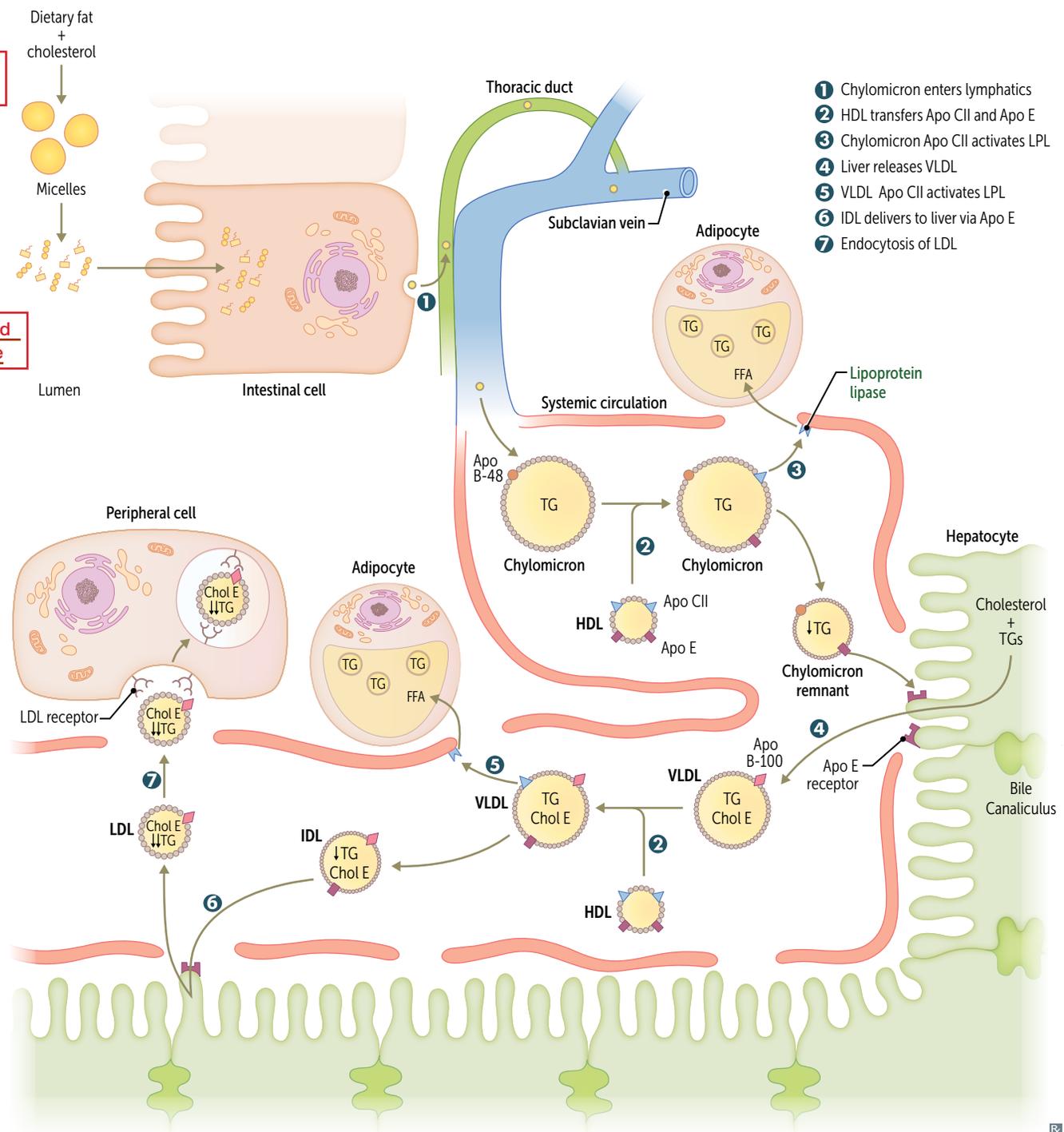


Lipid transport

Swapped Figure

Revised Figure



- 1 Chylomicron enters lymphatics
- 2 HDL transfers Apo CII and Apo E
- 3 Chylomicron Apo CII activates LPL
- 4 Liver releases VLDL
- 5 VLDL Apo CII activates LPL
- 6 IDL delivers to liver via Apo E
- 7 Endocytosis of LDL

Erythrocyte sedimentation rate

Products of inflammation (eg, fibrinogen) coat RBCs and cause aggregation. The denser RBC aggregates fall at a faster rate within a pipette tube → ↑ ESR. Often co-tested with CRP levels.

↑ ESR

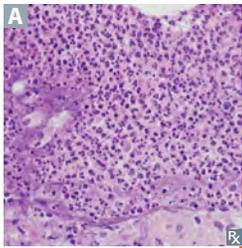
Most anemias
Infections
Inflammation (eg, giant cell [temporal] arteritis, polymyalgia rheumatica)
Cancer (eg, metastases, multiple myeloma)
Renal disease (end-stage or nephrotic syndrome)
Pregnancy

↓ ESR

Sickle cell anemia (altered shape)
Polycythemia (↑ RBCs “dilute” aggregation factors)
HF
Microcytosis
Hypofibrinogenemia

Acute inflammation

Transient and early response to injury or infection. Characterized by neutrophils in tissue **A**, often with associated edema. Rapid onset (seconds to minutes) and short duration (minutes to days). Represents a reaction of the innate immune system (ie, less specific response than chronic inflammation).



STIMULI

Infections, trauma, necrosis, foreign bodies.

MEDIATORS

Toll-like receptors, arachidonic acid metabolites, neutrophils, eosinophils, antibodies (pre-existing), mast cells, basophils, complement, Hageman factor (factor XII).

Inflammasome—Cytoplasmic protein complex that recognizes products of dead cells, microbial products, and crystals (eg, uric acid crystals) → activation of IL-1 and inflammatory response.

COMPONENTS

- Vascular: vasodilation (→ ↑ blood flow and stasis) and ↑ endothelial permeability
- Cellular: extravasation of leukocytes (mainly neutrophils) from postcapillary venules and accumulation in the focus of injury followed by leukocyte activation

To bring cells and proteins to site of injury or infection.

Leukocyte extravasation has 4 steps: margination and rolling, adhesion, transmigration, and migration (chemoattraction).

OUTCOMES

- Resolution and healing (IL-10, TGF-β)
- Persistent acute inflammation (IL-8)
- Abscess (acute inflammation walled off by fibrosis)
- Chronic inflammation (antigen presentation by macrophages and other APCs → activation of CD4⁺ Th cells)
- Scarring

Macrophages predominate in the late stages of acute inflammation (peak 2–3 days after onset) and influence the outcome of acute inflammation by secreting cytokines.

Congenital heart diseases (continued)

LEFT-TO-RIGHT SHUNTS

Acyanotic at presentation; cyanosis may occur years later. ⬇

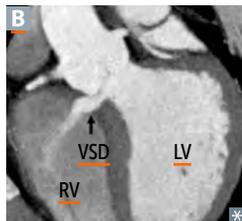
Right-to-Left shunts: ea**RL**y cyanosis.
Left-to-Right shunts: “**LateR**” cyanosis.

Ventricular septal defect

Most common congenital cardiac defect. Asymptomatic at birth, may manifest weeks later or remain asymptomatic throughout life. Most self resolve; larger lesions may lead to LV overload and HF.

O₂ saturation ↑ in RV and pulmonary artery. Frequency: VSD > ASD > PDA.

New Image



Atrial septal defect

Defect in interatrial septum **C**, wide, fixed split S2. Ostium secundum defects most common and usually an isolated finding; ostium primum defects rarer and usually occur with other cardiac anomalies. Symptoms range from none to HF. Distinct from patent foramen ovale in that septa are missing tissue rather than unfused.

O₂ saturation ↑ in RA, RV, and pulmonary artery. May lead to paradoxical emboli (systemic venous emboli use ASD to bypass lungs and become systemic arterial emboli).

Revised Figure

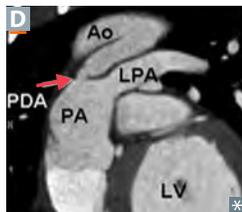


Swapped Image

Patent ductus arteriosus

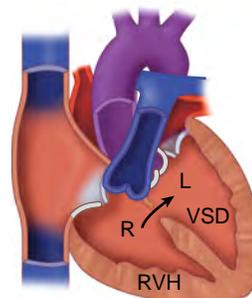
In fetal period, shunt is right to left (normal). In neonatal period, ↓ pulmonary vascular resistance → shunt becomes left to right → progressive RVH and/or LVH and HF. Associated with a continuous, “machine-like” murmur. Patency is maintained by PGE synthesis and low O₂ tension. Uncorrected PDA **D** can eventually result in late cyanosis in the lower extremities (differential cyanosis).

“**Endomethacin**” (indomethacin) **ends** patency of PDA; PGE keeps ductus **G**oing (may be necessary to sustain life in conditions such as transposition of the great vessels). PDA is normal in utero and normally closes only after birth.



Eisenmenger syndrome

Uncorrected left-to-right shunt (VSD, ASD, PDA) → ↑ pulmonary blood flow → pathologic remodeling of vasculature → pulmonary arterial hypertension. RVH occurs to compensate → shunt becomes right to left. Causes late cyanosis, clubbing **E**, and polycythemia. Age of onset varies.

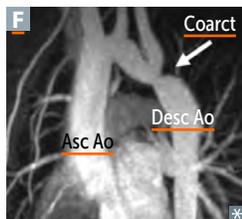


OTHER ANOMALIES

Coarctation of the aorta

Aortic narrowing **F**, near insertion of ductus arteriosus (“juxtaductal”). Associated with bicuspid aortic valve, other heart defects, and Turner syndrome. Hypertension in upper extremities and weak, delayed pulse in lower extremities (brachial-femoral delay). With age, intercostal arteries enlarge due to collateral circulation; arteries erode ribs → notched appearance on CXR. Complications include HF, ↑ risk of cerebral hemorrhage (berry aneurysms), aortic rupture, and possible endocarditis.

New Image



Calcitonin

SOURCE	Parafollicular cells (C cells) of thyroid.	Calcitonin opposes actions of PTH. Not important in normal Ca ²⁺ homeostasis. Calcitonin tones down serum Ca ²⁺ levels and keeps it in bones .
FUNCTION	↓ bone resorption of Ca ²⁺ .	
REGULATION	↑ serum Ca ²⁺ → calcitonin secretion.	

Thyroid hormones (T₃/T₄)

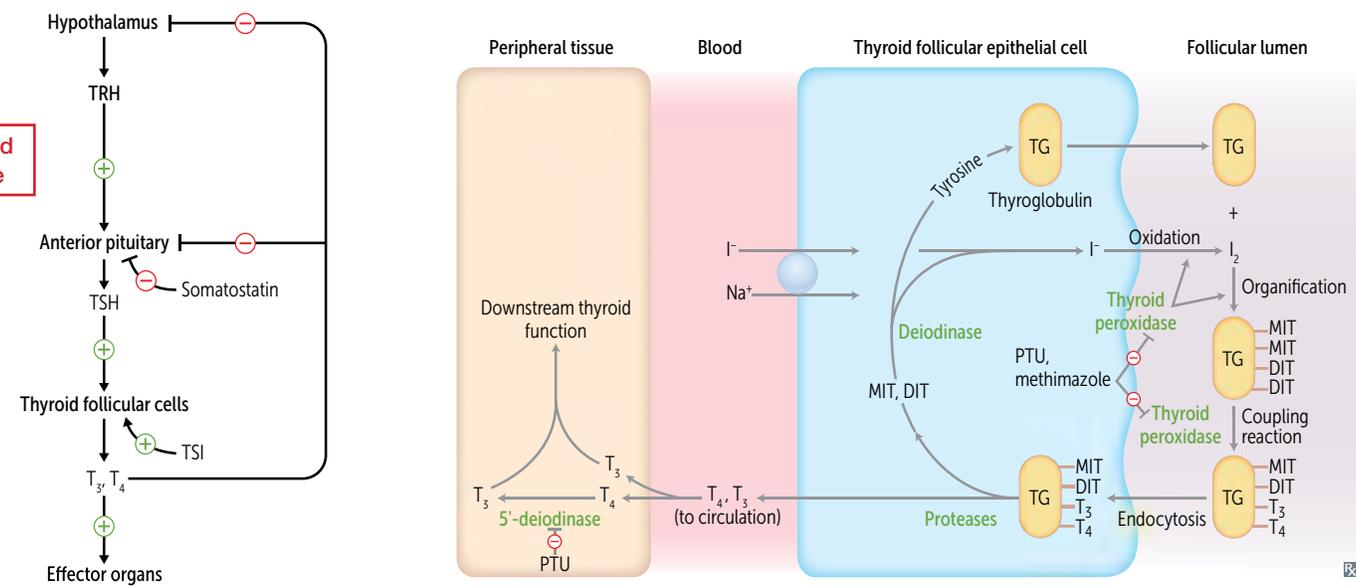
Iodine-containing hormones that control the body's metabolic rate.

Reset Fact

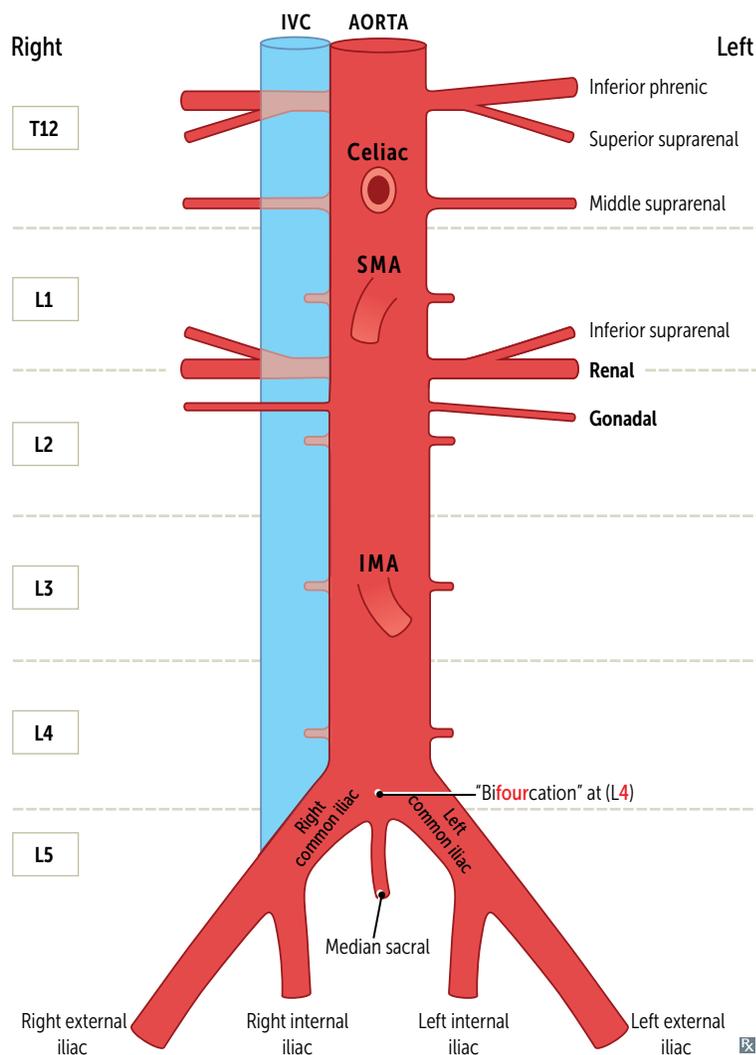
SOURCE	Follicles of thyroid. 5'-deiodinase converts T ₄ (the major thyroid product) to T ₃ in peripheral tissue (5, 4, 3). Peripheral conversion is inhibited by glucocorticoids, β-blockers and propylthiouracil (PTU). Functions of thyroid peroxidase include oxidation, organification of iodide and coupling of monoiodotyrosine (MIT) and diiodotyrosine (DIT). Inhibited by PTU and methimazole. DIT + DIT = T ₄ . DIT + MIT = T ₃ . Wolff-Chaikoff effect—excess iodine temporarily ⊖ thyroid peroxidase → ↓ T ₃ /T ₄ production.
FUNCTION	Only free hormone is active. T ₃ binds nuclear receptor with greater affinity than T ₄ . T ₃ functions —6 B's: <ul style="list-style-type: none"> ▪ Brain maturation ▪ Bone growth (synergism with GH) ▪ β-adrenergic effects. ↑ β₁ receptors in heart → ↑ CO, HR, SV, contractility; β-blockers alleviate adrenergic symptoms in thyrotoxicosis ▪ Basal metabolic rate ↑ (via Na⁺/K⁺-ATPase activity → ↑ O₂ consumption, RR, body temperature) ▪ Blood sugar (↑ glycogenolysis, gluconeogenesis) ▪ Break down lipids (↑ lipolysis)

REGULATION	TRH ⊕ TSH release → ⊕ follicular cells. Thyroid-stimulating immunoglobulin (TSI) may ⊕ follicular cells in Graves disease. Negative feedback primarily by free T ₃ /T ₄ : <ul style="list-style-type: none"> ▪ Anterior pituitary → ↓ sensitivity to TRH ▪ Hypothalamus → ↓ TRH secretion Thyroxine-binding globulin (TBG) binds most T ₃ /T ₄ in blood. Bound T ₃ /T ₄ = inactive. <ul style="list-style-type: none"> ▪ ↑ TBG in pregnancy, OCP use (estrogen → ↑ TBG) → ↑ total T₃/T₄ ▪ ↓ TBG in hepatic failure, steroids, nephrotic syndrome
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Revised Figure



Abdominal aorta and branches



Revised Figure

Arteries supplying GI structures are single and branch anteriorly.

Arteries supplying non-GI structures are paired and branch laterally and posteriorly.

Superior mesenteric artery syndrome—characterized by intermittent intestinal obstruction symptoms (primarily postprandial pain) when SMA and aorta compress transverse (third) portion of duodenum. Typically occurs in conditions associated with diminished mesenteric fat (eg, low body weight/malnutrition).

Two areas of the colon have dual blood supply from distal arterial branches (“watershed regions”) → susceptible in colonic ischemia:

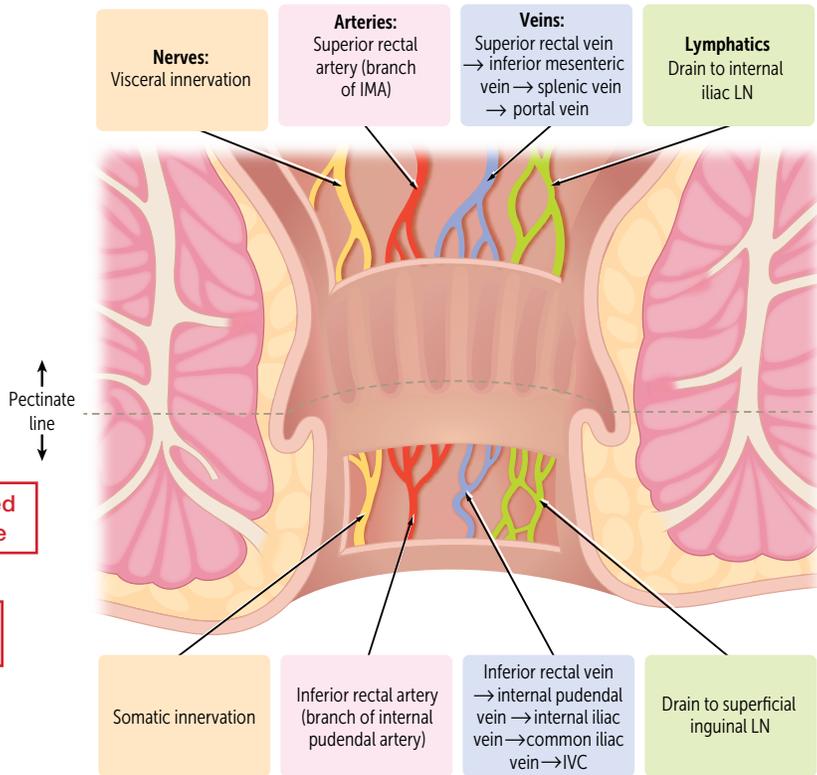
- Splenic flexure—SMA and IMA
- Rectosigmoid junction—the last sigmoid arterial branch from the IMA and superior rectal artery

Gastrointestinal blood supply and innervation

EMBRYONIC GUT REGION	ARTERY	PARASYMPATHETIC INNERVATION	VERTEBRAL LEVEL	STRUCTURES SUPPLIED
Foregut	Celiac	Vagus	T12/L1	Pharynx (vagus nerve only) and lower esophagus (celiac artery only) to proximal duodenum; liver, gallbladder, pancreas, spleen (mesoderm)
Midgut	SMA	Vagus	L1	Distal duodenum to proximal 2/3 of transverse colon
Hindgut	IMA	Pelvic	L3	Distal 1/3 of transverse colon to upper portion of rectum

Pectinate (dentate) line

Formed where endoderm (hindgut) meets ectoderm.



Above pectinate line—internal hemorrhoids, adenocarcinoma.

Internal hemorrhoids receive visceral innervation and are therefore **not painful**.

Below pectinate line—external hemorrhoids, anal fissures, squamous cell carcinoma.

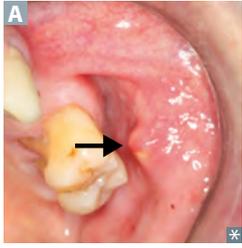
External hemorrhoids receive somatic innervation (inferior rectal branch of pudendal nerve) and are therefore **painful** if thrombosed.

Anal fissure—tear in the anal mucosa below the Pectinate line. **Pain** while **Pooping**; blood on toilet **Paper**. Located **Posteriorly** because this area is **Poorly Perfused**. Associated with low-fiber diets and constipation.

Revised Figure

New Figure

► GASTROINTESTINAL—PATHOLOGY

SialolithiasisNew
Fact

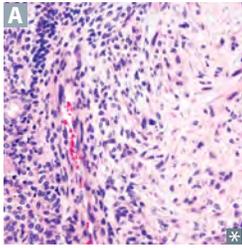
Stone(s) in salivary gland duct **A**. Can occur in 3 major salivary glands (parotid, submandibular, sublingual). Single stone more common in submandibular gland (Wharton duct).

Presents as recurrent pre-/periprincipal pain and swelling in affected gland.

Caused by dehydration or trauma.

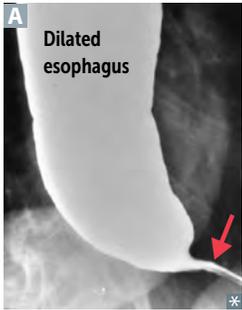
Treat conservatively with NSAIDs, gland massage, warm compresses, sour candies (to promote salivary flow).

Sialadenitis—inflammation of salivary gland due to obstruction, infection, or immune-mediated mechanisms.

Salivary gland tumors

Most commonly benign and in parotid gland. Tumors in smaller glands more likely malignant. Typically present as painless mass/swelling. Facial pain or paralysis suggests malignant involvement of CN VII.

- **Pleomorphic adenoma** (benign mixed tumor)—most common salivary gland tumor **A**. Composed of chondromyxoid stroma and epithelium and recurs if incompletely excised or ruptured intraoperatively. May undergo malignant transformation.
- **Mucoepidermoid carcinoma**—most common malignant tumor, has mucinous and squamous components.
- **Warthin tumor** (papillary cystadenoma lymphomatosum)—benign cystic tumor with **germinal** centers. Typically found in **smokers**. Bilateral in 10%; multifocal in 10%. “Warriors from Germany love smoking.”

Achalasia

Failure of LES to relax due to loss of myenteric (Auerbach) plexus due to loss of postganglionic inhibitory neurons (which contain NO and VIP).

Manometry findings include uncoordinated or absent peristalsis with high LES resting pressure → progressive dysphagia to solids and liquids (vs obstruction—solids only). Barium swallow shows dilated esophagus with an area of distal stenosis (“bird’s beak” **A**).

Associated with ↑ risk of esophageal cancer.

Achalasia = absence of relaxation.

2° achalasia (pseudoachalasia) may arise from Chagas disease (*T. cruzi* infection) or extraesophageal malignancies (mass effect or paraneoplastic).

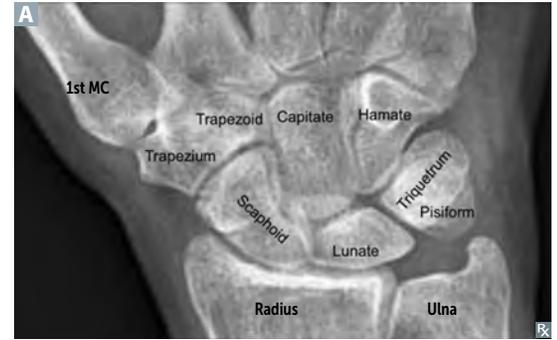
Wrist region



Scaphoid, Lunate, Triquetrum, Pisiform, Hamate, Capitate, Trapezoid, Trapezium **A**. (So Long To Pinky, Here Comes The Thumb).

Scaphoid (palpable in anatomic snuff box **B**) is the most commonly fractured carpal bone, typically due to a fall on an outstretched hand. Complications of proximal scaphoid fractures include avascular necrosis and nonunion due to retrograde blood supply. Fracture not always seen on initial x-ray.

Dislocation of lunate may cause acute carpal tunnel syndrome.



Metacarpal neck fracture

Also called boxer's fracture. Common fracture caused by direct blow with a closed fist (eg, from punching a wall or individual). Most commonly seen in 4th and 5th metacarpals.

Carpal tunnel syndrome



Entrapment of median nerve in carpal tunnel (between transverse carpal ligament and carpal bones); nerve compression → paresthesia, pain, and numbness in distribution of median nerve. Thenar eminence atrophies **C** but sensation spared, because palmar cutaneous branch enters hand external to carpal tunnel.

Suggested by ⊕ Tinel sign (percussion of wrist causes tingling) and Phalen maneuver (90° flexion of wrist causes tingling).

Associated with pregnancy (due to edema), rheumatoid arthritis, hypothyroidism, diabetes, acromegaly, dialysis-related amyloidosis; may be associated with repetitive use.

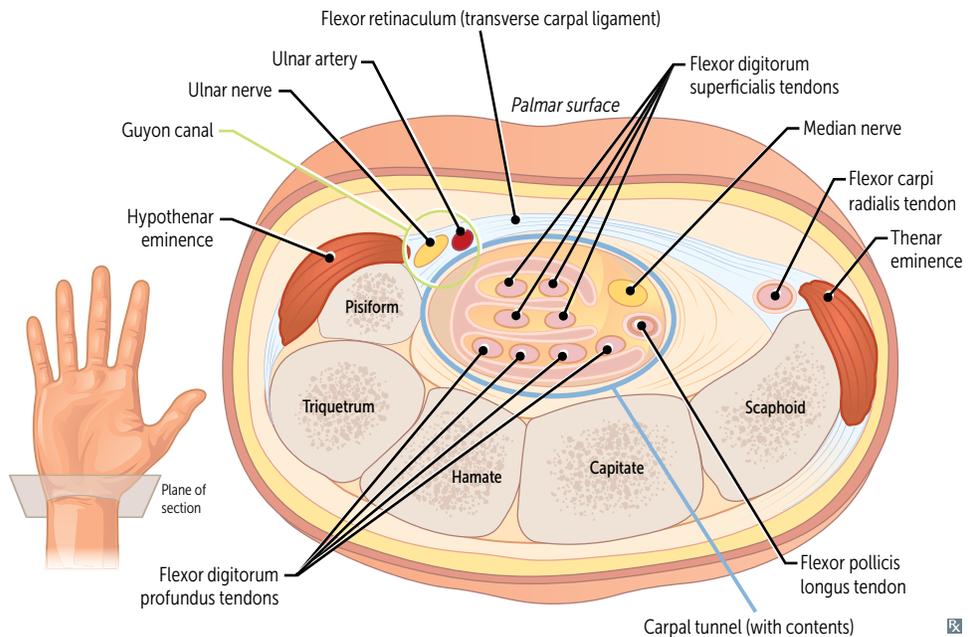
C = New Image

Guyon canal syndrome

Compression of ulnar nerve at wrist. Classically seen in cyclists due to pressure from handlebars.

New Figure

Revised Figure



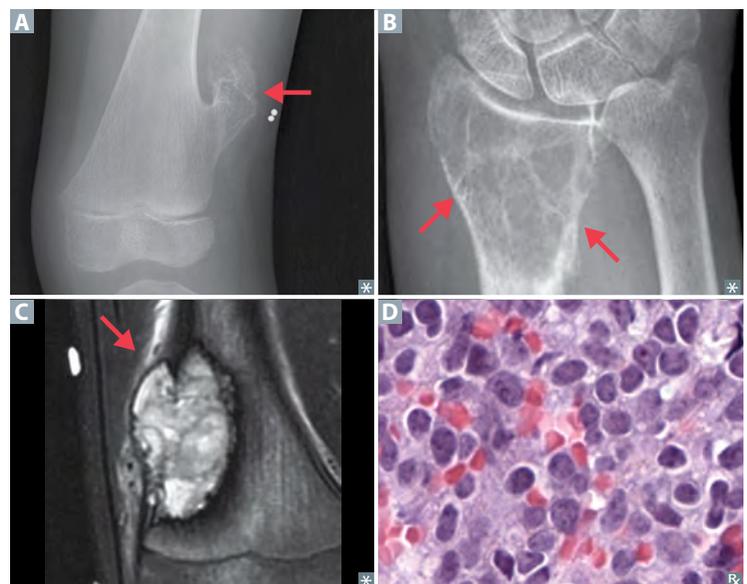
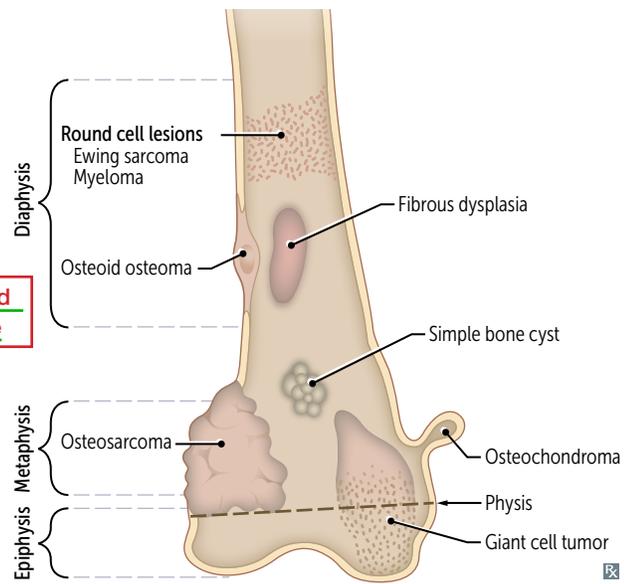
Primary bone tumors Metastatic disease is more common than 1° bone tumors.

TUMOR TYPE	EPIDEMIOLOGY	LOCATION	CHARACTERISTICS
Benign tumors			
Osteochondroma	Most common benign bone tumor. Males < 25 years old.	<u>Metaphysis of long bones.</u>	<u>Lateral bony projection of growth plate (continuous with marrow space) covered by cartilaginous cap A.</u> <u>Rarely transforms to chondrosarcoma.</u>
Osteoma	<u>Middle age.</u>	<u>Surface of facial bones.</u>	<u>Associated with Gardner syndrome.</u>
Osteoid osteoma	<u>Adults < 25 years old.</u> <u>Males > females.</u>	<u>Cortex of long bones.</u>	<u>Presents as bone pain (worse at night) that is relieved by NSAIDs.</u> <u>Bony mass (< 2 cm) with radiolucent osteoid core.</u>
Osteoblastoma		<u>Vertebrae.</u>	<u>Similar histology to osteoid osteoma.</u> <u>Larger size (> 2 cm), pain unresponsive to NSAIDs.</u>
Chondroma		<u>Medulla of small bones of hand and feet.</u>	<u>Benign tumor of cartilage.</u>
Giant cell tumor	<u>20–40 years old.</u>	<u>Epiphysis of long bones (often in knee region).</u>	<u>Locally aggressive benign tumor.</u> <u>Neoplastic mononuclear cells that express RANKL and reactive multinucleated giant (osteoclast-like) cells. “Osteoclastoma.”</u> <u>“Soap bubble” appearance on x-ray B.</u>
Malignant tumors			
Osteosarcoma (osteogenic sarcoma)	<u>Accounts for 20% of 1° bone cancers.</u> <u>Peak incidence of 1° tumor in males < 20 years.</u> <u>Less common in elderly; usually 2° to predisposing factors, such as Paget disease of bone, bone infarcts, radiation, familial retinoblastoma, Li-Fraumeni syndrome.</u>	<u>Metaphysis of long bones (often in knee region) C.</u>	<u>Pleomorphic osteoid-producing cells (malignant osteoblasts).</u> <u>Presents as painful enlarging mass or pathologic fractures.</u> <u>Codman triangle (from elevation of periosteum) or sunburst pattern on x-ray. Think of an osteocod (bone fish) swimming in the sun.</u> <u>Aggressive. 1° usually responsive to treatment (surgery, chemotherapy), poor prognosis for 2°.</u>
Chondrosarcoma		<u>Medulla of pelvis and central skeleton.</u>	<u>Tumor of malignant chondrocytes.</u>

Primary bone tumors (continued)

TUMOR TYPE	EPIDEMIOLOGY	LOCATION	CHARACTERISTICS
Ewing sarcoma	Most common in Caucasians. Generally boys < 15 years old.	Diaphysis of long bones (especially femur), pelvic flat bones.	<p>Anaplastic small blue cells of neuroectodermal origin (resemble lymphocytes) D.</p> <p>Differentiate from conditions with similar morphology (eg, lymphoma, chronic osteomyelitis) by testing for t(11;22) (fusion protein EWS-FLI1).</p> <p>“Onion skin” periosteal reaction in bone.</p> <p>Aggressive with early metastases, but responsive to chemotherapy.</p> <p>11 + 22 = 33 (Patrick Ewing’s jersey number).</p>

Revised Figure



Cerebral perfusion

Brain perfusion relies on tight autoregulation.

Cerebral perfusion is primarily driven by PCO_2 (PO_2 also modulates perfusion in severe hypoxia).

Cerebral perfusion relies on a pressure gradient between mean arterial pressure (MAP) and ICP. \downarrow blood pressure or \uparrow ICP \rightarrow \downarrow cerebral perfusion pressure (CPP).

Therapeutic hyperventilation \rightarrow \downarrow PCO_2

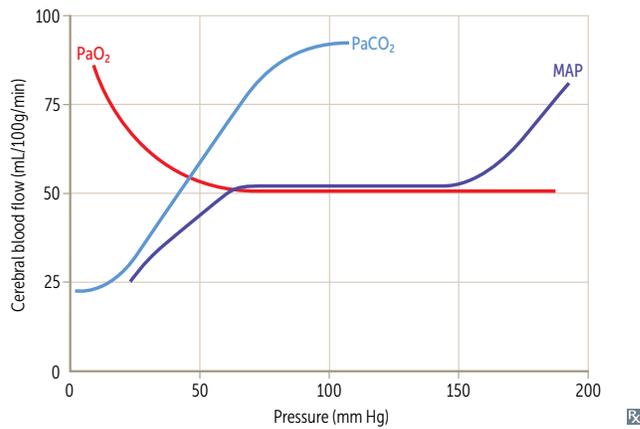
\rightarrow vasoconstriction \rightarrow \downarrow cerebral blood flow

\rightarrow \downarrow intracranial pressure (ICP). May be used to treat acute cerebral edema (eg, 2° to stroke) unresponsive to other interventions.

CPP = MAP - ICP. If CPP = 0, there is no cerebral perfusion \rightarrow brain death.

Hypoxemia increases CPP only if $PO_2 < 50$ mm Hg.

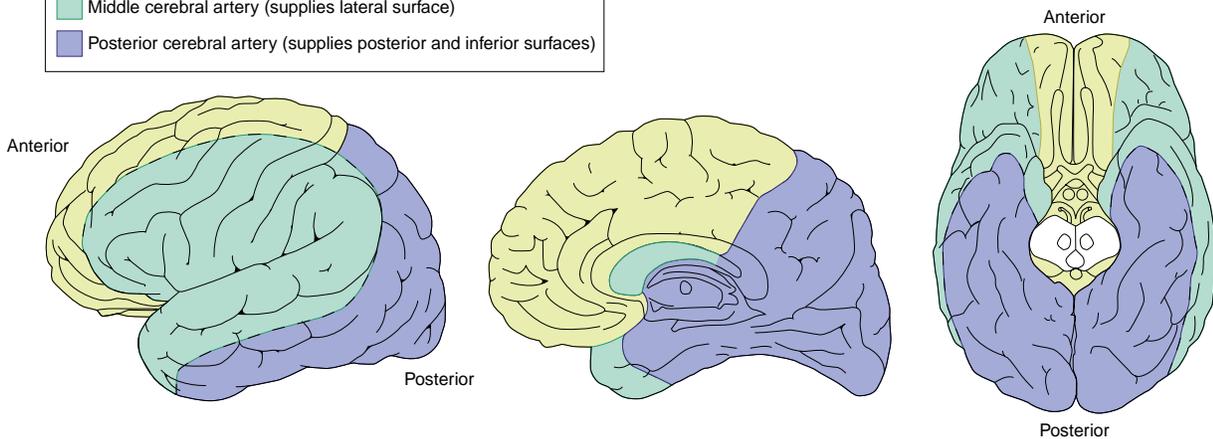
CPP is directly proportional to PCO_2 until $PCO_2 > 90$ mm Hg.



Revised Figure

Cerebral arteries—cortical distribution

- Anterior cerebral artery (supplies anteromedial surface)
- Middle cerebral artery (supplies lateral surface)
- Posterior cerebral artery (supplies posterior and inferior surfaces)



Art is reverted to previous version.

Revised Figure

Watershed zones



Between anterior cerebral/middle cerebral, posterior cerebral/middle cerebral arteries (cortical border zones) (blue areas in **A**); or may also occur between the superficial and deep vascular territories of the middle cerebral artery (internal border zones) (red areas in **A**).

Damage by severe hypotension \rightarrow proximal upper and lower extremity weakness (if internal border zone stroke), higher order visual dysfunction (if posterior cerebral/middle cerebral cortical border zone stroke).

Re-located Image

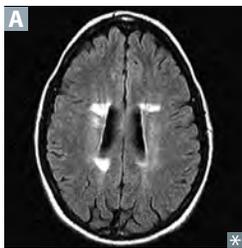
Swapped Figure

Multiple sclerosis

Autoimmune inflammation and demyelination of CNS (brain and spinal cord) with subsequent axonal damage. Can present with:

- Acute optic neuritis (painful unilateral visual loss associated with Marcus Gunn pupil)
- Brainstem/cerebellar syndromes (eg, diplopia, ataxia, scanning speech, intention tremor, nystagmus/INO (bilateral > unilateral))
- Pyramidal tract weakness
- Spinal cord syndromes (eg, electric shock-like sensation along spine on neck flexion [Lhermitte phenomenon], neurogenic bladder, paraparesis, sensory manifestations affecting the trunk or one or more extremity)

Symptoms may exacerbate with increased body temperature (eg, hot bath, exercise). Relapsing and remitting is most common clinical course. Most often affects women in their 20s and 30s; more common in Caucasians living farther from equator.

FINDINGS

↑ IgG level and myelin basic protein in CSF. Oligoclonal bands are diagnostic. MRI is gold standard. Periventricular plaques A (areas of oligodendrocyte loss and reactive gliosis). Multiple white matter lesions disseminated in space and time.

TREATMENT

Stop relapses and halt/slow progression with disease-modifying therapies (eg, β -interferon, glatiramer, natalizumab). Treat acute flares with IV steroids. Symptomatic treatment for neurogenic bladder (catheterization, muscarinic antagonists), spasticity (baclofen, GABA_B receptor agonists), pain (TCAs, anticonvulsants).

New Fact Other demyelinating and dysmyelinating disorders**Osmotic demyelination syndrome**

Also known as central pontine myelinolysis. Massive axonal demyelination in pontine white matter **A** 2° to rapid osmotic changes, most commonly iatrogenic correction of hyponatremia but also rapid shifts of other osmolytes (eg, glucose). Acute paralysis, dysarthria, dysphagia, diplopia, loss of consciousness. Can cause “locked-in syndrome.”

Correcting serum Na⁺ too fast:

- “From low to high, your pons will die” (osmotic demyelination syndrome).
- “From high to low, your brains will blow” (cerebral edema/herniation).

**Acute inflammatory demyelinating polyradiculopathy**

Most common subtype of **Guillain-Barré syndrome**. Autoimmune condition associated with infections (eg, *Campylobacter jejuni*, viruses [eg, Zika]) that destroys Schwann cells by inflammation and demyelination of peripheral nerves (including cranial nerves III-XII) and motor fibers likely due to molecular mimicry, inoculations, and stress, but no definitive link to pathogens.

Results in symmetric ascending muscle weakness/paralysis and depressed/absent DTRs beginning in lower extremities. Facial paralysis (usually bilateral) and respiratory failure are common. May see autonomic dysregulation (eg, cardiac irregularities, hypertension, hypotension) or sensory abnormalities. Almost all patients survive; majority recover completely after weeks to months.

↑ CSF protein with normal cell count (albuminocytologic dissociation)

Respiratory support is critical until recovery. Disease-modifying treatment: plasmapheresis, IV immunoglobulins. No role for steroids.

Acute disseminated (postinfectious) encephalomyelitis

Multifocal inflammation and demyelination after infection or vaccination. Presents with rapidly progressive multifocal neurologic symptoms, altered mental status.

Charcot-Marie-Tooth disease

Also known as hereditary motor and sensory neuropathy. Group of progressive hereditary nerve disorders related to the defective production of proteins involved in the structure and function of peripheral nerves or the myelin sheath. Typically autosomal dominant inheritance pattern and associated with foot deformities (eg, pes cavus, hammer toe), lower extremity weakness (eg, foot drop), and sensory deficits. Most common type, CMT1A, is caused by PMP22 gene duplication.

Progressive multifocal leukoencephalopathy

Demyelination of CNS **B** due to destruction of oligodendrocytes (2° to reactivation of latent JC virus infection). Seen in 2–4% of patients with AIDS. Rapidly progressive, usually fatal. Predominantly involves parietal and occipital areas; visual symptoms are common. ↑ risk associated with natalizumab, rituximab.

**Other disorders**

Krabbe disease, metachromatic leukodystrophy, adrenoleukodystrophy.

Urethral injury

Occurs almost exclusively in men. Suspect if blood seen at urethral meatus. Urethral catheterization is relatively contraindicated.

Anterior urethral injury

Bulbar (spongy) urethra

Perineal straddle injury

Blood accumulates in scrotum

If Buck fascia is torn, urine escapes into perineal space

Blood at urethral meatus and scrotal hematoma

Posterior urethral injury

Membranous urethra

Pelvic fracture

Urine leaks into retropubic space

Blood at urethral meatus and high-riding prostate

Reset
Fact

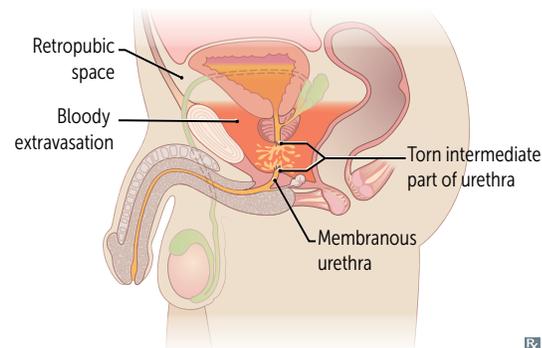
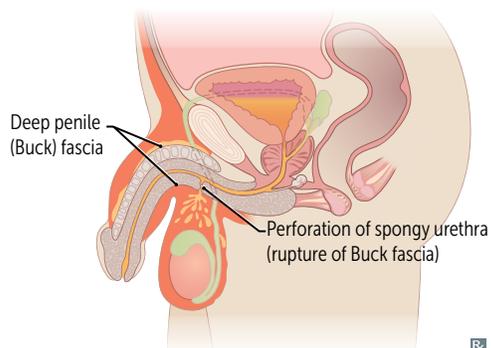
PART OF URETHRA

MECHANISM

LOCATION OF URINE LEAK/BLOOD

ACCUMULATION

PRESENTATION

Revised
FiguresNew
Figures**Autonomic innervation of male sexual response**

Erection—Parasympathetic nervous system (pelvic splanchnic nerves, S2-S4):

- NO → ↑ cGMP → smooth muscle relaxation → vasodilation → proerectile.
- Norepinephrine → ↑ $[Ca^{2+}]_{in}$ → smooth muscle contraction → vasoconstriction → antierectile.

Emission—Sympathetic nervous system (hypogastric nerve, T11-L2).

Ejaculation—visceral and Somatic nerves (pudendal nerve).

Point, Squeeze, and Shoot.

PDE-5 inhibitors (eg, sildenafil) ↓ cGMP breakdown.