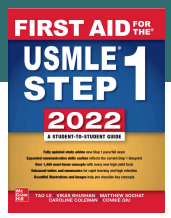

new image for 2022 2nd pass

art revised for 2022 3rd pass

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Cilia structure

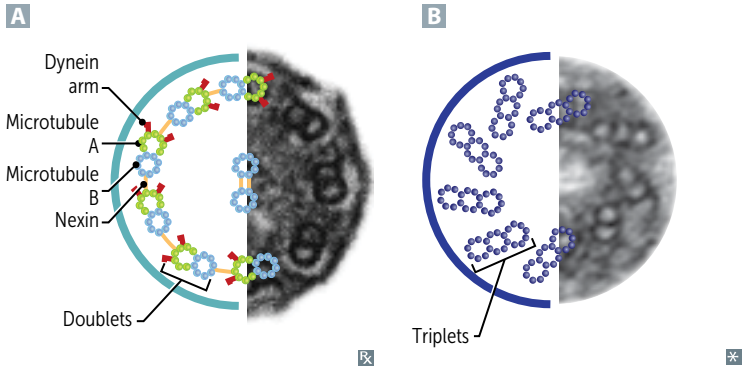
Motile cilia consist of 9 doublet + 2 singlet arrangement of microtubules (axoneme) A.

Basal body (base of cilium below cell membrane) consists of 9 microtubule triplets B with no central microtubules.

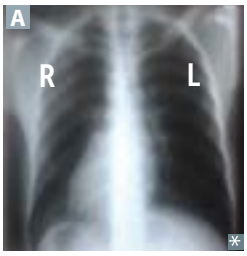
Nonmotile (primary) cilia work as chemical signal sensors and have a role in signal transduction and cell growth control. Dysgenesis may lead to polycystic kidney disease, mitral valve prolapse, or retinal degeneration.

Axonemal dynein—ATPase that links peripheral 9 doublets and causes bending of cilium by differential sliding of doublets.

Gap junctions enable coordinated ciliary movement.



Primary ciliary dyskinesia



Also called Kartagener syndrome. Autosomal recessive. Dynein arm defect → immotile cilia → dysfunctional ciliated epithelia.

Developmental abnormalities due to impaired migration and orientation (eg, situs inversus A, hearing loss due to dysfunctional eustachian tube cilia); recurrent infections (eg, sinusitis, ear infections, bronchiectasis due to impaired ciliary clearance of debris/pathogens); infertility (↑ risk of ectopic pregnancy due to dysfunctional fallopian tube cilia, immotile spermatozoa).

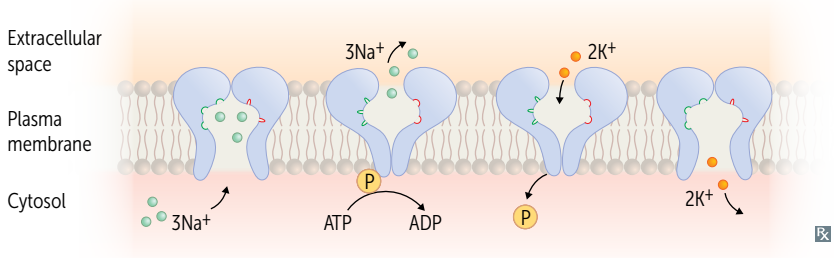
Lab findings: ↓ nasal nitric oxide (used as screening test).

Sodium-potassium pump

Na^+/K^+-ATPase is located in the plasma membrane with ATP site on cytosolic side. For each ATP consumed, 2 K^+ go in to the cell (pump dephosphorylated) and 3 Na^+ go out of the cell (pump phosphorylated).

2 strikes? K, you're still in. 3 strikes? Nah, you're out!

Cardiac glycosides (digoxin and digitoxin) directly inhibit Na^+/K^+-ATPase → indirect inhibition of Na^+/Ca^{2+} exchange → ↑ $[Ca^{2+}]_i$ → ↑ cardiac contractility.



Phenylketonuria

Fact revised for 2022 4th pass

Caused by ↓ phenylalanine hydroxylase (PAH). Tyrosine becomes essential. ↑ phenylalanine → ↑ phenyl ketones in urine.

Tetrahydrobiopterin (BH_4) deficiency—BH_4 essential cofactor for PAH. BH_4 deficiency → ↑ phenylalanine. Varying degrees of clinical severity. Untreated patients typically die in infancy.

Phenylalanine embryopathy—↑ phenylalanine levels in pregnant patients with untreated PKU can cause fetal growth restriction, microcephaly, intellectual disability, congenital heart defects. Can be prevented with dietary measures.

Autosomal recessive.

Screening occurs 2–3 days after birth (normal at birth because of maternal enzyme during fetal life).

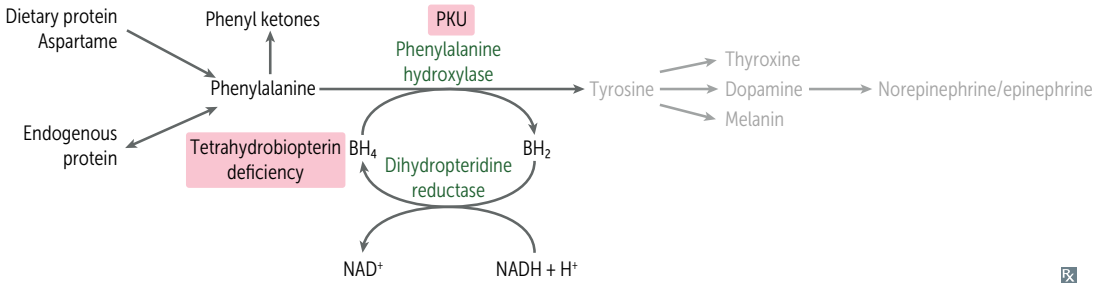
Findings: intellectual disability, microcephaly, seizures, hypopigmented skin, eczema, musty body odor.

Treatment: ↓ phenylalanine and ↑ tyrosine in diet (eg, soy products, chicken, fish, milk), tetrahydrobiopterin supplementation.

Phenyl ketones—phenylacetate, phenyllactate, and phenylpyruvate.

Disorder of aromatic amino acid metabolism → musty body odor.

Patients with PKU must avoid the artificial sweetener aspartame, which contains phenylalanine.



art revised for 2022 4th pass

Maple syrup urine disease

Blocked degradation of branched amino acids (Isoleucine, leucine, valine) due to ↓ branched-chain α-ketoacid dehydrogenase (B_1). Causes ↑ α-ketoacids in the blood, especially those of leucine.

Treatment: restriction of isoleucine, leucine, valine in diet, and thiamine supplementation.

Autosomal recessive.

Presentation: vomiting, poor feeding, urine smells like maple syrup/burnt sugar. Causes progressive neurological decline.

I love Vermont maple syrup from maple trees (with B_1ranches).

Alkaptonuria

Congenital deficiency of homogentisate oxidase in the degradative pathway of tyrosine to fumarate → pigment-forming homogentisic acid builds up in tissue A. Autosomal recessive. Usually benign.

Findings: bluish-black connective tissue, ear cartilage, and sclerae (ochronosis); urine turns black on prolonged exposure to air. May have debilitating arthralgias (homogentisic acid toxic to cartilage).

This page: 5 new images for 2022 3rd pass

This page: 5 images removed for 2022 4th pass

Vaccination

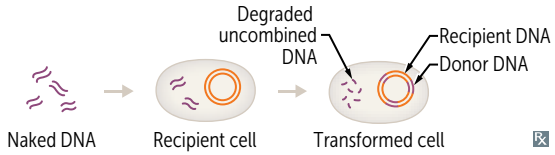
Induces an active immune response (humoral and/or cellular) to specific pathogens.

VACCINE TYPE	DESCRIPTION	PROS/CONS	EXAMPLES
Live attenuated vaccine	Microorganism rendered nonpathogenic but retains capacity for transient growth within inoculated host. MMR and varicella vaccines can be given to people living with HIV without evidence of immunity if CD4+ cell count ≥200 cells/mm^3.	Pros: induces cellular and humoral responses. Induces strong, often lifelong immunity. Cons: may revert to virulent form. Contraindicated in pregnancy and patients with immunodeficiency.	Adenovirus (nonattenuated, given to military recruits), typhoid (Ty21a, oral), polio (Sabin), varicella (chickenpox), smallpox, BCG, yellow fever, influenza (intranasal), MMR, rotavirus. "Attention teachers! Please vaccinate small, Beautiful young infants with MMR regularly!"
Killed or inactivated vaccine	Pathogen is inactivated by heat or chemicals. Maintaining epitope structure on surface antigens is important for immune response. Mainly induces a humoral response.	Pros: safer than live vaccines. Cons: weaker cell-mediated immune response; booster shots usually needed.	Hepatitis A, Typhoid (Vi polysaccharide, intramuscular), Rabies, Influenza (intramuscular), Polio (SalK). A TRIP could Kill you.
Subunit, recombinant, polysaccharide, and conjugate	All use specific antigens that best stimulate the immune system.	Pros: targets specific epitopes of antigen; lower chance of adverse reactions. Cons: expensive; weaker immune response.	HBV (antigen = HBsAg), HPV, acellular pertussis (aP), *Neisseria meningitidis* (various strains), *Streptococcus pneumoniae* (PPSV23 polysaccharide primarily T-cell–independent response; PCV13 conjugated polysaccharide produces T-cell–dependent response), *Haemophilus influenzae* type b, herpes zoster.
Toxoid	Denatured bacterial toxin with an intact receptor binding site. Stimulates immune system to make antibodies without potential for causing disease.	Pros: protects against the bacterial toxins. Cons: antitoxin levels decrease with time, thus booster shots may be needed.	*Clostridium tetani*, *Corynebacterium diphtheriae*.
mRNA	A lipid nanoparticle delivers mRNA, causing cells to synthesize foreign protein (eg, spike protein of SARS-CoV-2). Induces cellular and humoral immunity.	Pros: high efficacy, safe in pregnancy. Cons: local and transient systemic (fatigue, headache, myalgia) reactions are common. Rare myocarditis, pericarditis particularly in young males.	SARS-CoV-2

Bacterial genetics

Transformation

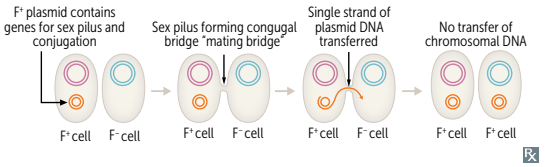
Competent bacteria can bind and import short pieces of environmental naked bacterial chromosomal DNA (from bacterial cell lysis). The transfer and expression of newly transferred genes is called transformation.
A feature of many bacteria, especially ***S pneumoniae***, ***H influenzae*** type b, and ***Neisseria*** (**SHiN**).
Adding deoxyribonuclease degrades naked DNA, preventing transformation.



Conjugation

$F^+ \times F^-$

F^+ plasmid contains genes required for sex pilus and conjugation. Bacteria without this plasmid are termed F^-. Sex pilus on F^+ bacterium contacts F^- bacterium. A single strand of plasmid DNA is transferred across the conjugal bridge ("mating bridge"). No transfer of chromosomal DNA.



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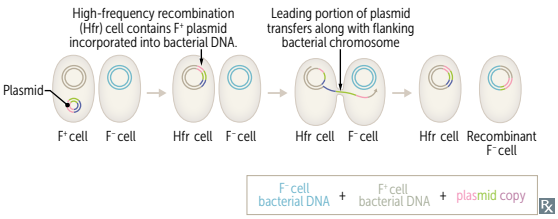
Hfr × F^-

F^+ plasmid can become incorporated into bacterial chromosomal DNA, termed high-frequency recombination (Hfr) cell. Transfer of leading part of plasmid and a few flanking chromosomal genes. High-frequency recombination may integrate some of those bacterial genes. Recipient cell remains F^- but now may have new bacterial genes.



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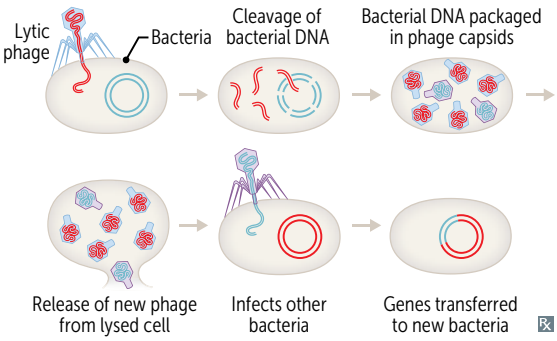
art revised for 2022 3rd pass

Transduction

Generalized

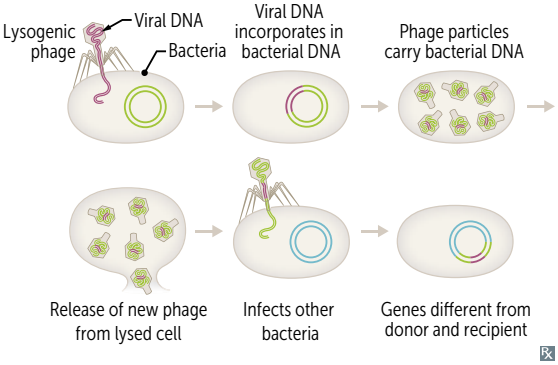
A "packaging" error. Lytic phage infects bacterium, leading to cleavage of bacterial DNA. Parts of bacterial chromosomal DNA may become packaged in phage capsid. Phage infects another bacterium, transferring these genes.



art revised for 2022 4th pass

Specialized

An "excision" event. Lysogenic phage infects bacterium; viral DNA incorporates into bacterial chromosome. When phage DNA is excised, flanking bacterial genes may be excised with it. DNA is packaged into phage capsid and can infect another bacterium.
Genes for the following 5 bacterial toxins are encoded in a lysogenic phage (**ABCD'S**): Group **A** strep erythrogenic toxin, **B**otulinum toxin, **C**holera toxin, **D**iphtheria toxin, **S**higa toxin.



Opportunistic fungal infections

Candida albicans

alba = white. Dimorphic; forms pseudohyphae and budding yeasts at 20°C A, germ tubes at 37°C B.

Systemic or superficial fungal infection. Causes oral C and esophageal thrush in immunocompromised (neonates, steroids, diabetes, AIDS), vulvovaginitis (diabetes, use of antibiotics), diaper rash, infective endocarditis (people who inject drugs), disseminated candidiasis (especially in neutropenic patients), chronic mucocutaneous candidiasis.

Treatment: oral fluconazole/topical azoles for vaginal; nystatin, azoles, or, rarely, echinocandins for oral; fluconazole, echinocandins, or amphotericin B for esophageal or systemic disease.

Aspergillus fumigatus

Septate hyphae that branch at 45° Acute Angle D.

Causes invasive aspergillosis in immunocompromised patients, especially those with neutrophil dysfunction (eg, chronic granulomatous disease) because *Aspergillus* is catalase ⊕.

Can cause aspergillomas E in pre-existing lung cavities, especially after TB infection.

Some species of *Aspergillus* produce Aflatoxins (associated with hepatocellular carcinoma).

Treatment: voriconazole or echinocandins (2nd-line).

Allergic bronchopulmonary aspergillosis (ABPA) F—hypersensitivity response to *Aspergillus* growing in lung mucus. Associated with asthma and cystic fibrosis; may cause bronchiectasis and eosinophilia.

Cryptococcus neoformans

5–10 µm with narrow budding. Heavily encapsulated yeast. Not dimorphic. ⊕ PAS staining.

Found in soil, pigeon droppings. Acquired through inhalation with hematogenous dissemination to meninges. Highlighted with India ink (clear halo G) and mucicarmine (red inner capsule H). Latex agglutination test detects polysaccharide capsular antigen and is more sensitive and specific.

Causes cryptococcosis, which can manifest with meningitis, pneumonia, and/or encephalitis ("soap bubble" lesions in brain), primarily in immunocompromised.

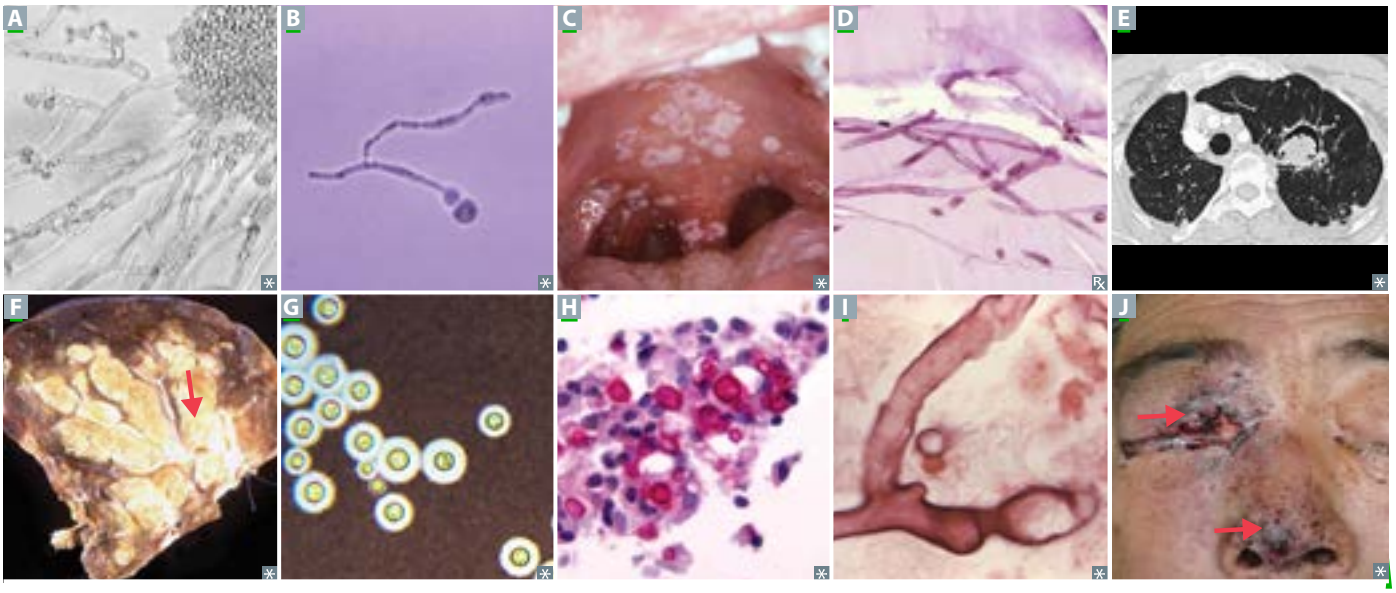
Treatment: amphotericin B + flucytosine followed by fluconazole for cryptococcal meningitis.

Mucor and *Rhizopus* spp

Irregular, broad, nonseptate hyphae branching at wide angles I.

Causes mucormycosis, mostly in patients with DKA and/or neutropenia (eg, leukemia). Inhalation of spores → fungi proliferate in blood vessel walls, penetrate cribriform plate, and enter brain. Rhinocerebral, frontal lobe abscess; cavernous sinus thrombosis. Headache, facial pain, black necrotic eschar on face J; may have cranial nerve involvement.

Treatment: surgical debridement, amphotericin B or isavuconazole.



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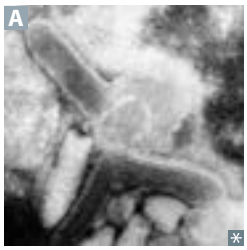
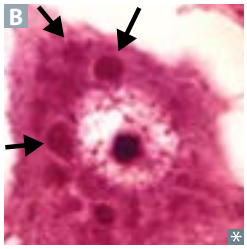
images E, F swapped for 2022 2nd pass

new image (B) for 2022 3rd pass

Rabies virus





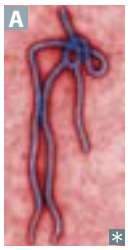
Bullet-shaped virus A. Negri bodies (cytoplasmic inclusions B) commonly found in Purkinje cells of cerebellum and in hippocampal neurons. Rabies has long incubation period (weeks to months) before symptom onset. Postexposure prophylaxis is wound cleaning plus immunization with killed vaccine and rabies immunoglobulin. Example of passive-active immunity.

Travels to the CNS by migrating in a retrograde fashion (via dynein motors) up nerve axons after binding to ACh receptors.

Progression of disease: fever, malaise → agitation, photophobia, hydrophobia, hypersalivation → paralysis, coma → death.

Infection more commonly from bat, raccoon, and skunk bites than from dog bites in the United States; aerosol transmission (eg, bat caves) also possible.

Ebola virus



A filovirus A. Following an incubation period of up to 21 days, presents with abrupt onset of flulike symptoms, diarrhea/vomiting, high fever, myalgia. Can progress to DIC, diffuse hemorrhage, shock.

Diagnosed with RT-PCR within 48 hr of symptom onset. High mortality rate.

Transmission requires direct contact with bodily fluids, fomites (including dead bodies), infected bats or primates (apes/monkeys); high incidence of healthcare-associated infection.

Supportive care, no definitive treatment. Vaccination of contacts, strict isolation of infected individuals, and barrier practices for healthcare workers are key to preventing transmission.

Fact revised for 2022 2nd pass

Severe acute respiratory syndrome coronavirus 2

SARS-CoV-2 is a novel ⊕ ssRNA coronavirus and the cause of the COVID-19 pandemic.

Clinical course varies; often asymptomatic.

Symptoms include
- Common: fever, dry cough, shortness of breath, fatigue.
- More specific: anosmia (loss of smell), dysgeusia (altered taste).

Complications include acute respiratory distress syndrome, hypercoagulability (→ thrombotic complications including cryptogenic and/or ischemic stroke), shock, organ failure, death.

Risk factors for severe illness or death include increasing age (strongest risk factor), obesity, diabetes, hypertension, chronic kidney disease, severe cardiopulmonary illness.

Diagnosed by NAAT (most commonly RT-PCR). Tests detecting viral antigen are typically less sensitive than NAATs, but can be performed rapidly and may be more accessible.

Spreads through respiratory droplets and aerosols. Host cell entry occurs by attachment of viral spike protein to ACE2 receptor on cell membranes. Anti-spike protein antibodies confer immunity.

Vaccination induces humoral and cellular immunity, which decreases risk of contracting or transmitting the virus and prevents more serious disease, hospitalization, and death.

Supplemental oxygen and supportive care remain the mainstay of therapy for hospitalized patients. Dexamethasone, remdesivir, and IL-6 pathway inhibitors may benefit some severely ill patients.

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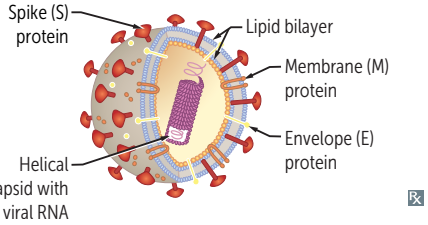


New content for 2022 1st Pass

▸ PATHOLOGY—AGING

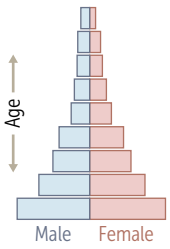
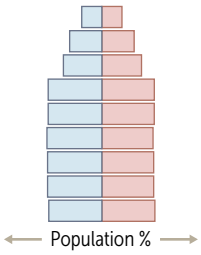
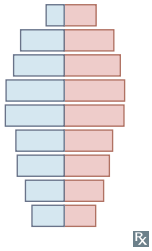
Normal aging	Time-dependent progressive decline in organ function resulting in ↑ susceptibility to disease. Associated with genetic (eg, telomere shortening), epigenetic (eg, DNA methylation), and metabolic (eg, mitochondrial dysfunction) alterations.
Cardiovascular	↓ arterial compliance (↑ stiffness), ↑ aortic diameter, ↓ left ventricular cavity size and sigmoid-shaped interventricular septum (due to myocardial hypertrophy), ↑ left atrial cavity size, aortic and mitral valve calcification, ↓ maximum heart rate.
Gastrointestinal	↓ LES tone, ↓ gastric mucosal protection, ↓ colonic motility.
Hematopoietic	↓ bone marrow mass, ↑ bone marrow fat; less vigorous response to stressors (eg, blood loss).
Immune	Predominant effect on adaptive immunity: ↓ naive B cells and T cells, preserved memory B cells and T cells. Immunosenescence impairs response to new antigens (eg, pathogens, vaccines).
Musculoskeletal	↓ skeletal muscle mass (sarcopenia), ↓ bone mass (osteopenia), joint cartilage thinning.
Nervous	↓ brain volume (neuronal loss), ↓ cerebral blood flow; function is preserved despite mild cognitive decline.
Special senses	Impaired accommodation (presbyopia), ↓ hearing (presbycusis), ↓ smell and taste.
Skin	Atrophy with flattening of dermal-epidermal junction; ↓ dermal collagen and ↓ elastin (wrinkles, senile purpura), ↓ sweat glands (heat stroke), ↓ sebaceous glands (xerosis cutis). ▪ Intrinsic aging (chronological aging)—↓ biosynthetic capacity of dermal fibroblasts. ▪ Extrinsic aging (photoaging)—degradation of dermal collagen and elastin from sun exposure (UVA); degradation products accumulate in dermis (solar elastosis).
Renal	↓ GFR (↓ nephrons), ↓ RBF, ↓ hormonal function. Voiding dysfunction (eg, urinary incontinence).
Reproductive	Males—testicular atrophy (↓ spermatogenesis), prostate enlargement, slower erection/ejaculation, longer refractory period. Less pronounced ↓ in libido as compared to females. Females—vulvovaginal atrophy; vaginal shortening, thinning, dryness, ↑ pH.
Respiratory	↑ lung compliance (↓ elastic recoil), ↓ chest wall compliance (↑ stiffness), ↓ respiratory muscle strength; ↓ FEV_1, ↓ FVC, ↑ RV (TLC is unchanged); ↑ A-a gradient, ↑ $\dot{V}/\dot{Q}$ mismatch. Ventilatory response to hypoxia/hypercapnia is blunted. Less vigorous cough, slower mucociliary clearance.

Quantifying risk *(continued)*

TERM	DEFINITION	EXAMPLE	FORMULA
Mortality rate	Number of deaths (in general or due to specific cause) within a population over a defined period.	If 80 people in a town of 10,000 die over 2 years, mortality rate is 4 per 1000 per year.	Deaths/1000 people per year.
Attack rate	Proportion of exposed people who become ill.	If 80 people in a town are exposed and 60 people become ill, attack rate is 75%.	$\frac{\text{People who become ill}}{\text{Total people exposed}}$

Demographic transition

As a country proceeds to higher levels of development, birth and mortality rates decline to varying degrees, changing the age composition of the population.

Population pyramid			
Birth rate	↑↑	↓	↓↓
Mortality rate	↑	↓	↓
Life expectancy	Short	Long	Long
Population	Growing	Stable	Declining

Likelihood ratio

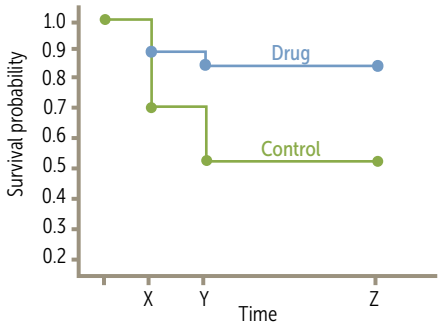
$$LR^{+} = \frac{\text{probability of positive result in patient with disorder}}{\text{probability of positive result in patient without disorder}} = \frac{\text{sensitivity}}{1 - \text{specificity}} = \frac{\text{TP rate}}{\text{FP rate}}$$

$$LR^{-} = \frac{\text{probability of negative result in patient with disorder}}{\text{probability of negative result in patient without disorder}} = \frac{1 - \text{sensitivity}}{\text{specificity}} = \frac{\text{FN rate}}{\text{TN rate}}$$

$LR^{+} > 10$ indicates a highly specific test, while $LR^{-} < 0.1$ indicates a highly sensitive test.
Pretest probability × LR = posttest odds. Posttest probability = posttest odds / (posttest odds + 1).

Kaplan-Meier curve

Graphic representation of event probability (y-axis) vs length of time (x-axis). Useful for displaying "time-to-event" data. Outcomes examined may include any event, but frequently include mortality. Survival probability = 1 – (event probability).



High-output heart failure

Uncommon form of HF characterized by ↑ CO. High-output state is due to ↓ SVR from either vasodilation or arteriovenous shunting. Causes include severe obesity, advanced cirrhosis, severe anemia, hyperthyroidism, wet beriberi, Paget disease of bone.

Presents with symptoms and signs of pulmonary and/or systemic venous congestion.

Shock

Fact revised for 2022 1st pass

Inadequate organ perfusion and delivery of nutrients necessary for normal tissue and cellular function. Initially may be reversible but life threatening if not treated promptly.

TYPE	CAUSED BY	MECHANISM	SKIN	CVP (RIGHT HEART PRELOAD)	PCWP (LEFT HEART PRELOAD)	CO	SVR (AFTERLOAD)	SVO_2 (MIXED VENOUS CONTENT)
Hypovolemic shock	Hemorrhage, dehydration, burns	Volume depletion	Cold, clammy	↓	↓↓	↓	↑	↓
Cardiogenic shock	MI, HF, vascular dysfunction, arrhythmia	Left heart dysfunction		↑	↑	↓↓	↑	↓
Obstructive shock	Cardiac tamponade, PE, tension pneumothorax	Right heart dysfunction		↑	↑[a]	↓↓	↑	↓
Distributive shock	Sepsis (early), anaphylaxis	Systemic vasodilation	Warm, dry	↓	↓	↑	↓↓	↑
	CNS injury			↓	↓	↓	↓↓	normal/↑

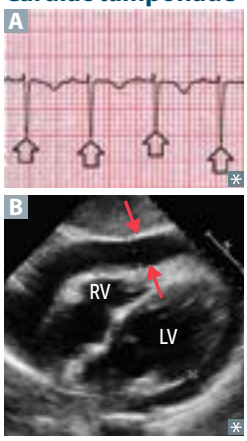
Double arrow = primary physiologic disorder driving the shock.

[a] ↑ in cardiac tamponade.

Cardiac tamponade

Fact revised for 2022 2nd pass

art revised for 2022 2nd pass



Compression of the heart by fluid (eg, blood, effusions) → ↓ CO. Equilibration of diastolic pressures in all 4 chambers.

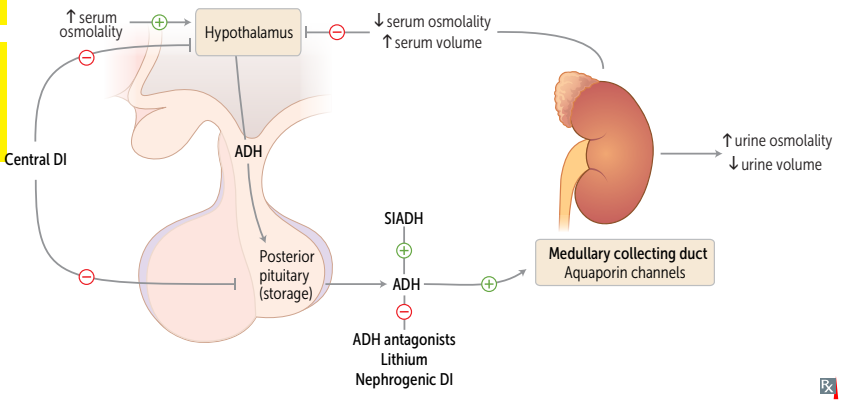
Findings: Beck triad (hypotension, distended neck veins, distant heart sounds), ↑ HR, pulsus paradoxus. ECG shows low-voltage QRS and electrical alternans A (due to "swinging" movement of heart in large effusion). Echocardiogram shows pericardial effusion (arrows in B), systolic RA collapse, diastolic RV collapse, and IVC plethora.

Treatment: pericardiocentesis or surgical drainage.

Pulsus paradoxus—↓ in amplitude of systolic BP by > 10 mm Hg during inspiration. ↑ venous return during inspiration → ↑ RV filling → interventricular septum bows toward LV (due to ↓ pericardial compliance) → ↓ LV ejection volume → ↓ systolic BP. Seen in constrictive pericarditis, obstructive pulmonary disease (eg, Croup, OSA, Asthma, COPD), cardiac Tamponade (pea COAT).

▸ ENDOCRINE—PATHOLOGY

Syndrome of inappropriate antidiuretic hormone secretion



Characterized by excessive free water retention, euvolemic hyponatremia with continued urinary Na^+ excretion, urine osmolality > serum osmolality.

Body responds to water retention with ↓ aldosterone and ↑ ANP and BNP → ↑ urinary Na^+ secretion → normalization of extracellular fluid volume → euvolemic hyponatremia.

Treatment: fluid restriction (first line), salt tablets, IV hypertonic saline, diuretics, ADH antagonists (eg, conivaptan, tolvaptan, demeclocycline).

SIADH causes include (HEELD-up water):

- Head trauma/CNS disorders
- Ectopic ADH (eg, small cell lung cancer)
- Exogenous hormones (eg, vasopressin, desmopressin, oxytocin)
- Lung disease
- Drugs (eg, SSRIs, carbamazepine, cyclophosphamide)

Primary polydipsia and diabetes insipidus

Characterized by the production of large amounts of dilute urine +/– thirst. Urine specific gravity < 1.006. Urine osmolality usually < 300 mOsm/kg. Central DI may be transient if damage is below hypothalamic median eminence or in the posterior pituitary (ADH in hypothalamus can still be secreted systemically via portal capillaries in median eminence).

	Primary polydipsia	Central DI	Nephrogenic DI
DEFINITION	Excessive water intake	↓ ADH release	ADH resistance
CAUSES	Psychiatric illnesses, hypothalamic lesions affecting thirst center	Idiopathic, brain injury (trauma, hypoxia, tumor, surgery, infiltrative diseases)	Hereditary (ADH receptor mutation), drugs (eg, lithium, demeclocycline), hypercalcemia, hypokalemia
SERUM OSMOLALITY	↓	↑	↑
ADH LEVEL	↓ or normal	↓	Normal or ↑
WATER RESTRICTION[a]	Significant ↑ in urine osmolality (> 700 mOsm/kg)	No change or slight ↑ in urine osmolality	No change or slight ↑ in urine osmolality
DESMOPRESSIN ADMINISTRATION[b]	—	Significant ↑ in urine osmolality (> 50%)	Minimal change in urine osmolality
TREATMENT	Water restriction	Desmopressin (DDAVP)	Manage the underlying cause; low-solute diet, HCTZ, amiloride, indomethacin

[a]No water intake for 2–3 hours followed by hourly measurements of urine volume and osmolality as well as plasma Na^+ concentration and osmolality.

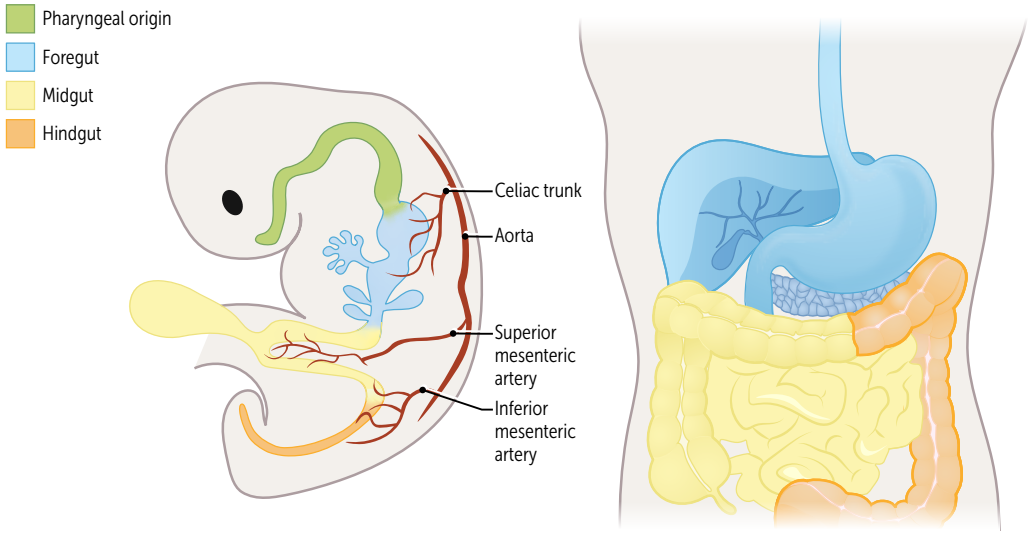
[b]Desmopressin (ADH analog) is administered if serum osmolality > 295–300 mOsm/kg, plasma Na^+ ≥ 145 mEq/L, or urine osmolality does not increase despite ↑ plasma osmolality.

▸ GASTROINTESTINAL—EMBRYOLOGY

Normal gastrointestinal embryology

Foregut—esophagus to duodenum at level of pancreatic duct and common bile duct insertion (ampulla of Vater).
Midgut—lower duodenum to proximal 2/3 of transverse colon.
Hindgut—distal 1/3 of transverse colon to anal canal above pectinate line.
Midgut:

- 6th week of development—physiologic herniation of midgut through umbilical ring
- 10th week of development—returns to abdominal cavity + rotates around superior mesenteric artery (SMA), total 270° counterclockwise



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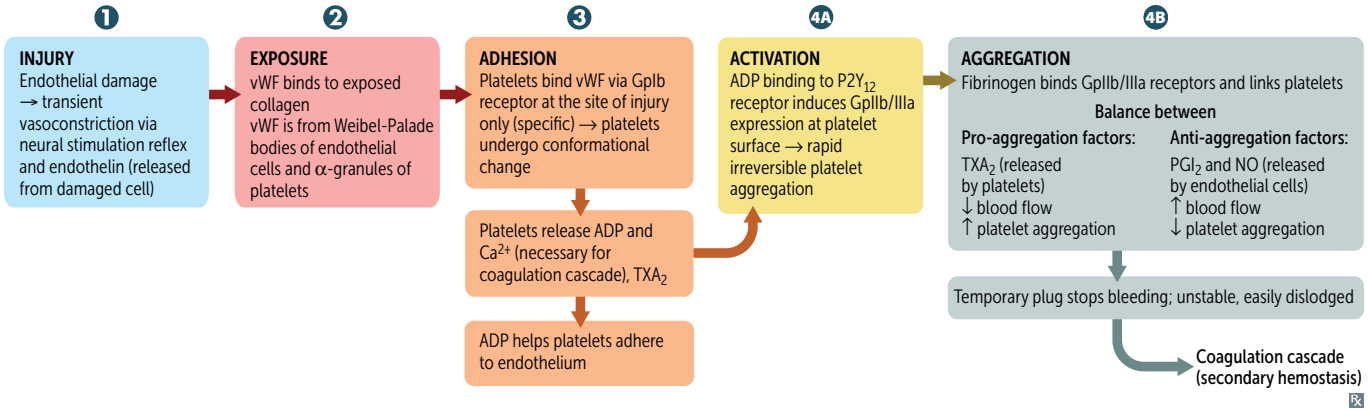
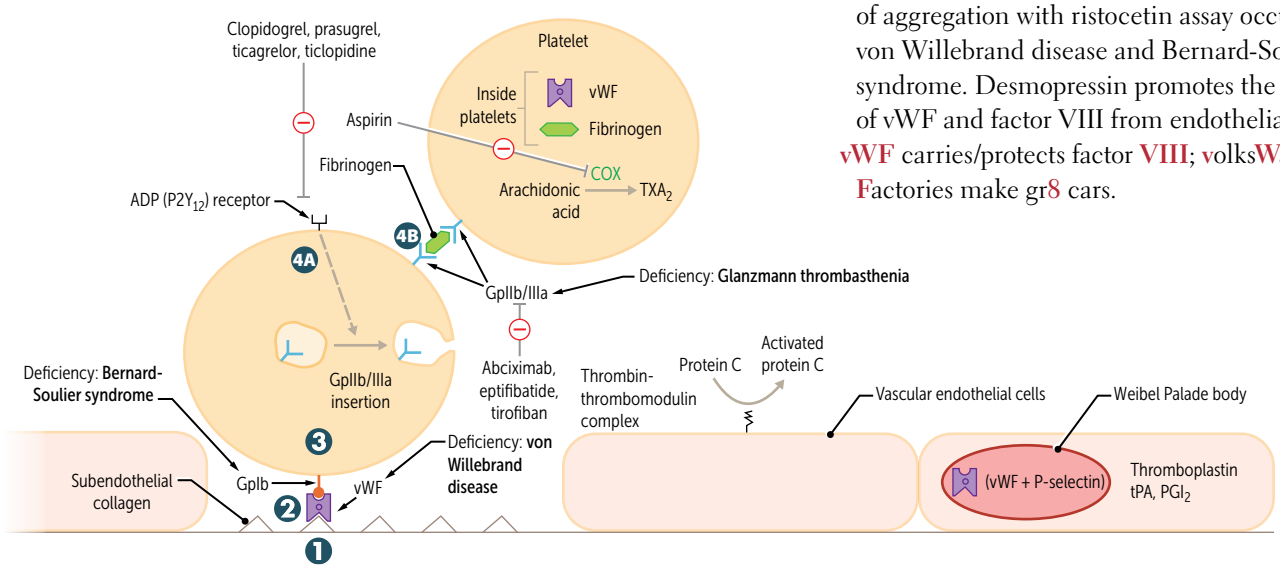
Platelet plug formation (primary hemostasis)



Thrombogenesis



Formation of insoluble fibrin mesh.

Aspirin irreversibly inhibits cyclooxygenase, thereby inhibiting TXA_2 synthesis.

Clopidogrel, prasugrel, ticagrelor, and ticlopidine inhibit ADP-induced expression of GpIIb/IIIa by blocking $P2Y_{12}$ receptor.

Abciximab, eptifibatide, and tirofiban inhibit GpIIb/IIIa directly.

Ristocetin activates vWF to bind GpIb. Failure of aggregation with ristocetin assay occurs in von Willebrand disease and Bernard-Soulier syndrome. Desmopressin promotes the release of vWF and factor VIII from endothelial cells.

vWF carries/protects factor VIII; volksWagen Factories make gr8 cars.

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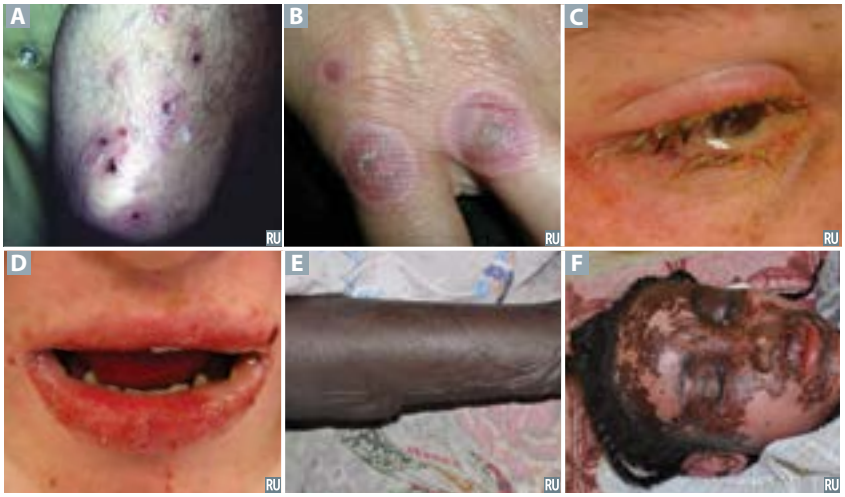
Other blistering skin disorders

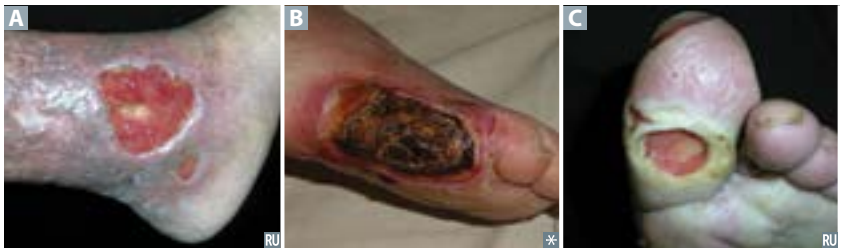
Dermatitis herpetiformis	Pruritic papules, vesicles, and bullae (often found on elbows, knees, buttocks) A. Deposits of IgA at tips of dermal papillae. Associated with celiac disease. Treatment: dapsone, gluten-free diet.
Erythema multiforme	Associated with infections (eg, *Mycoplasma pneumoniae*, HSV), drugs (eg, sulfa drugs, β-lactams, phenytoin). Presents with multiple types of lesions—macules, papules, vesicles, target lesions (look like targets with multiple rings and dusky center showing epithelial disruption) B.
Stevens-Johnson syndrome	Characterized by fever, bullae formation and necrosis, sloughing of skin at dermal-epidermal junction (⊕ Nikolsky), high mortality rate. Typically mucous membranes are involved C D. Targetoid skin lesions may appear, as seen in erythema multiforme. Usually associated with adverse drug reaction. Toxic epidermal necrolysis (TEN) E F is more severe form of SJS involving > 30% body surface area. 10–30% involvement denotes SJS-TEN.



Lower extremity ulcers

	Venous ulcer	Arterial ulcer	Neuropathic ulcer
ETIOLOGY	Chronic venous insufficiency; most common ulcer type	Peripheral artery disease (eg, atherosclerotic stenosis)	Peripheral neuropathy (eg, diabetic foot)
LOCATION	Gaiter area (ankle to midcalf), typically over malleoli	Distal toes, anterior shin, pressure points	Bony prominences (eg, metatarsal heads, heel)
APPEARANCE	Irregular border, shallow, exudative A	Symmetric with well-defined punched-out appearance B	Hyperkeratotic edge with undermined borders C
PAIN	Mild to moderate	Severe	Absent
ASSOCIATED SIGNS	Telangiectasias, varicose veins, edema, stasis dermatitis (erythematous eczematous patches)	Signs of arterial insufficiency including cold, pale, atrophic skin with hair loss and nail dystrophy, absent pulses	Claw toes, Charcot joints, absent reflexes

new images for 2022 2nd pass



new images (B, C) for 2022 3rd pass

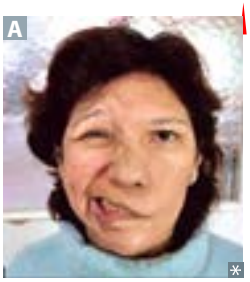
Common cranial nerve lesions

CN V motor lesion	Jaw deviates **toward** side of lesion due to unopposed force from the opposite pterygoid muscle.
CN X lesion	Uvula deviates **away** from side of lesion. Weak side collapses and uvula points away.
CN XI lesion	Weakness turning head to contralateral side of lesion (SCM). Shoulder droop on side of lesion (trapezius).
CN XII lesion	LMN lesion. Tongue deviates **toward** side of lesion ("lick your wounds") due to weakened tongue muscles on affected side.

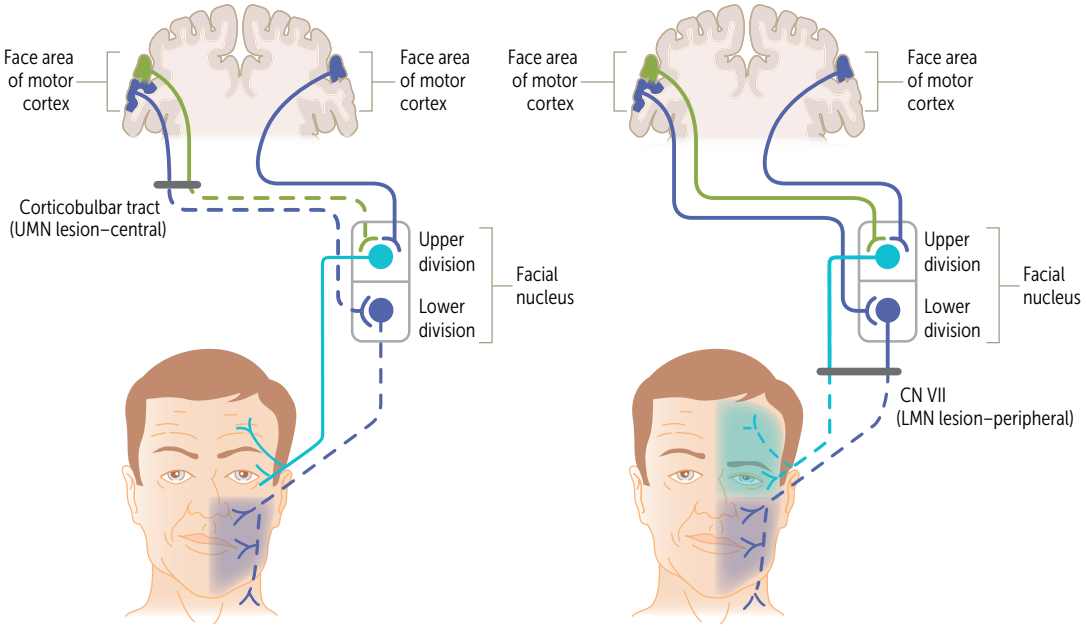
Facial nerve lesions

Bell palsy is the most common cause of peripheral facial palsy A. Usually develops after HSV reactivation. Treatment: glucocorticoids +/– acyclovir. Most patients gradually recover function, but aberrant regeneration can occur. Other causes of peripheral facial palsy include Lyme disease, herpes zoster (Ramsay Hunt syndrome), sarcoidosis, tumors (eg, parotid gland), diabetes mellitus.

A

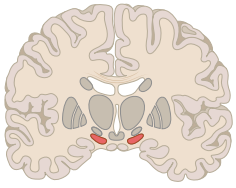
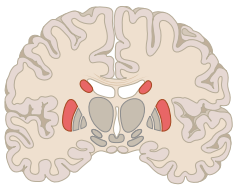
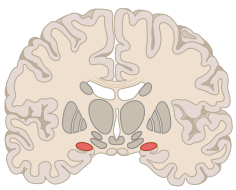


	Upper motor neuron lesion	Lower motor neuron lesion
LESION LOCATION	Motor cortex, connection from motor cortex to facial nucleus in pons	Facial nucleus, anywhere along CN VII
AFFECTED SIDE	Contralateral	Ipsilateral
MUSCLES INVOLVED	Lower muscles of facial expression	Upper and lower muscles of facial expression
FOREHEAD INVOLVED?	Spared, due to bilateral UMN innervation	Affected
OTHER SYMPTOMS	Variable; depends on size of lesion	Incomplete eye closure (dry eyes, corneal ulceration), hyperacusis, loss of taste sensation to anterior tongue



Neurodegenerative disorders

↓ in cognitive ability, memory, or function with intact consciousness.
Must rule out depression as cause of dementia (called pseudodementia). Other reversible causes of dementia: hypothyroidism, vitamin B_{12} deficiency, neurosyphilis, normal pressure hydrocephalus.

DISEASE	DESCRIPTION	HISTOLOGIC/GROSS FINDINGS
Parkinson disease 	Parkinson **TRAPSS** your body: **T**remor (pill-rolling tremor at rest) **R**igidity (cogwheel) **A**kinesia (or bradykinesia) **P**ostural instability **S**huffling gait **S**mall handwriting (micrographia) Dementia is usually a late finding. MPTP, a contaminant in illegal drugs, is metabolized to MPP+, which is toxic to substantia nigra.	Loss of dopaminergic neurons (ie, depigmentation) of substantia nigra pars compacta. Lewy bodies: composed of α-synuclein (intracellular eosinophilic inclusions A).
Huntington disease 	Autosomal dominant trinucleotide $(CAG)_n$ repeat expansion in the **hunt**ingtin *(HTT)* gene on chromosome **4** (**4 letters**) → toxic gain of function. Symptoms manifest between ages 20 and 50: chorea, athetosis, aggression, depression, dementia (sometimes initially mistaken for substance use). Anticipation results from expansion of **CAG** repeats. **C**audate loses **A**Ch and **G**ABA.	Atrophy of caudate and putamen with ex vacuo ventriculomegaly. ↑ dopamine, ↓ GABA, ↓ ACh in brain. Neuronal death via NMDA-R binding and glutamate excitotoxicity.
Alzheimer disease 	Most common cause of dementia in older adults. Advanced age is the strongest risk factor. Down syndrome patients have ↑ risk of developing early-onset Alzheimer disease, as APP is located on chromosome 21. ↓ ACh. Associated with the following altered proteins: ▪ ApoE-2: ↓ risk of sporadic form ▪ ApoE-4: ↑ risk of sporadic form ▪ APP, presenilin-1, presenilin-2: familial forms (10%) with earlier onset ApoE-2 is "protwoctive", apoE-4 is "four" Alzheimer disease.	Widespread cortical atrophy (normal cortex B; cortex in Alzheimer disease C), especially hippocampus (arrows in B and C). Narrowing of gyri and widening of sulci. Senile plaques D in gray matter: extracellular β-amyloid core; may cause amyloid angiopathy → intracranial hemorrhage; Aβ (amyloid-β) synthesized by cleaving amyloid precursor protein (APP). Neurofibrillary tangles E: intracellular, hyperphosphorylated tau protein = insoluble cytoskeletal elements; number of tangles correlates with degree of dementia. Hirano bodies—intracellular eosinophilic proteinaceous rods in hippocampus.
Frontotemporal dementia	Formerly called Pick disease. Early changes in personality and behavior (behavioral variant), or aphasia (primary progressive aphasia). May have associated movement disorders.	Frontotemporal lobe degeneration F. Inclusions of hyperphosphorylated tau (round Pick bodies G) or ubiquitinated TDP-43.

Renal clearance

$C_x = (U_x V)/P_x$ = volume of plasma from which the substance is completely cleared in the urine per unit time.
If $C_x <$ GFR: net tubular reabsorption and/or not freely filtered.
If $C_x >$ GFR: net tubular secretion of X.
If $C_x =$ GFR: no net secretion or reabsorption.

C_x = clearance of X (mL/min).
U_x = urine concentration of X (eg, mg/mL).
P_x = plasma concentration of X (eg, mg/mL).
V = urine flow rate (mL/min).

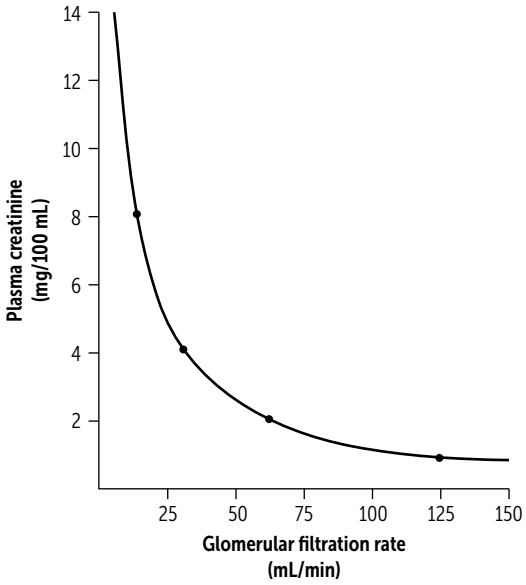
Glomerular filtration rate

Inulin clearance can be used to calculate GFR because it is freely filtered and is neither reabsorbed nor secreted.

$$C_{inulin} = GFR = U_{inulin} \times V/P_{inulin}$$
$$= K_f [(P_{GC} - P_{BS}) - (\pi_{GC} - \pi_{BS})]$$

(P_{GC} = glomerular capillary hydrostatic pressure; P_{BS} = Bowman space hydrostatic pressure; π_{GC} = glomerular capillary oncotic pressure; π_{BS} = Bowman space oncotic pressure; π_{BS} normally equals zero; K_f = filtration coefficient).

Normal GFR ≈ 100 mL/min.
Creatinine clearance is an approximate measure of GFR. Slightly overestimates GFR because creatinine is moderately secreted by renal tubules.



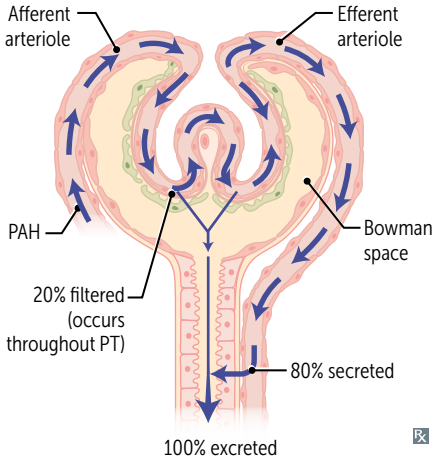
New fact for 2022 1st pass

Renal blood flow autoregulation

Autoregulatory mechanisms help maintain a constant RBF and GFR to protect the kidney from rapid increases or decreases in renal perfusion pressure that could cause renal injury or decrease glomerular filtration. Mechanisms:
Myogenic: ↑ arterial pressure → stretch of afferent arteriole → mechanical activation of vascular smooth muscle → vasoconstriction of afferent arteriole → ↓ RBF.
Tubuloglomerular: ↑ NaCl or tonicity of the filtrate sensed by macula densa cells → paracrine-driven vasoconstriction of afferent arteriole → ↓ RBF.

Effective renal plasma flow

Effective renal plasma flow (eRPF) can be estimated using *para*-aminohippuric acid (PAH) clearance. Between filtration and secretion, there is nearly 100% excretion of all PAH that enters the kidney.
$eRPF = U_{PAH} \times V/P_{PAH} = C_{PAH}$.
Renal blood flow (RBF) = RPF/(1 – Hct).
Usually 20–25% of cardiac output, remaining constant due to autoregulation.
eRPF underestimates true renal plasma flow (RPF) slightly.



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New fact for 2022 1st pass

Uterine rupture

Full-thickness disruption of uterine wall. Risk factors: prior C-section (usually occurs during labor in a subsequent pregnancy), abdominal trauma.

Presents with painful vaginal bleeding, fetal heart rate abnormalities (eg, bradycardia), easily palpable fetal parts, loss of fetal station. May be life threatening for both mother and fetus.

New fact for 2022 1st pass

Postpartum hemorrhage

Greater-than-expected blood loss after delivery. Leading cause of maternal mortality worldwide.

Etiology (4 T's): Tone (uterine atony → soft, boggy uterus; most common), Trauma (eg, lacerations, incisions, uterine rupture), Tissue (retained products of conception), Thrombin (coagulopathy).

Treatment: uterine massage, oxytocin. If refractory, surgical ligation of uterine or internal iliac arteries (fertility is preserved since ovarian arteries provide collateral circulation).

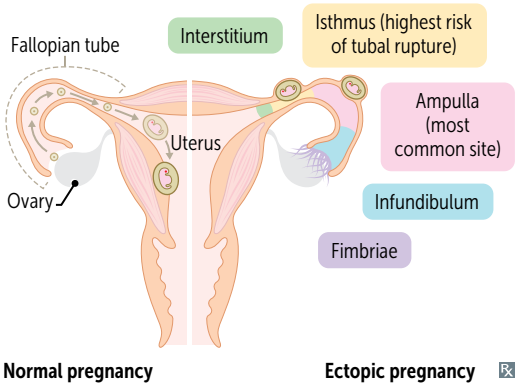
Fact revised for 2022 1st pass

Ectopic pregnancy

Implantation of fertilized ovum in a site other than the uterus, most often in ampulla of fallopian tube A. Risk factors: tubal pathologies (eg, scarring from salpingitis [PID] or surgery), previous ectopic pregnancy, IUD, IVF.

Presents with first-trimester bleeding and/or lower abdominal pain. Often clinically mistaken for appendicitis. Suspect in patients with history of amenorrhea, lower-than-expected rise in hCG based on dates. Confirm with ultrasound, which may show extraovarian adnexal mass.

Treatment: methotrexate, surgery.

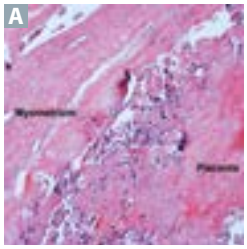


New fact for 2022 1st pass

Placental disorders

Placenta accreta spectrum

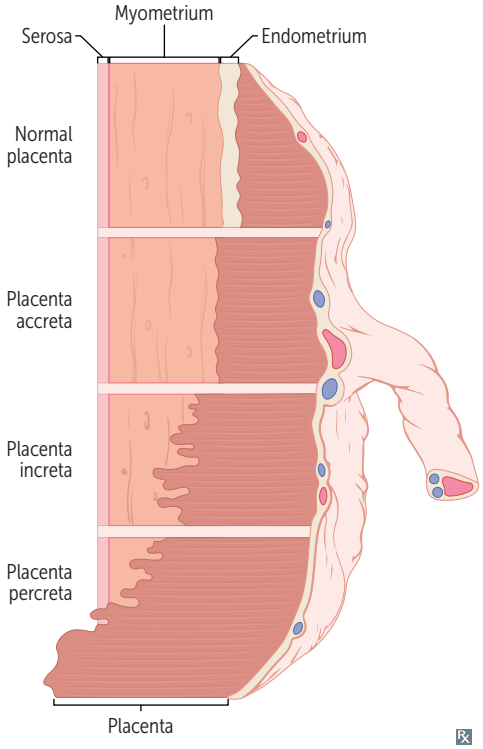
new image for 2022 2nd pass



Formerly called morbidly adherent placenta. Abnormal invasion of trophoblastic tissue into uterine wall A. Risk factors: prior C-section or other uterine surgery (areas of uterine scarring impair normal decidualization), placenta previa, ↑ maternal age, multiparity. Three types depending on depth of trophoblast invasion:

- Placenta accreta—attaches to myometrium (instead of overlying decidua basalis) without invading it. Most common type.
- Placenta increta—partially invades into myometrium.
- Placenta percreta—completely invades ("perforates") through myometrium and serosa, sometimes extending into adjacent organs (eg, bladder → hematuria).

Presents with difficulty separating placenta from uterus after fetal delivery and severe postpartum hemorrhage upon attempted manual removal of placenta (often extracted in pieces).



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Placenta previa

Attachment of placenta over internal cervical os (a "preview" of the placenta is visible through cervix). Risk factors: prior C-section, multiparity.

Presents with painless vaginal bleeding in third trimester.

Low-lying placenta—located < 2 cm from, but not covering, the internal cervical os.

Vasa previa

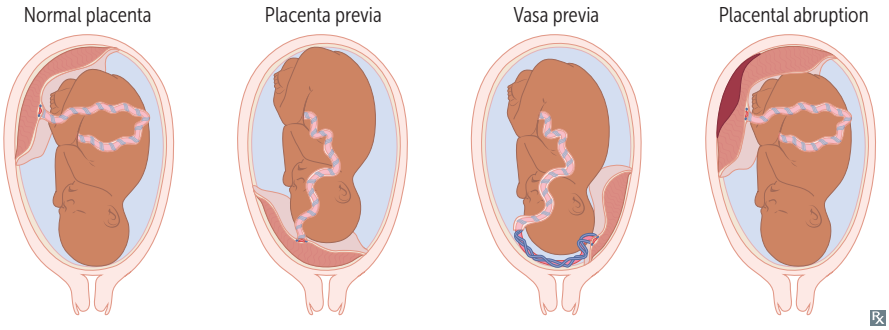
Fetal vessels run over, or < 2 cm from, the internal cervical os. Risk factors: velamentous insertion of umbilical cord (inserts in chorioamniotic membrane rather than placenta → fetal vessels travel to placenta unprotected by Wharton jelly), bilobed or succenturiate placenta.

Presents with painless vaginal bleeding (fetal blood from injured vessels) upon rupture of membranes accompanied by fetal heart rate abnormalities (eg, bradycardia). May lead to fetal death from exsanguination.

Placental abruption

Also called abruptio placentae. Premature separation of placenta from uterus prior to fetal delivery. Risk factors: maternal hypertension, preeclampsia, smoking, cocaine use, abdominal trauma.

Presents with abrupt, painful vaginal bleeding in third trimester; can lead to maternal hypovolemic shock (due to hemorrhage) and DIC (due to release of tissue factor from injured placenta), fetal distress (eg, hypoxia). May be life threatening for both mother and fetus.



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