Multisystem Processes & Disorders

United States Medical Licensing Examination (USMLE) Step 1

8 to 12% of Step 1 · 9 sections · content outline and specifications

Multisystem Processes and Disorders covers problems that affect many organs at once. On Step 1, this is where much of biochemistry, genetics, nutrition, general pharmacology, toxicology, and general pathology is tested. Questions describe a patient, then ask about an enzyme, a vitamin, a gene, a drug calculation, a toxin's mechanism, or an organism. Most items need two steps: name the disorder, then explain its mechanism. Many items use a small table of laboratory values that you must read with care.

You should be able to: After this guide, you should be able to name a multisystem disorder from a vignette and explain its enzyme, vitamin, gene, toxin, or immune mechanism, and do the basic dosing and acid-base calculations Step 1 expects.

Every section: the key point and the trap

1 Inborn errors of metabolism and storage diseases

Most inborn errors are autosomal recessive; Fabry disease, Hunter syndrome, and ornithine transcarbamylase deficiency are X-linked.

Trap: Do not choose the deficient enzyme when the question asks what a treatment acts on. In porphyria, the deficient enzyme is porphobilinogen deaminase, but hemin works by lowering aminolevulinic acid synthase.

2 Genetic mechanisms and inheritance patterns

Autosomal dominant diseases often affect structural proteins (Marfan syndrome: fibrillin-1); autosomal recessive diseases often affect enzymes.

Trap: Learners often use 1/2 for the carrier chance of a healthy sibling. Once you know the sibling is not affected, only three outcomes remain, and two of them are carriers, so the chance is 2/3.

3 Nutrition: vitamins, minerals, and malnutrition

Thiamine (B1) is a cofactor for pyruvate dehydrogenase, alpha-ketoglutarate dehydrogenase, transketolase, and branched-chain ketoacid dehydrogenase; deficiency causes Wernicke encephalopathy and beriberi.

Trap: Bleeding in scurvy happens with normal platelets and normal clotting times, because the problem is weak vessel collagen. Bleeding with long clotting times points to vitamin K instead.

4 Pharmacokinetics and pharmacodynamics

Loading dose = target concentration x volume of distribution / bioavailability.

Trap: Check the route of the dose. Many wrong answers come from dividing an intravenous dose by oral bioavailability, or from forgetting to multiply by the dosing interval.

5 Poisoning: mechanisms and antidotes

Acetaminophen is changed by CYP2E1 into NAPQI; N-acetylcysteine restores glutathione, and liver injury is worst in zone 3.

Trap: A normal pulse oximetry reading does not rule out carbon monoxide poisoning. Standard oximeters read carboxyhemoglobin as oxyhemoglobin.

6 Environmental extremes: heat, cold, altitude, and pressure

Heat stroke is a core temperature above 40°C (104°F) with brain dysfunction; heat exhaustion has normal mental function.

Trap: Do not confuse the time course. Nitrogen narcosis happens while deep and goes away on rising. Arterial gas embolism starts within minutes of surfacing with stroke-like signs. Decompression sickness starts minutes to hours later.

7 Multisystem infections, sepsis, and shock

Gram-negative lipopolysaccharide binds Toll-like receptor 4 (with CD14); tumor necrosis factor-alpha and interleukin-1 cause septic shock.

Trap: In neurogenic shock, resistance is also low, but the heart rate is often slow and cardiac output is low. A warm, fast-heart patient with infection points to septic shock.

8 Cell injury, neoplasia, and paraneoplastic syndromes

Free radicals injure cells by lipid peroxidation; carbon tetrachloride is changed by CYP2E1 into the CCl_3 radical and damages zone 3 of the liver.

Trap: Lambert-Eaton weakness improves with repeated effort; myasthenia gravis weakness gets worse with use. Check which way strength changes before choosing the antibody.

9 Immune injury, transplantation, and fluid, electrolyte, and acid-base balance

Hyperacute rejection happens within minutes, from preformed antibodies against donor ABO or HLA antigens (type II hypersensitivity).

Trap: A normal pH does not mean a normal acid-base state. Compensation never fully corrects the pH, so a normal pH with abnormal bicarbonate and PCO_2 means two disorders.

Key terms

Inborn error of metabolism: An inherited enzyme defect that blocks a chemical pathway in the body.

Cofactor: A helper molecule, often made from a vitamin, that an enzyme needs to work.

Bioavailability: The fraction of a dose that reaches the blood unchanged.

Volume of distribution: The amount of drug in the body divided by its plasma concentration.

Clearance: The volume of plasma cleared of a drug per unit of time.

Paraneoplastic syndrome: Signs caused by substances a tumor makes, not by the tumor mass itself.

Superantigen: A toxin that activates many T cells at once by binding outside the normal antigen site.

Genomic imprinting: A gene is switched on or off depending on which parent it came from.

Anion gap: Sodium minus the sum of chloride and bicarbonate; a high value means extra acids.

Free radical: An unstable molecule with an unpaired electron that damages cell parts.

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