PATHOPHYSIOLOGY · CHAPTER 19

Parts 3 & 4

Disease at the Cellular Level

Disease at the Tissue Level

Paramedic Program · Instructor Presentation with Teaching Notes

Part 3

Disease at the Cellular Level

1. The cell & membrane
2. Transport & tonicity
3. Fluids & electrolytes
4. Energy production
5. Adaptation & injury

The Cell

The basic unit of all living organisms

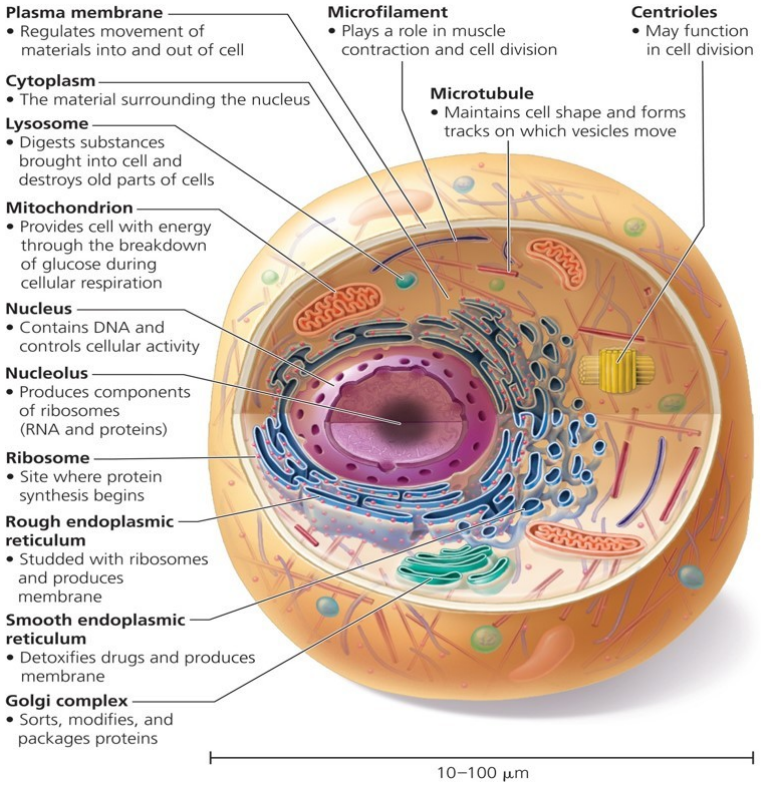

Figure 19-33 Generalized eukaryotic animal cell

P Prokaryotic

No true nucleus and no membrane-bound organelles — genetic material sits free in the cytoplasm. Bacteria are prokaryotes, which is exactly why antibiotics can attack them without destroying our cells.

E Eukaryotic

Contains a true nucleus and membrane-bound organelles that compartmentalize biological work. All human cells are eukaryotic; size range is roughly 10–100 micrometers.

Key vocabulary

Nucleus Control center; holds the cell's DNA

Organelle Specialized internal structure with a job

Cytoplasm Gel-like interior suspending the organelles

Cytosol / ICF The water component of cytoplasm

The Plasma Membrane

A phospholipid bilayer — the cell's gatekeeper

Structure

- Two layers of phospholipids arranged tail-to-tail
- Hydrophilic heads face outward toward ECF and inward toward cytoplasm
- Hydrophobic tails face each other in the middle
- Cholesterol and proteins embedded throughout
- Lipid-soluble substances cross easily; charged particles need a protein
- Selective, not sealed — "semipermeable"

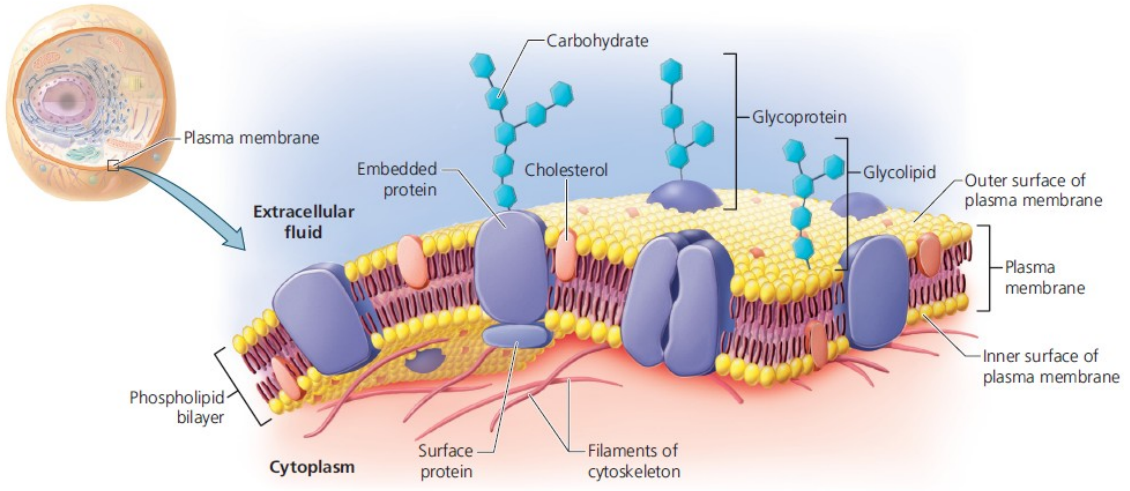

Figure 19-34 Detail of the plasma membrane

Four jobs of membrane proteins

1 Linkers

Anchor the cell to neighbors and the cytoskeleton.

2 Enzymes

Catalyze reactions at the membrane surface.

3 Receptors

Bind hormones and drugs; trigger internal change.

4 Transporters

Move specific substances across the membrane.

Cell Junctions and Communication

How individual cells become a working tissue

1 Tight junctions

Adjacent membranes fuse into a continuous seal, so nothing slips between the cells.

Found wherever a barrier must be absolute: the blood-brain barrier, the lining of the bladder, the gut epithelium.

2 Desmosomes

Rivets. Protein plaques anchored to the internal cytoskeleton hold neighboring cells together mechanically.

Concentrated in tissue that takes physical stress — skin, cervix, and the myocardium.

3 Gap junctions

Protein channels that connect the cytoplasm of one cell directly to the next, letting ions and small molecules pass between them.

This is how cardiac and smooth muscle cells share an electrical signal.

Cell adhesion and recognition

Cell adhesion molecules (CAMs) on the membrane surface let cells stick to one another and to the extracellular matrix. Cell-cell recognition is the related ability of a cell to distinguish one cell type from another — the basis of both tissue organization and immune self-recognition.

When cancer cells lose their adhesion molecules, they stop staying put. That loss is part of what makes a malignancy invasive.

Why the heart works the way it does

Cardiac muscle cells are joined by intercalated discs that combine both kinds of junction: desmosomes hold the cells together mechanically so the contraction does not tear them apart, and gap junctions let the depolarization wave pass cell to cell without a nerve.

That single anatomic arrangement is why the myocardium contracts as one unit, and why a single irritable focus can capture a whole chamber.

Transport Across the Plasma Membrane

Passive mechanisms need no energy; active mechanisms spend ATP

Mechanism	Energy	How it works	Field example
Simple diffusion	Passive	Molecules move down a concentration gradient until equilibrium is reached	O_2 and CO_2 across the alveolar membrane
Facilitated diffusion	Passive	Down the gradient, but requires a carrier or channel protein	Glucose entering most body cells
Osmosis	Passive	Water moves toward the higher solute concentration	Fluid shifting after a hypertonic dose
Active transport	ATP	Moves substances against the gradient using a carrier protein	Sodium–potassium pump maintaining membrane potential
Endocytosis	ATP	Membrane engulfs material and draws it inward in a vesicle	Neutrophil phagocytosing bacteria
Exocytosis	ATP	Internal vesicle fuses with the membrane and releases contents	Neurotransmitter release at a synapse

Why this matters in the field: Active transport is the first thing to fail when a cell runs out of ATP. The Na^+/K^+ pump alone consumes a large share of a resting cell's energy. Lose perfusion, lose ATP, lose the pump — sodium and water flood in, potassium leaks out, and the cell swells and dies.

The Sodium–Potassium Pump

The single most important example of active transport

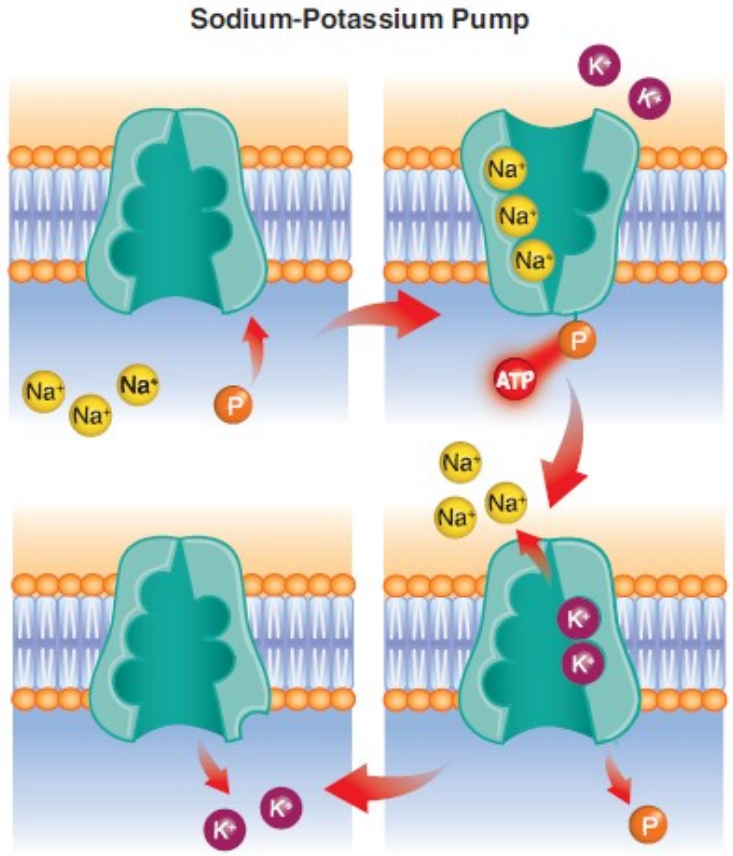

Figure 19-43 Sodium–potassium pump

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How it works

- Three sodium ions are pumped OUT of the cell
- Two potassium ions are pumped IN
- One molecule of ATP is spent per cycle
- Both ions move AGAINST their concentration gradients — this is why it costs energy
- Net loss of one positive charge from the interior helps make the inside of the cell negative

Why every ECG depends on this pump

The pump creates and maintains the resting membrane potential — the electrical gradient that makes depolarization possible. It also consumes a large share of a resting cell's ATP. Lose perfusion and the pump stops: sodium and water flood into the cell, potassium leaks out into the bloodstream, and the cell swells and dies. That single failure links shock, crush injury, prolonged arrest and hyperkalemia.

The Resting Membrane Potential

Where the ECG comes from

The gradient is stored energy

Because the sodium-potassium pump works continuously, a cell at rest holds potassium inside and sodium outside at very different concentrations. The membrane is far more permeable to potassium than to sodium, so potassium leaks outward and leaves negative charge behind.

The result is an electrical charge across the membrane — the resting membrane potential — of roughly −70 mV in a nerve cell and −90 mV in a cardiac myocyte, with the inside negative relative to the outside.

Spending it: the action potential

- A stimulus makes the membrane slightly less negative
- At threshold, voltage-gated sodium channels open and sodium rushes in — depolarization
- In cardiac and smooth muscle, calcium entry sustains the plateau and triggers contraction
- Potassium channels open and potassium exits — repolarization
- The Na^+/K^+ pump restores the original distribution, at the cost of ATP
- During the refractory period, the cell cannot be restimulated

Typical ion distribution across the membrane

Ion	Predominant location	Approximate serum range	Primary role
Sodium (Na^+)	Extracellular	135–145 mEq/L	Depolarization; extracellular osmolarity and water distribution
Potassium (K^+)	Intracellular	3.5–5.0 mEq/L	Sets the resting potential; repolarization
Calcium (Ca^{2+})	Extracellular and stored intracellularly	8.5–10.5 mg/dL	Excitation-contraction coupling; the coagulation cascade
Magnesium (Mg^{2+})	Intracellular	1.5–2.5 mEq/L	Enzyme cofactor; stabilizes cardiac conduction

Tonicity

Water follows solute — every time

↓ Hypotonic

Fewer solutes than the cell.

Water moves INTO the cell.

Cell swells and may lyse.

Example: 0.45% NaCl; D5W once dextrose is metabolized.

= Isotonic

Solute concentration equal on both sides.

No net water movement.

Cell stays normal.

Example: 0.9% NaCl, lactated Ringer's.

↑ Hypertonic

More solutes than the cell.

Water moves OUT of the cell.

Cell shrinks and crenates.

Example: 3% NaCl, mannitol.

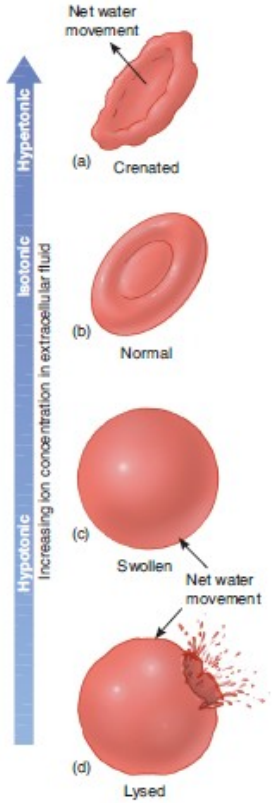


Figure 19-52 Effect on red cells

Related terms

- Osmotic pressure — the pressure osmosis generates
- Oncotic pressure — the share of it produced by plasma proteins
- Osmolarity — solute particles per liter of solution
- Osmolality — particles per kg of solvent; normal roughly 275–295 mOsm/kg

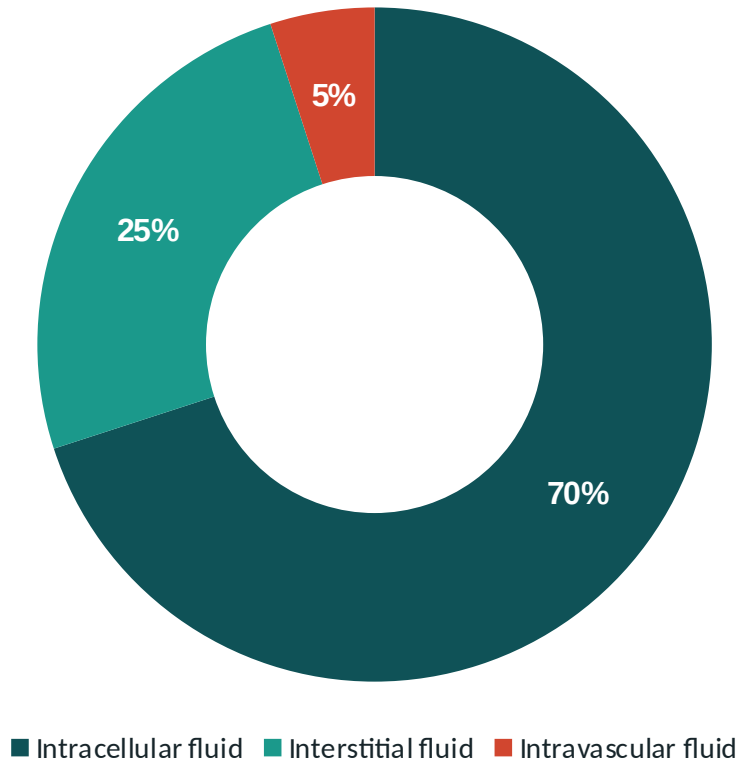
Field application

Choosing a fluid is choosing where the water will go. Isotonic fluid stays extracellular and expands volume. Hypotonic drifts into cells and does little for perfusion. Hypertonic pulls water out of cells — useful for cerebral edema, dangerous elsewhere.

Body Fluid Compartments

Water is about 60% of adult body weight — but it is not all in one place

Distribution of total body water (%)



60%

of adult body weight is water (total body water, TBW)

42 L

total body water in a 70 kg adult

29.4 L

sits inside cells — the intracellular compartment

2.1 L

is intravascular — the only volume we can reach with an IV

Age changes the math: infants are 75–80% water; older adults are lower. Both tolerate fluid loss poorly.

Fluid Imbalance

Intake must equal output — thirst is the primary regulator

- Dehydration

Abnormal decrease in total body water

Causes

- GI losses — vomiting, diarrhea, NG suction
- Increased insensible loss — fever, tachypnea, burns
- Increased sweating — exertion, heat exposure
- Internal (third-space) losses — bowel obstruction, ascites
- Plasma losses — burns, open wounds

Assessment findings

- Dry mucous membranes, poor skin turgor
- Excessive thirst, decreased urine output
- Tachycardia, orthostatic changes, delayed capillary refill
- Sunken fontanelle and absent tears in infants

+ Overhydration

Excess total body water

Causes

- Excessive or overly rapid IV fluid administration
- Renal failure with impaired excretion
- Heart failure with fluid retention
- Excessive ADH activity

Assessment findings

- Peripheral edema, JVD, weight gain
- Crackles, dyspnea, hypoxia from pulmonary edema
- Bounding pulses, hypertension
- In severe cases, frank heart failure

Electrolytes

Substances that dissociate into charged particles in water; measured in mEq/L

Cations (positive charge)

Sodium (Na^+) — Principal ECF cation; governs extracellular osmolarity and water distribution

Potassium (K^+) — Principal ICF cation; sets resting membrane potential — narrow safe range

Calcium (Ca^{2+}) — Muscle contraction, coagulation cascade, neurotransmitter release

Magnesium (Mg^{2+}) — Enzyme cofactor; neuromuscular and cardiac conduction stability

Anions (negative charge)

Chloride (Cl^-) — Principal ECF anion; follows sodium and helps maintain neutrality

Bicarbonate (HCO_3^-) — The body's primary buffer; central to acid–base balance

Phosphate (PO_4^{3-}) — Component of ATP and cell membranes; intracellular buffer

Potassium is the one that kills

Roughly 98% of total body potassium is inside cells. Because the gradient across the membrane is so steep, small shifts produce large changes in cardiac conduction. Crush injury, prolonged cardiac arrest, missed dialysis, DKA, and severe burns all dump intracellular potassium into the bloodstream. Peaked T waves, widening QRS, and a sine-wave rhythm are the ECG story of that gradient collapsing.

When Electrolytes Go Wrong

The four abnormalities most likely to be in front of you

Hyponatremia

Sodium too low

Causes Excess free water intake, SIADH, diuretics, adrenal insufficiency, endurance exercise with water-only replacement, psychogenic polydipsia.

Presentation Water shifts INTO cells, including brain cells. Nausea, headache, confusion, lethargy, and at low levels seizures. The signs are neurologic because the brain swells.

Hypernatremia

Sodium too high

Causes Dehydration with inadequate water intake, prolonged vomiting or diarrhea, diabetes insipidus, tube feeding without free water.

Presentation Water shifts OUT of cells. Thirst, dry mucous membranes, restlessness and irritability progressing to lethargy and seizures.

Hypokalemia

Potassium too low

Causes Diuretics, vomiting and diarrhea, poor intake, insulin therapy driving potassium into cells, alkalosis.

Presentation Weakness, cramping, ileus, and cardiac irritability. ECG may show flattened T waves, ST depression, and prominent U waves. Potentiates digoxin toxicity.

Hyperkalemia

Potassium too high

Causes Renal failure and missed dialysis, crush injury and rhabdomyolysis, extensive burns, DKA, prolonged cardiac arrest, potassium-sparing diuretics and ACE inhibitors.

Presentation Weakness and paresthesias, but the danger is cardiac. Peaked T waves, then a flattening P wave and widening QRS, then a sine wave and arrest.

Prehospital providers do not have lab values — recognize the history and the pattern, not the number.

Starling Forces and Edema

Filtration at the capillary is a tug-of-war between two pressures

Hydrostatic pressure

Blood pressure — the force generated by cardiac contraction pushing against the vessel wall. It PUSHES water out of the capillary and into the interstitial space (filtration).

Oncotic (colloid osmotic) pressure

Generated mainly by plasma proteins, especially albumin, which are too large to leave the vessel. It PULLS water back into the capillary. In health, filtration and reabsorption roughly balance — net filtration near zero.

Four ways that balance breaks — and edema results

1 Low oncotic force

Not enough plasma protein to hold water in.

Liver failure, malnutrition, nephrotic syndrome.

2 High hydrostatic pressure

Too much pressure pushing water out.

Heart failure, venous obstruction, fluid overload.

3 Leaky capillaries

Membrane permeability increases; protein escapes.

Sepsis, anaphylaxis, burns, inflammation.

4 Lymphatic obstruction

Drainage route is blocked.

Tumor, surgical node removal, filariasis.

Intravenous Fluids

Colloids and crystalloids behave very differently once they are in the vein

C Colloids

Contain proteins or other large molecules that cannot cross the capillary membrane, so they stay in the intravascular space and draw water in with them. Small volumes expand circulating volume substantially.

Examples: plasma protein fraction, salt-poor albumin, dextran, hetastarch.

Expensive, require storage, and are uncommon in prehospital use.

X Crystalloids

Water with dissolved electrolytes and no large molecules. They cross the capillary membrane freely and redistribute into the interstitial space within roughly an hour.

The primary compounds used in prehospital fluid therapy.

Isotonic, hypertonic, and hypotonic preparations exist — each with different indications.

Common prehospital crystalloids

Fluid	Tonicity	Typical prehospital use
0.9% sodium chloride (normal saline)	Isotonic	Volume replacement, medication dilution, keep-open access
Lactated Ringer's	Isotonic	Volume replacement; electrolyte profile closer to plasma; lactate is metabolized to bicarbonate
5% dextrose in water (D5W)	Isotonic in bag, functionally hypotonic in patient	Medication drips and free water; not a volume resuscitation fluid

Blood and Blood Components

The fluid of the cardiovascular system: plasma plus formed elements

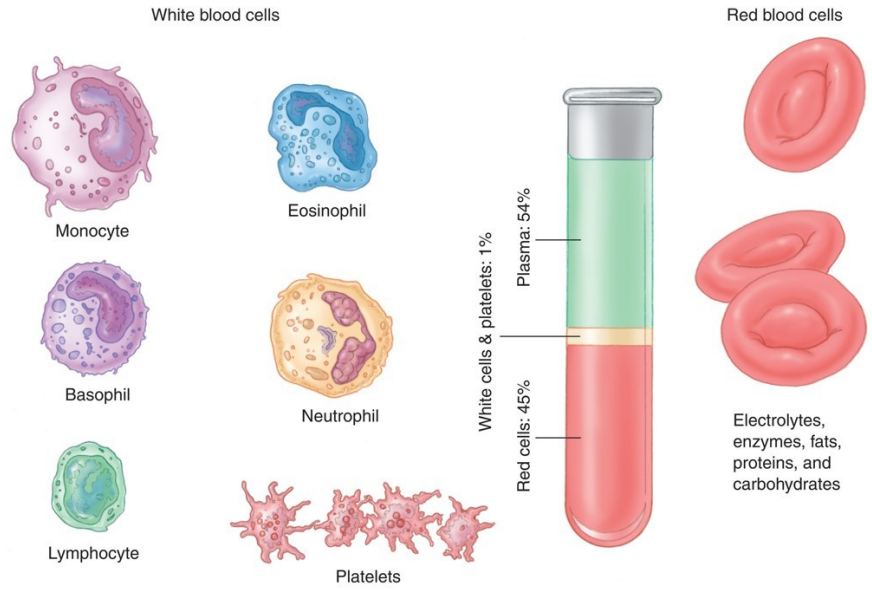


Figure 19-50 Blood components

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The formed elements

Erythrocytes (RBCs)
Carry oxygen bound to hemoglobin, an iron-based compound. About 99% of all blood cells.

Leukocytes (WBCs)
Immunity and infection control. Monocytes, neutrophils, basophils, eosinophils, lymphocytes.

Thrombocytes (platelets)
Initiate and support clotting.

Whole blood is roughly 54% plasma, 45% red cells (the hematocrit), and 1% white cells and platelets.

Transfusion and blood products

Whole blood is the ideal replacement for blood loss because it restores oxygen-carrying capacity as well as volume — something no crystalloid can do. Blood must be typed and crossmatched to prevent a transfusion reaction; O negative serves as the universal donor when there is no time. Transfusion reactions may present with fever, chills, hives, hypotension, tachycardia, flushing, headache, nausea, dyspnea, or loss of consciousness.

The Internal Cell: Organelles

Compartmentalized departments, each with a defined job

Nucleus

Largest organelle. Holds the cell's DNA on 46 chromosomes (23 pairs). Bounded by a double nuclear envelope pierced by nuclear pores.

Nucleolus

Region within the nucleus that produces ribosomal RNA.

Ribosomes

Sites of protein synthesis. Some float free in cytoplasm; others bind to the ER.

Endoplasmic reticulum

Rough ER carries ribosomes and processes protein. Smooth ER lacks them and handles lipid synthesis and drug detoxification.

Golgi apparatus

Sorts, modifies, and packages proteins for delivery.

Lysosomes

The cell's garbage disposal — digests foreign material and worn-out organelles.

Peroxisomes

Generate and degrade hydrogen peroxide; detoxify harmful substances.

Mitochondria

The powerhouses. Site of cellular respiration and the vast majority of ATP production.

From Gene to Protein

What the organelles are actually doing all day

1 Transcription

In the nucleus, a segment of DNA is read and copied into a strand of messenger RNA. DNA never leaves the nucleus — the working copy does.

2 Export

The mRNA passes out through a nuclear pore into the cytoplasm, carrying the instructions for one protein.

3 Translation

A ribosome reads the mRNA three bases at a time and assembles the matching amino acids into a polypeptide chain, joined by peptide bonds.

4 Processing

The chain folds and is modified in the rough ER, then travels to the Golgi apparatus, which sorts, modifies and packages it for delivery.

Why every cell is different

Every nucleated cell in the body carries the same 46 chromosomes and the same complete set of genes. A liver cell and a cardiac myocyte differ because they express different genes — they transcribe different sections of the same library.

That is what differentiation means, and it is why the loss of differentiation in cancer is such a serious finding.

Where drugs and disease intervene

- A genetic mutation is an error in the DNA that produces a faulty protein — sickle cell disease is one changed amino acid in hemoglobin
- Many antibiotics work by blocking bacterial ribosomes, which differ from ours
- mRNA vaccines supply a ready-made message so our own ribosomes build one viral protein for the immune system to learn
- Viruses hijack this entire pathway to build copies of themselves

The Cytoskeleton and Cell Movement

The internal scaffold — structure, transport and motion

1 Microtubules

Long hollow rods built from the protein tubulin. Maintain cell shape and act as tracks along which vesicles travel. They also form the spindle that separates chromosomes during cell division.

2 Microfilaments

Thinner strands made from the protein actin. Central to muscle contraction, to cell division, and to changes in cell shape and movement.

3 Intermediate filaments

Rope-like fibers that give the cell tensile strength and resist mechanical stress. They anchor desmosomes and hold the nucleus in place.

4 Centrioles

Paired cylindrical structures made of microtubule groups. Organize the spindle and function in cell division.

Surface projections

Cilia

Short, numerous hairlike structures that beat in a coordinated back-and-forth motion. They sweep debris and mucus away from the cell surface — the mucociliary escalator of the respiratory tract, and transport in the reproductive tract.

Flagella

Much longer than cilia and far fewer in number. They move in an undulating, wavelike manner to propel the cell itself. In humans, the only flagellated cell is the sperm cell.

Cellular Respiration

Aerobic metabolism: three stages, roughly 36 ATP per glucose molecule

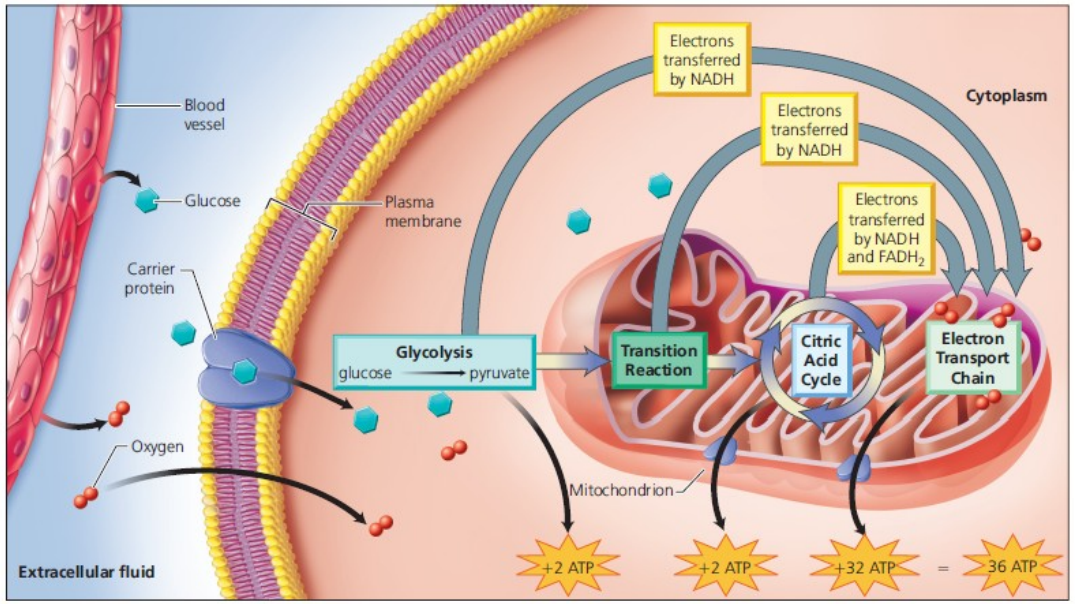


Figure 19-62 Summary of cellular respiration

1 Glycolysis — +2 ATP

In the cytoplasm. Glucose is split into two pyruvate molecules.

2 Citric acid cycle — +2 ATP

In the mitochondria. Krebs or TCA cycle. Fully oxidizes the rest of the glucose; releases CO_2.

3 Electron transport chain — +32 ATP

On the inner mitochondrial membrane. Oxygen is the final electron acceptor.

Fermentation — the anaerobic backup

Without oxygen, glycolysis continues but pyruvate becomes the final electron acceptor. Lactic acid fermentation yields only 2 ATP per glucose and produces lactate.

The 18-fold problem

Aerobic metabolism yields about 36 ATP; anaerobic yields 2. An oxygen-deprived cell runs on roughly one-eighteenth of its energy budget while its workload is unchanged. Pumps fail and lactate accumulates.

Cellular Adaptation

Physiologic and structural change in response to stress

1

Hyperplasia

Increase in the NUMBER of cells

Hormonal (puberty, pregnancy) or compensatory (liver regeneration after partial resection). Can also be pathological.

2

Hypertrophy

Increase in the SIZE of cells

Physiologic from increased demand (athlete's heart, skeletal muscle). Pathological from abnormal stress (LVH from chronic hypertension).

3

Atrophy

Decrease in the SIZE of cells

Disuse, reduced blood supply, loss of nerve supply, poor nutrition, loss of hormonal stimulation, aging.

4

Metaplasia

One adult cell type replaced by ANOTHER

Reversible and protective. Ciliated columnar airway epithelium replaced by squamous cells in a smoker.

5

Dysplasia

Abnormal, DISORDERED growth

Not a normal adaptation. More common in rapidly reproducing cells. A recognized precursor to cancer.

Adaptation is not failure. These changes are the cell's attempt to survive an altered environment. They become pathological when the stress is chronic, excessive, or the wrong kind — and dysplasia is the point where adaptation has crossed into disordered growth.

Cellular Adaptation — What It Looks Like

The same normal epithelium, responding five different ways

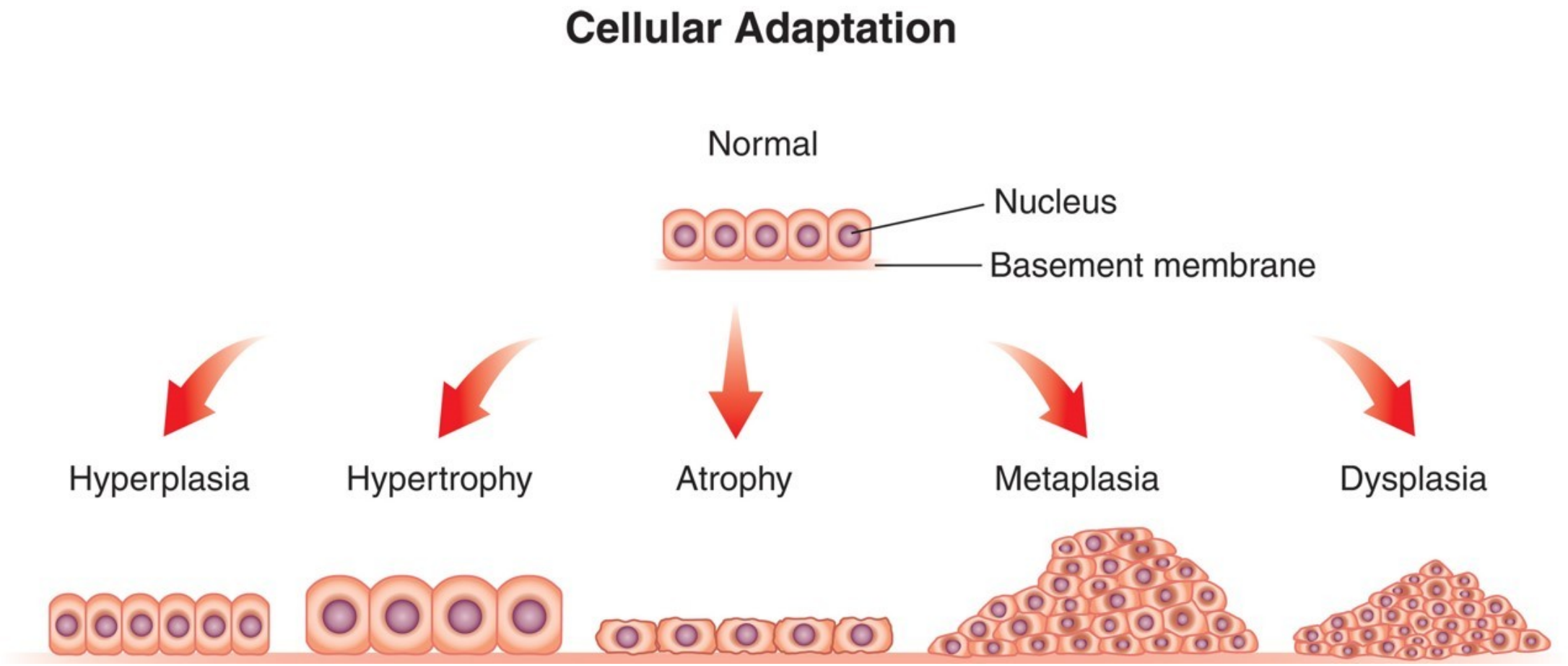


Figure 19-68 Abnormal cell responses to stress

Cell Injury

When a cell can no longer adapt

Ischemic and hypoxic injury

Ischemia — diminished blood flow. The delivery pipe is blocked.
Hypoxia — decreased availability of oxygen. The cargo is missing.

Either way, cellular respiration is impaired and energy production falls back to glycolysis alone. Ischemia is worse than pure hypoxia, because the blocked vessel also fails to remove accumulating waste.

Causes of cell injury

- Hypoxia and ischemia
- Physical agents — trauma, temperature extremes, radiation, electricity
- Chemical agents — toxins, drugs, poisons
- Infectious agents
- Immune and inflammatory reactions
- Genetic defects and nutritional imbalances

Oxidative stress and reperfusion injury

When blood flow is restored to ischemic tissue, oxygen free radicals are generated. A free radical steals an electron from a neighboring compound, creating a new radical — a chain reaction that can continue until cellular components are consumed. Some reversibly injured cells die anyway once flow returns.

Practice implication: titrate oxygen

Supplemental oxygen should be guided by pulse oximetry, not given reflexively. Hyperoxia increases free radical production and has been associated with worse outcomes in several conditions. Give oxygen to correct hypoxia — not as a ritual.

Reversible and Irreversible Injury

There is a point of no return — and our job is to reach the patient before it

R Reversible injury

Restore perfusion and the cell recovers

- ATP falls and the sodium-potassium pump slows — sodium and water enter
- Cellular swelling: the earliest visible change in any injured cell
- Ribosomes detach from the rough ER and protein synthesis declines
- Glycogen stores are consumed; lactate accumulates and intracellular pH falls
- Fatty change may appear in organs with high metabolic demand, such as the liver

I Irreversible injury

The cell dies whether or not perfusion returns

- Severe mitochondrial damage — ATP production cannot restart
- Membrane integrity is lost; the cell can no longer control its interior
- Lysosomal enzymes are released and begin digesting the cell from within
- Nuclear changes: the nucleus condenses, fragments, then dissolves
- Intracellular contents leak into the bloodstream — the source of every biomarker

Approximate tolerance to complete ischemia — why some minutes matter more than others

Tissue	Rough ischemic tolerance	Clinical consequence
Brain (neurons)	Minutes	The basis of the cardiac arrest and stroke time windows — "time is brain"
Myocardium	Tens of minutes	Infarct size grows with delay — "time is muscle"
Kidney and liver	Hours	Acute kidney injury after prolonged hypoperfusion or crush injury
Skeletal muscle	Several hours	Rhabdomyolysis and compartment syndrome after prolonged entrapment
Skin, bone, cartilage	Longest	Why a replanted digit can survive a long transport

Cell Death: Necrosis vs. Apoptosis

Two very different endings

N Necrosis

Cell murder — death from outside forces

- Caused by injury: ischemia, infection, toxins, trauma, temperature extremes
- The cell swells and ruptures
- Contents spill into surrounding tissue
- Provokes inflammation and can injure neighbors
- Always pathological

A Apoptosis

Programmed death — from within

- An internal program destroys nuclear DNA and selected cytoplasmic proteins
- The cell shrinks and breaks into apoptotic bodies
- Fragments cleared quietly by phagocytes
- Little or no inflammation
- Can be physiologic or pathological

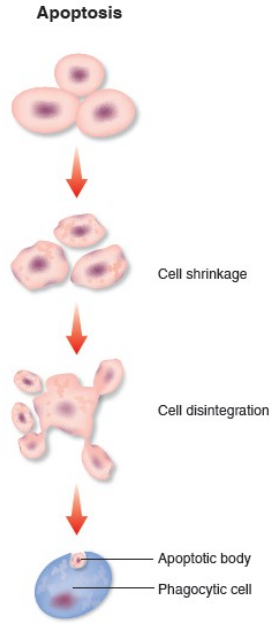


Figure 19-70 Apoptosis

Why the distinction matters: Necrosis is messy and inflammatory — it is why an infarcted myocardium releases troponin, why crush injury releases myoglobin, and why an ischemic bowel produces a systemic inflammatory response. Apoptosis is orderly; too little of it contributes to cancer, and too much contributes to neurodegenerative disease.

Part 3 — Key Takeaways

1

The membrane controls everything.

Selective permeability is what lets a cell maintain an internal environment different from its surroundings. Damage it and the cell loses control.

2

Water follows solute.

Tonicity determines where infused fluid goes. Isotonic stays extracellular and expands volume; that is why it is the resuscitation default.

3

Only about 5% of body water is intravascular.

That small compartment determines blood pressure, and it is the only one we can reach directly with an IV.

4

Oxygen is the final electron acceptor.

Without it, ATP production collapses from roughly 36 to 2 per glucose. This is the endpoint of every shock state.

5

Cells adapt until they cannot.

Hyperplasia, hypertrophy, atrophy, and metaplasia are survival strategies. Dysplasia is the point where growth has become disordered.

6

Necrosis is inflammatory; apoptosis is quiet.

The biomarkers we measure in the hospital are the contents of cells that ruptured rather than shut down in an orderly way.

Part 4

Disease at the Tissue Level

1. Origin of body tissues
2. The four tissue types
3. Neoplasia
4. Carcinogenesis
5. Tumor classification

Origin of Body Tissues

Roughly two weeks after conception, embryonic cells differentiate into three germ layers

1 Endoderm

The innermost germ layer. Gives rise to liver and associated ducts, pancreas, lining of the trachea, bronchi and alveoli, urinary bladder and part of the urethra, and epithelial linings of the thyroid and thymus.

2 Mesoderm

The middle germ layer. Gives rise to skeletal, cardiac and smooth muscle, bone and cartilage, kidney tissue, fibrous and adipose tissue, blood and lymph vessels, and blood cells.

3 Ectoderm

The outermost germ layer. Gives rise to skin, hair, nails and glands, lens and cornea, the entire nervous system including brain and spinal cord, the retina, adrenal medulla, and the meninges.

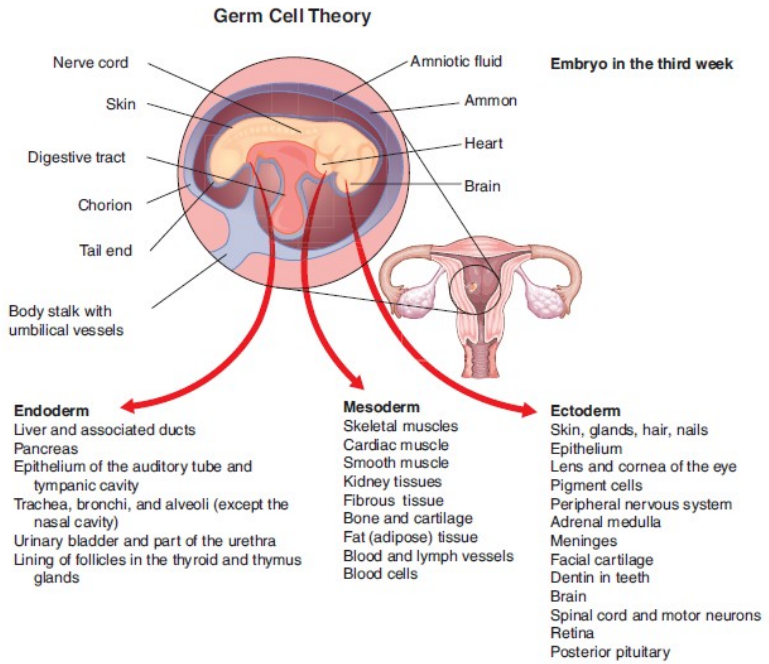


Figure 19-72 Embryonic germ layers

Why an EMS provider should care: Shared embryonic origin explains clinical patterns that otherwise look random. The adrenal medulla arises from the same ectodermal neural crest as the sympathetic nervous system — which is why it secretes epinephrine and behaves like a giant sympathetic ganglion. Congenital anomalies also cluster across organs that seem unrelated.

The Four Primary Tissue Types

Every organ in the body is built from combinations of these four

1 Epithelial

Covers internal and external body surfaces

- Provides physical protection
- Controls permeability
- Provides special senses
- Produces specialized secretions
- Avascular — nourished by diffusion from below
- Regenerates rapidly

2 Connective

Provides the framework everything else rests on

- Binds and supports other tissues
- Cells dispersed in an extracellular matrix
- Collagen, elastic and reticular fibers
- Includes bone, cartilage, blood and lymph
- Never exposed to the external environment

3 Muscle

Specialized for contraction

- Skeletal — voluntary, striated
- Cardiac — involuntary, striated, self-exciting
- Smooth — involuntary, non-striated
- Converts chemical energy into movement
- Moves the body and its contents

4 Nervous

Coordinates the body's activities

- Found in brain, spinal cord, peripheral nerves
- Conducts electrical impulses
- Neurons transmit the signal
- Neuroglia support and insulate neurons
- Least tolerant of hypoxia of any tissue

Which Tissues Heal, and Which Do Not

Regenerative capacity is the single most useful thing to know about a tissue

L Labile

Cells divide continuously throughout life, constantly replacing themselves.

Surface epithelium of skin and gut, bone marrow and blood cells, the lining of the respiratory tract.

Heal completely and quickly — and are the tissues chemotherapy and radiation damage most, because those treatments target rapidly dividing cells.

S Stable

Cells normally rest but retain the ability to divide when stimulated by injury.

Liver, kidney tubules, pancreas, smooth muscle, bone, fibrous tissue, vascular endothelium.

Can regenerate substantially — the liver is the classic example, capable of regrowing after partial removal.

P Permanent

Cells cannot meaningfully divide after development is complete.

Neurons of the central nervous system, cardiac muscle, and skeletal muscle to a large degree.

Do not regenerate. Injury is replaced by scar, which fills the space but does not do the job.

What scar actually costs you

Scar is fibrous connective tissue. It is strong and it closes the defect, but it does not conduct an impulse, it does not contract, and it does not secrete. A scarred myocardium is why ventricular aneurysm and reentrant dysrhythmias develop after an infarct.

Why this drives every time-critical protocol

Both tissues in the permanent column — CNS neurons and cardiac muscle — are also the least tolerant of ischemia. Least tolerant and unable to repair is the worst possible combination, and it is exactly why stroke and STEMI have time targets that a femur fracture does not.

Epithelial Tissue

Classified by cell shape and number of layers

Shape	Layers	Example locations	Function
Squamous (flat, scale-like)	Simple (single layer)	Lining of heart and blood vessels; alveoli	Passage of materials by diffusion
Squamous	Stratified (multilayer)	Mouth, esophagus, vagina; outer skin	Protects against abrasion
Cuboidal (cube-shaped)	Simple	Kidney tubules; secretory portions of glands	Secretion and absorption
Cuboidal	Stratified	Ducts of sweat, mammary, salivary glands	Protects underlying areas
Columnar (tall, slender)	Simple	Digestive tract; bronchi; uterus	Absorbs; secretes mucus and enzymes
Columnar	Stratified	Rare — urethra; esophagus-stomach junction	Protects; secretes mucus

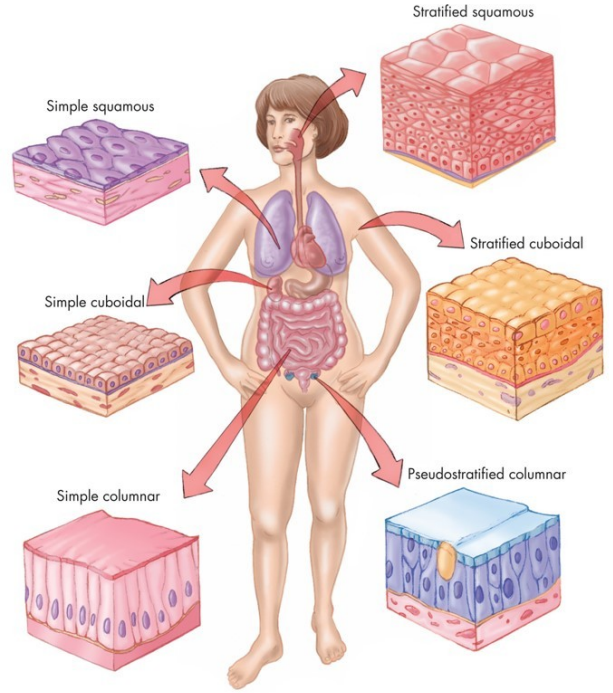


Figure 19-74 Types of epithelial tissue

Bledsoe, Porter & Cherry, Paramedic Care: Principles & Practice, 6th ed.

Field relevance: Simple squamous epithelium exists exactly where diffusion must happen — the alveolar membrane and the capillary wall. It is one cell thick because anything thicker would slow gas exchange. Thicken it with fluid, as in pulmonary edema, and oxygenation fails.

Connective Tissue

Deep tissue that binds, supports, and never touches the outside world

Fiber types

- Collagen — strong, resists stretch
- Elastic — recoils after stretch
- Reticular — fine branching support

Suspended in a ground substance called the extracellular matrix.

Cell types

- Fibroblasts — manufacture fibers; central to wound healing
- Macrophages — phagocytose debris and pathogens
- Adipocytes — store fat
- Mast cells — release histamine and heparin

Mast cells matter

Mast cells sit in connective tissue throughout the skin, airway and gut — exactly the places allergens enter. Degranulation releases histamine, producing vasodilation, capillary leak, bronchospasm and urticaria.

This is the cellular basis of anaphylaxis.

Classes of connective tissue

Class	Examples	Location	Function
Loose (areolar)	Areolar tissue	Between muscles, around glands, wrapping small vessels and nerves	Wraps and cushions organs
Adipose	Fat	Beneath the skin, around kidneys and heart	Stores energy, insulates, cushions
Dense (fibrous)	Tendons, ligaments	Joints and muscle attachments	Ligament binds bone to bone; tendon binds muscle to bone
Specialized	Cartilage, bone, blood, lymph	Skeleton, ear and nose, airway rings, vessels	Support, protection, leverage, and transport

Types and Locations of Connective Tissue

One limb, six different connective tissues

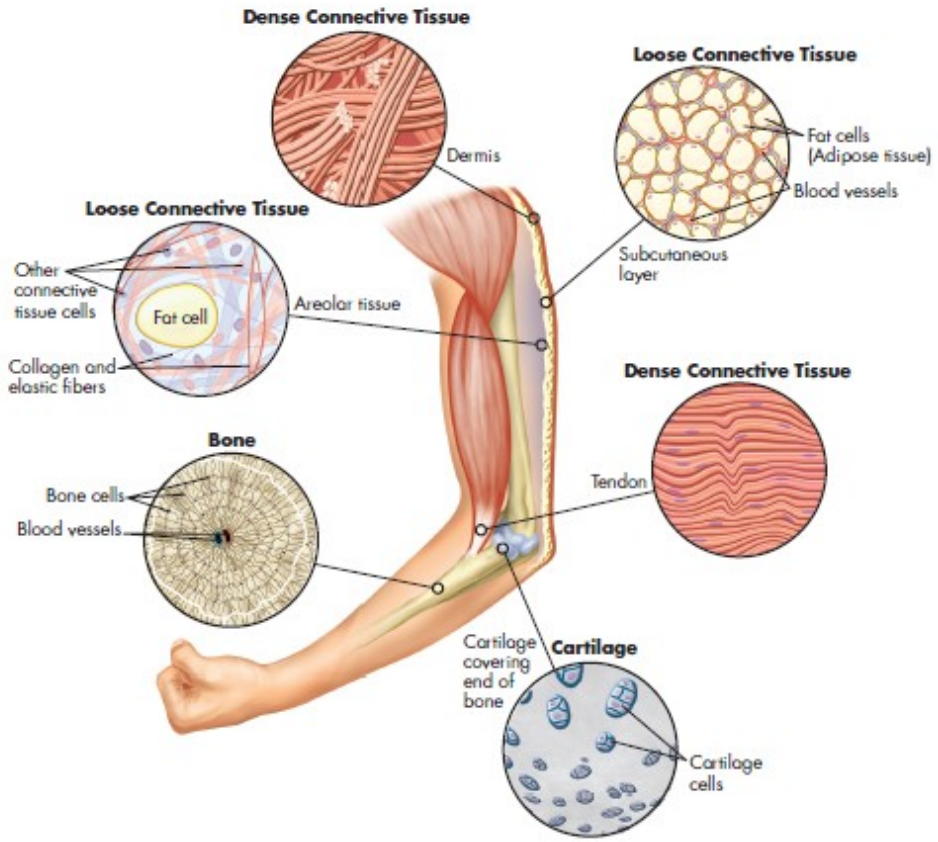


Figure 19-76 Types and locations of connective tissue

1. **Dermis**
   Dense connective tissue — long strands bundled in many directions
2. **Subcutaneous layer**
   Loose connective tissue with adipose cells among blood vessels
3. **Areolar tissue**
   Loose connective tissue — fat and other cells among collagen and elastic fibers
4. **Tendon**
   Dense connective tissue — strands bundled in one direction for tensile strength
5. **Cartilage**
   Oval cartilage cells covering the articular surface of bone
6. **Bone**
   Rectangular cells arranged in concentric rings around a central blood vessel

Muscle and Nervous Tissue

Contraction and coordination

Muscle type	Description	Location	Control & function
Skeletal	Long cylindrical cells, multiple nuclei, obvious striations	Attached to bones	Voluntary — moves the skeleton
Cardiac	Branching striated cells, one nucleus, intercalated discs	Wall of the heart only	Involuntary — propels blood; generates its own impulses
Smooth	Cells taper at each end, single nucleus, no striations	Digestive tract, blood vessels, bronchioles, urinary tubules	Involuntary — propels substances through passageways

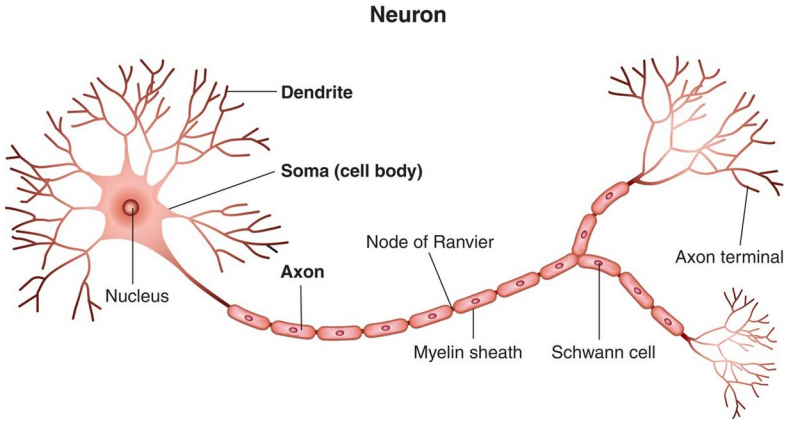


Figure 19-78 Neuron

Neurons

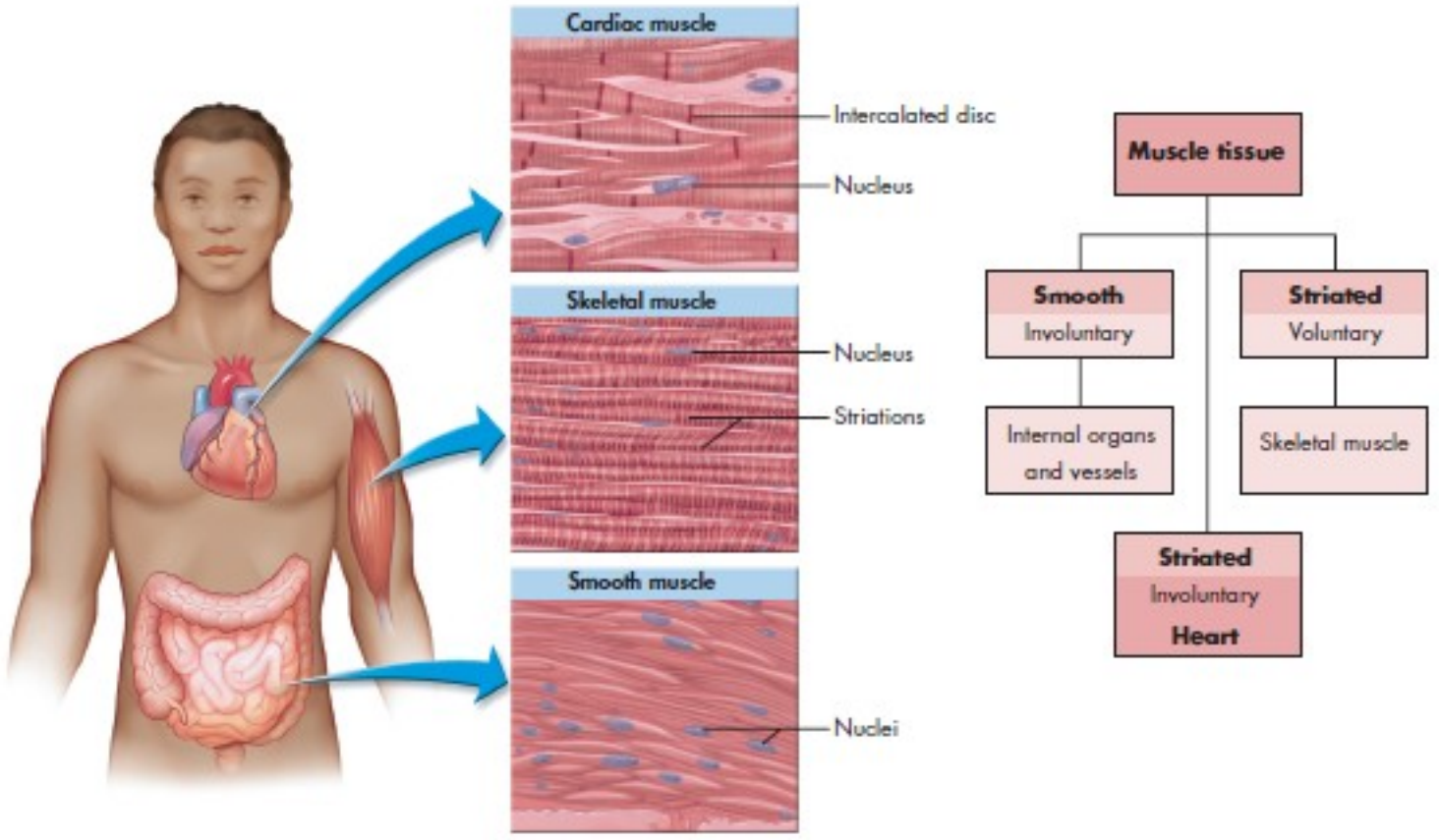
The signal-transmitting cells. Dendrites receive input, the soma holds the nucleus, the axon carries the impulse, and the axon terminal passes it on. Myelin sheath with nodes of Ranvier speeds conduction.

Neuroglia (glial cells)

Support, insulate, nourish and protect neurons; they do not transmit impulses. Astrocytes maintain the blood-brain barrier, oligodendrocytes produce central myelin, microglia are the immune cells of the CNS.

The Three Muscle Tissue Types

Striated or smooth, voluntary or involuntary



Quick sort

Skeletal

Striated
Voluntary
Attached to bone

Cardiac

Striated
Involuntary
Heart only — self-exciting

Smooth

Not striated
Involuntary
Vessels, gut, airways

Figure 19-77 Diagram and chart of the three muscle tissue types

Neoplasia

Abnormal tissue growth — cells multiplying in an uncontrolled fashion

Neoplasia is uncontrolled cell growth. **Tumor** is the resulting mass. Primitive nonspecialized cells (stem cells) normally mature into specific cell types according to function; in neoplasia, that orderly differentiation is lost and **dysplastic (atypical)** cells develop abnormal growth patterns.

B Benign

- Slow growing
- Usually encapsulated by adherent cells
- Does not invade local tissue
- Does not spread to other body areas
- Does not recur once completely removed

M Malignant

- Rapid, disorganized growth
- Not encapsulated; invades along tissue planes
- Locally invasive and destructive
- Metastasizes — sheds cells to distant sites via blood and lymph
- Recurrence is common after treatment

Contributing factors

1 Carcinogens

Chemical agents — tobacco, asbestos, benzene.

2 Radiation

Ionizing and ultraviolet exposure.

3 Oncogenic viruses

HPV, hepatitis B and C, Epstein-Barr.

4 Genetics & hormones

Inherited susceptibility; hormone-driven cancers.

Carcinogenesis

The process of developing a malignant neoplasia occurs in three stages

1 Initiation

A carcinogen, radiation, viral insertion or spontaneous error damages DNA, which may recombine incorrectly and form an oncogene. The change is permanent — but one initiated cell is not yet cancer.

2 Promotion

A promoter drives the initiated cell to divide repeatedly. Promotion is necessary for continued tumor development and speeds the process. Removing the promoter here may still halt progression.

3 Progression

Malignancy exists. Cells become anaplastic — they have lost their differentiated features. Growth, local invasion and possible metastasis follow along tissue planes.

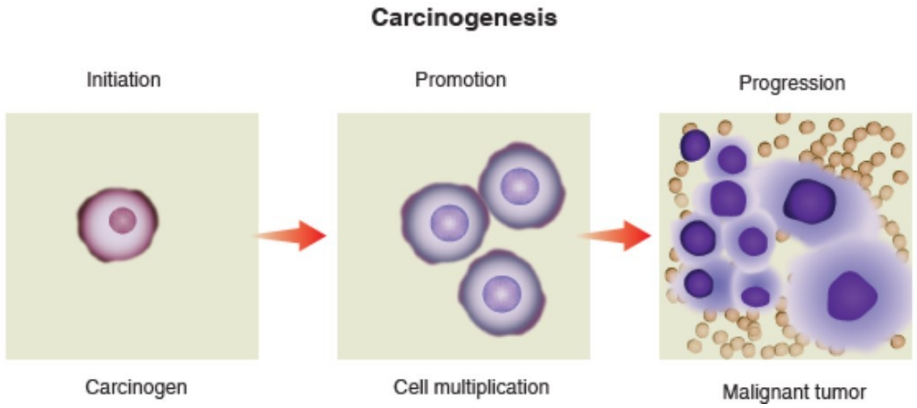


Figure 19-83 Carcinogenesis

Grading by differentiation

Cancer cells are graded by how much they still resemble the tissue of origin. Grade X cannot be assessed; Grade 1 is well differentiated; Grade 4 is undifferentiated (anaplastic). Less resemblance means more aggressive behavior.

Metastasis

Malignant cells shed into the bloodstream and lymphatics and establish colonies in distant organs. Once a tumor has spread, treatment becomes far more difficult. Common destinations include lung, liver, bone and brain.

Tumor Origins and Names

Learn the pattern and the vocabulary decodes itself

The rule: **-oma generally indicates a benign tumor. carcinoma indicates a malignancy of epithelial origin. sarcoma indicates a malignancy of connective or supporting tissue origin.**

Origin / prefix	Cell type	Benign tumor	Malignant tumor
Adeno-	Gland	Adenoma	Adenocarcinoma
Melano-	Pigmented cell	Mole	Melanoma
Squamous cell	Squamous cell	Keratoacanthoma	Squamous cell carcinoma
Osteo-	Bone	Osteoma	Osteosarcoma
Lipo-	Fat	Lipoma	Liposarcoma
Leiomyo-	Smooth muscle	Leiomyoma	Leiomyosarcoma
Rhabdomyo-	Striated muscle	Rhabdomyoma	Rhabdomyosarcoma
Hemangio-	Blood vessel	Hemangioma	Hemangiosarcoma
Meningio-	Meninges	Meningioma	Meningiosarcoma
Lympho- / Myelo-	Lymphocyte / bone marrow	—	Lymphoma; myeloma or leukemia

Oncologic Emergencies

EMS rarely diagnoses cancer — we transport its complications constantly

Neutropenic fever

Chemotherapy suppresses bone marrow, removing the neutrophils that mount the inflammatory response.

Any fever within roughly two weeks of treatment is an emergency. The patient may look unimpressive and be septic — the signs you look for are the response they cannot make.

Spinal cord compression

Vertebral metastasis compresses the cord or nerve roots.

New back pain with any neurologic change in a cancer patient is time-critical. Nervous tissue does not regenerate, so delayed decompression means permanent deficit.

Pathologic fracture

Metastasis weakens bone; the cortex fails under normal load.

Fracture from minimal or no mechanism. Handle and package gently, and do not dismiss a low-energy mechanism in a patient with known malignancy.

Hypercalcemia of malignancy

Tumor-driven bone breakdown releases calcium into the blood.

Confusion, weakness, nausea, constipation, polyuria and dehydration. Frequently mistaken for simple decline or dementia.

Superior vena cava syndrome

A mediastinal tumor obstructs venous return from the head and upper body.

Facial and upper extremity swelling, distended neck and chest veins, dyspnea worse when supine. Sit the patient up.

Malignant effusions

Fluid accumulates in the pericardial or pleural space.

Pericardial effusion produces obstructive shock physiology; pleural effusion produces progressive dyspnea and decreased breath sounds on one side.

Also expect indwelling ports and central lines. Know your system’s policy on accessing them before you are standing next to one.

Part 4 — Key Takeaways

1 **All tissue comes from three germ layers.**

Endoderm, mesoderm, ectoderm. Shared origin explains why seemingly unrelated organs are affected together in some congenital conditions.

2 **There are four primary tissue types.**

Epithelial covers, connective supports, muscle contracts, nervous coordinates. Every organ is a combination of these four.

3 **Structure predicts function.**

Thin where diffusion must happen, thick where abrasion must be resisted. Change the structure and you change the physiology.

4 **Regenerative capacity varies enormously.**

Epithelium regenerates constantly; cardiac muscle and CNS neurons barely at all. This is why "time is muscle" and "time is brain."

5 **Malignancy is defined by invasion and spread.**

Benign tumors can still kill by location. Malignant tumors seed distant organs, which is what makes them so difficult to treat.

6 **Carcinogenesis has three stages.**

Initiation is permanent; promotion is often modifiable. That distinction is the basis of nearly all cancer prevention — including your own.

Putting It Together

Work these as a class — each one requires both parts

A The trapped construction worker

A 34-year-old has been pinned beneath a collapsed wall for two hours with his legs entrapped. He is alert, talking, and his vital signs are stable.

Trace the cellular events in his legs right now. Predict what happens the instant the weight is lifted, and explain why.

B The vomiting toddler

A 2-year-old has had vomiting and diarrhea for three days. She is listless, has dry mucous membranes and a sunken fontanelle, and is tachycardic with a normal blood pressure.

Which fluid compartments have been depleted? Why is her blood pressure still normal? What fluid would you choose, and why not one of the others?

C The oncology patient

A 61-year-old with a history of adenocarcinoma of the lung calls for new mid-back pain and difficulty walking that began yesterday. He finished chemotherapy ten days ago and feels feverish.

Decode his diagnosis from the name. Name two time-critical complications you should be worried about, and explain the tissue-level reason for each.