	Lost
Anaplasia	Absent	Present
Mitoses	Present, few, typical	Present, many, atypical as well as typical
Tumour giant cells	Rare, without atypia	Common, with atypia
Cytogenetic changes	Rare	Common
Physiology of cells/function	Maintained	Lost
Growth rate	Low	High
Local invasion	Rare	Common
Metastasis	Absent	Present

TABLE 6.6. Differences between anti-oncogenes and proto-oncogenes

Features	Anti-oncogenes	Proto-oncogenes
Other name	Tumour suppressor genes	Precursor genes for oncogene
Function	They suppress cell proliferation, and promote differentiation and maturation of cells	They promote normal cell growth and differentiation
Inheritance	Recessive. Homozygous inactivation, ie, loss of both normal copies of gene is required for carcinogenesis	Dominant. Mutation in a single copy may lead to oncogenic conversion
Action	Act passively, ie, cancer-promoting genes dominate and lead to tumour formation due to loss of normal function of anti-oncogenes	Act actively, ie, gene products of oncogenes directly lead to tumour formation
Examples	*P53*, *RB* gene, *BRCA*-1 and 2, *TGF*-β, *APC*, *WT-1* and *NF*	*myc*, *N-myc*, *erb*B1/2/3

TABLE 6.7. Contrasting features of initiators and promoters

Features	Initiators	Promoters
Sequence of application	Applied first	Applied after initiator
Mechanism	Induction of mutation	Not mutagenic; instead are mitogenic Induce cell cycling and reinforce the action of initiators rather than inducing a mutation
Dose	Single for a short time	Repeated over a long time
Response	Sudden	Delayed
Molecular change	Initiation causes irreversible changes and has memory	Promoters induce reversible changes
Examples	Most chemical carcinogens, radiation	Hormones, phorbol esters

TABLE 6.8. Differences between DNA and RNA oncogenic viruses

Features	DNA oncogenic virus	RNA oncogenic virus
Viruses	HPV, EBV, HBV, KSHV	HTLV-1
Genome	Double-stranded DNA	Single-stranded RNA
Reverse transcriptase	Absent	Present
Interaction with host genome	Linear DNA genome forms a double-stranded circle within infected cell and then covalently integrates into the host genome	First RNA is transcribed into DNA, which then integrates into host genome
Name of gene	*Early region A* gene	*src* gene
Name of protein	T antigen	*src* protein
Function of protein	Protein kinase, ATPase activity, binding to DNA and stimulation of DNA	Protein kinase that phosphorylates tyrosine and disturbs the growth control process
Location of protein	Primarily nuclear, but sometimes in plasma membrane	Plasma membrane

TABLE 6.11. Role of tumour markers in neoplasia

Tumour marker	Associated neoplasm
AFP (α-fetoprotein)	Hepatocellular carcinoma, nonseminomatous-germ-cell tumours
PSA (prostate-specific antigen)	Prostatic carcinoma
HCG (human chorionic gonadotropin)	Trophoblastic tumours
Calcitonin	Medullary carcinoma of thyroid
Vanillylmandelic acid (VMA)	Pheochromocytoma
CA-125	Carcinoma of ovary
CEA (carcinoembryonic antigen)	Cancer of bowel, pancreas and breast
CA-15.3	Carcinoma of breast

IMPORTANT FLOWCHARTS

Dysplasia

↓

Carcinoma in situ

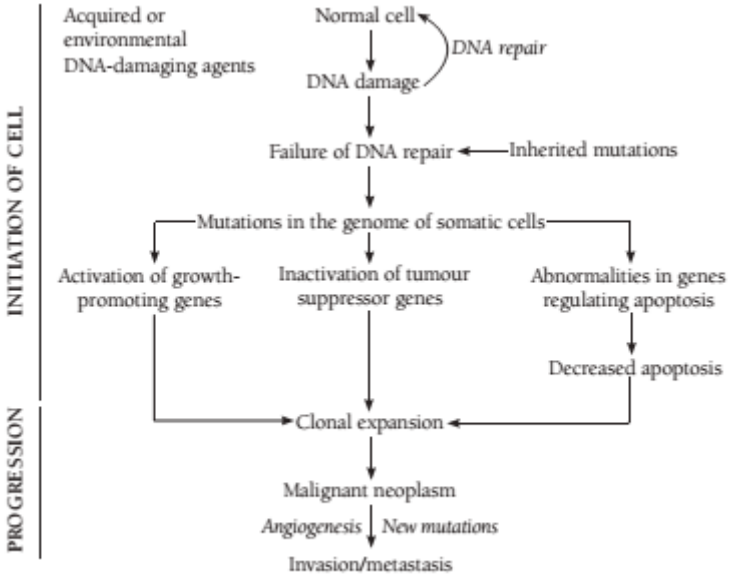
(Dysplasia involving the entire thickness of the epithelium)

↓

Invasive carcinoma

(Frank invasion into the stroma by malignant cells)

FLOWCHART 6.1. Steps in the progression of dysplasia to invasive carcinoma.



FLOWCHART 6.2. Steps involved in carcinogenesis.

External signals (growth factors, integrins)

↓

Activation of MYC, RAS and other genes

↓

Synthesis of cyclin D

↓

Cyclin D + CDK4 form an active complex

↓ *P16, INK4, P21*

RB phosphorylation in E2F/DP1/RB complex

(in its hypophosphorylated form, RB binds to and sequesters a transcription activator called E2F; RB is removed from E2F by phosphorylation and free E2F is made available)

↓

Free E2F

↓

Cyclin E transcription

↓

Cyclin E

↓

Cyclin E/CDK 2 (active complex)

↓ *P27*

G1 → S

Note: The cell cycle is blocked by P21, P27, P16 and INK4.

FLOWCHART 6.3. Role of cyclins, CDKs and CDK inhibitors in regulating G1/S cell cycle transition.

Receptors for growth factors undergo mutations or are overexpressed
↓
Mutant receptor proteins deliver continuous signals
↓
Continuous activation of signal-transducing proteins on the inner leaflet of plasma membrane
↓
Signal transduced from cytosol to nucleus via second messengers
↓
Activation of nuclear regulatory factors
↓
DNA transcription

FLOWCHART 6.4. Role of growth factor receptors in evolution of carcinogenesis.

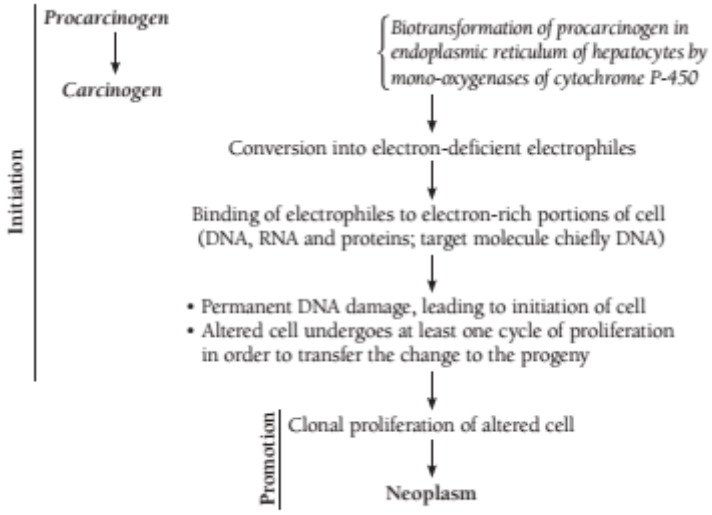
Mutated RAS (rat sarcoma) gene
↓ *Growth factors bind to extracellular receptor domain and activate the intracellular domain of the same*
Conformational changes and activation of RAS
GDP ⇄ GTP *Intrinsic GTPase activity of RAS may reconvert GTP into GDP; GAPs (GTPase-activating proteins) also prevent uncontrolled RAS activation*
Stimulation of RAF mitogen-activated protein (MAP) kinase mitogenic cascade
↓
Cell proliferation

FLOWCHART 6.5. Role of RAS-signalling pathway in cancer.

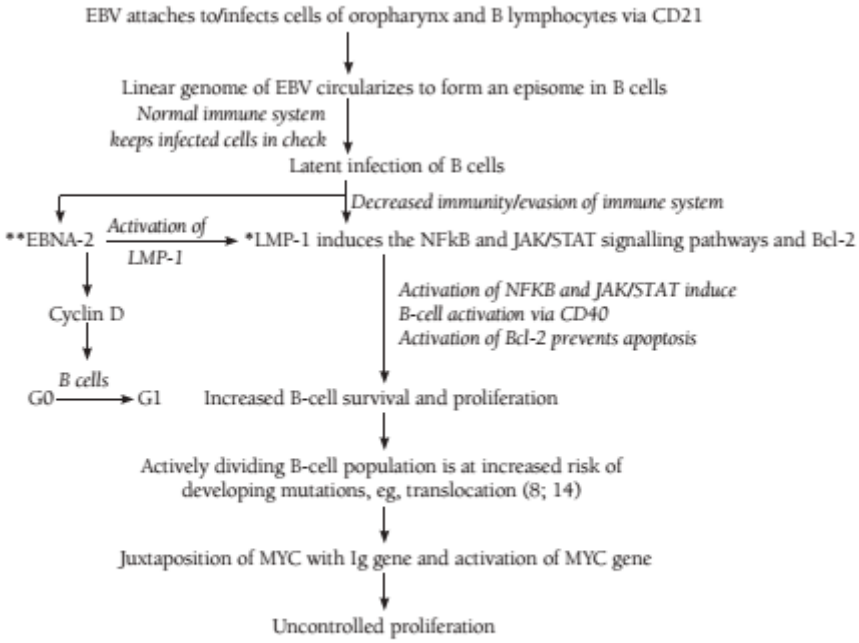
Development of a rapidly proliferating clone of cancer cells
↓
Emergence of a subpopulation of tumour cells with the biological characteristics essential for metastases
↓
Adhesion to and invasion of basement membrane by tumour cells
Tumour cell–ECM interactions and degradation of ECM due to:
- ↑ *Metalloproteinase expression on tumour cells*
- ↑ *Proteases (MMPs, cathepsin D, urokinase plasminogen activator)*
- ↓ *Tissue inhibitors of metalloproteinases (TIMPs)*

Cleavage of basement membrane proteins collagen laminin by MMP2 and MMP9
↓
Invasion of ECM
↓
Development of leaky blood vessels with endothelial gaps having direct contact with cancer cells
↓
Intravasation (entry into vessels) by tumour cells
↓
Interaction with host lymphoid cells to form tumour cell emboli
↓
Adhesion to basement membrane of vessel wall
↓
Extravasation at a distant site
↓
Metastatic deposit
↓
Proliferation as a secondary colony aided by angiopoietins 1 and 2

FLOWCHART 6.6. Sequence of events in invasion and metastasis.

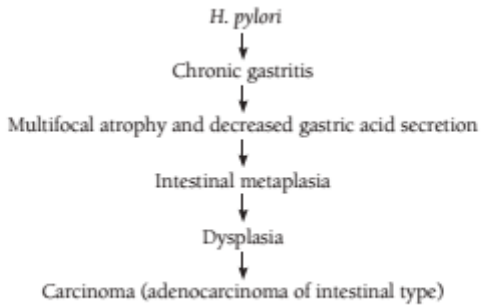


FLOWCHART 6.7. Stages of chemical carcinogenesis.



*LMP-1 – Latent membrane protein-1. **EBNA-2 – Epstein–Barr nuclear antigen 2.

FLOWCHART 6.8. Mechanism of EBV-induced oncogenesis.



FLOWCHART 6.9. Mechanism of *Helicobacter pylori*-induced oncogenesis.

GENETICS

IMPORTANT DIFFERENCES

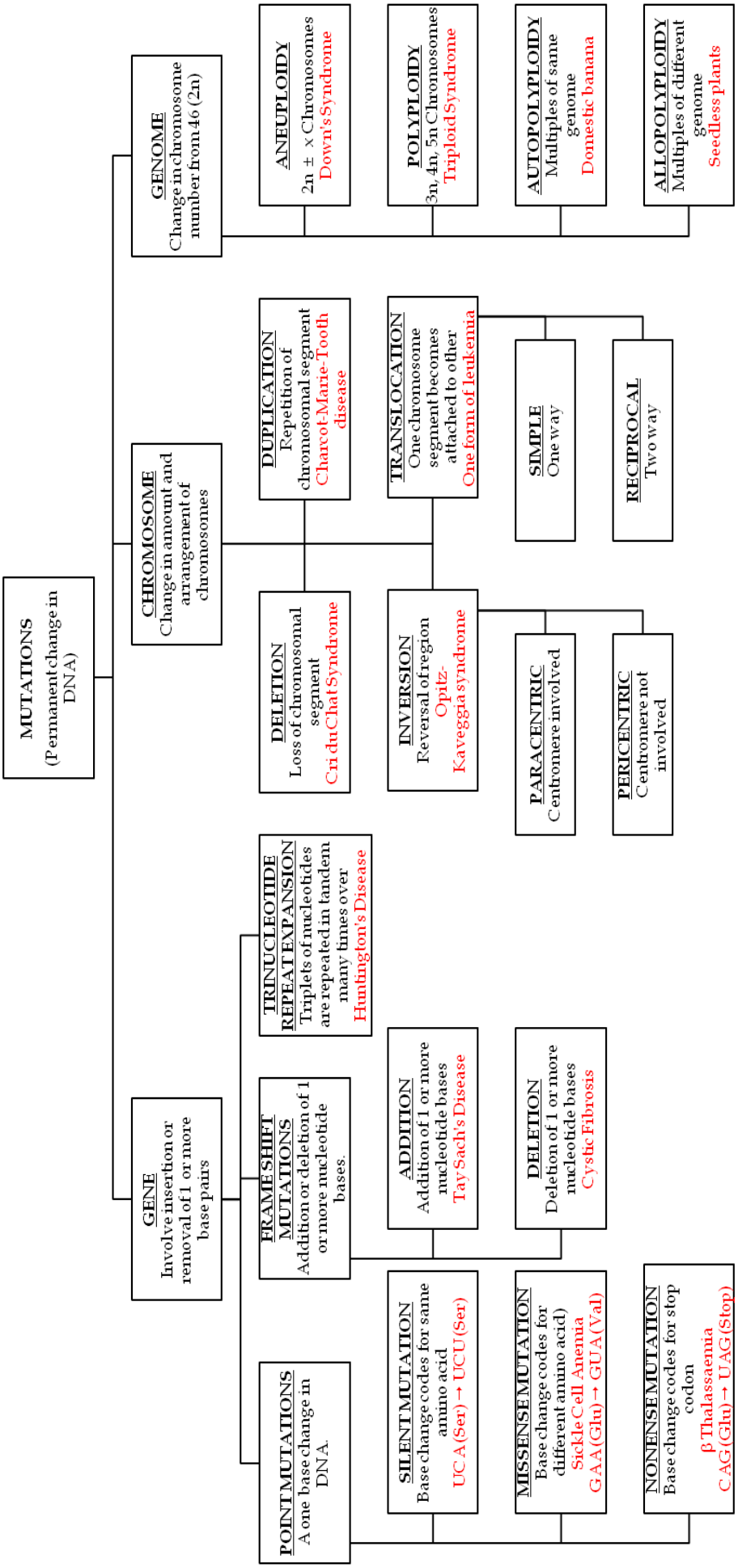
TABLE 7.1. Karyotypic Abnormalities of Important Syndromes

Down's Syndrome	Klinefelter's Syndrome	Turner's Syndrome
Meiotic Non-disjunction type: (95%) 47,XX, +21	***Classical type: (90%)*** 47,XXY	***Classic type: (57%)*** 45,X
Robersonian Translocation type: (4%) 46,XX,der(14;21)(q10;q10),+21	***Mosaic type: (10%)*** 46,XY/47,XXY 47,XXY/48,XXXY	***Defective 2nd X chromosome: (14%)*** 46,X,i(Xq) 46,XXq– 46,XXp– 46,X, r(X)
Mosaic type (Mitotic Non-disjunction during embryogenesis): (1%) 46,XX/47,XX, +21	***Variant types: (<1%)*** 48,XXYY 48,XXXY 49,XXXYY 49,XXXXY	***Mosaic type: (29%)*** 45,X/46,XX 45,X/46,XY 45,X/47,XXX 45,X/46,X,i(X)(q10)

TABLE 7.2. Difference between Disorders with an Extra Chromosome

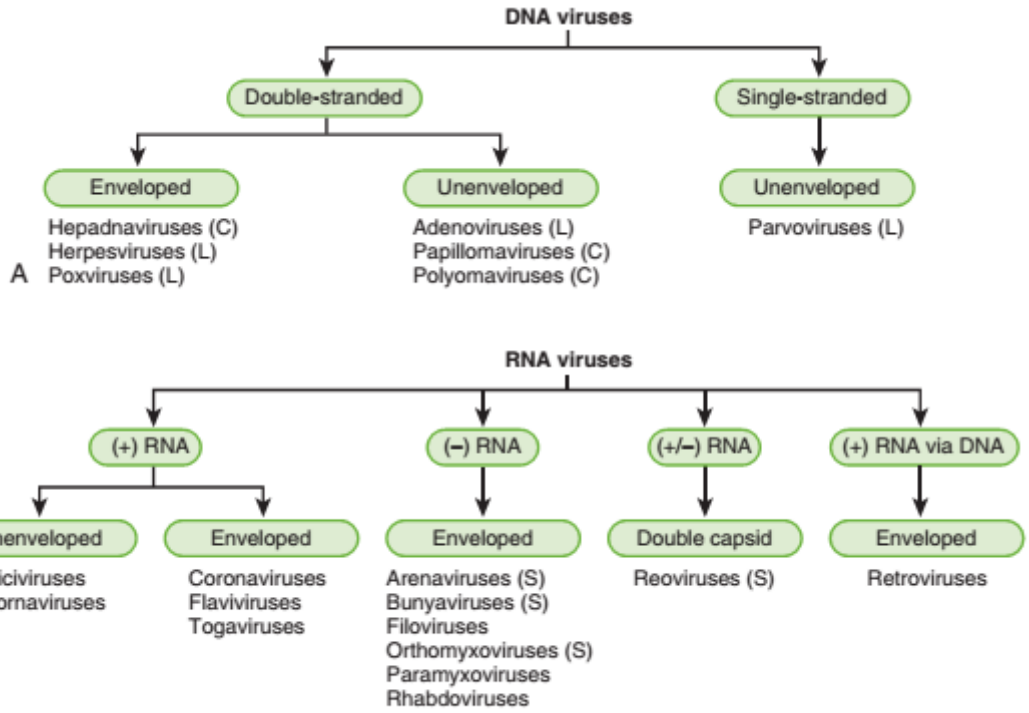
Feature	Down Syndrome	Edward Syndrome	Patau Syndrome
Trisomy	21	18	13
Common Karyotype	Meiotic Non-disjunction type: (95%) 47,XX, +21	Meiotic Non-disjunction type: 47,XX, +18	Meiotic Non-disjunction type: 47,XX, +13
Risk	↑ with maternal age to incidence of 1/25 live births in woman age ≥ 45	↑ with maternal age	↑ with maternal age
Intellectual Disability	✓	✓	✓
Skull Defects	×	Prominent occiput	Microcephaly Holoprosencephaly
Facial Defects	Low-bridged nose Flat face Epicanthial folds	Low set ears Micrognathia	Cleft lip or palate
Eyes Defects	Brushfield spots	×	Microophthalmia
Neck Defects	Broad short neck	Short neck	×
Congenital Heart Defects	✓	✓	✓
Renal Defects	×	✓	✓
Umbilical Hernia	✓	×	✓
Hand Defects	Simian Crease	Overlapping flexed fingers	Polydactyly
Foot Defects	Gap between 1st & 2nd toe	Rocker-bottom feet	Rocker-bottom feet
Others	Muscular Hypotonia Intestinal Stenosis		

IMPORTANT FLOWCHARTS



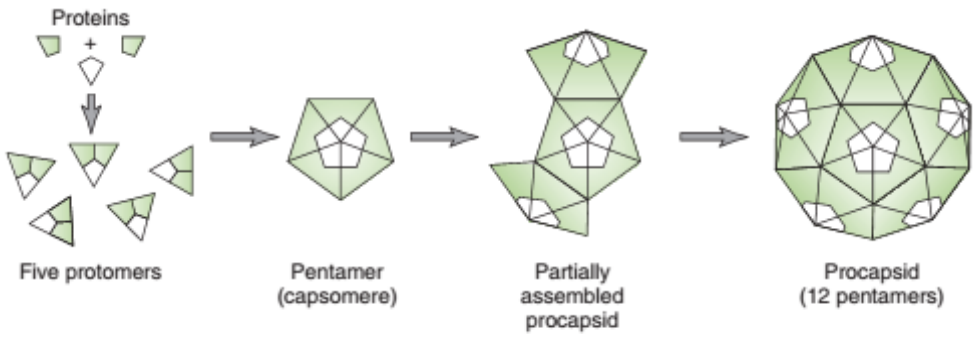
VIROLOGY

CLASSIFICATION OF VIRUSES



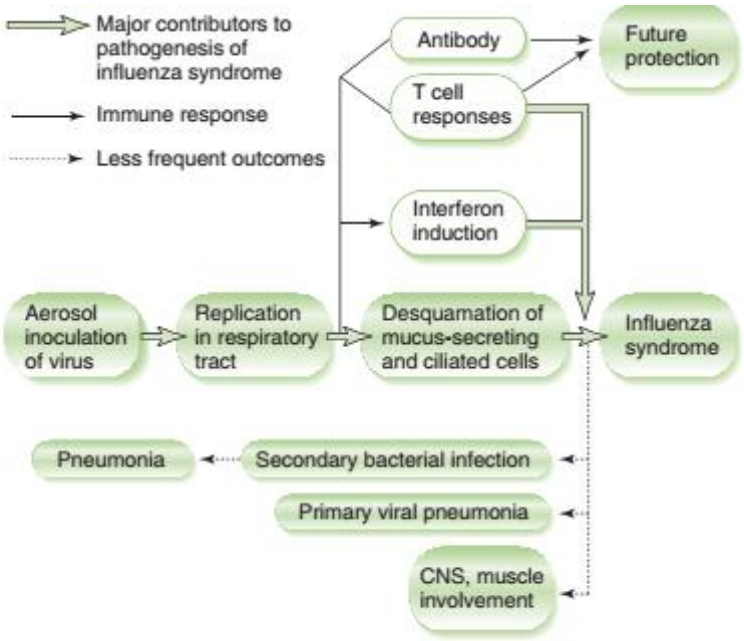
18-1: Classification of major viral families based on genome structure and virion morphology. **A,** DNA viruses. L, linear genome; C, circular genome. **B,** RNA viruses. S, segmented genome.

VIRAL STRUCTURE



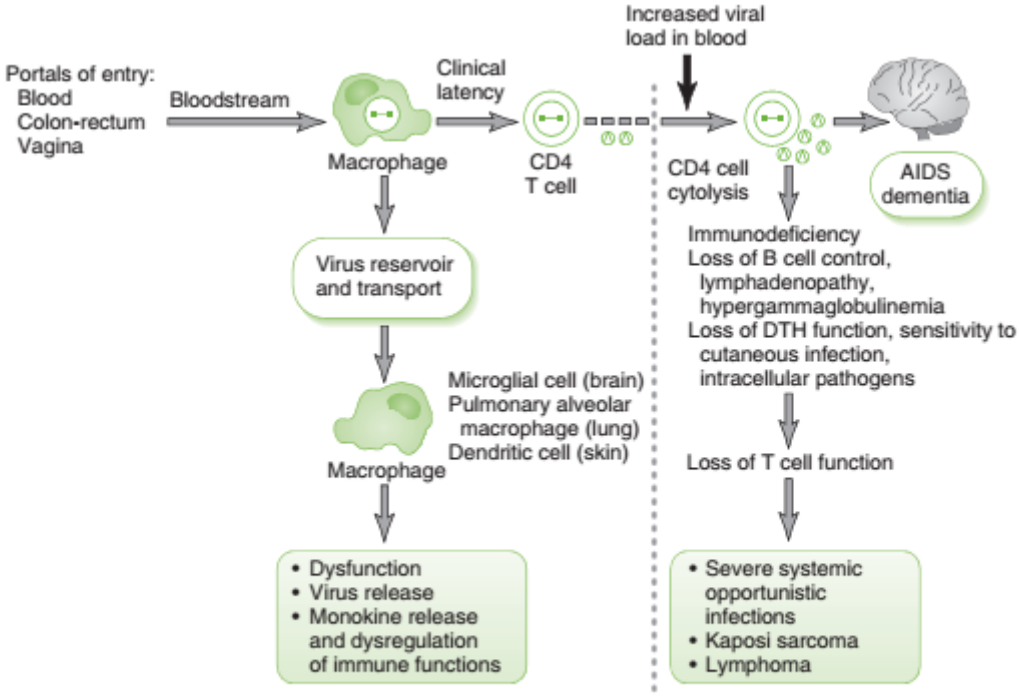
18-4: Assembly of the icosahedral capsid of a picornavirus. Individual proteins associate into subunits, which associate into protomers, capsomeres, and an empty procapsid. Insertion of the (+) RNA genome triggers conversion of procapsid to the final capsid (not shown).

INFLUENZA VIRUS



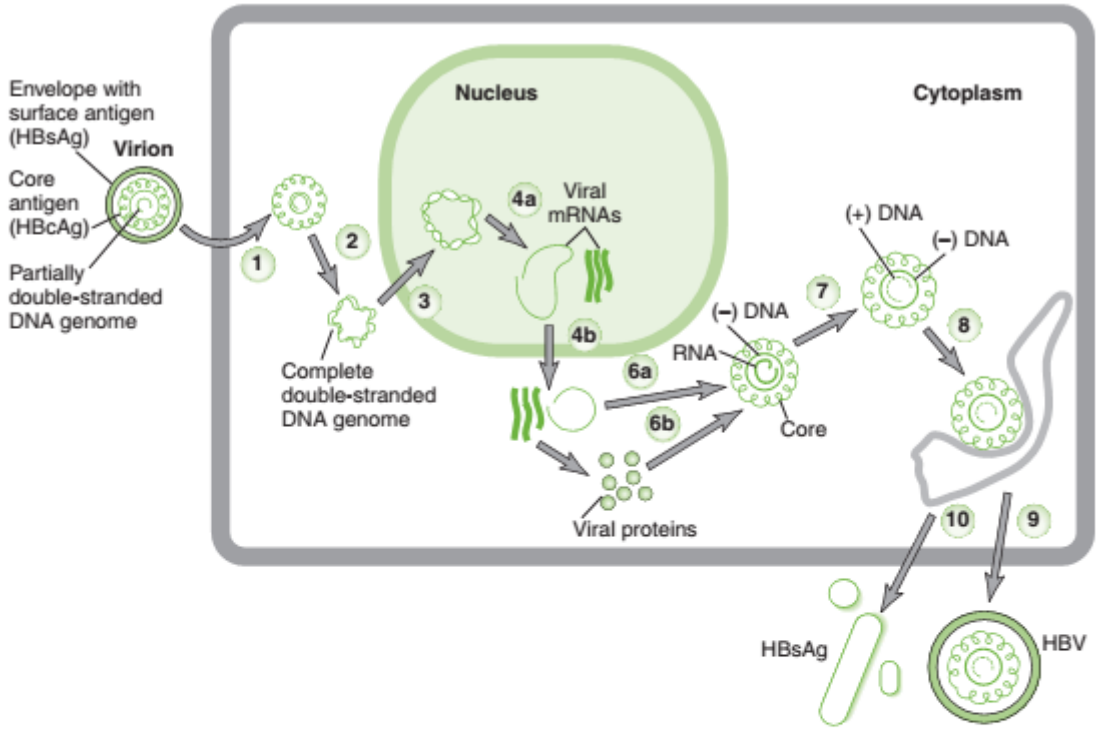
24-2: Pathogenesis of influenza A virus. Viral damage to the respiratory epithelium and host immune responses are responsible for the symptoms of influenza. Infection may also promote secondary bacterial infection. CNS, central nervous system.

HUMAN IMMUNODEFICIENCY VIRUS (HIV)



26-3: Pathogenesis of human immunodeficiency virus (HIV). HIV causes lytic and latent infection of CD_4 T cells and persistent infection of cells of the monocyte-macrophage family, and it disrupts neurons. The outcomes of these actions are immunodeficiency and acquired immunodeficiency syndrome (AIDS) dementia. DTH, delayed-type hypersensitivity.

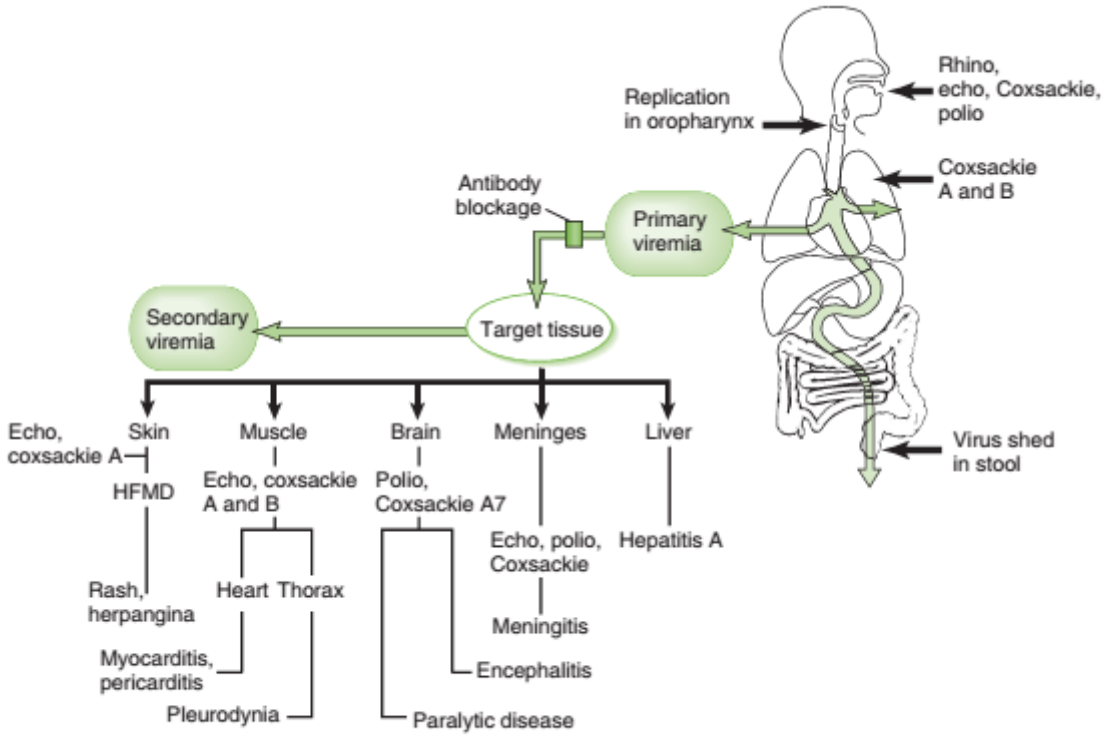
HEPATITIS B VIRUS



1. Binding and endocytosis of HBV virion into target cell; and release of nucleocapsid core into cytoplasm
2. Uncoating of core and completion of partially double-stranded DNA genome by viral DNA polymerase
3. Transport of completed genome to nucleus
4. Transcription of viral genome by host enzymes (4a) and transport of mRNAs to cytoplasm (4b)
5. Translation of viral mRNAs into proteins on host ribosomes
6. Synthesis of (–) DNA strand by viral reverse transcriptase using longest mRNA as template (6a) and assembly of core proteins around RNA/DNA hybrid (6b)
7. Degradation of RNA strand and synthesis of (+) DNA strand to replace it
8. Envelopment of nucleocapsid by intracellular membrane before entire (+) DNA strand is completed
9. Exocytosis of HBV virion
10. Exocytosis of noninfectious HBsAg particles

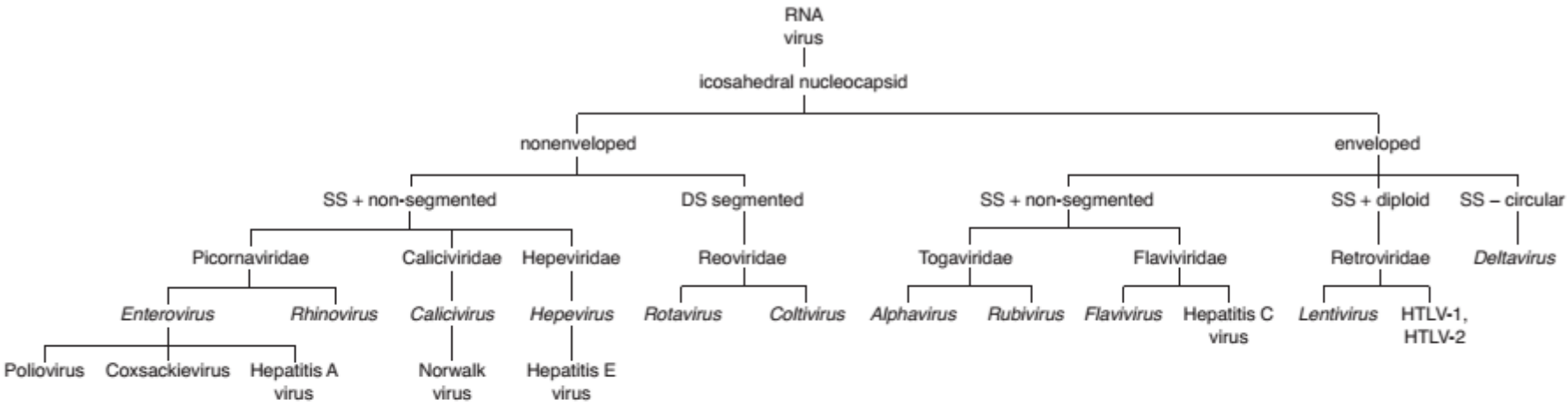
27-1: Proposed pathway for replication of hepatitis B virus (HBV). HBcAg, hepatitis B core antigen; HBsAg, hepatitis B surface antigen; mRNA, messenger RNA.

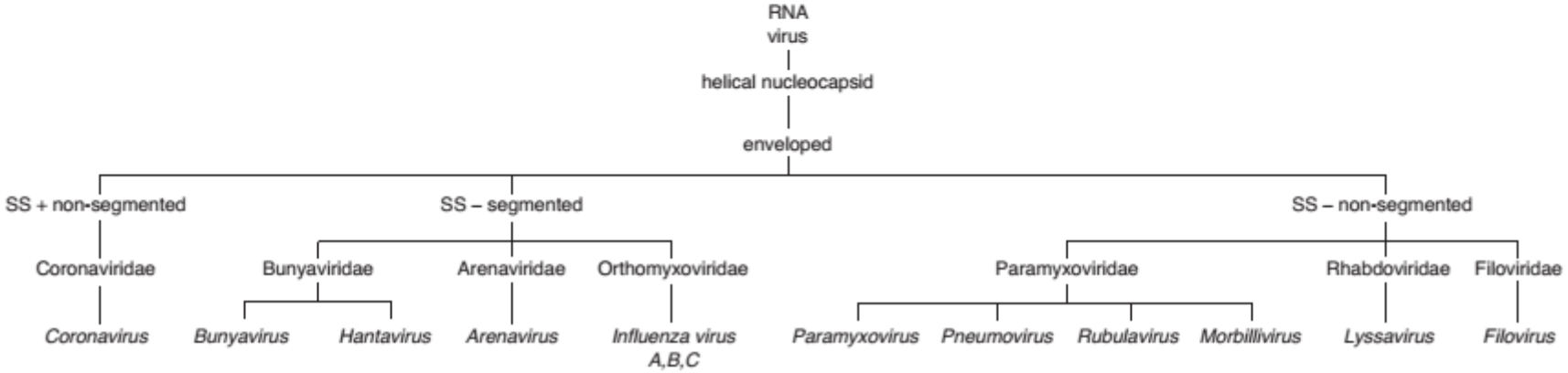
PICORNAVIRUSES



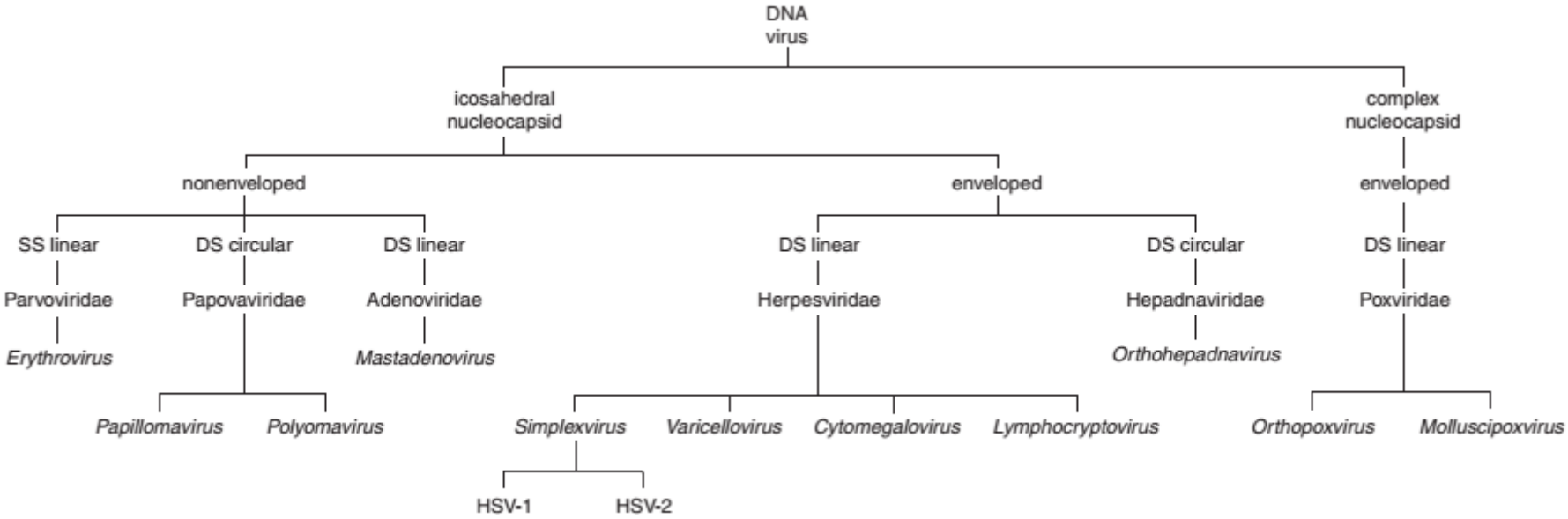
23-1: Pathogenesis of picornaviruses. All of the enteroviruses can be spread by the fecal-oral route but cause different diseases depending on the target tissue that is infected. Some enteroviruses, like the rhinoviruses, can be spread by respiratory means and cause symptoms of the common cold. HFMD, hand-foot-and-mouth disease.

ALGORITHM FOR RNA VIRUSES



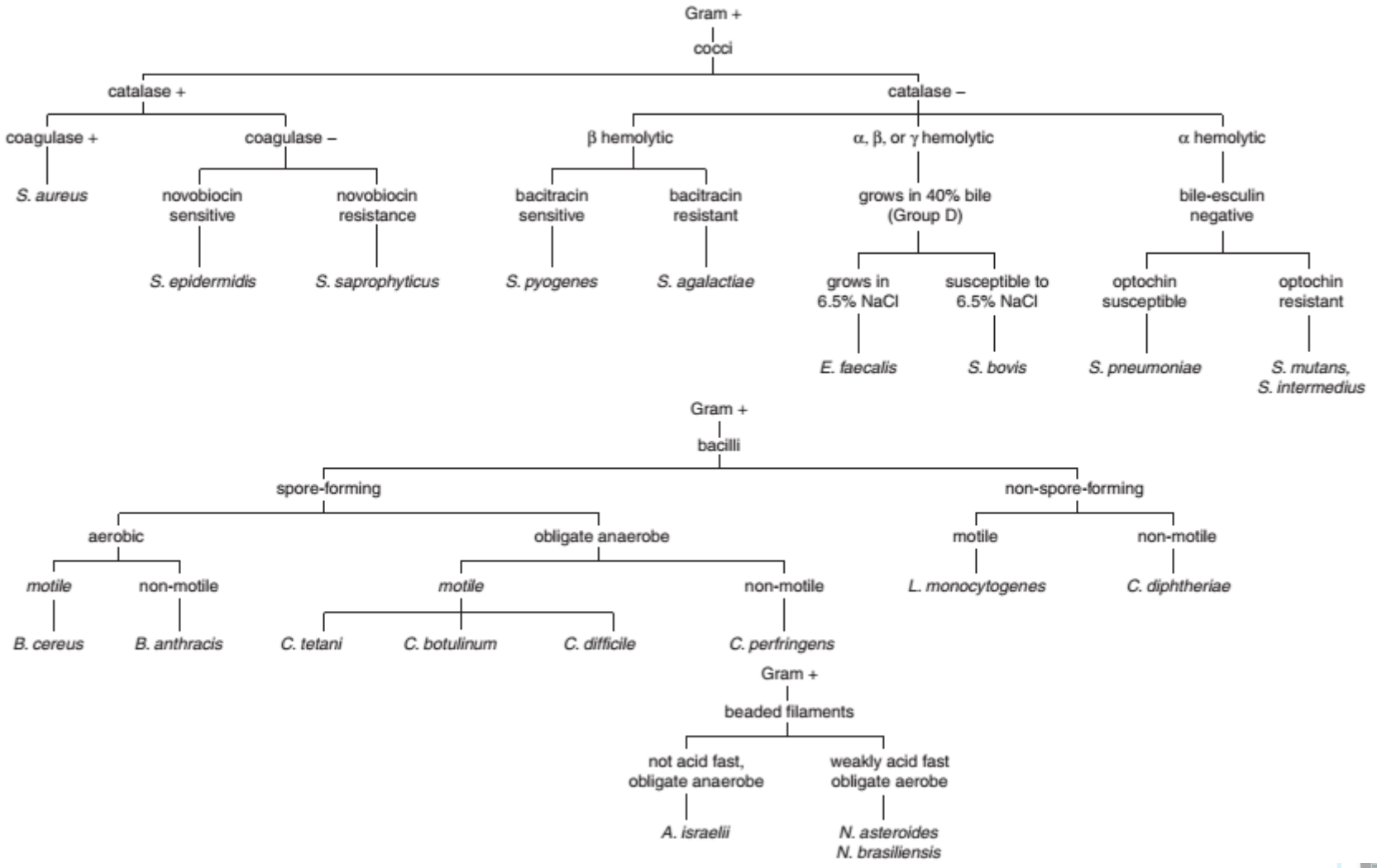


ALGORITHM FOR DNA VIRUSES



BACTERIOLOGY

ALGORITHM FOR GRAM POSITIVE BACTERIA



GRAM POSITIVE COCCI

Staphylococcus aureus *(virulent)* *(nonmotile, nonsporeforming, facultative anaerobe)* *Gm+ cocci*

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
***Skin infections:** impetigo, cellulitis, erysipelas, abcess, furuncle, carbuncle ***Bacteremia/sepsis:** hematogenous spread ***Acute endocarditis:** DESTRUCTIVE (compare to S.*viridans* and S.*faecalis*) ***Pneumonia –**damaging process, cavitations, empyema, effusions ***Osteomyelitis/septic arthritis-** hematogenous and traumatic spread ***Food poisoning –** 1-8 hr onset, vomiting, <u>preformed</u> toxin ***Tox shock syndrome-** fever, vomiting, diarrhea, diffuse <u>erythematous rash</u>	Gm + cocci in grapes/clusters Catalase + coagulase +	Ubiquitous in environment; normal flora of skin/nose Spread through lesions, fomites	**Enterotoxin-** vomiting, diarrhea, heat resistant, (actually released in gut) **TSST-1** – tampon use, wounds, *superantigen* **Exfoliatin-** scalded skin <u>TISSUE SPREAD:</u> **Alpha toxin**(lechthinase)- skin necrosis;hemolysis **Hyaluronidase-** degrades proteoglycans **Fibrinolysin-** lysis fibrin clots <u>IMMUNE EVASION:</u> **Protein A-** binds IgG-Fc, blocks opsonization and complement fixation **Coagulase-** activates prothrombin **Hemolysin-** destroys RBCs, PMNs, M0s, platelets **Leukocidin-** destroys WBCs	Gm + cocci in grapes, **Catalase** differentiates from Strep. S.*aureus:* **Beta hemolysis, coagulase, Yellow (Au) pigment** (coagulase *causes coagulation!*) **Coagulase neg:** S. *epidermidis:* **novobiocin <u>sensitive</u>** "sensitive skin" S. *saprophyticus:* **Novobiocin resistant**	**Beta lactamase production is common!** Use methicillin, nafcillin, dicloxacillin **MRSA-** vancomycin	none
S. *epidermitis:* associated w/ IV catheters, damaged/prosthetic **heart valves: INSIDIOUS onset, Nosocomial, LESS virulent**. Blood culture Contaminant S. *saprophyticus:* **Community acquired UTI** in young women						

Streptococcus viridans* (GABHS) *(nonmotile, nonsporeforming)							***Gm+ cocci***
Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention	
***Pharyngitis**- "strep throat", erythema, tonsillar exudate, fever ***Skin/soft tissue infections**- impetigo, cellulitis, necrotizing fascitis ***Scarlet fever**- centrifugal, red rash, erythrogenic toxin, slap cheek, strawberry tongue ***Tox shock syndrome**- clinically like *Staph* TSS ***Rheumatic fcver**- fever, myocarditis, polyarthritis, chorea, subcutaneous nodules, erythema marginatum rash. **Mitral valve disease** follows **pharyngitis,** NOT skin infections. Abs vs. bacteria cross react w/ joint and heart antigens ***Acute GN**- hypertension, hematuria, edema of face/ankles. Follows both pharyngitis AND skin infections. Cross reactive antigens deposited in GBM.	Gm + cocci in **chains or pairs** **Beta-hemolytic** are classified by Lancefield groups (A,B,D) according to **C-carbohydrates**	Human throat/skin, Transmission by respiratory droplets	**Hyaluronidase**- degrades proteoglycans (TISSUE SPREAD) **Erythrogenic toxin**- scarlet fever, **lysogenized** S.*pyogenes* **Streptolysin 0**- results in **beta hemolysis**, target of ASO antibodies **M protein**- antibody target, but inhibits complement/phagocytosis **Streptokinase**- converts plasminogen to plasmin, dissolves fibrin clots **IgA protease** "**HE'S** an **MSI**"	**All** Strep are Catalase – **Beta hemolysis** and Bacitracin sensitivity point to GABHS, esp with inc. ASO titer.	**Penicillin** to prevent rheumatic fever. Penicillin DOES NOT treat post strep disease or enterococcus.		
S. *agalactiae* (Group B strep)							
Neonatal menigitis, sepsis pneumonia	**Beta-hemolytic**	Female urinary tract					
S. *faecalis* (enterococcus)							
Subacute endocarditis, UTI "Oh **crap!** I've got **Heart** problems!"	Not hemolytic	GI tract		Grows in 6.5% NaCl			
S. *bovis* (group D)							
UTI	Not hemolytic	GI tract		Hydrolyze esculin in presence of bile. NOT grow in 6.5% bile			
S. *pneumoniae* (pneumococcus)							
Lobar pneumonia, ADULT meningitis, URI (kids)	**Alpha-hemolytic**	Nasopharynx	85 different **capsular polysaccarides**	**Quellung rxn**		23 valent vaccine, for AIDS, elderly, **asplenics**	
S. *Mutans , mitis* (Viridans group)							
Subacute endocarditis, caries	**Alpha-hemolytic**	Oropharynx					

GRAM POSITIVE RODS

Clostridium *(Anaerobic, spore-forming, with Exotoxin)* *Gm+ Rods*

C. *tetani*

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
Tetanus – tetany, **risus sardonicus** "joker smile", exaggerated reflexes, **respiratory failure**		**Spores, ubiquitous in soil, enter wounds and** germinate in anaerobic environment of necrotic tissue	**Tetanus toxin** travels intra axonally to CNS, **blocks release of inhibitory glycine neurotransmitter**		**Penicillin,** ventilatory support, muscle relaxants **Tetanus immune globulin,** preformed Ig	**Tetanus toxoid** (formaldehyde treated tox)

C. *botulinum*

Botulism "flaccid paralysis", descending weakness, diplopia, flaccid paralysis, resp failure. **Wound botulism-** spores to wounds, germinate, release toxin **Infant botulism-** ingestion of spores in honey- **floppy baby**		**Spores, in soil, inadequate sterilization of canned foods.** Alkaline veggies, smoked fish.	**Botulinum toxin** ingested **preformed.** Tox spreads in blood, to nerves **blocks Ach RELEASE** **Toxin** can be used to Tx torticollis, blepharospasm		**Antitoxin,** ventilatory support **NO PENICILLIN!!** Will burst cells and release toxin	Watch swollen cans!

C. *perfingens*

Gas gangrene (myonecrosis): war wounds, septic abortions **Food poisoning- ingestion** of cooking resistant spores in foods. **Watery diarrhea, cramps, little vomiting**	Results in **crepitus-** gas production and **Hemolysis**	**Normal flora of colon and vagina**	**Alpha tox-** lecithinase degrades cell membranes- hemolytic	Morphology, exudate smears, culture, sugar fermentation, organic acid production	Debridement, **O2 gas, Penicillin**	

C. *difficile*

Antibiotic associated pseudomembranous colitis- esp in hospitalized pts.		Normal flora in 3% of people	**Suppression of normal flora allows overgrowth, usually by clindamycin, ampicillin, cephalosporins** Exotox A (severe diarrhea Exotox B (damage to colonic mucosa)	ID C-diff tox in stool	**Metronidazole-** poorly absorbed orally, inc. colonic dose Vancomycin	

Bacillus *(Aerobic, spore-forming, with Exotoxin)* *Gm+ Rods*

B. *anthracis*

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
Woolsorter's disease- pulmonary anthrax, pneumonia	Large w/ square ends, nonmotile	Common in animals. Humans infected by **spores on animal products (skins/hides)** **Transmission** through skin, GI tract, respiratory tract	**Antiphagocytic capsule** made of **d-glutamate** [only one w/ Amino acids!] (not a polysaccharide) **Tripartite anthrax toxin:** protective antigen, lethal factor, edema factor. Protective factor inhibits phagocytosis.	Morphology and blood agar growth.	Penicillin	Sterilization of animal products, and **vaccination of animals.** Vaccine (protective antigen) for humans at risk

B. *cereus*

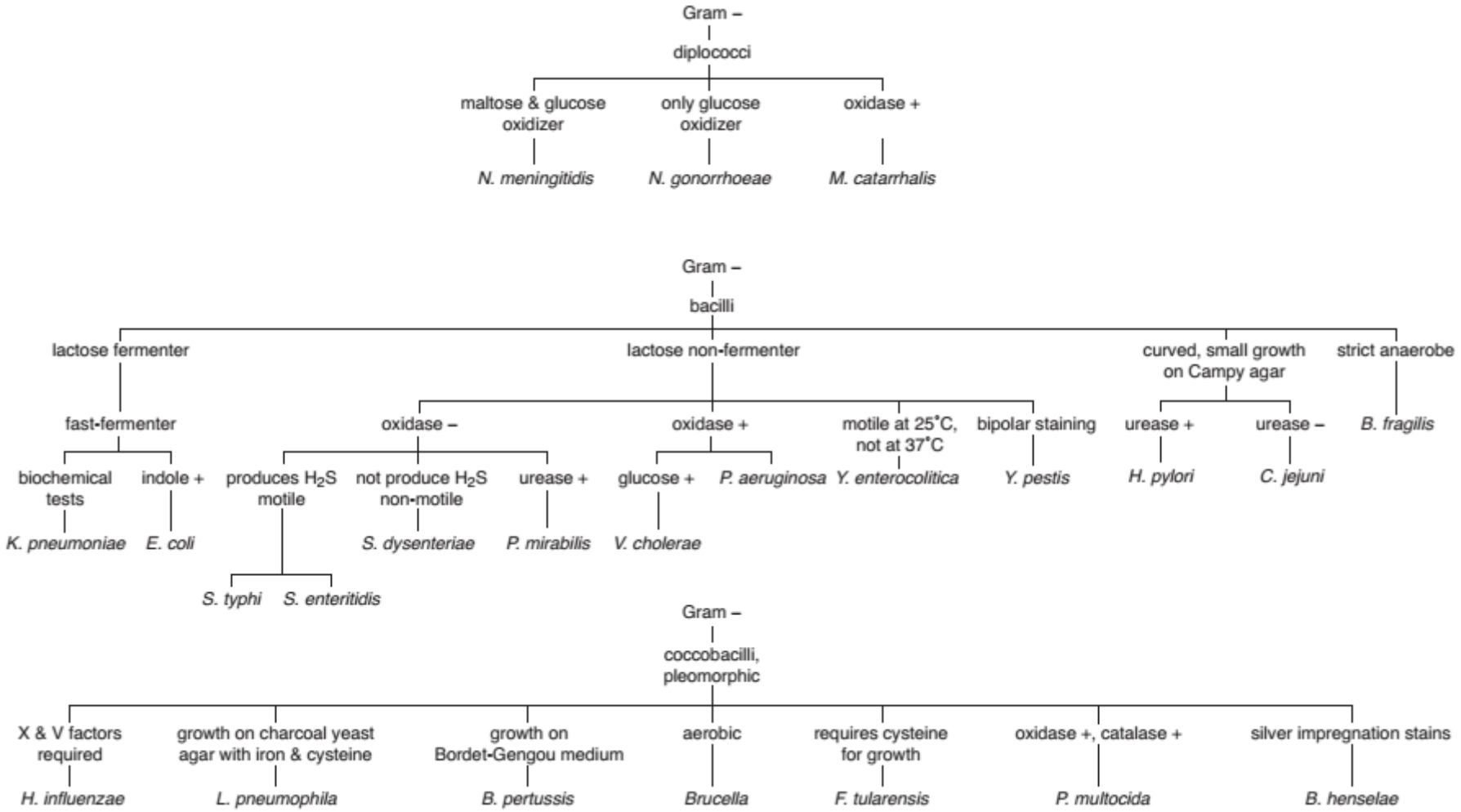
Vomiting with 4 hr incubation period (like S.*aureus*)- **heat stable toxin**--	Distinguished from B. *anthracis* by **motility** and **lack of capsule.**	**Spores** on grains survive cooking and germinate when food is warmed.	**Preformed heat-labile** enterotoxin (like E.*coli, Cholera tox*) - diarrhea		Treat symptoms	Avoid reheated rice

Corynebacterium *diptheriae* *(nonmotile, nonsporeforming, Chinese)* *Gm+ Rods*

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
Diptheria – throat inflammation, **gray fibrinous exudate** (pseudomembrane), airway obstruction, **myocarditis, recurrent laryngeal nerve palsy**	**Club shaped**, in **palisades, Chinese characters** Polyphosphate granules stain **metachromatically**	**Airborne droplets**, colonization of throat and production of Diptheria tox.	Diptheria tox: inhibits protein syn by **ADP ribosylation of eukaryotic ef-2**. Toxin produced by **lysogenized** bacteria (like erythrogenic toxin of GABHS)	**Tellurite plate, Loefller's** Toxin assessed by animal inoculation or gel diffusion precipitin test.	**Antitoxin**, **Penicillin** to reduce transmission	**Diptheria toxoid vaccine**. (disease in US is *iatrogenic* due to innoculation by inadequately killed toxin.

Listeria *monocytogenes* *(Facultative intracelluar anerobes, Non-sporeforming, tumbling motility)*						***Gm+ Rods***
Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
Neonatal meningitis and sepsis, abortion, premature delivery	Gm + rods, in clumps, Chinese characters, **NON-sporeforming, Tumbling** distinguishes it from corynebacterium	Newborns, immunocompromised are high risk groups. Transmitted to humans from animal feces, veggies, **unpasteurized milk/cheese.**	**Only Gm+ with LPS** **Infects monocytes and** induces granulomas. **Listeriolysin O** punches holes in cells	**Gm+ rods, beta hemolysis,** motility	Ampicillin	No vaccine

ALGORITHM FOR GRAM NEGATIVE BACTERIA



GRAM NEGATIVE COCCI

Neisseria (*Chocolate agar, Oxidase +, kedney bean shape*) *Gm- cocci*

N. *meningitidis* (meningococcus)

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
***Meningococcemia**- fever, arthralgias, myalgias, **petechial rash,** inc. in people w/ **complement deficiencies** ***meningitis**- fever, headache, stiff neck, photophobia, **inc.PMNs** in CSF *** Waterhouse-Friedrichsen**- fever, purpura, DIC, adrenal insufficiency due to *bilateral adrenal hemorrhage*, shock, death (like a bad meningococcemia)	**Gm –** cocci **kidney beans.** **Thayer-Martin, chocolate agar**	Airborne droplets, colonized **nasopharynx,** establishes carrier states in some	**Polysaccharide capsule, endotoxin (LPS), IgA protease** Capsular polysaccharides are **antigenic** serve as markers for classification.	**Ferments maltose** Presumptive diagnosis by Gm stain of petechiae or CSF **LATEX agglutination test b/c** capsular polysaccharides	Penicillin or **Ceftriaxone (G3)**	Chemoprophylaxis with **Rifampin** (excreted into saliva) **Polysaccharide vaccine in** military recruits.

N. *gonnorhoeae (gonnococcus)* *(most common notifiable disease in US)*

Males- symptomatic dysuria, penile discharge b/c of **urethritis.** Leads to **epididymitis,** prostatitis, urethral strictures **Female**- asymptomatic, vaginal discharge, dyspareunia, due to **cervicitis, Infertility, PID, ectopic,** tubo-ovarian abcess, perihepatitis (**Fitz-Hugh-Curtis syndrome)**, **opthalmia neonatorum** **Both: Septic arthritis**	**NO CAPSULE** **Gm –** cocci **kidney beans.** **Thayer-Martin, chocolate agar**	Sexual transmission OFTEN coexistent WITH Chlamydia AND Syphilllis (tx w/ tetracycline or chloramphenacol)	**Pili/fimbriae (ANTIGENIC** variation) **LPS** OMPs **IgA protease** NO CAPSULE!	**Men: Gm – diplococci in PMNs** **Does NOT** ferment maltose No serologic testing, no capsule!	**Ceftriaxone (G3**) b/c penicillinase producing N.*gonnorhoeae PPNG common*	**Erythromycin** eye drops in newborns (also protects vs. Chlamydia) No Vaccine.

NOTE: bacterial meningitis: 0-6 months (Group B *Strep*, E.*coli, Listeria*); 6 months – 3 years (H.*influenzae B)*, 3-15 years (N. *meningitidis),* >15 years (S. *pneumoniae)*

GRAM NEGATIVE RODS

ENTERIC *(Intestinal AND non-Intestinal disease)* *Gm- Rods*

Not all gram negative enterics belong to ***Enterobacteriaciae family: 1) colonic location 2) facultative anaerobes 3)ferment glucose, 4)oxidase negative, and 5)reduce nitrates to nitrites***. *ALL are members here EXCEPT:* Vibrio, Campylobacter, Helicobacter, Pseudomonas, Bacteriodes. ("**V**ile **P**eople **C**an't **B**e **H**appy") As a group, ***Enterobacteriaciae*** are often **normal flora.** Pathogenisis is by endotoxin/LPS, exotoxins. **O** (**O**uter polysaccharides), **H** (flag**H**ella), **K** (**K**apsular polysaccharides) **are important antigens.** Inoculation on **MacConkey's** or **Eosin-Methylene Blue (EMB)** agar differentiates family members by **lactose fermenting** ability. Fermenters are pink-purple, non-fermenters are colorless. Also keep an eye on **motility.**

E. *coli* *(Enterobacteriaciae)*

Diseases	Character	Hab/Trans	Pathogenesis	Diagnosis	Treatment	Prevent
Most common **UTI, Gm- sepsis, traveller's diarrhea.** 2nd most common cause of **Neonatal meningitis.** **Enterotoxigenic** strains: Do NOT invade! **heat labile** enterotox binds **GM1 ganglioside** receptor, activates adenylate cyclase via ADPribosylation of G protein. (like *Cholera tox*) **Watery diarrhea.** **Enterohemorragic**: **verotoxin** inhibits 60s ribosome (like *Shigella)* **Bloody diarrhea. 0157:H7 type** causes **hemolytic-uremic syndrome** (anemia, thrombocytopenia, renal failure) associated w/ fast food outbreaks **Enteroinvasive:** factor mediated **invasion** of epithelial cells, sepsis. **Bloody diarrhea with WBCs.**	As other *enterobacteria ciae* family	Normal flora, but need virulence factors to cause disease.	**Pathogenisis by pilus and enterotox, capsule,** and **endotoxin.** Serotype ID by **O,H,K antigens**	**Ferments lactose,** unlike *Salmonella, Shigella*	G3 **Cephalosporin**	No vaccine

Salmonella *(Enerobacteriaciae)*

S. *enteritidis* causes **gasteroenteritis** via Cholera like tox. **Large inoculum** needed. (Peptic acid kills) Tx symptoms. **S.*typhi* –Typhoid fever**, init by asymptomatic infection of gut phagocytes and dissemination to liver, **Gall bladder** (carrier state), Fever, RLQ abdominal pain, **rose spots**. Tx **Cipro or ceftriaxone.** **S. *cholerae-suis***- Gm- **sepsis.** Esp patients with **Sickle cell** (risk for **osteomyelitis** b/c func. **Asplenia**)	As other *enterobacteria ciae* family	Normal flora of *animals*. Contamination food, **poultry / eggs**	K anitgen/Vi antigen **Flagella antigenic variation**	**Does NOT** ferment **lactose.** Production of H_2S gas distinguish from *Shigella*.	S. *typhi*- by **Cipro or ceftriaxone**	Hand washing, cooking, water chlorination

ENTERIC *(INTESTIAL disease)* *Gm- Rods*

Shigella (Enterobacteriaciae)

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
Enterocolitis (dysentary) by S.*dysentariae*, S.*sonnei*, S. *flexneri*, S. *boydii*	Nonmotile **Small innoculum <100 bugs**	Not normal flora. Humans only host. 4Fs: fingers flied food feces (fecal-oral)	Distal ileal and colonic mucosal **invasion** and cell death. Does NOT enter bloodstream (unlike *Salmonella*)	**NO H_2S gas, nonmotile. Non lactose** fermenting on EMB, MacConkey's agar **PMNs in smear** w/ fever suggest invasive bug.	Fluid replacement, avoid antiperistaltic drugs which prolong excretion of organism.	

Vibrio (Not Enterobacteriaciae)

Cholera - Massive watery diarrhea (Rice water stool) like enterotoxic E.*coli* V.*parahemolyticus* is a marine bug in contaminated raw seafood. Japan	**Comma shaped, single flagella. Large innoculum needed.**	Infects humans only, **transmission** by **fecal-oral**.	Mucinase aided colonization of small intestine, **bipartite enterotox:** binds **GM1 gangliosides** on enterocyte, **ADP-ribosylation of G protein**. (like ETEC)	Diagnosis clinically in endemic areas: Asia, Africa, Latin America.	Oral rehydration	No effective vaccine.

Campylobacter (Not Enterobacteriaciae)

More frequently causes **enterocolitis than *Salmonella* or *Shigella*.** Can cause **bloody Diarrhea**	**Comma or S-shaped, Microaerophilic, urease negative**	Domestic animals via fecal oral, unpasteurized milk	Probably enterotoxin	Blood agar w/antibiotics, C.*jejuni* **grows at 42C, produces oxidase**, nalidixix acid sensitive C.*intestinalis* grows at **25C, oxidase neg,** resistant to nalidixic acid	Antibiotics	No Vaccine

Helicobacter *pylori* *(Not Enterobacteriaciae)*

Gastritis, peptic ulcer, risk factor **Gastric carcinoma**	Urease + (protects from stomach acid)	Fecal-oral.	Attaches to gastric mucosa, mediated by NH3 production, host inflammatory response		**Bismuth sulfate, tetracycline, metronidazole**	No vaccine.

ENTERIC *(EXTRAINTESTIAL disease)* *Gm- Rods*

Klebsiella-Enterobacter-Serratia (Enterobacteriaciae)

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
Opportunistic pathogens cause **UTI, pneumonia,** usually nosocomial *Klebsiella* is nonmotile, with capsule, **mucoid** colony appearance. *Klebsiella* pneumo renowned for severity, bloody "**currant jelly**" sputum, lung cavitations. *Serratia*- **bright red pigment. Nosocomial**- Ab resistant	All ferment **Lactose** K.*pneumoniae*, E.*cloacae*, S.*marcescens* difficult to distinguish clinically	Large intestine, soil water		**Ferment lactose** on EMB, MacConkey's agar		No vaccine

Proteus-Providencia-Morganella (Enterobacteriaciae)

Community and **nosocomial UTI, b/c high motility** (important species: *Proteus mirabilis, Proteus vularis Providencia rettgretii* M. *morganii*)	**Non** lactose fermenting, **urease +** (alkalinizes urine) Only enterobac that makes **phenylalanine deaminase**	Large intestine, soil water		**Swarming** appearance on blood agar. Use antigens from *Rickettsiae* cross react with *Proteus*. P.*mirabilis* is **indole neg** unlike others of this group.		No vaccine

Pseudomonas (Not Enterobacteriaciae)

P *aeruginosa*: opportunistic, nosocomial: Pneumonia, osteomyelitis, burn infections, sepsis, UTI, endocarditis, **malignant otitis externa,** corneal infections. **P. *cepacia*** colonizes CF patients	**Strict aerobe, Not glucose fermenting, Not reduce nitrates, oxidase +**	Normal flora of **colon**.	Exotox like C.*diptheriae* **(ADP-reibosylation)**	Produces **pyocyanin, pyoverdin**	Highly resistant. Combo pipercillin, ticarcillin and aminoglycoside. **Ceftazidime**	

Bacteroides fragilis (Not Enterobacteriaciae)

Peritoneal abscesses. Growth favored by growth w/ facultative anaerobes to exhause local oxygen	**Anaerobic, non sporeforming, non LPS, polysaccharide capsule.** No exotox, No LPS	**Predominant** flora of **colon.** NOT communicable. Exits colon via break in mucosa (Chronic disease, PID, trauma)	Polysaccharide capsule provides virulence factor		Treat as **mixed** infection. **Clindamycin, or metronidazole**	No Vaccine

RESPIRATORY — *Gm- Rods*

H. Influenzae *(chocolate agar w/ heme and NAD)*

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
Leading cause of **meningitis** in kids. Peak at 6m to 1 yr. (decline in maternal IgG, inability of infants to mount attack vs. polysaccharide capsule) Fatal **epiglottitis** by type **B** *influenzae*.	**Coccobacillus w/** polysaccharide **Capsule**	Upper respiratory tract, respiratory droplets	**ONLY encapsulated** forms like type B cause invasive disease. Nonencapsulated cause URI, pneumonia in pts with preexisting lung disease (COPD). **IgA protease,**	**Chocolate agar, w/ heme and NAD.** **Quellung rxn** "Hmmmm Chocolaaate!"  **H.*Simpson***	**Rifampin** prevents meningitis and transmission from close contacts b/c **secreted into saliva** better than Ampicillin	HIB vaccine of **capsular polysaccharide conjugated to carrier protein.**

Legionella pneumophilia *(Cysteine and Iron agar)*

Atypical pneumonia with **high fever, nonproductive cough**(differentiate from *Mycoplasma*, influenza, psittacosis, Q fever)	Poor gm stain	Airborne from water sources. Smoking EtOH, Immunosuppressed are at risk.		High concentration **Error! No table of figures entries found.**of **cysteine and iron**. Urine antigen test. Suspect when inc. **PMNs** with no organisms!	**Erythromycin** (also good for *Mycoplasma)*	Disinfect water sources

Bordetella pertussis *(Bordet-genou agar)*

Whooping cough- acute tracheobronchitis with **URI symptoms, paroxysmal hacking cough** 1-4 wks, **copious mucus**	Small gm- rods	Airborn droplets **(highly contagious)**	**Polysaccharide capsule and pili** are essential for virulence. Does NOT invade. **Pertussis tox (ADP-ribosylation), and tracheal cytotoxin.**	Culture on **Bordet-genou** agar. Ab agglutination, stain	Erythromycin reduces complications, doesn't change clinical course. Resp tract already damaged.	Killed **B.*pertussis*** vaccine 2,4,6 months, Boosters at age 1, school. **Acellular** vax for booster only.

ZOONOTIC — *Gm- Rods*

Brucella (virulent, facultative intracellular, tx: aminoglycoside)

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
Brucellosis- influenza like syndrome w/ **undulating fever**(higher during day, lower at night). Lymphadenopathy, H/Smegaly, no boboes/ulcers.	Small gm- rods	Animal reserviors: B *melitensisi* (goats/sheep) B. *abortus* (cattle) B. *suis* (pigs) **Non pasteurized milk products**(travelers), **through skin** (meat packers, vets, farmers)	Organisms localize in **RES**. Persist in macrophages, induce granulomas	Serology, biochemistry	Antibiotics	**Animal vaccination, pasteurization.** No Human vaccine.

Francisella tularensis *(virulent, facultative intracellular, tx: aminoglycoside)*

Tularemia- influenza like syndrome w/ **ulceroglandular lesions** (hole in skin, black base, swollen LN, draining pus)	Small gm- rods	Ubiquitous in US in **wide variety of animals. Tick/mite vectors.** Humans as accidental dead end hosts by **bites** or **animal skin handling.**	Enters through skin, localizes in **RES**. Persist in macrophages, induce granulomas	Serology	Streptomycin	**Live attenuated vaccine** (like BCG)

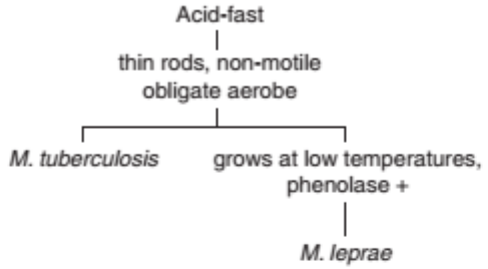
Yersinia pestis *(virulent, facultative intracellular, tx: aminoglycoside)*

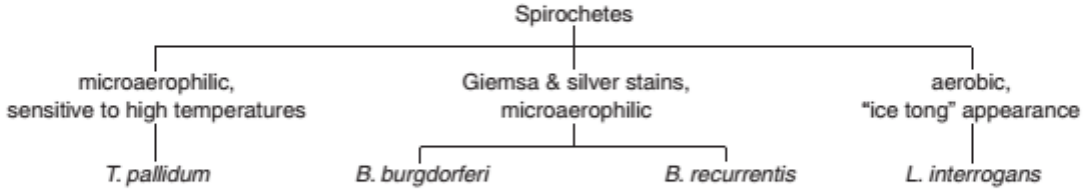
Plague- Hematogenous spread **results in fever myalgias, hemorrhage. Also septic shock, pneumonia.**	Small gm- rods with bipolar stain	Endemic in prairie dogs in US, 99% cases in SE Asia. Rats/flease in **urban centers. Also wound-person respiratory droplets.**	Bacteria spread to **regional LN, enlarged tender buboes.**	Immunoflorescence	Antibiotics	Quarantine. No Vaccine.

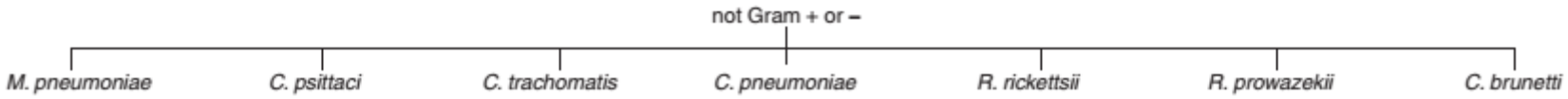
Pasteurella multocida

Cellulitis rapid onset at bite site. **Osteomyelitis as complication**. **Sutures** predispose to infection	Small gm- rods	**Normal flora of dogs and cats.** Transmitted to humans by animal bite.		Presumptive Dx by rapid onset **cellulitis** at animal bite.	Penicillin	Ampicillin prophylax.

ALGORITHM FOR OTHER BACTERIA







MYCOBACTERIA *(Obligate aerobe, facultative intracellular organisms)* *Acid Fast Rods*

M. tuberculosis

Diseases	Character	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
Tuberculosis: chronic low grade fever, night sweats, productive cough, hemoptysis, weight loss. Elderly, immunocomp, malnourished at risk.	Obligate aerobe, intracellular, infect M0, persist for years. Mycolic acid walls	**Only infects humans.** Respiratory aerosol. Infects M0s in **mid/lower lobes**, init granuloma formation, widely disseminate the infection. T cells help M0 kill some intracellular mycobacteria at expense of bystander cell damage. Result: necrotic host cells, viable mycobacteria. Walled off w/ giant cells, fibroblasts, collagen, calcification to form **granuloma** or **tubercle.** This **1' infection** = **Ghon focus** on CXR (when including Ca tubercles in perihilar lymph nodes = **Ghon complex.**) Reactivation prefers **upper lobe (obligate aerobe)** of lung. Reactivation can infect any organ. Cervical LN (**scrofula),**spine **(Pott's disease.)**	**Mycolic acids** confer acid fastness. **WaxD** is active ingredient in **Freund's adjuvant. Cord factor** is **virulence factor** (mycoside= 2 mycolic acids + disaccharide)	**PPD** tests for **prior exposure** or to **BCG vax.** Positive test if **both redness, induration 48-72 hr** after injection (DTH rxn.) Note: *candida* and mumps as controls in immunocomp. **Acid fast stain. NaOH** concentrate on **Lowenstein-Jensen medium**. Slow culture, 6-8 wks. **Niacin production**	**Prolonged, multiple Tx. (INH, rifampin, pyrazinamide, ehtambutol)** **Protracted tx** b/c: intracellular life cycle, granuloma blocks penetration of drug, metabolically inactive mycobac persist in lesion	Chemoproph ylax w/ INH (watch hepatotox in people >35 y.o.) **Live attenuated M.*bovis* (BCG)** induces some protective immunity.

M. avium- intracellulare

Clincal TB indistinguishable from M *tuberculosis* in AIDS.	**Atypical mycobacterium**	Found in water, soil, **not pathogenic** in guinea pigs (infects birds)			**Azithromycin Clarithromycin**	Macrolide prophylax when CD4 count < 50

M. leprae

Leprosy- preferential growth in < 37C, **skin, superficial nerves.** **Tuberculoid- good** cellular immune response, **few** AFB, **granulomas, positive** lepromin skin test. Anethetized skin lesions & thickened superficial nerves. **Lepromatous- poor** cellular immune response, **lots** of organisms, **foamy histiocytes**, **negative** lepromin skin test (poor response.) Skin lesions, lion facies. Skin anesthesia, bone resorption, skin thickening, **disfiguring.**	Never has been grown in lab.	**Brazil, India, Sudan** Humans only natural hosts. **Mouse footpad and armadillo** growth only. Transmission by nasal secretions, skin lesions to persons with **prolonged** contact w/pts.	Intracellular replication (skin histiocytes, endothelial cells, Schwann cells)		**Rifampin Dapsone** Up to **2 years!**	Prophylax exposed persons with **Dapsone.**

ACTINOMYCETES — *Gm- Branching Rods*

A. israelii

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
Actinomycosis- hard non-tender swelling, drains pus through sinus. (abscess that spreads to neck, chest, abdomen.)	Aanerobic Gm-branching rods	**Normal anaerobic flora oral cavity/GI tract.** Not communicable.	**Invasion after** local trauma **(risk factor for anaerobic growth)**	**Anaerobic Gm-branching rods, sulfur granules** in pus	**Penicillin**	No vaccine

Nocardia asteroids *(Acid Fast Branching)*

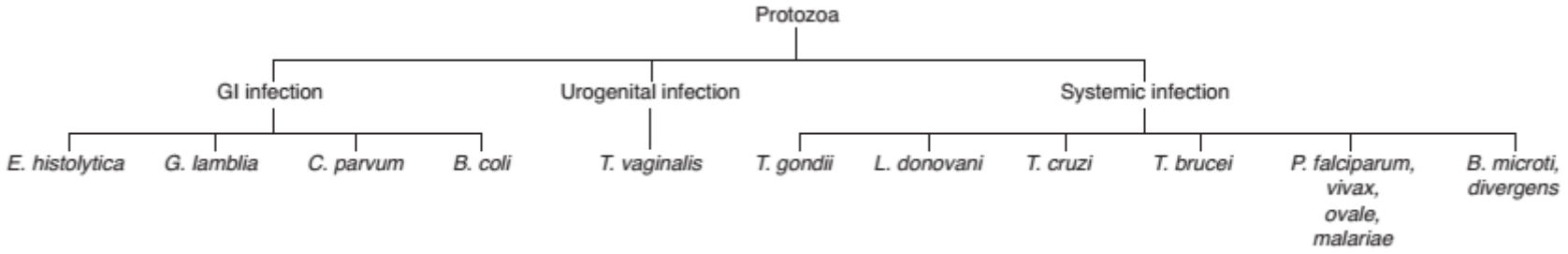
Nocardiosis- pneumonia that progresses to abscess formation, sinus tract drainage, dissemination to brain/kidney (immunosuppressed)	Aerobic Gm-branching rods.	**Soil, NOT normal flora**		**Acid fast branching, NO sulfur, aerobic**	**Bactrim** (trimethorprim + sulfamethoxazole)	No vaccine

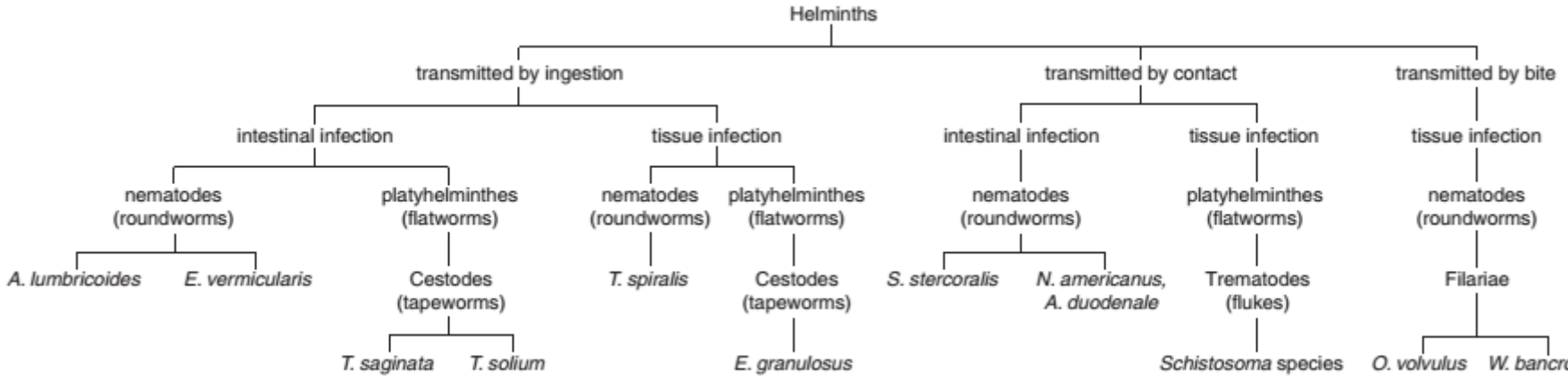
Mycoplasma pneumoniae *(No cell wall, poor gm stain)* — *Small free living organism*

Diseases	Characteristics	Habitat/Transmission	Pathogenesis	Diagnosis	Treatment	Prevention
"Walking pneumonia" (dry nonproductive cough, horrible CST, generally feel well) **Most common pneumonia in young adults** (college students).	Smallest free living organism, **no cell wall** so poor gm stain, resists **penicillins, cephalosporins**. Cell membrane has **chol** which are not in other bacteria. "Fried egg" colonies on **Eaton's agar.** (**"Eat Fried Eggs w/ chol"**)	**Respiratory droplets.** Attaches but does NOT invade respiratory epithelium, like B.*pertussis*.	Pathogenic only for humans. Arrests cilliary motion, induces epithelial cell necrosis. Cross reactive antigens induce anti RBC autoantibodies (**cold agglutinins.**)	Elevated titer of cold agglutinins or specific anitbodies	**Erythromycin Tetracycline**	No vaccine

PARASITOLOGY

ALGORITHM FOR PARASITES





PROTOZOA – INTESTINAL and UROGENITAL

Entamoeba Histolytica *(bloody diarrhea)*

Diseases	Characteristics	Habitat/Trans	Pathogenesis	Diagnosis	Treatment
Amebic dysentery- bloody, mucus diarrhea, **liver and pulmonary abcess.** **Mostly asymptomatic.**	Trophozoite has **single nucleus and ingested RBC**, cysts have **4 small nuclei.** Prevalent among male homosexuals.	No animal reservoir. **Fecal-oral transmision.**	Excyst in ileum, invade colonic epithelium, cause necrosis (**teardrop ulcer**), spread (**liver, lung**)	**ID trophozoites and cysts** in stool. **Serology positive** in invasive amebiasis **Absence of PMNs.**	Metronidazole, iodoquinol. Cysts removed by filtration, killed by boiling, not chlorination.

Giardia lamblia *(Nonbloody diarrhea)*

Giardiasis- nonbloody, foul smelling diarrhea, nausea, anorexia, flatulence, abdominal cramps for wks/months. Outbreaks at **day care centers, mental hospitals.**	**Pear shaped trophozoite,** 2 nuclei, 4 pairs flagella, suction disk. **Thick walled oval cyst w/ 4 nuclei** 5% US stools have cysts, 50% asymptomatic carriers.	**Fecal contamination of food/water.** Homosexual transmission.	Excyst in duodenum, attaches-NO invasion, inflammation, malabsorption of protein/fat.	**Trophozoites/cysts** in stool, **string test**, serology.	Metronidazole Cysts removed by filtration, killed by boiling, iodine, not chlorination.

Cryptosporidium *(Nonbloody diarrhea)*

Cryptosporidiosis in immunocompromised- watery nonbloody diarrhea, fluid loss, Malnutrition		**Fecal-oral transmision** of oocysts from **human/animal** sources.	Complex cycle occurs in epithelial cells of jejunum, NO invasion	ID **kinyoun acid-fast** (red) oocytes in stool smear.	**No effective therapy. Try azithromycin**

Trichomonas vaginalis *(NO cyst form)*

Trichomoniasis- vaginal itching w/ watery **foul smelling, green** vaginal discharge. Men asymptomatic.	**No cyst. Pear shaped trophozoites, 4 anterior flagella, undulating membrane** (jerky movement) 25-50% sexually active women infected	Sexual contact.	Infects vagina, prostate. Predisposing factor is loss of vaginal acidity		Both partners: **metronidazole**

PROTOZOA – BLOOD and TISSUE

Plasmodium

Diseases	Characteristics	Habitat/Trans	Pathogenesis	Diagnosis	Treatment
Malaria- fever, chills, HA, myalgias, arthralgias two wks post bite. Fever spikes accompanied by nausea, vomiting, abdominal pain, **drenching sweats. Splenomegaly** is common. **Anemia** due to **lysis of RBCs, splenic sequestration** of damaged RBCs. P. *falciparum* causes most severe malaria-can infect RBCs at all stages and causes adherence of RBCs to cerebral vascular endothelium via **knob proteins ("cerebral malaria".)** P.*ovale*, P. *vivax* cause **benign malaria**. P. *malariae* produces fevers each 72 hours, others every 48 hrs. P. *falciparum* can cause almost constant fever.	Endemic to 91 countries, 300-500 million cases, mostly **sub-Saharan Africa.**	Female ***Anopheles*** mosquito	**Asexual Schizogony** in humans Exoerythrocytic phase: Mosquito injects **sporozoites** which attack **hepatocytes**, sporozoites replicate, differentiate into **merozoites** which infect RBCs. Erythrocytic phase: **Merozoites** in RBCs, diferentiate into **ring shaped trophozoites,** develop into **schizonts** filled with merozoites. Merozoites lyse RBCs **at regular intervals** and further infect RBCs. **Sexual Sporogony** in mosquitoes Some blood merozoites develop into male/female **gametocytes** in RBCs. Female mosquito eats these RBCs, form one female **macrogamete** or 8 spermlike **microgamete** in gut. **Diploid zygote** differentiates into **motile ookinete** which burrows through gut wall. **Oocyst** w/ haploid **sporozoites** form on stomach wall, sporozoites released and migrate to mosquito **salivary glands.** Female mosquito injects **sporozoites** into next human victim (sucker.)	**Thick and thin Giemsa stained smears**. Usually ring shaped trophozoites are ID.	Acute malaria w/ **chloroquine** which kills merozoites, sporozoites in blood. **Mefloquine** used in P.*falciparum* resistant to chloroquine. **Primaquine** to get **hepatic** stages of P. *ovale* and P. *vivax.* Prophylax w/ chloroquine/ mefloquine. Prevent w/ **pyrimethamine** impregnated bednets. (kills mosquito cycle)

Toxoplasma gondii

Toxoplasmosis- usually asymptomatic, can cause hererophil antibody-negative **infectious mononucleosis.** Life threatening encephalitis in immunocompromised b/c **reactivation of dormant cysts. Transplacental transmission** results in stillbirth or fetal infection (encephalitis, retinitis, microcephaly, mental retardation)	5-50% seropositivity rate in US	Cat host. Humans eat **cysts in meat or cat feces**	Cysts rupture and invade gut mucosa, ingested by macrophages, differentiate into tachyzoites (rapidly multiplying trophozoites), disseminate to **brain, muscle.**	**Serology** or crescent shaped trophozoites	**Sulfadiazine and pyrimethamine**

Trypanosoma cruzi *(Chagas disease)*

Chagas diesease- Acute: edematous nodule (Chagoma) at bite site (**periorbital,** perioral), fever lymphadenopathy, H/Smegaly, resolves in 2 months **Indeterminate**- low levels of parasitemia, serological evidence of infection **Chronic- myocarditis** (arrythmia, dilated cardiomyopathy, CHF), **megacolon, megaesophagus**. Death usually by arrythmia.	**Rural Central and South America, Southern US**	**Humans, animal reservoirs. Reduviid** (kissing) bug as vector	Reduviid bug ingests **trypomastigotes** from animal's blood, trypomastigotes multiply in gut, **excreted** at bite, invade skin, disseminate in blood, amastigotes proliferate **inside macrophages and myocardium,** amastigotes differentiated into blood borne trypomastigotes which are taken up by reduviid bug at next meal.	**Thick and thin** blood smears for trypomastigotes. **Serology Muscle biopsy** revealing amastigotes. **Xenodiagnosis**	**Nifurtimox** kills trypomastigotes, NO therapy for chronic form.

Trypanosoma gambiense/rhodesiense ***(African sleeping sickness)***					
Trypanosomal chancre (many organisms) at bite site. **African sleeping sickness- Cyclical fever**, **lymphadenopathy, demyelinating encephalitis,** HA, insominia, slurred speech, ataxia, mood changes, **somnolence**, coma.	Trypomastigotes, **no amastigotes.** **Sub-Saharan Africa**	**Tsetse fly** vector. **"Sleep-Sleep fly"** Human and **animal** reservoirs.	Skin to blood/LN to CNS **Antigenic variation** of **VSGs** –variable surface glycoproteins	ID trypomastigotes in **blood smear**, LN or CSF.	**Suramin** in pre encephalitis stage. **Melarsoprol** for CNS involvement.
Leishmania donovani ***(Kala-azar)***					
Kala-azar (visceral leishmaniasis)- RES involvement. Chronic low grade fever, anorexia, weight loss, **skin hyperpigmentation.** Bone marrow involvement results in **anemia, leukopenia, thrombocytopenia** and **secondary infections, coagulopathies. Massive splenomegaly.** Disease lasts months to years.	Mediterranean/ Middle East, Saharan Africa, India	**Sandfly vector. Dog, fox, rodent reservoirs**	Female sandfly **ingests macrophages** containing **amastigotes,** amastigotes differentiate into **promastigotes** in sandfly gut, multiply, migrate to **pharyx,** transmitted to humans w/ bite, in human **macrophages** promastigotes differentiate back into amastigotes.	ID amastigotes **in spleen, LN, BM biopsy**. **Leshmanin** DTH skin test negative, poor cellular response.	**Sodium stibogluconate**
Leishmania tropica, mexicana, braziliensis ***(Cutaneous, mucocutaneous)***					
Ulcers confined to **skin/mucous membranes**, often **superinfected** by bacteria. Multiple satellite nodules coalesce and ulcerate. **In diffuse cutaneous leishmaniasis,** lesions grow/spread all over skin. **Disfiguring granulomatous lesions** destroy **nasal cartilage** (like lepromatous leprosy) L. *tropica* – Cutaneous – Old world L. *mexicana* – Cutaneous – Americas L. *braziliensis* – Mucocutaneous -- Central/South America		**Sandfly vector. Forest rodent reservoirs**	Basically like L. *donovani*	ID **amastigotes in skin lesions**	**Sodium stibogluconate**
Pneumocystis carinii ***(PCP)***					
Pneumonia- acute fever, nonproductive cough, dyspnea, tachypnea. CXR shows **diffuse, bilateral infiltrates** or may be normal. **Untreated cases fatal.**	**Classified as a fungus**	Inhalation of **cysts. NOT person-person**	Cysts establish life long latent infection in lungs. In immunocompromised, **cysts reactivate** and induce exudative inflammation which compromises gas exchange in the alveoli.	**Silver stained** induced **sputum** specimen, **bronchoalveolar lavage fluid, bronchial tissue biopsy** reveal *pneumocystis.*	**TMP-SMZ** **Pentamidine** Prophylax when CD4 < 200

CESTODES — *Hermaphroditic flatworms*

Taenia solium *(Pork tapeworm)*

Diseases	Characteristics	Habitat/Trans	Pathogenesis	Diagnosis	Treatment
Cysticercosis- HA, vomiting, seizures, uveitis, retinitis **Taeniasis**- usually asymptomatic	**Solex w/ 4 suckers, circle of hooks**		Gravid proglottids ingested by pigs (intermediate hosts), develop into larvae which burrow holes in blood vessels, go to skeletal muscle. Humans eat raw pork containing **cysticerci** (encysted larvae), mature in gut. If humans eat eggs, larvae spread to **eyes/brain** where they encyst to form cysticerci. **Space filled/calcified lesions.**	**ID gravid proglottids w/ 5-10 uterine branches** in stool. Cysts by Xray or CT. Larvae may be **floating in vitreous.**	**Niclosamide** **Praziquantel** Treat asymtomatics to prevent autoinnoculation, **cysticercosis**

Taenia saginata *(Beef tapeworm)*

Taeniasis- asymptomatic **No cysticercosis** in humans	**Solex w/ 4 suckers, no hooklets**		Same life cycle, except cattle host.	**Gravid proglottids w/ 15-25 uterine branches.** (remember COWS are bigger than PIGS, more branches)	**Niclosamide** **Praziquantel**

Diphyllobothrium latum *(Fish tapeworm)*

Mostly asymptomatic or Megaloblastic anemia (B12 deficiency) due to preferred uptake of B12 by worm.	**Solex w/sucking grooves, no hooks. Gravid uterus in rosette form. Eggs oval w/ operculum.** (diagnostic)	**Scandinavia** and Japan.	Eggs in fresh water, ingested into **crustaceans,** differentiate into larvae for **fish**. Humans infected by eating **undercooked fish.**		**Niclosamide** **Praziquantel**

Echinococcus granulosus *(Dog tapeworm)*

Unilocular hydatid cyst disease- usually **asymptomatic**, may cause hepatic dysfunction. Cyst contents cause **anaphylaxis**	**Scolex and 3 proglottids** (small)	**Dogs definitive hosts, sheep intermediate, humans dead end.**	Worms in dog intestine dump eggs, ingested by sheep or humans. **Oncospheres** form and spread to organs (**liver**), form **hydatid cysts.** Dogs eat slaughtered sheep, cycle complete		**Niclosamide** **Praziquantel** Stop feeding the dogs sheep bits!

Hymenolepsis nana *(Dwarf tapeworm)*

Usually asymptomatic	Most common tapeworm in US, esp. **SE USA**	No intermediate host	Eggs directly infectious for humans. **Many worms found**, unlike others which exist singly	Eggs in stool	**Niclosamide** **Praziquantel**

TREMATODES *Flukes*

Schistosoma *(snails)*

Diseases	Characteristics	Habitat/Trans	Pathogenesis	Diagnosis	Treatment
Schistosomiasis- itching at site of penetration ("swimmer's itch"), fever, chills, diarrhea, lyphadenopathy, **eosinophilia**. Chronic infection leads to GI hemorrhage, H/Smegaly, death by **ruptured esophogeal varicies.** **S. *haemoatobium*** infection can cause **bladder cancer.**	Schistosomes are separate sexes that live attached to each other. **Females reside in male grooves.** 200 million cases worldwide		**Free swimming cercariae penetrate human skin,** differentiate into larvae, enter venous circulation, mature into adult form. Females lay eggs spread to **gut or bladder**, excreted in **feces or urine.** Eggs hatch in fresh water, **penetrate snails**, differentiate to **free swimming cercariae.** Pathogenesis mediated by host granuloma response to antigenic **eggs** in organs. Schistosomes coast themselves in host antigens, **immune evasion.**	**Characteristic eggs in feces, urine.**	**Prizaquantel**

Trematode	Affected veins	Eggs	Endemic areas
S. *mansoni*	**L**arge intestine	**L**arge lateral spine	Africa, Caribbean
S. *japonicum*	**S**mall intestine	**S**mall lateral spine	Orient
S. *haematobium*	Bladder	Large **Terminal** spine	Africa, Mid East

(think of bladder as **terminal** organ of GU system)

Chlonorchis sinensis *(snails, fish)*

Oriental liver fluke- mostly asymptomatic, or upper abdominal pain, anorexia, hepatomegaly, **eosinophilia** with high worm burden		**Korea, China, Japan**	Humans infected by eating **undercooked fish** containing encysted larvae. Larvae excyst in duodenum, immature flukes enter **biliary ducts**. Host inflammatory response causes **hyperplasia/fibrosis of biliary tree.** Adults pass eggs in feces. Eggs eaten by **fresh water snails** (1st intermediate host), hatch in snail gut into **free swimming cercariae**. Cercariae encyst under scales of **fish** (2nd intermediate host) and cycle repeats	**Typical operculated eggs in stool**	**Prizaquantel**

Paragonimus westermani *(snails, crabs)*

Lung fluke- chronic cough w/ **bloody sputum** (resembles TB), Dyspnea, pleuritic chest pain, recurrent **secondary bacterial pneumonias.**		**Orient, India**	Humans eat **undercooked crabs**, containing encysted larvae which excyst in small intestine. Larvae penetrate intestinal wall and **through diapragm into lung.** Adults make eggs which are coughed up, swallowed, excreted into fresh water. Eggs develop into miracidia and enter **fresh water snails** (1st host) in which they develop into **free-swimming cercariae** which enter **crabs** (2nd host) and cycle repeats.	ID **operculated eggs in sputum or feces**	**Prizaquantel**

NEMATODES - INTESTINAL *Roundworms*

Enterobius vermicularis *(Pinworm)*

Diseases	Characteristics	Pathogenesis	Diagnosis	Treatment
Perianal itching	Life cycle confined to humans	Humans infected by ingesting eggs. Eggs hatch in small intestine, larvae migrate to colon. Male/female mating, **female migrates to anus at night to release eggs.** Larvae carried to mouth my fingers which have scratched itchy skin, cycle repeats	**Recover eggs by famous Scotch tape method** **Eggs NOT in stool**	Mebendazole kills adults.

Trichuris trichiura *(Whipworm)*

Mostly asymptomatic, maybe diarrhea	Worldwide, **Southern US**	Humans eat eggs in **soil** contaminated with **human feces.** Adult worms burrow into intestinal mucosa, **do not cause anemia**, unlike hookworms	**Eggs in stool**	Mebendazole

Ascaris lumbricoides

Ascariasis- mostly asymptomatic, but **ascaris pneumonia** can result from damage of **larvae migration through lung, inducing inflammation with eosinophilic exudate**	Common in tropics. Largest nematodes, 25cm.	Humans eat eggs in **soil** contaminated with **human feces.** Eggs hatch in small intestine, larvae migrate through gut mucosa into bloodstream to lungs, coughed up and swallowed. Mature in small intestine, persist in lumen, **do not attach, live off ingested food.** Thousands of eggs laid daily, passed in feces, form embryos in warm soil. Human ingestion completes cycle.	ID corrugated eggs in Stool	**Mebendazole** Pyrantel pamoate

Ancylostoma/Necator *(Hookworm)*

Microcytic anemia- weakness pallor, pneumonia with eosinophilia		Cycle like *Ascaris*, except *larvae* in soil penetrate skin. Adults use cutting plates to attach to intestine. Major damage is by **loss of blood**.	Eggs in stool.	**Mebendazole** Pyrantel pamoate

Strongyloides stercoralis

Strongyloidiasis- mostly asymptomatic, **pnemonitis can occur,** and gut mucosal damage. **<u>Eosinophilia can be striking.</u>**	**Tropics, SE Asia, Southern US**	Two life cycles. One in humans, one in soil. Infectious **larvae penetrate skin, migrate to lungs, alveoli, trachea** where they are swallowed. In small intestine, larvae become adults, enter mucosa and produce eggs. Eggs hatch, larvae passed in stool. In **soil**, larvae differentiate into male/females, mate, produce **infectious larvae.**	**LARVAE, not eggs in stool**	Thiabendazole

Trichinella spiralis

Trichinosis- Gastroenteritis, followed 1-2 wks later with fever, muscle pain, **periorbital edema, eosinophilia.**	Worldwide, esp. E. Europe, W. Africa	**Pigs reservoir in US.** Infection by eating raw pork (or Bear!) containing larvae encysted in muscle. Adult forms arise and release larvae into blood with dissemination to organs. **Larvae only develop in striated muscle.**	**Muscle biopsy.**	No Treatment for trichinosis. **Thiabendazole for early infections** kills adult worms.

NEMATODES - TISSUE — *Roundworms*

Wuchereria bancrofti *(Filariasis)*

Diseases	Characteristics	Pathogenesis	Diagnosis	Treatment
Filariasis- adult worms cause obstruction of lymphatics, causing **edema.** Fever, lymphangitis, cellulitis develop. **Elephantiasis-** occur in patients repeatedly infected.	Tropics, 200-300 million infected	**Female *Anopheles* mosquito** deposits infective larvae on skin while biting. Larvae penetrate skin, enter LN, mature **one year later** into adults that produce **microfilariae. These circulate in blood, esp. at night**, and are ingested by mosquitoes in which they produce infective larvae. Microfilariae do NOT cause symptoms	**Thick blood smears taken at night** show microfilariae	**Diethylcarbamzaine** effective vs. microfilariae. No tx vs. adults

Oncocerca volvulus *(River Blindness)*

Subcutaneous inflammation, pruritis, papules, nodules form in response to adult worm proteins. Microfilariae migrate through tissues, ultimately concentrating in the eyes. Leads to **blindness.**	Millions infected in Africa, Central America	**Female blackfly** (THINK BLACK=blindness)deposits infective larvae on skin while biting. Larvae enter wound, migrate to subcutaneous tissue, where they differentiate into adults in **dermal nodules.** Female produces microfilariae that are ingested when another blackfly bites. Microfilariae develop into infective larvae to complete the cycle.	**Microfilariae in tissue biopsy**	Ivermectin vs. microfilariae. Suramin vs. adults.

Loa loa

Loiasis- hypersensitivity rxn results in localized subcutaneous edema. Adult worm may be seen **crawling across conjuctiva,** usually harmless.	Only tropical central and western **Africa**	**Deer fly (mango fly)** deposits infective larvae on skin. Larvae enter wound, wander around body, develop into adults. Females release **microfilariae** which enter blood **during the day** (compare to *Wuchereria*). Deer fly infests microfilariae which differentiate into infective larvae.	**Microfilariae in blood smear**	**Diethylcarbamazine**

Dracunculis medinensis *(Guinea fire worm disease)*

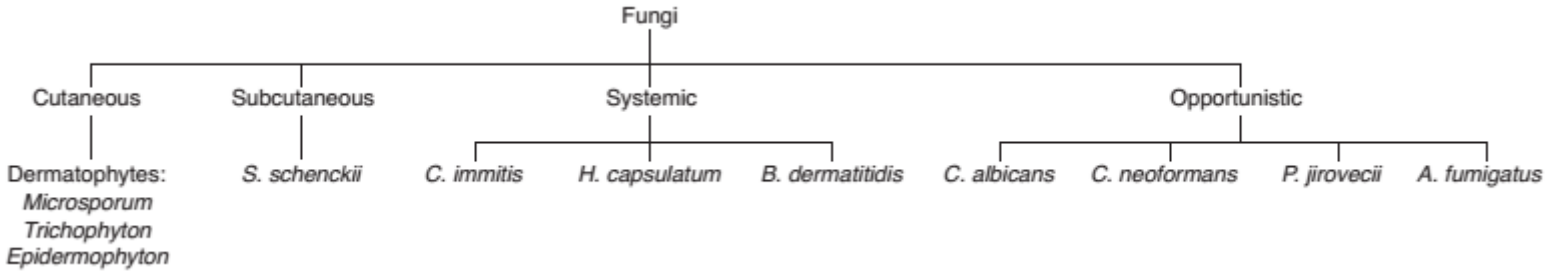
Dracunculiasis- worm protrudes from skin ulcer, wind up on stick over days.	**W.H.O. says just 17 countries have this disease as of 4/3/98. All in Africa.** (109 countries *Dracunculis free!)*	Humans infected by tiny crustaceans (copepods) swallowed in drinking water. Larvae released in small intestine, migrate to body, develop into adults. Adult females ulcerate skin, release larvae which are eaten by copepods.		Wind worm up on a stick over days.

Toxocara canis *(Visceral larva migrans)*

Visceral larva migrans- Blindness due to retinal involvement. Fever, hepatomegaly, eosinophilia are common.	**Dog is definitive host**	Dog sheds T.*canis* in eggs in soil. Humans eat eggs, hatch in small intestine, larvae migrate to organs (**eyes, liver, brain**), but are eventually encapsulated and die. Life cycle NOT completed in humans (**dead end host**.)	Larvae in tissue. **Hypergammaglobulinemia, eosinophilia.**	Diethylcarbamazine

MYCOLOGY

ALGORITHM FOR FUNGI



FUNGUS MORPHOLOGIES CHART

	FUNGUS	YEAST FORM	MOLD FORM
Cutaneous/ Subcutaneous	**Tinea:** (*Malassezia furfur, Exophiala weneckii)*	Spherical yeast	Branched Hyphae
	Dermatophytoses: (*Microsporum, trichophyton, epidermophyton)*	NONE	Branched hyphae w/ macro and microconidia
	Sporotrichosis	Round or cigar shaped budding yeast	**Branched hyphae w/ oval conidia at tip of conidiophores ("daisies")**
Systemic	**Coccidioides**	"Spherule" containing endospores	Branched hyphae w/ alternating **arthrospores** and empty cells
	Histoplasma	Oval budding yeast INSIDE macrophages	Branched hyphae w/ macro and microconidia
	Blastomyces	Round yeast w/ **doubly refractive wall**, single broad based bud	Branched hyphae w/ small conidia
	Paracoccidioides	Round yeast w/ thick wall and multiple buds	Branched hyphae w/ small conidia
Opportunistic	**Candida**	Oval yeast w/ single bud and "psuedohyphae" C. *albicans* germ tubes w/ chamydospores at 37°C	NONE
	Cryptococcus	Oval budding yeast w/ polysccharide capsule	NONE
	Aspergillus	NONE	**V-shaped septate** hyphae w/ radiating chains of conidia
	Mucor/Rhizopus	NONE	**Right-angle branched** nonseptate hyphae w/ sporangium

SUPERFICIAL MYCOSES — *Spherical yeasts, branched Hyphae*

Malassezia furfur

Diseases	Diagnosis	Treatment
Tinea versicolor- chronic superficial skin infection w/ hypo or hyperpigmented areas. **Asymptomatic** lesions identified by **pigment changes/failure to tan. More frequent in hot/humid** weather	**Branched hyphae, spherical yeasts in KOH** treated skin scrapings	**Selenium sulfide shampoo, imidazoles**

Exophiala werneckii

Tinea nigra- chronic superficial infection, black lesions on **palms and Soles**	**Branched hyphae, spherical yeasts in KOH** treated skin scrapings	**Selenium sulfide shampoo, imidazoles**

CUTANEOUS MYCOSES — *No Yeast / Branched Hyphae, micro/macroconidia*

Dermatophytoses: *Microsporum spp., Trichophyton spp., Epidermophyton floccosum*

Diseases	Habitat/Trans	Pathogenesis	Diagnosis	Treatment
Puritic papules, vesicles, Hypersensitivity to fungal antigens may present as "**dermatophytid"** rxns (NOT an infection! NO hyphae/organisms) Chronic infection esp. w/ **heat/humidity.** **Tinea corporis-** ringworm – body **Tiniea cruris –** jock itch- groin **Tinea pedis-** athlete's foot- toes **Tinea capitis-** head **Tinea unguium-** onychomycosis- nails **Tinea barbae-** beard	Infect superficial keratinized structures, **skin, hair, nails.** **Spread by direct contact.**	**Keratinase-** results in scaly skin, hair loss, brittle nails	**Branched hyphae** in KOH treated skin/nail scrapings. **Wood's light** for some ***Microsporum***	Topical **imidazoles.** Tinea capitis, barbae, unguium, w/ oral **griseofulvin** (hair/nail involvement)

SUBCUTANEOUS MYCOSES — *Round/Cigar budding yeast/ Branched hyphae w/ oval conidia at tip of conidiophores*

Sporothrix schenckii *(gardener's disease)*

Diseases	Habitat/Trans	Diagnosis	Treatment
Causes local pustule/ulcer with nodules along draining lymphatics (think linear distribution)	Soil/vegetation (thorns, splinters) **Gardeners at risk.** Introduced by **trauma**	**Round or cigar shaped budding yeasts in tissue or 37' Branching hyphae w/ oval conidia** at tip of conidiophores at **25'**. (like a daisy—Think of a**Gardener planting daisies smoking a cigar!)**	**Potassium Iodide** Amphotericin B

SYSTEMIC MYCOSES — *Dimorphic Fungi*

ALL dimorphic, YEASTS in humans (molds in dirt), Human infection by **SPORE inhalation**, so **NO Person-Person transmission** (remember yeasts DO NOT make spores), **most infections asymptomatic or mild pneumonia.** Dissemination results when **IMMUNOCOMPROMISED.** Grows as **MOLD (mycelia w/ spores) at 25'C in Sabouraud's agar** and as a **YEAST** at **37'C in blood agar.** Diagnosis by serology or biopsy/culture w/ **silver stain.** DTH tests useful to **RULE OUT** diagnoses. Systemic mycoses need the BIG GUNS: **amphotericin B or itraconazole**

Coccidioides immitis *(SW USA, Latin America)*

Diseases	Characteristics	Habitat/Trans	Pathogenesis	Diagnosis	Treatment
Coccidiomycosis- mild lung infection, usually asymptomatic or mild pneumonia. Dissemination leads to bone granulomas or **meningitis**. 10% develop **erythema nodosum** (red tender nodules on extensor surfaces, indicated **DTH rxn to fungal antigens – NO** organisms in lesions**) and arthragias- "valley fever", "desert rheumatism"**	In soil, hyphae with alternating **arthrospores** and empty cells. "**Spherules"** in tissue	Endemic in **arid** parts of **SW USA, Latin America.**	**Arthrospores are inhaled.** **Arthrospores** make **spherules w/ doubly refractive wall** filled with **endospores.** On rupture, endospores released to form new spherules which spread by direct extension or via blood.	**Skin tests w/ coccidiodin or spherulin**	Amphotericin B Itraconazole

Histoplasma capsulatum *(Ohio and Mississippi river valleys)*

Histoplasmosis- asymptomatic infrection or mild pneumonia, disseminated in immunocompromised	NO capsule. Two kinds of asexual spores: tuberculate **macroconidia, microconidia**	Worldwide, but endemic to **Ohio, Mississippi river valleys**. (Think **OHI**st**O**plama) **Bird/bat** droppings in soil.	**Inhaled** microconidia **develop into yeasts** within macrophages**.** (**Hi**stoplasma **Hi**des in macrophages) **Spreads quickly, calcified granulomas.**	**ID budding yeasts WITHIN macrophages.** DTH skin test w/ **histoplasmin**	Amphotericin B Itraconazole

Blastomyces dermatitidis *(East of Mississippi, Central America)*

Blastomycosis- ALMOST ALWAYS SYMPTOMATIC! (IT BLASTS YOU!) - disseminates w/ fever, night sweats, weight loss, skin and lung **granulomas**	**Round yeast w/ doubly refractive wall** (like coccidio) **, single broad based bud**	**East of Missisippi, and Central America.** **Soil, rotton wood.**	**Inhaled conidia**		Amphotericin B Itraconazole

Paracoccidiodes brasiliensis *(rural Latin America)*

Asymptomatic lung lesions, **mild** pneumonia	**Thick walled yeast, multiple buds**	**Latin America** Soil fungus	**Spores** inhaled		Amphotericin B Itraconazole

OPPORTUNISTIC MYCOSES — *All Monomorphic*

Candida albicans *(yeast only)*

Diseases	Characteristics	Habitat/Trans	Pathogenesis	Diagnosis	Treatment
Vulvovaginitis- vaginal itching/discharge, favored by high pH, diabetes, antibiotics, oral contraceptives, menses, pregancy **Cutaneous candidiasis-** skin invasion favored by warmth, moisture: inframammary folds, groin **Oral thrush-** white exudate in immunocompromised **Esophogeal candidiasis-** AIDS defining illness w/ substernal chest pain, dysphagia **Disseminated candidiasis-** Immunocompromised and IVDA	**Oval yeast w/ single bud.** Can appear as **"pseudohyphae"** w/in tissue	**Normal flora** of upper respiratory, GI, female GU, so NO person-person transmission. NEVER in the blood		**C.*albicans*** differentiated from other *Candida* by **germ tubes in serum at 37'C and chlamydospores.** Skin tests are positive in normal adults, indicator of good **cellular immunity.**	Skin infections w/ topical clotrimazole, vaginitis w/ imidazole suppositories, oral thrush w/ "swish 'n swallow" nystatin, systemic candidiasis w/ amphotericin B

Cryptococcus neoformans *(yeast only)*

Usually asymptomatic, can cause pneumonia, bone/skin granulomas. Dissemination causes **cryptococcal meningitis, subacute.**	**Oval budding yeast w/ wide polysaccardide capsule (India ink stain)**	Soil w/ **pigeon crap.** (Think: crypto**COCCUS**= pigeon **CACA**)	Humans inhale Yeast	**CSF culture, cryptococcal antigen test, India Ink stain**	Meningitis takes 6+ months of amphotericin B, Flucytosine Document care via serial lumbar punctures

Aspergillus fumigatus *(mold only)*

Invasive necrotizing pneumonia in AIDS, Molds grow in pulmonary cavities and produce **aspergilloma** (FUNGUS BALL), requiring **surgery.** Can also induce **allergic bronchopulmonary aspergillosis,** type I hypersensitivity rxn like asthma. **A.*flavus*-** *grows on* ***cereal or nuts*** *produces* ***aflatoxins (toxic, carcinogenic to liver)***	**Septate** hyphae, **V-shapted branches**. **Conidia form radiating chains.** (compare w/ *mucor/rhizopus)*	Saprophytic molds EVERYWHERE!	**Transmission by airborne conidia** colonize and invade **abraded skin,** wounds, burns, ear, cornia	Sputum culture, or Fungus Ball on CXR or CT	**Amphotericin B**

Mucor/Rhizopus *(mold only)*

Rhinocerebral mucormycosis- associated w/ diabetes, caused by infection of nasal mucosa with invasion of sinuses/orbit. Molds proliferate in walls of **blood vessels.** (Think **MUCOR**/Rhizopus invades **MUCOSA**)	**Nonseptate hyphae w/ broad irregular walls and right angle branches** (compare w/ *aspergillus)* Endospores inside of **sporangium**	Saprophytic molds EVERYWHERE!		Biopsy	Amphotericin B, Surgical resection


HUMAN
FOUNTAINS