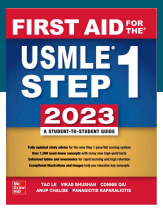
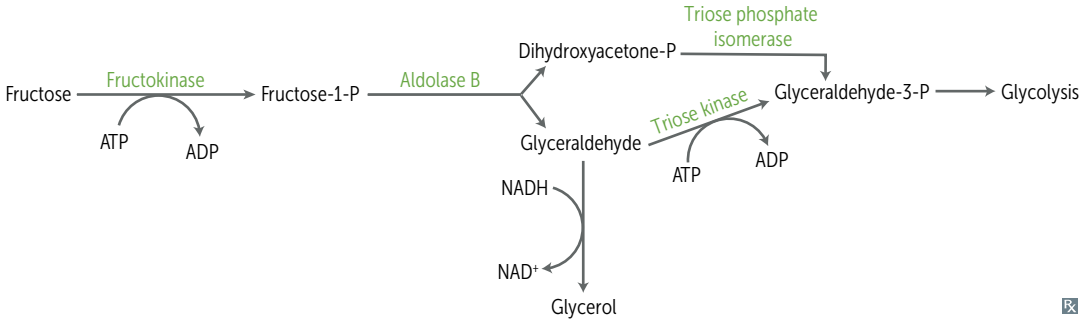


updated fact for 2023 1st pass

Disorders of fructose metabolism

	Essential fructosuria	Hereditary fructose intolerance
ENZYME DEFICIENCY	Fructokinase (autosomal recessive)	Aldolase B (autosomal recessive)
PATHOPHYSIOLOGY	Fructose is not trapped into cells. Hexokinase becomes 1° pathway for converting fructose to fructose-6-phosphate.	Fructose-1-phosphate accumulates → ↓ available phosphate → inhibition of glycogenolysis and gluconeogenesis.
PRESENTATION (SIGNS/SYMPTOMS)	Asymptomatic, benign. Fructose appears in blood and urine (fructo**kin**ase deficiency is **kin**der).	Hypoglycemia, jaundice, cirrhosis, vomiting. Symptoms only present following consumption of fruit, juice, or honey.
ADDITIONAL REMARKS	Urine dipstick will be ⊖ (tests for glucose only); reducing sugar can be detected in the urine (nonspecific test for inborn errors of carbohydrate metabolism).	
TREATMENT	–	↓ intake of fructose, sucrose (glucose + fructose), and sorbitol (metabolized to fructose).

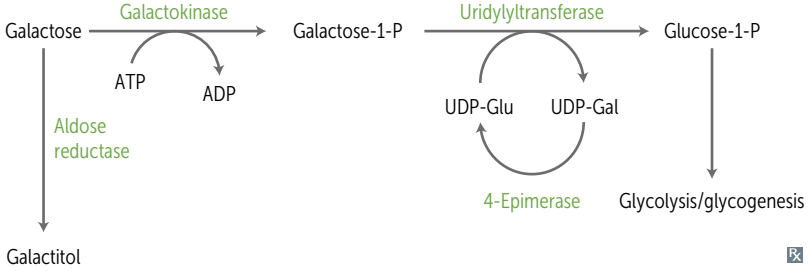


Disorders of galactose metabolism

updated fact for 2023 1st pass

	Galactokinase deficiency	Classic galactosemia
ENZYME DEFICIENCY	Galactokinase (autosomal recessive)	Galactose-1-phosphate uridyltransferase (autosomal recessive)
PATHOPHYSIOLOGY	Galactitol accumulates if diet has galactose.	Damage caused by accumulation of toxic substances (eg, galacitol).
PRESENTATION (SIGNS/SYMPTOMS)	Relatively mild/benign condition (galacto**kin**ase deficiency is **kin**der). Galactose appears in blood (galactosemia) and urine (galactosuria); infantile cataracts. May present as failure to track objects or develop social smile.	Symptoms start when infant is fed formula or breast milk → failure to thrive, jaundice, hepatomegaly, infantile cataracts (galacitol deposition in eye lens), intellectual disability. Can predispose neonates to *E coli* sepsis.
TREATMENT	–	Exclude galactose and lactose (galactose + glucose) from diet.

art revised for 2023 4th 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 from asymptomatic to critical; most infections are mild.

Predominant presenting symptoms can differ by variant:

- Common: fever, myalgia, headache, nasal congestion, sneezing, cough, sore throat, GI symptoms (eg, nausea, diarrhea).
- More specific: anosmia (loss of smell), dysgeusia (altered taste).

Pneumonia is the most frequent serious manifestation, but complications can include acute respiratory distress syndrome, hypercoagulability (→ thromboembolic complications including DVT, PE, stroke), myocardial injury, neurologic sequelae, shock, organ failure, death.

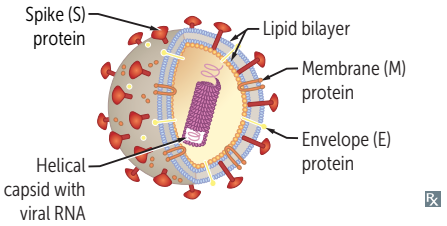
Strongest risk factors for severe illness or death include advanced age and pre-existing medical comorbidities (eg, obesity, hypertension).

Diagnosed by NAAT (most commonly RT-PCR). Tests detecting viral antigen are rapid and more accessible, but typically less sensitive than NAATs; negative results may warrant additional testing if there is a high suspicion of disease.

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

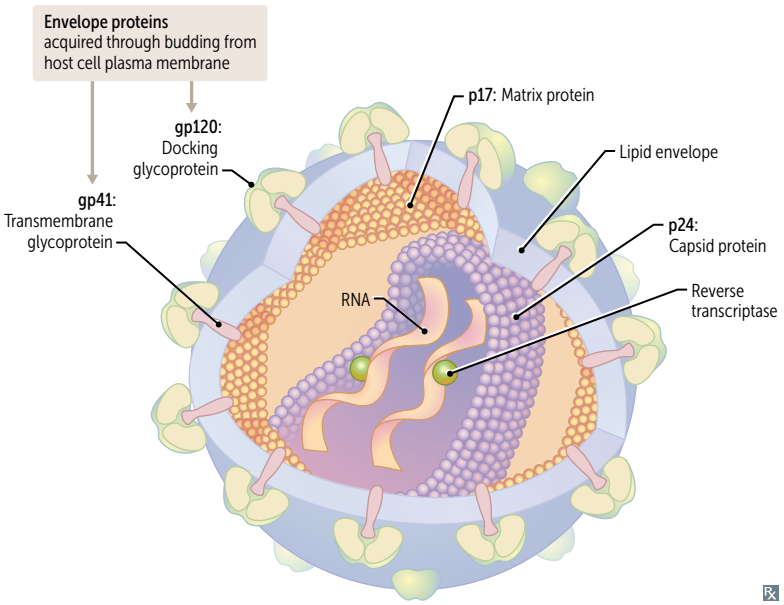
Vaccination (primary series and booster) induces humoral and cellular immunity, which decreases risk of contracting or transmitting the virus and confers high rates of protection against severe disease and death.

Virus-specific options include antivirals (remdesivir, nirmatrelivir-ritonavir, molnupiravir), and antibody-based therapies. Therapies directed against the inflammatory response include dexamethasone and immunomodulators (baricitinib, IL-6 pathway inhibitors).



updated fact for 2023 2nd pass

HIV



Diploid genome (2 molecules of RNA).

The 3 structural genes (protein coded for):

- *Env* (gp120 and gp41)—formed from cleavage of gp160 to form envelope glycoproteins.
  - gp120—attachment to host CD4+ T cell.
  - gp41 (forty-one)—fusion and entry.
- *gag* (p24 and p17)—capsid and matrix proteins, respectively.
- *pol*—Reverse transcriptase, Integrase, Protease; RIP "Pol" (Paul)

Reverse transcriptase synthesizes dsDNA from genomic RNA; dsDNA integrates into host genome.

Virus binds CD4 as well as a coreceptor, either CCR5 on macrophages (early infection) or CXCR4 on T cells (late infection).

Homozygous CCR5 mutation = immunity.

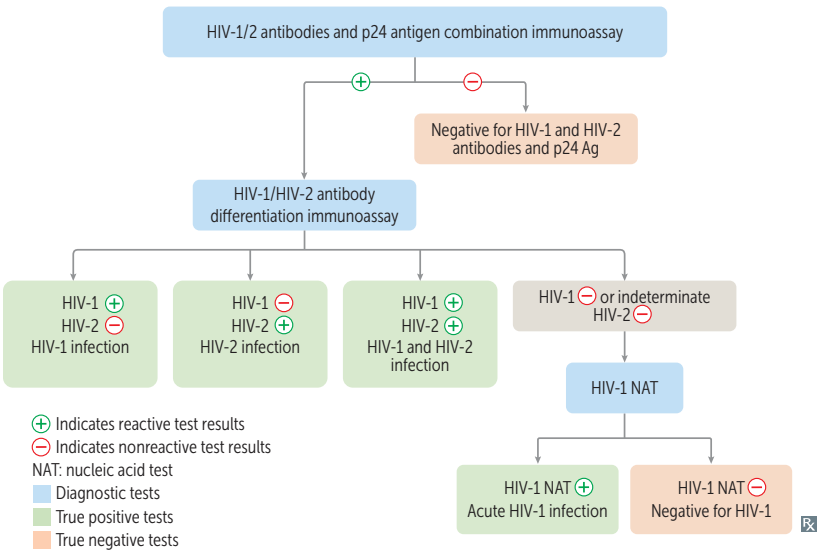
Heterozygous CCR5 mutation = slower course.

HIV diagnosis

updated fact for 2023 2nd pass

art revised for 2023 3rd pass

art revised for 2023 4th pass



HIV-1/2 Ag/Ab immunoassays detect viral p24 antigen capsid protein and IgG and/or IgM to HIV-1/2.

- Use for diagnosis. Very high sensitivity/specificity, but may miss early HIV disease if tested within first 2 weeks of infection.
- A positive screening test is followed by a confirmatory HIV-1/2 differentiation immunoassay.

HIV RNA tests detect elevated HIV RNA and can be qualitative or quantitative.

- NAAT is qualitative, and is a sensitive method to detect HIV viremia in antibody-negative patients.
- Viral load tests (RT-PCR) are quantitative and determine amount of viral RNA in the plasma. Use to monitor response to treatment and transmissibility.

Western blot tests are no longer recommended by the CDC for confirmatory testing.

HIV-1/2 Ag/Ab testing is not recommended in babies with suspected HIV due to maternally transferred antibody. Use HIV viral load instead.

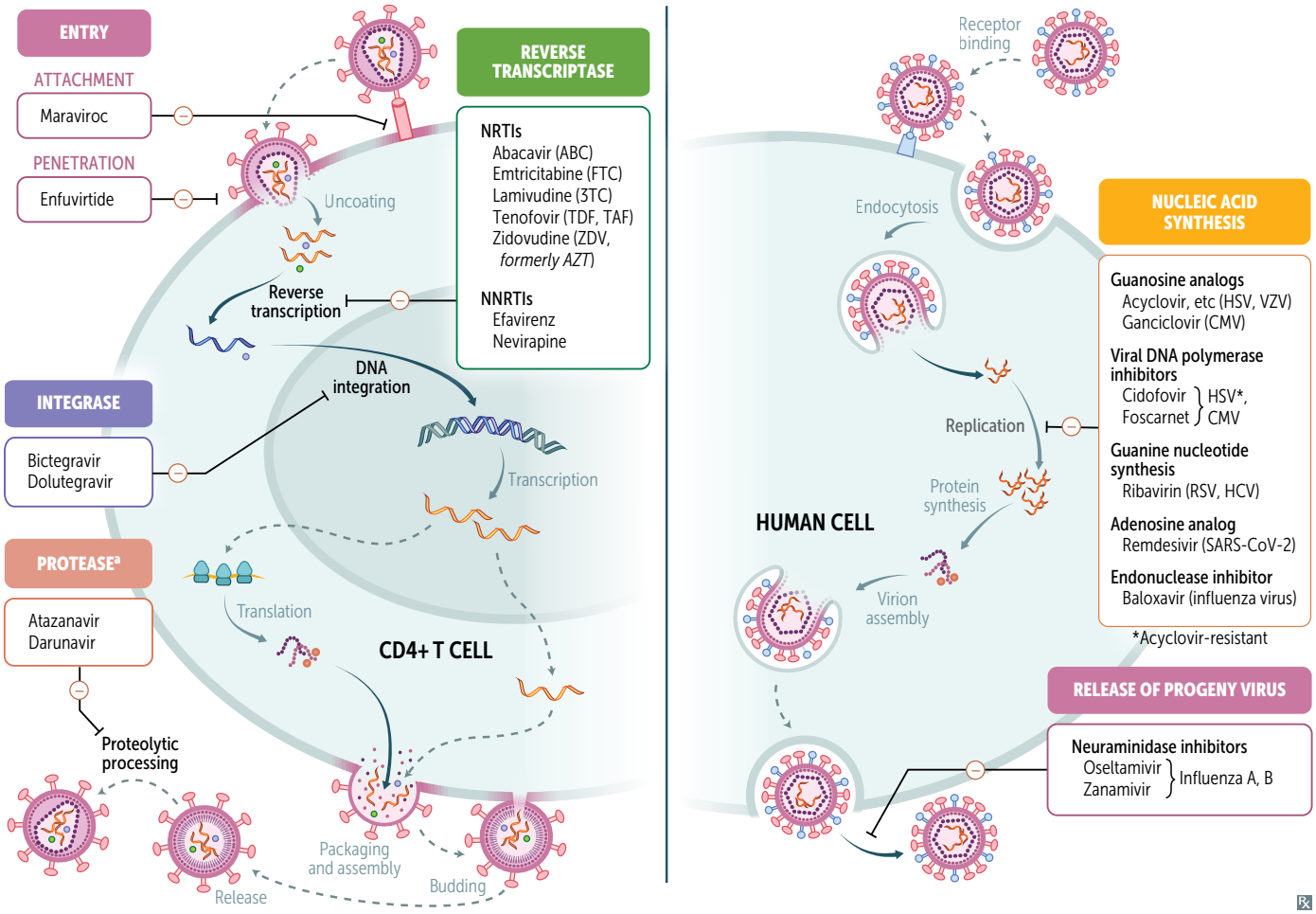
AIDS diagnosis: ≤ 200 CD4+ cells/mm^3 (normal: 500–1500 cells/mm^3) or HIV ⊕ with AIDS-defining condition (eg, *Pneumocystis pneumonia*).

Antihelminthic therapy

Pyrantel pamoate, ivermectin, mebendazole (microtubule inhibitor to treat "bendy worms"), praziquantel (↑ Ca^{2+} permeability, ↑ vacuolization), diethylcarbamazine.

Antiviral therapy

art revised for 2023 4th pass



[a]All protease inhibitors require boosting with either ritonavir (protease inhibitor only used as a boosting agent) or cobicistat (cytochrome P450 inhibitor).

Oseltamivir, zanamivir

MECHANISM	Inhibit influenza neuraminidase → ↓ release of progeny virus.
CLINICAL USE	Treatment and prevention of influenza A and B. Beginning therapy within 48 hours of symptom onset may shorten duration of illness.

Baloxavir

MECHANISM	Inhibits the "cap snatching" (transfer of the 5′ cap from cell mRNA onto viral mRNA) endonuclease activity of the influenza virus RNA polymerase → ↓ viral replication.
CLINICAL USE	Treatment within 48 hours of symptom onset shortens duration of illness.

Clinical therapeutic trial

Experimental study involving humans. Compares therapeutic benefits of ≥ 2 interventions (eg, treatment vs placebo, treatment vs treatment). Study quality improves when clinical trial is randomized, controlled, and double-blinded (ie, neither subject nor researcher knows whether the subject is in the treatment or control group). Triple-blind refers to additional blinding of the researchers analyzing the data.

Crossover clinical trial—compares the effect of a series of ≥ 2 treatments on a subject. Order in which subjects receive treatments is randomized. Washout period occurs between treatments. Allows subjects to serve as their own controls.

Intention-to-treat analysis—all subjects are analyzed according to their original, randomly assigned treatment. No one is excluded. Attempts to avoid bias from attrition, crossover, and nonrandom noncompliance, but may dilute the true effects of intervention.

As-treated analysis—all subjects are analyzed according to the treatment they actually received. ↑ risk of bias.

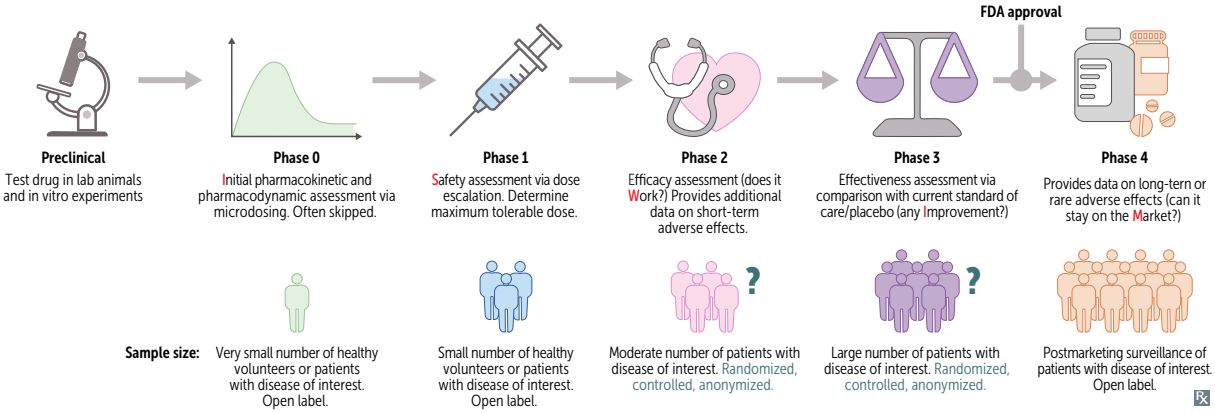
Per-protocol analysis—subjects who fail to complete treatment as originally, randomly assigned are excluded. ↑ risk of bias.

Clinical trials occur after preclinical studies and consist of five phases ("Can I SWIM?").

updated fact/new art for 2023 2nd pass

art revised for 2023 3rd pass

art revised for 2023 4th pass



Off-label drug use

Use of a drug to treat a disease in a form, population group, or dosage that is not specifically approved by the FDA. Reasons for off-label use include treatment of an illness with no approved pharmacologic treatment or exploring alternative treatments after failure of approved options.

Example: use of tricyclic antidepressants for treating neuropathic/chronic pain.

Bradford Hill criteria

A group of principles that provide limited support for establishing evidence of a causal relationship between presumed cause and effect.

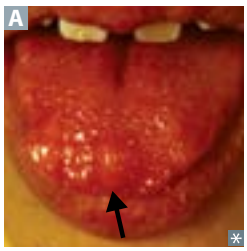
Strength	Association does not necessarily imply causation, but the stronger the association, the more evidence for causation.
Consistency	Repeated observations of the findings in multiple distinct samples.
Specificity	The more specific the presumed cause is to the effect, the stronger the evidence for causation.
Temporality	The presumed cause precedes the effect by an expected amount of time.
Biological gradient	Greater effect observed with greater exposure to the presumed cause (dose-response relationship).
Plausibility	A conceivable mechanism exists by which the cause may lead to the effect.
Coherence	The presumed cause and effect do not conflict with existing scientific consensus.
Experiment	Empirical evidence supporting the presumed cause and effect (eg, animal studies, in vitro studies).
Analogy	The presumed cause and effect are comparable to a similar, established cause and effect.

fact revised for 2023 3rd pass

Multiple endocrine neoplasias

All MEN syndromes have autosomal dominant inheritance.
The X-MEN are dominant over villains.

SUBTYPE	CHARACTERISTICS
MEN1	Pituitary tumors (prolactin or GH) Pancreatic endocrine tumors—Zollinger-Ellison syndrome, insulinomas, VIPomas, glucagonomas (rare) Parathyroid adenomas Associated with mutation of *MEN1* (tumor suppressor, codes for menin, chromosome 11), angiofibromas, collagenomas, meningiomas
MEN2A	Parathyroid hyperplasia Medullary thyroid carcinoma—neoplasm of parafollicular C cells; secretes calcitonin; prophylactic thyroidectomy required Pheochromocytoma (secretes catecholamines) Associated with mutation in *RET* (protooncogene, codes for receptor tyrosine kinase, chromosome 10)
MEN2B	Medullary thyroid carcinoma Pheochromocytoma Mucosal neuromas A (oral/intestinal ganglioneuromatosis) Associated with marfanoid habitus; mutation in *RET* gene



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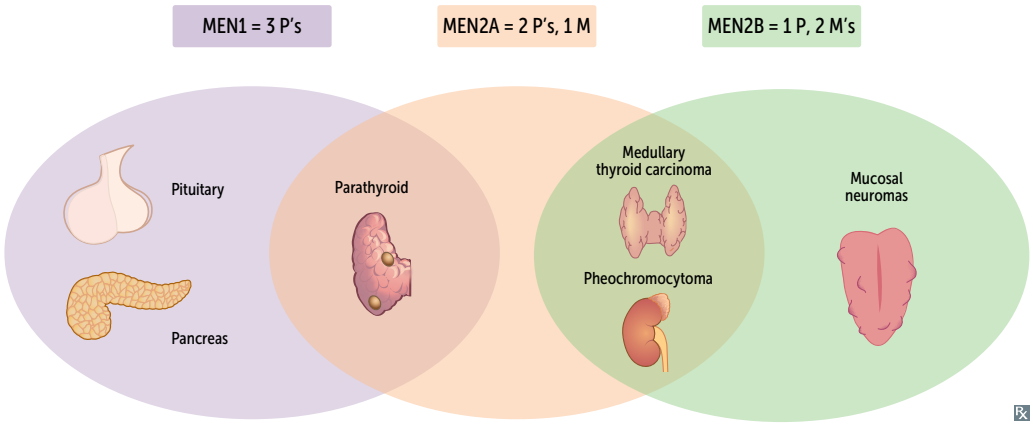


updated fact for 2023 2nd pass

Microcytic, hypochromic anemias

MCV < 80 fL.

Iron deficiency

↓ iron due to chronic bleeding (eg, GI loss, heavy menstrual bleeding), malnutrition, absorption disorders, GI surgery (eg, gastrectomy), or ↑ demand (eg, pregnancy) → ↓ final step in heme synthesis.

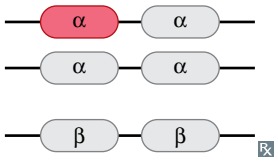
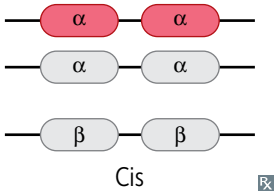
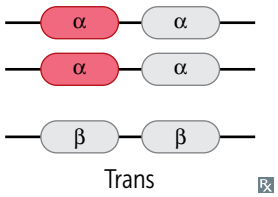
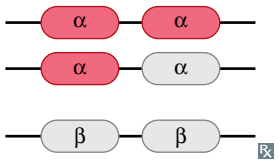
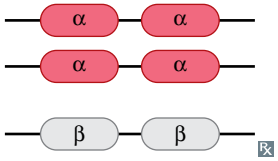
Labs: ↓ iron, ↑ TIBC, ↓ ferritin, ↑ free erythrocyte protoporphyrin, ↑ RDW, ↓ RI. Microcytosis and hypochromasia (↑ central pallor) A.

Symptoms: fatigue, conjunctival pallor B, restless leg syndrome, pica (persistent craving and compulsive eating of nonfood substances), spoon nails (koilonychia).

May manifest as glossitis, cheilosis, Plummer-Vinson syndrome (triad of iron deficiency anemia, esophageal webs, and dysphagia).

α-thalassemia

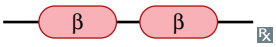
α-globin gene deletions on chromosome 16 → ↓ α-globin synthesis. May have *cis* deletion (deletions occur on same chromosome) or *trans* deletion (deletions occur on separate chromosomes). Normal is αα/αα. Often ↑ RBC count, in contrast to iron deficiency anemia. ↑ prevalence in people of Asian and African descent. Target cells C on peripheral smear.

# OF α-GLOBIN GENES DELETED[a]	DISEASE	CLINICAL OUTCOME
1 	α-thalassemia minima	No anemia (silent carrier)
2  Cis or  Trans	α-thalassemia minor	Mild microcytic, hypochromic anemia
3 	Hemoglobin H disease (HbH); excess β-globin forms β_4	Moderate to severe microcytic hypochromic anemia
4 	Hemoglobin Barts disease; no α-globin, excess γ-globin forms γ_4	Hydrops fetalis; incompatible with life

Microcytic, hypochromic anemias *(continued)*

β-thalassemia

Point mutation in splice sites or Kozak consensus sequence (promoter) on chromosome 11 → ↓ β-globin synthesis (β^+) or absent β-globin synthesis (β^0). ↑ prevalence in people of Mediterranean descent.

# OF β-GLOBIN GENES MUTATED±	DISEASE	CLINICAL OUTCOME
1 	β-thalassemia minor	Mild microcytic anemia. ↑ HbA_2.
2 (β^+/β^+ or β^+/β^0)	β-thalassemia intermedia	Variable anemia, ranging from mild/asymptomatic to severe/transfusion-dependent.
2 	β-thalassemia major (Cooley anemia)	Severe microcytic anemia with target cells and ↑ anisopoikilocytosis requiring blood transfusions (↑ risk of 2° hemochromatosis), marrow expansion ("crew cut" on skull x-ray) → skeletal deformities, extramedullary hematopoiesis → HSM. ↑ risk of parvovirus B19-induced aplastic crisis. ↑ HbF and HbA_2, becomes symptomatic after 6 months when HbF declines (HbF is protective). Chronic hemolysis → pigmented gallstones.
1 (β^+/HbS or β^0/HbS)	Sickle cell β-thalassemia	Mild to moderate sickle cell disease depending on whether there is ↓ (β^+/HbS) or absent (β^0/HbS) β-globin synthesis.

Lead poisoning

Lead inhibits ferrochelatase and ALA dehydratase → ↓ heme synthesis and ↑ RBC protoporphyrin. Also inhibits rRNA degradation → RBCs retain aggregates of rRNA (basophilic stippling).

Symptoms of LLEEAAD poisoning:

- **L**ead **L**ines on gingivae (Burton lines) and on metaphyses of long bones D on x-ray.
- **E**ncephalopathy and **E**rythrocyte basophilic stippling.
- **A**bdominal colic and sideroblastic **A**nemia.
- **D**rops—wrist and foot drop.

Treatment: chelation with succimer, EDTA, dimercaprol.

Exposure risk ↑ in old houses (built before 1978) with chipped paint (children) and workplace (adults).

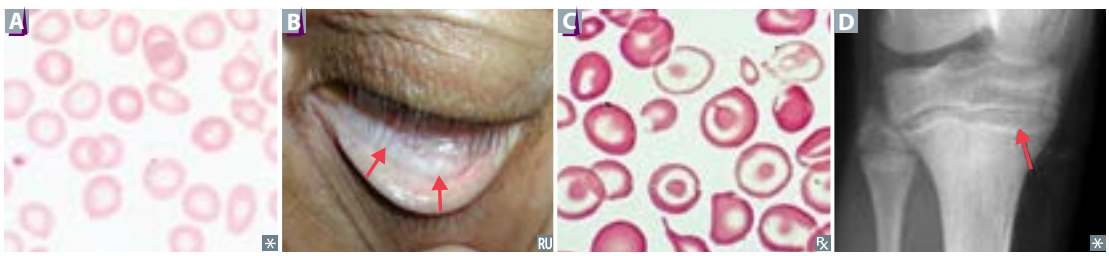
Sideroblastic anemia

Causes: genetic (eg, X-linked defect in ALA synthase gene), acquired (myelodysplastic syndromes), and reversible (alcohol is most common; also lead poisoning, vitamin B_6 deficiency, copper deficiency, drugs [eg, isoniazid, linezolid]).

Lab findings: ↑ iron, normal/↓ TIBC, ↑ ferritin. Ringed sideroblasts (with iron-laden, Prussian blue–stained mitochondria) seen in bone marrow. Peripheral blood smear: basophilic stippling of RBCs. Some acquired variants may be normocytic or macrocytic.

Treatment: pyridoxine (B_6, cofactor for ALA synthase).

art reordered for 2023 4th pass



new fact started for 2023 1st pass. needs text and then correct formatting will be done with photos at bottom, etc.

updated art and fact format for 2023 2nd pass moved to spread due to being a continued fact now

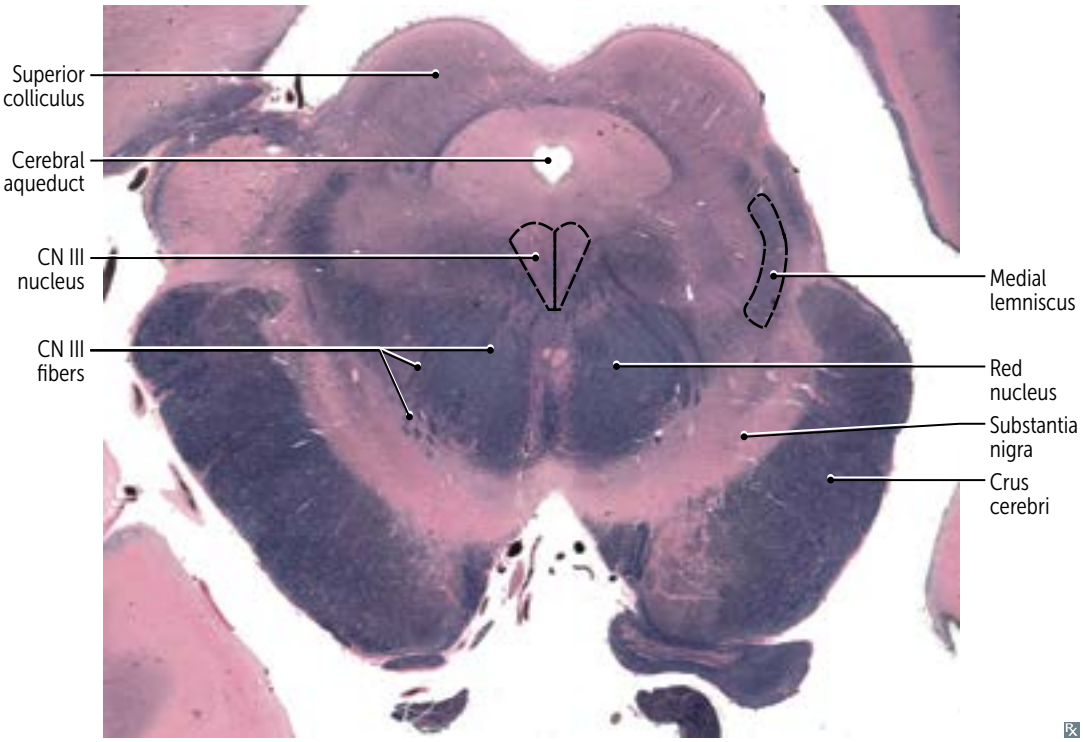
art revised for 2023 3rd pass

art revised for 2023 4th pass

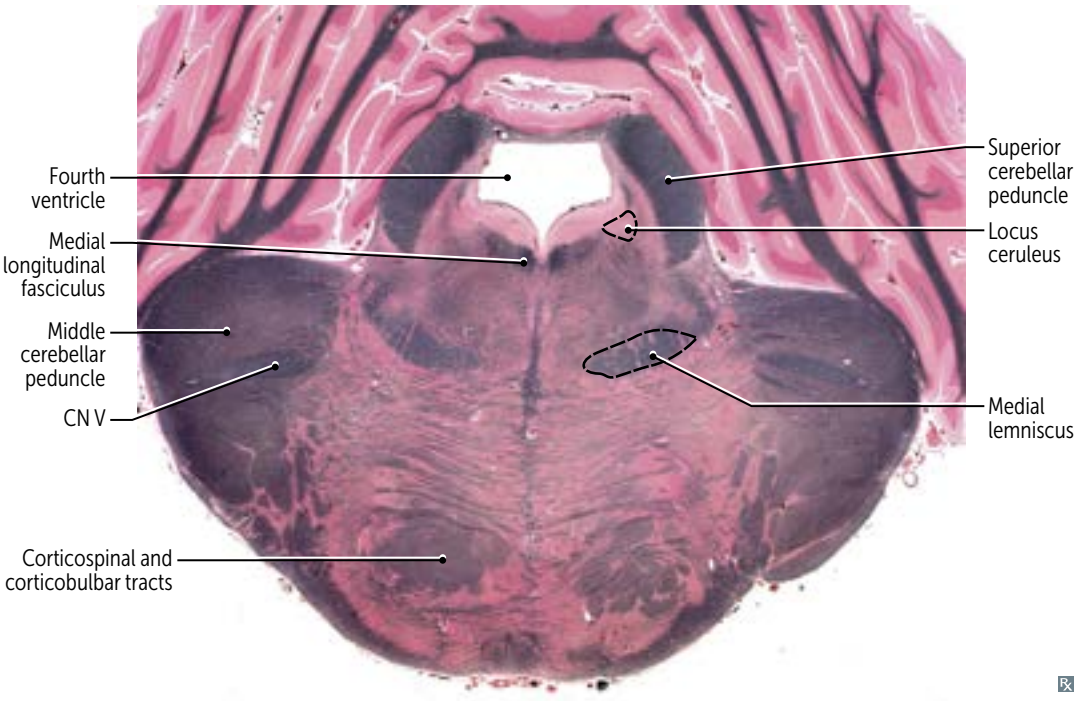
art revised for 2023 3rd pass

Brainstem cross sections

Midbrain



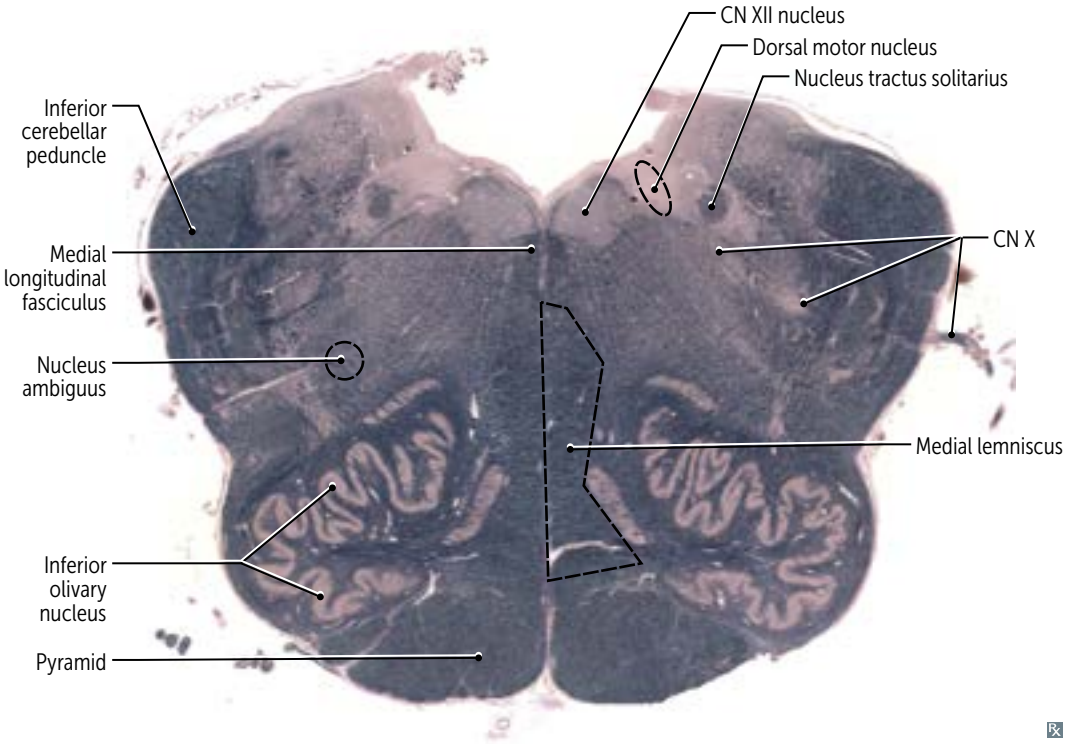
Pons



Brainstem cross sections *(continued)*

art revised for 2023 3rd pass

Medulla



Psychosis — Distorted perception of reality characterized by delusions, hallucinations, and/or disorganized thought/speech. Can occur in patients with psychiatric illness or another medical condition, or secondary to substance or medication use.

Delusions — False, fixed, idiosyncratic beliefs that persist despite evidence to the contrary and are not typical of a patient's culture or religion (eg, a patient who believes that others are reading his thoughts). Types include erotomanic, grandiose, jealous, persecutory, somatic, mixed, and unspecified.

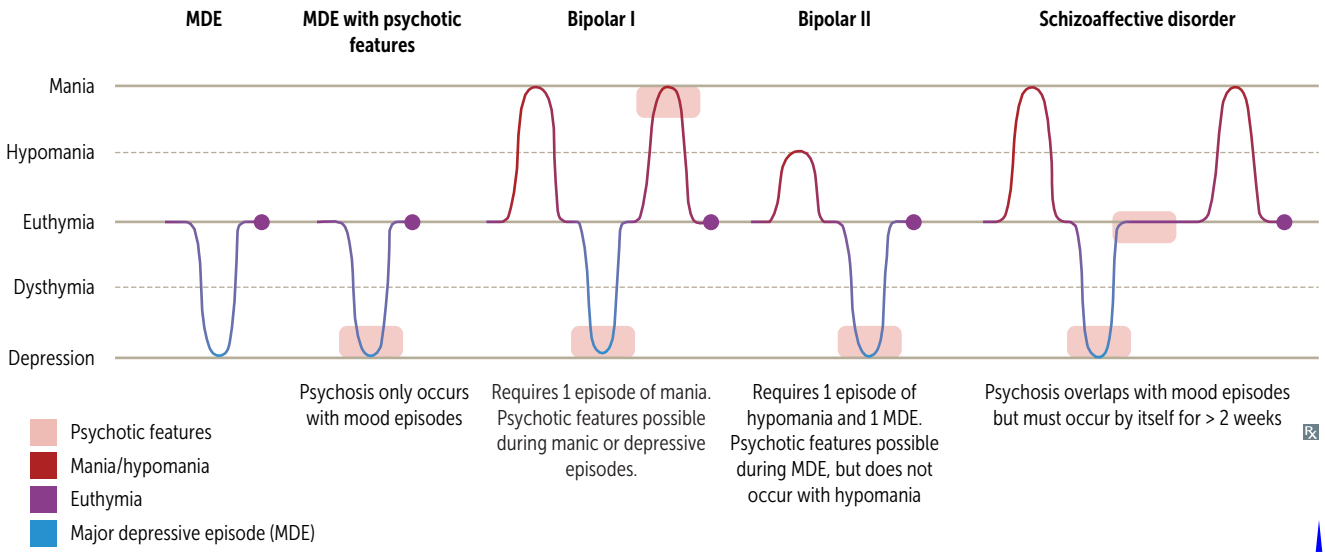
Disorganized thought — Speech may be incoherent ("word salad"), tangential, or derailed ("loose associations").

Hallucinations — Perceptions in the absence of external stimuli (eg, seeing a light that is not actually present). Contrast with misperceptions (eg, illusions) of real external stimuli. Types include:

- Auditory—more commonly due to psychiatric illness (eg, schizophrenia) than neurologic disease.
- Visual—more commonly due to neurologic disease (eg, dementia), delirium, or drug intoxication than psychiatric illness.
- Tactile—common in alcohol withdrawal and stimulant use (eg, "cocaine crawlies," a type of delusional parasitosis).
- Olfactory—often occur as an aura of temporal lobe epilepsy (eg, burning rubber) and in brain tumors.
- Gustatory—rare, but seen in epilepsy.
- Hypnagogic—occurs while going to sleep. Sometimes seen in narcolepsy.
- Hypnopompic—occurs while waking from sleep ("get pomped up in the morning"). Sometimes seen in narcolepsy.

Contrast with illusions, which are misperceptions of real external stimuli (eg, mistaking a shadow for a black cat).

Mood disorder — Characterized by an abnormal range of moods or internal emotional states and loss of control over them. Severity of moods causes distress and impairment in social and occupational functioning. Includes major depressive, bipolar, dysthymic, and cyclothymic disorders. Episodic superimposed psychotic features (delusions, hallucinations, disorganized speech/behavior) may be present at any time during mood episodes (other than hypomania).



art new for 2023 2nd pass

art revised for 2023 3rd pass

art revised for 2023 4th pass

Trauma and stress-related disorders

Adjustment disorder

Emotional or behavioral symptoms (eg, anxiety, outbursts) that occur within 3 months of an identifiable psychosocial stressor (eg, divorce, illness) lasting < 6 months once the stressor has ended. Symptoms do not meet criteria for another psychiatric illness. If symptoms persist > 6 months after stressor ends, reevaluate for other explanations (eg, MDD, GAD). Treatment: CBT is first line; antidepressants and anxiolytics may be considered.

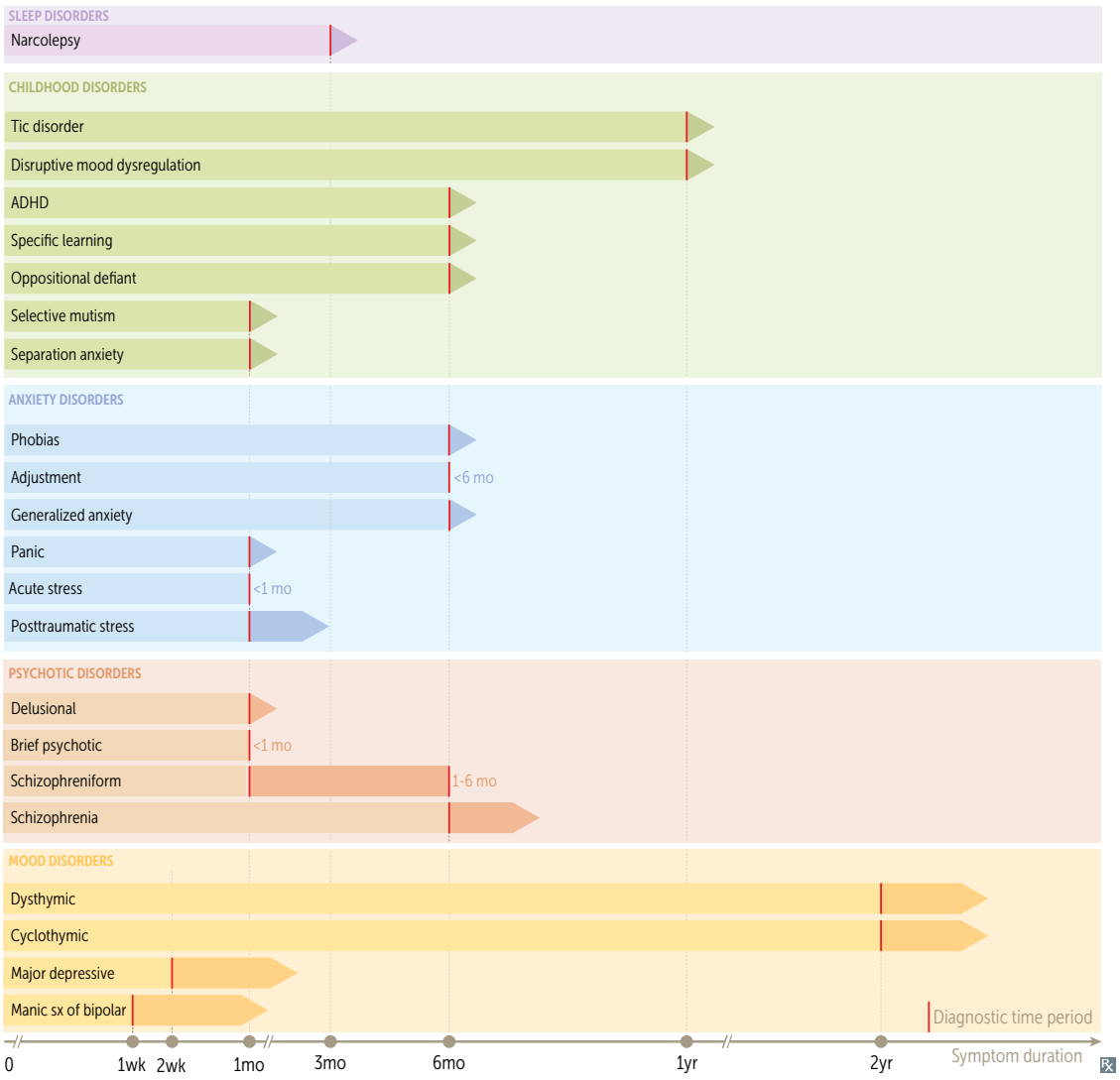
Post-traumatic stress disorder

Experiencing, witnessing, or discovering that a loved one has experienced a life-threatening situation (eg, serious injury, sexual assault) → persistent **H**yperarousal, **A**voidance of associated stimuli, intrusive **R**e-experiencing of the event (eg, nightmares, flashbacks), changes in cognition or mood (eg, fear, horror, **D**istress) (having PTSD is **HARD**). Disturbance lasts > 1 month with significant distress or impaired functioning. Treatment: CBT, SSRIs, and venlafaxine are first line. Prazosin can reduce nightmares.

Acute stress disorder—lasts between 3 days and 1 month. Treatment: CBT; pharmacotherapy is usually not indicated.

Diagnostic criteria by symptom duration

art revised for 2023 4th pass



Rapid Review

"Study without thought is vain: thought without study is dangerous."
—Confucius

"It is better, of course, to know useless things than to know nothing."
—Lucius Annaeus Seneca

"For every complex problem there is an answer that is clear, simple, and wrong."
—H. L. Mencken

The following tables represent a collection of high-yield associations between diseases and their clinical findings, treatments, and key associations. They can be quickly reviewed in the days before the exam.

We have added a high-yield Pathophysiology of Important Diseases section for review of disease mechanisms and removed the Classic/Relevant Treatments section to accommodate the change in focus of the USMLE from pharmacology to pathophysiology.

▸ PATHOPHYSIOLOGY OF IMPORTANT DISEASES

new section for 2023 1st pass

CONDITION	MECHANISM	PAGE
Lesch-Nyhan syndrome	Absent HGPRT → ↑ de novo purine synthesis → ↑ uric acid production	35
β-thalassemia	Mutation at splice site or promoter sequences → retained intron in mRNA	38, 425
Lynch syndrome	Failure of mismatch repair during the S phase → microsatellite instability	37, 395
I-cell disease	N-acetylglucosaminyl-1-phosphotransferase defect → Golgi mediated mannose residues phosphorylation failure (↓ mannose-6-phosphate) → ↑ cellular debris in lysosomes	45
Osteogenesis imperfecta	Type 1 collagen defect due to inability to form triple helices	49
Menkes disease	Defective *ATP7A* protein → impaired copper absorption and transport → ↓ lysyl oxidase activity → ↓ collagen cross-linking	49
Marfan syndrome	*FBN1* mutation on chromosome 15 → defective fibrillin (normally forms sheath around elastin)	50
Prader-Willi syndrome	Uniparental disomy or imprinting leading to silencing of maternal gene. Disease expressed when paternal allele deleted or mutated	56
Angelman syndrome	Silenced gene leading to mutation, lack of expression, or deletion of *UBE3A* on maternal chromosome 15	56
Cystic fibrosis	Autosomal recessive ΔF508 deletion in *CFTR* gene on chromosome 7 → impaired ATP-gated Cl^- channel (secretes Cl^- in lungs and GI tract and reabsorbs Cl^- in sweat glands)	58
Duchenne muscular dystrophy	Dystrophin gene frameshift mutations → loss of anchoring protein to ECM (dystrophin) → myonecrosis	59
Myotonic dystrophy	CTG trinucleotide repeat expansion in *DMPK* gene → abnormal expression of myotonin protein kinase → myotonia	59
Fragile X syndrome	Trinucleotide repeat in *FMR1* gene → hypermethylation → ↓ expression	60
Bitot spots in vitamin A deficiency	↓ differentiation of epithelial cells into specialized tissue → squamous metaplasia	64
Wernicke encephalopathy in alcoholic patient given glucose	Thiamine deficiency → impaired glucose breakdown → ATP depletion worsened by glucose infusion	64
Pellagra in malignant carcinoid syndrome	Tryptophan is diverted towards serotonin synthesis → B_3 deficiency (B_3 is derived from tryptophan)	65
Kwashiorkor	Protein malnutrition → ↓ oncotic pressure (→ edema), ↓ apolipoprotein synthesis (→ liver fatty change)	69
Lactic acidosis, fasting hypoglycemia, hepatic steatosis in alcoholism	↑ $NADH/NAD^+$ ratio due to ethanol metabolism	70
Aspirin-induced hyperthermia	↑ permeability of mitochondrial membrane → ↓ proton $[H^+]$ gradient and ↑ O_2 consumption → uncoupling	76
Hereditary fructose intolerance	Aldolase B deficiency → Fructose-1-phosphate accumulates → ↓ available phosphate → inhibition of glycogenolysis and gluconeogenesis	78
Classic galactosemia	Galactose-1-phosphate uridyltransferase deficiency → accumulation of toxic substances (eg, galactitol in eyes)	78

CONDITION	MECHANISM	PAGE
Cataracts, retinopathy, peripheral neuropathy in DM	Lens, retina, Schwann cells lack sorbitol dehydrogenase → intracellular sorbitol accumulation → osmotic damage	79
Recurrent *Neisseria* bacteremia	Terminal complement deficiencies (C5–C9) → failure of MAC formation	105
Hereditary angioedema	C1 esterase inhibitor deficiency → unregulated activation of kallikrein → ↑ bradykinin	105
Paroxysmal nocturnal hemoglobinuria	*PIGA* gene mutation → ↓ GPI anchors for complement inhibitors (DAF/CD55, MIRL/CD59) → complement-mediated intravascular hemolysis	105
Type I hypersensitivity	Immediate (minutes): antigen cross links IgE on mast cells → degranulation → release of histamine and tryptase Late (hours): mast cells secrete chemokines (attract eosinophils) and leukotrienes → inflammation, tissue damage	110
Type II hypersensitivity	Antibodies bind to cell-surface antigens → cellular destruction, inflammation, cellular dysfunction	110
Type III hypersensitivity	Antigen-antibody complexes → activate complement → attracts neutrophils	111
Type IV hypersensitivity	T cell-mediated (no antibodies involved). $CD8^+$ directly kills target cells, $CD4^+$ releases cytokines	111
Acute hemolytic transfusion reaction	Type II hypersensitivity reaction against donor RBCs (usually ABO antigens)	112
X-linked (Bruton) agammaglobulinemia	Defect in *BTK* gene (tyrosine kinase) → no B-cell maturation → absent B cells in peripheral blood, ↓ Ig of all classes	114
DiGeorge syndrome	22q11 microdeletion → failure to develop 3rd and 4th branchial (pharyngeal) pouches	114
Hyper-IgM syndrome	Defective CD40L on Th cells → class switching defect	115
Leukocyte adhesion deficiency (type 1)	LFA-1 integrin (CD18) defect → impaired phagocyte migration and chemotaxis	115
Chédiak-Higashi syndrome	*LYST* mutation → microtubule dysfunction → phagosome-lysosome fusion defect	115
Chronic granulomatous disease	NADPH oxidase defect → ↓ ROS, ↓ respiratory burst in neutrophils	115
Candida infection in immunodeficiency	↓ granulocytes (systemic), ↓ T cells (local)	116
Graft-versus-host disease	Type IV HSR; HLA mismatch → donor T cells attack host cells	117
Recurrent *S aureus*, *Serratia*, *B cepacia* infections in CGD	Catalase ⊕ organisms degrade H_2O_2 before it can be converted to microbicidal products by the myeloperoxidase system	126
Hemolytic uremic syndrome	Shiga/Shiga-like toxins inactivate 60S ribosome → ↑ cytokine release	130
Tetanus	Tetanospasmin prevents release of inhibitory neurotransmitters (GABA and glycine) from Renshaw cells	130
Botulism	Toxin (protease) cleaves SNARE → ↓ neurotransmitter (ACh) release at NMJ	130
Gas gangrene	Alpha toxin (phospholipase/lecithinase) degrades phospholipids → myonecrosis	131
Toxic shock syndrome, scarlet fever	TSST-1 and erythrogenic exotoxin A (scarlet) cross-link β region of TCR to MHC class II on APCs outside of antigen binding site → ↑↑ IL-1, IL-2, IFN-γ, TNF-α	131