USMLE session 4

- 12.10.2013
- 8 Qs with discussion and review

Q1

A 52-year-old overweight male steamroller operator presents to his primary care physician complaining of itchy, watery eyes and runny nose in the springtime. He says that he has had this problem for as long as he can remember but does not like going to doctors. His wife finally convinced him to come today to see what his physician might be able to do for him.

What is the most appropriate treatment for this patient?

(A) Albuterol

(B) Diphenhydramine

(C) Epinephrine

(D) Hydroxyzine

(E) Loratadine

Q - hints

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What is the most appropriate treatment for this patient?

(A) Albuterol - short-acting beta-agonist

(B) Diphenhydramine - H1-antagonist (1st gen.)

(C) Epinephrine - alpha- and beta- adrenergic agonist

(D) Hydroxyzine - H1-antagonist (1st gen.)

(E) Loratadine - H1-antagonist

A

Itchy, watery eyes with runny nose in spring is likely **allergic rhinitis**, commonly called hay fever.

These symptoms are caused primarily by histamine acting on H1 receptors. Histamine is released from mast cells when they encounter the antigen to which they have been sensitized. Interrupting histamine release (i.e., cromolyn sodium), blocking H1 receptors (diphenhydramine, loratadine, and hydroxyzine), and physiologically antagonizing the effects of histamine (epinephrine) are all methods employed to reduce symptoms of allergic rhinitis.

Epinephrine may be useful for a severe acute attack but not the best choice for chronic symptom management.

The H1 antagonists are divided into **first-generation (diphenhydramine, hydroxyzine)** and **second-generation (loratadine)** drugs. The second-generation drugs are more specific for the H1 receptor and **do not cross the blood–brain barrier** as readily so they have **fewer anticholinergic and antihistaminic side effects (such as drowsiness).** This is important for the patient because he operates heavy equipment.

subQ

What drugs have anticholinergic (antimuscarinic) properties?

- decreased secretions (salivation, bronchial, sweat..)
- mydriasis
- hyperthermia => vasodil.
- tachycardia
- sedation
- urinary retention, constipation
- behaviour excitatition and halucinations

subA

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OLD Drugs:

- antihistamines (1st gen.): Diphenhydramine, Hydroxyzine, ...
- tricyclic antidepresants: amitriptylin, imipramin, ...
- antipsychotics (typical, low potency): thioridazine
- meperidin (=opioid)
- ...
- /many others/

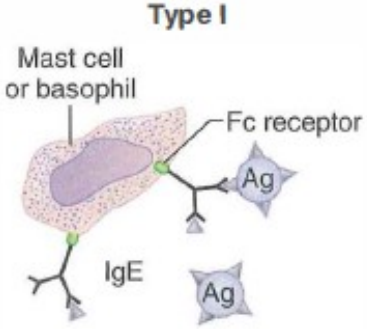
subQ

What type of hypersensitivity reaction (according to Coombs) is allergic rhinitis?

Review

Hypersensitivity

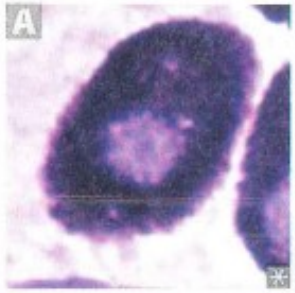
Type I



Anaphylactic and atopic—free antigen cross-links IgE on presensitized mast cells and basophils, triggering release of vasoactive amines that act at postcapillary venules (i.e., histamine). Reaction develops rapidly after antigen exposure due to preformed antibody.

First and **F**ast (anaphylaxis). Types I, II, and III are all antibody mediated.
Test: scratch test and radioimmunosorbent assay.

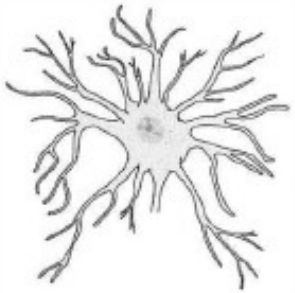
Mast cell



Mediates allergic reaction. Degranulation—histamine, heparin, and eosinophil chemotactic factors. Can bind the Fc portion of IgE to membrane. Mast cells resemble basophils A structurally and functionally but are not the same cell type. Found in tissue.

Involved in type I hypersensitivity reactions. Cromolyn sodium prevents mast cell degranulation (used for asthma prophylaxis).

Dendritic cells



Professional (APCs). Express MHC II and Fc receptor (FcR) on surface. Main inducers of 1° antibody response. Called Langerhans cells on skin.

Review

Mast cells release:

- 1/ immediate (degranulation of preformed vesicles):
  - **histamine**,
  - serotonin;
- 2/ late (new synthesis&release):
  - **Leukotriens**,
  - cytokines (Eosinophil chemotactic factor)

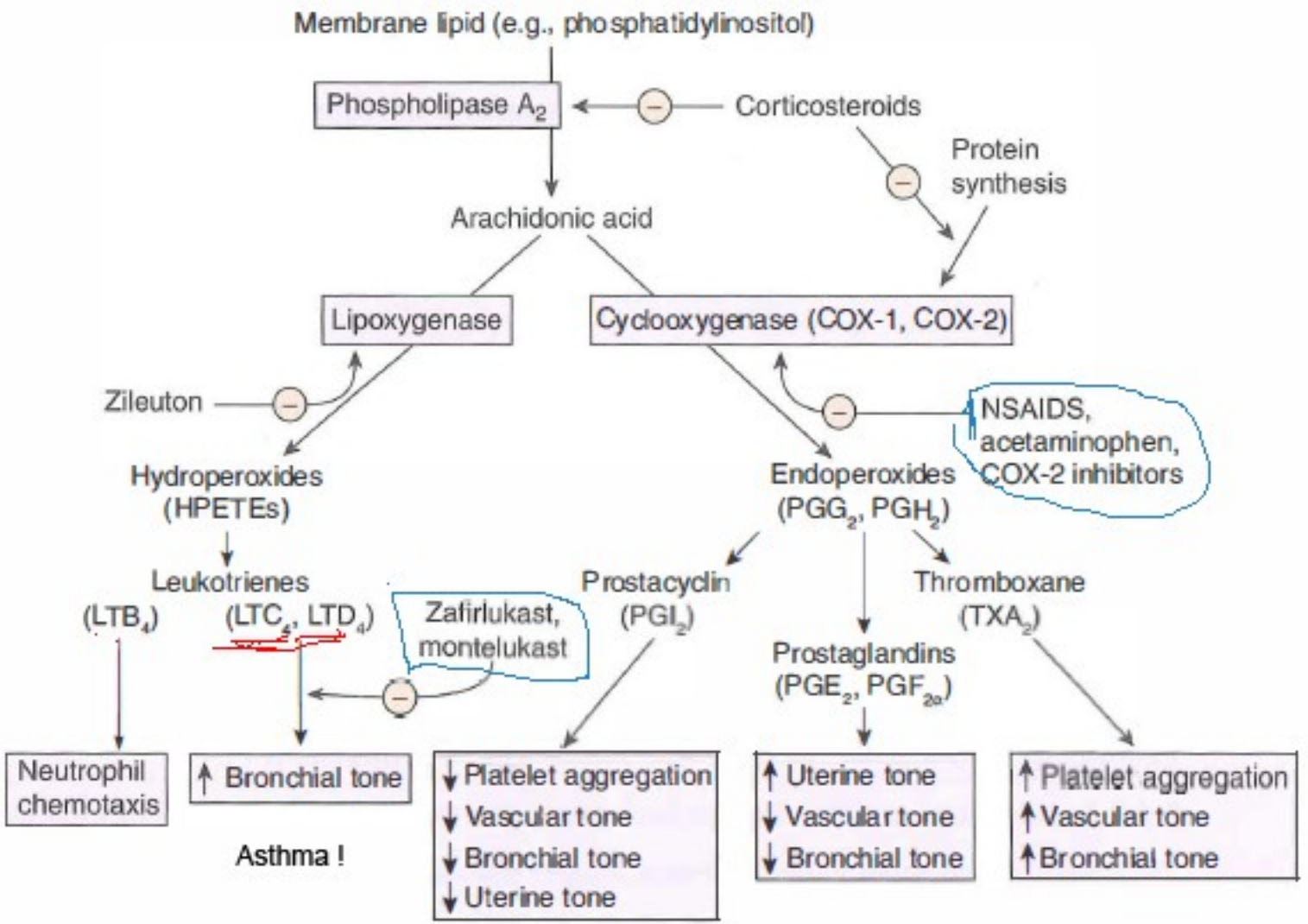
Arachidonic acid products

Lipoxygenase pathway yields Leukotrienes.
LTB_4 is a neutrophil chemotactic agent.
LTC_4, D_4, and E_4 function in bronchoconstriction, vasoconstriction, contraction of smooth muscle, and ↑ vascular permeability.
PGI_2 inhibits platelet aggregation and promotes vasodilation.

L for Lipoxygenase and Leukotriene.
Neutrophils arrive "B4" others.
Platelet-Gathering Inhibitor.

Related patfyz:

•aspirin induced asthma
•aspirin as an antithrombotic



Q2

A 5-year-old boy is brought to his primary care physician by his parents who say that he often has trouble catching his breath when he has been playing hard outside. He is allergic to peanuts. At the moment, he is breathing fine. Which of the following drugs is commonly used to diagnose suspected asthma?

(A) Albuterol

(B) Methacholine

(C) Neostigmine

(D) Nicotine

(E) Pilocarpine

Q - hints

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(A) Albuterol - short-acting beta2 agonist

(B) Methacholine - M-agonist

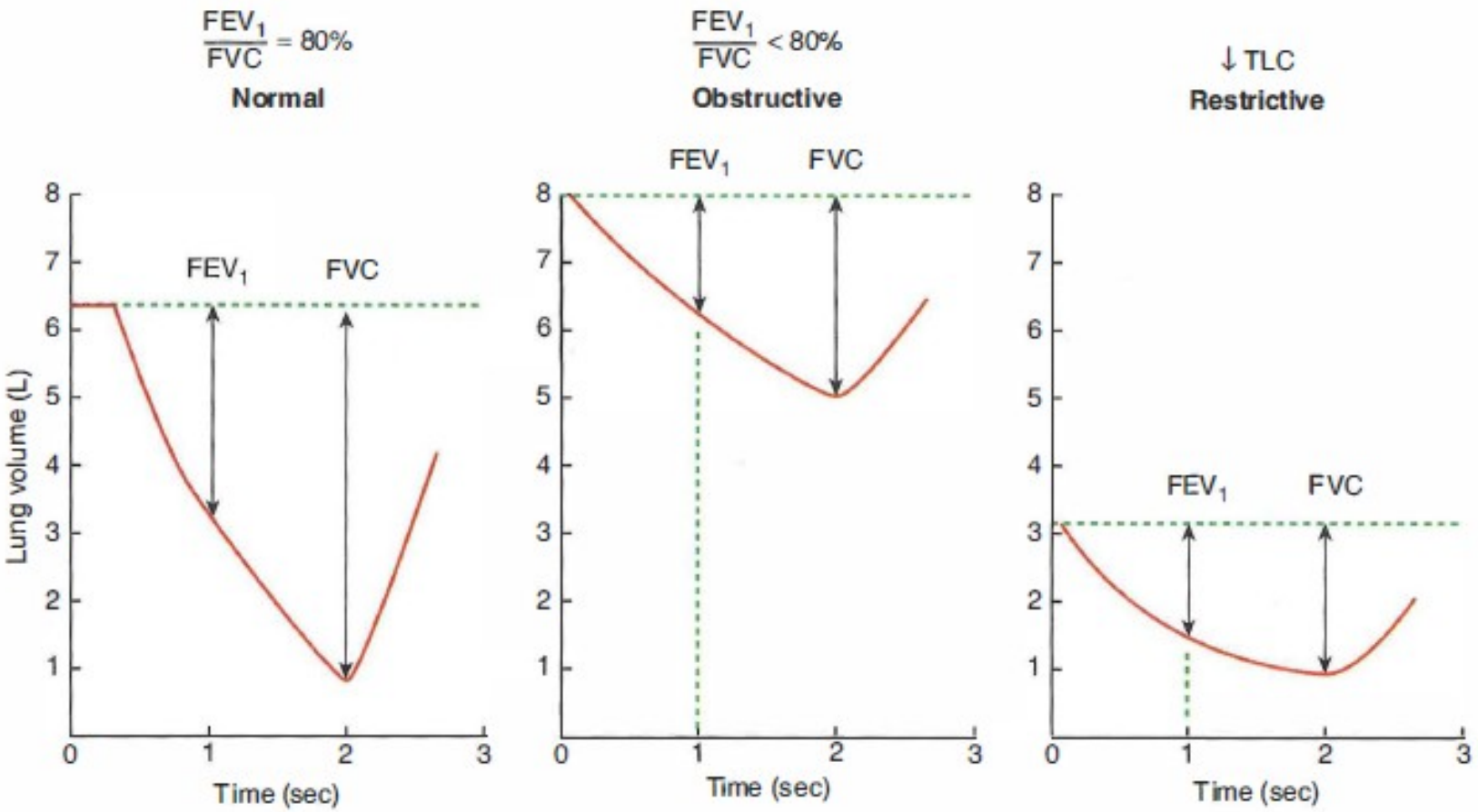
(C) Neostigmine - AchE inhibitor

(D) Nicotine - N-agonst

(E) Pilocarpine - M-agonist

A

Obstructive vs. restrictive lung disease



Note: Obstructive lung volumes > normal (↑ TLC, ↑ FRC, ↑ RV); restrictive lung volumes < normal. In both obstructive and restrictive, FEV_1 and FVC are reduced, but in obstructive, FEV_1 is more dramatically reduced, resulting in a ↓ FEV_1/FVC ratio.

A

In asthma, constriction of terminal bronchioles is **episodic** (in response to irritants), not persistent.

Patients with **airway hyperreactivity** will **react to lower doses of an inhaled cholinergic** agent. Methacholine is commonly used to diagnose asthma in this way. It binds to muscarinic receptors on bronchiolar smooth muscle, causing bronchoconstriction. Methacholine is a synthetic choline ester that is degraded by cholinesterase more slowly than acetylcholine.

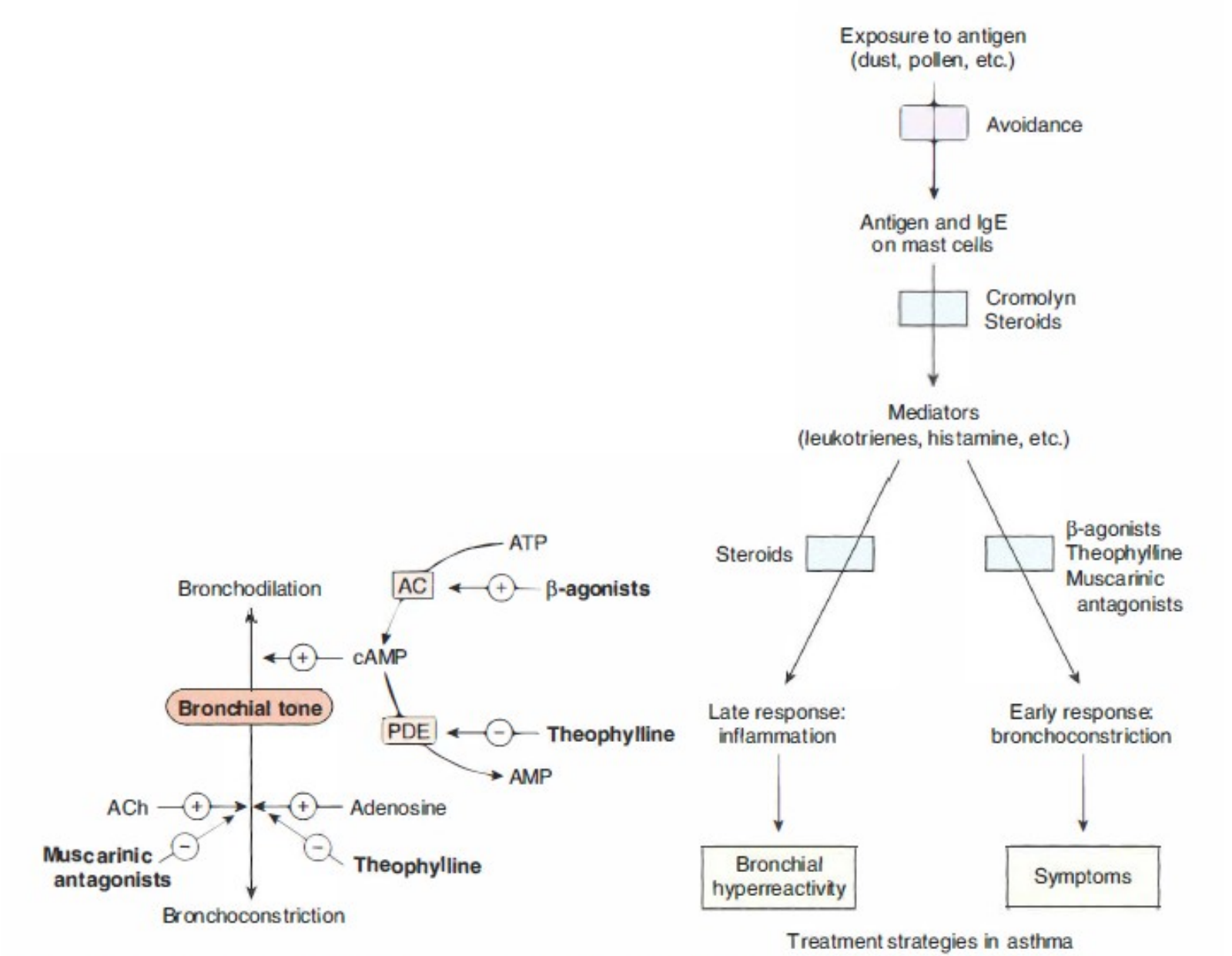
(A) Albuterol is used in the treatment of asthma. It is an adrenergic b2-agonist and causes relaxation of bronchial smooth muscle.

(C) Neostigmine is an acetylcholinesterase inhibitor. It is used in the treatment of myasthenia gravis and neuromuscular blockade reversal. Neostigmine's halflife is too long to be useful in diagnosing asthma.

(D) Nicotine binds to nicotinic receptors, not the muscarinicreceptors found on bronchiolar smooth muscle. It would not be useful in causing bronchoconstriction

(E) Pilocarpine is used in the treatment of glaucoma. Its half-life is too long to be useful in diagnosing asthma.

- Asthma treatment is another story



Treatment strategies in asthma

(Adapted, with permission, from Katzung BG, Trevor AJ. *Pharmacology: Examination & Board Review*, 5th ed. Stamford, CT: Appleton & Lange, 1998: 159 and 161.)

Q3

A 22-year-old woman ingests an entire bottle of acetaminophen in an attempted suicide. She unexpectedly feels well for the next 24 h, at which time her boyfriend discovers what she has done and takes her to the ER. The toxic metabolite of acetaminophen exerts its deleterious effect by what mechanism?

(A) Depletion of endogenous antioxidant

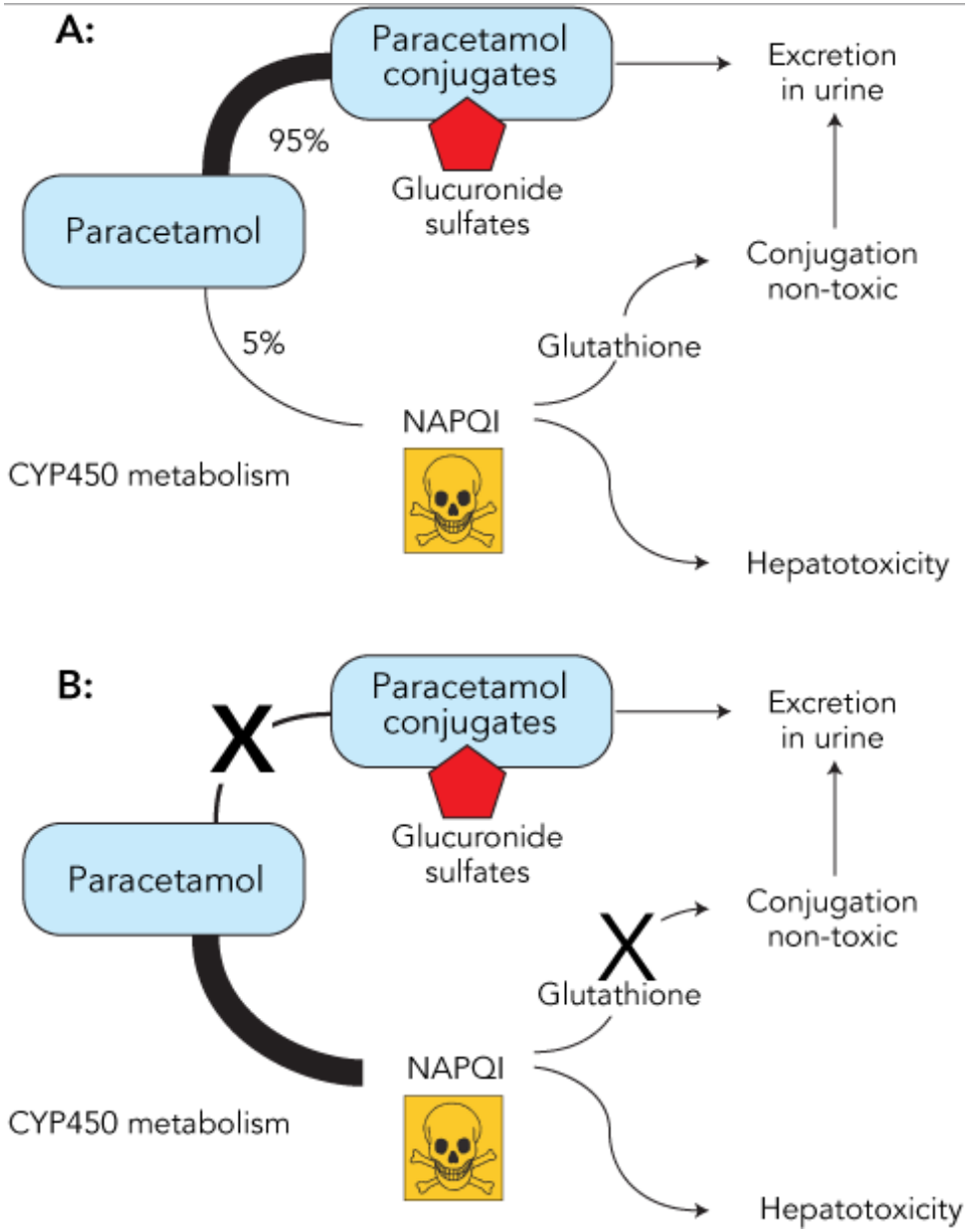
(B) Hapten formation leading to autoantibody production

(C) Inhibition of cytochrome C oxidase

(D) Ischemia from decreased hepatic blood flow

(E) Paralysis of gall bladder causing bile stasis

A


A:
Paracetamol conjugates
Excretion in urine
95%
Glucuronide sulfates
Paracetamol
Conjugation non-toxic
5%
Glutathione
NAPQI
CYP450 metabolism
Hepatotoxicity
B:
Paracetamol conjugates
Excretion in urine
Glucuronide sulfates
Paracetamol
Conjugation non-toxic
Glutathione
NAPQI
CYP450 metabolism
Hepatotoxicity

A

Acetaminophen metabolism follows one of two pathways in the liver. Most (more than 90%) undergoes phase II metabolism (=conjugation to glucuronide) directly and is excreted via the kidney. The remainder undergoes phase I metabolism by CYP1A2 or CYP2E1 to produce NAPQI (N-acetyl-p-benzoquinone imine), the toxic metabolite of acetaminophen. NAPQI **requires glutathione** for its next step of metabolism.

Excess acetaminophen in the body produces so much NAPQI that liver glutathione (a natural, endogenous antioxidant) is depleted. Oxidative damage then occurs.

(B) **Penicillin** in high doses can induce immune mediated **hemolysis** via the **hapten mechanism** in which antibodies are targeted against the combination of penicillin in association with red blood cells. Complement is activated by the attached antibody leading to the removal of red blood cells by the spleen.

(C) **Cyanide inhibits cytochrome C oxidase**. This leads to blockage of the electron transport chain in the mitochondria.

(D) (Rare) thrombosis of portal or hepatic vein may cause hepatic ishemia

(E) Neither acetaminophen nor its metabolites cause paralysis of the gall bladder.

Q4

A 63-year-old woman with history of CAD, MI 2 years ago, years begins to have lower extremity swelling. Heart sounds are regular and S3 is present, on lung auscultation there are bibasilar crackles. She starts taking a diuretic and the swelling improves significantly. Over the next few days, however, she develops ringing in her ears. Which of the following diuretics is she taking?

(A) Acetazolamide

(B) Furosemide

(C) Hydrochlorothiazide

(D) Mannitol

(E) Spironolactone

Q4 - hints

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(A) Acetazolamide - carbonic anhydrase inhibitor

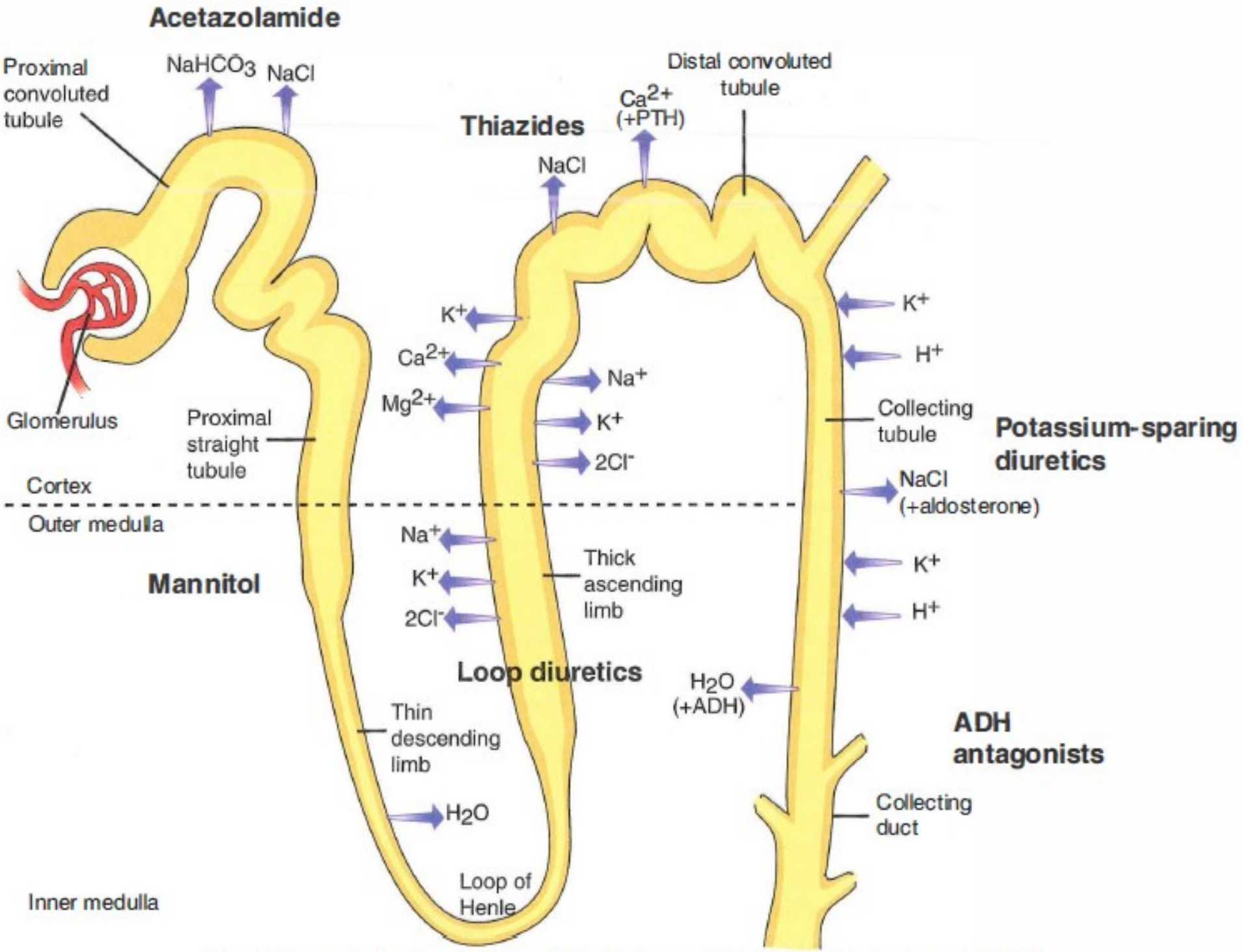
(B) Furosemide - Na/K/2Cl cotransporter inhibitor

(C) Hydrochlorothiazide - inhibits Na/Cl cotransport in early dist. tubule

(D) Mannitol - osmotic diuretic

(E) Spironolactone - competitive aldosterone antagonist

Diuretics: site of action



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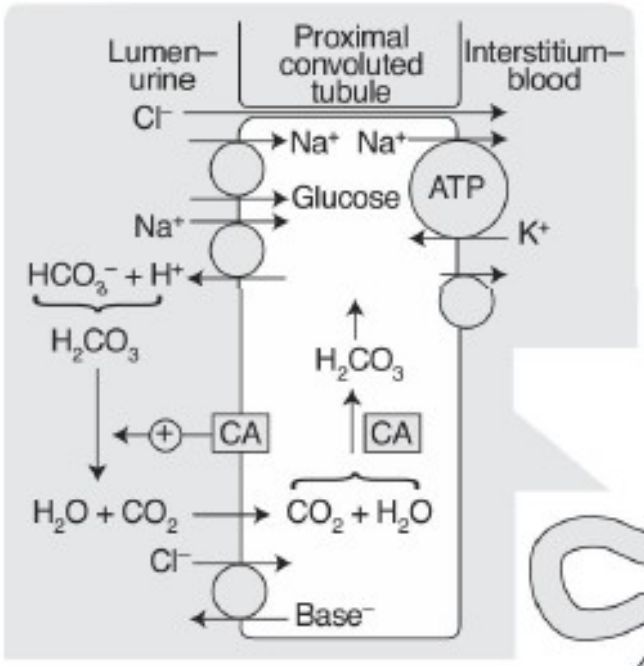
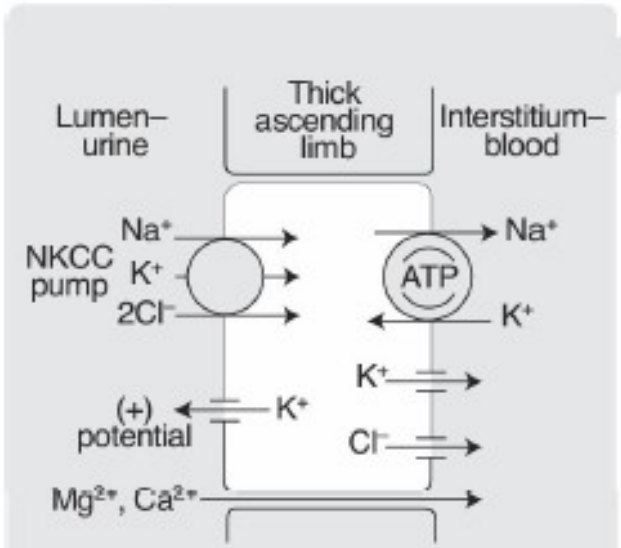
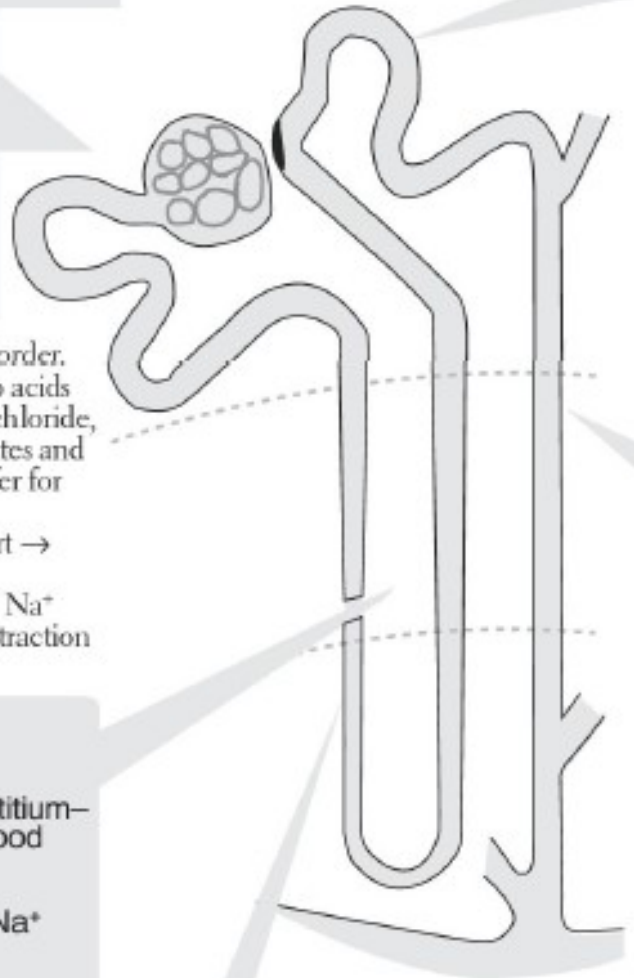


Early proximal tubule—contains brush border. Reabsorbs all of the glucose and amino acids and most of the bicarbonate, sodium, chloride, and water. Isotonic absorption. Generates and secretes ammonia, which acts as a buffer for secreted H^+.

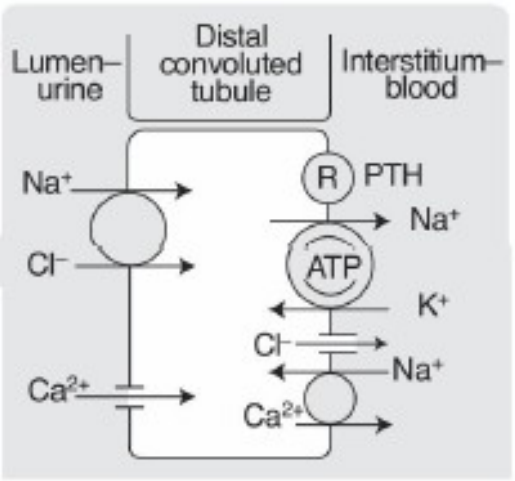
PTH—inhibits Na^+/phosphate cotransport → phosphate excretion.

AT II—stimulates Na^+/H^+ exchange → ↑ Na^+ and H_2O reabsorption (permitting contraction alkalosis).



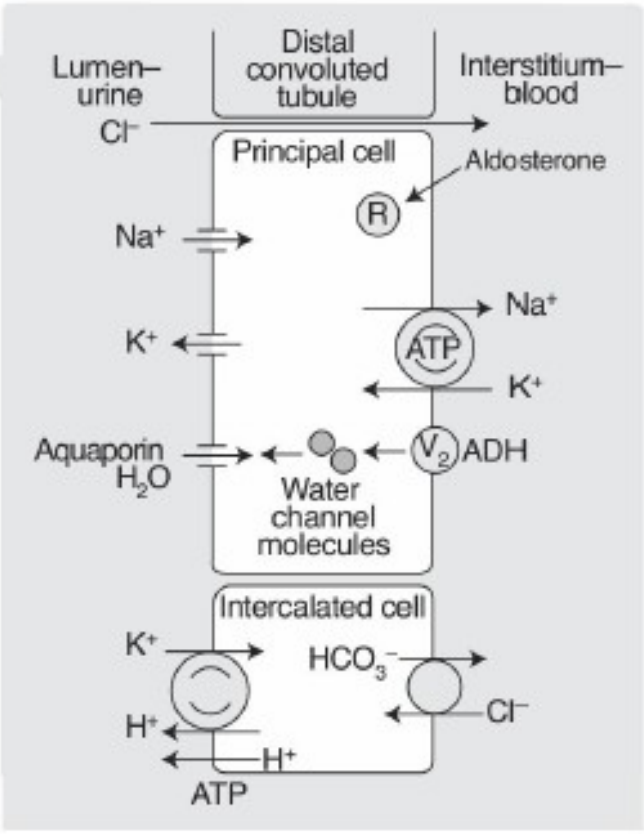


Thin descending loop of Henle—passively reabsorbs water via medullary hypertonicity (impermeable to sodium). Concentrating segment. Makes urine hypertonic.



Early distal convoluted tubule—actively reabsorbs Na^+, Cl^-. Diluting segment. Makes urine hypotonic.

PTH—↑ Ca^{2+}/Na^+ exchange → Ca^{2+} reabsorption.



A4: side effects overview

(A) Acetazolamide - carbonic anhydrase inhibitor
- H ?

(B) Furosemide - Na/K/2Cl cotransporter inhibitor (subQ: barter sy. ?)
- Ca++, Mg++ ?
- K ?
- gout?

(C) Hydrochlorothiazide - inhibits Na/Cl cotransport in early dist. tubule
- Ca++ ?
- K+, H+ ?
- glycemia, lipidemia?
- gout exacerbation

(D) Mannitol - osmotic diuretic

(E) Spironolactone - competitive aldosterone antagonist
- K+ ?
- endocrine?

A4: side effects overview

(A) Acetazolamide - carbonic anhydrase inhibitor
- acidosis

(B) Furosemide - Na/K/2Cl cotransporter inhibitor (subQ: barter sy. ?)
- increased Ca++, Mg++ excretion
- hypoKalemia
- allergy (sulfa)
- interstitial nephritis
- gout exacerbation

(C) Hydrochlorothiazide - inhibits Na/Cl cotransport in early dist. tubule
- increased Ca++ excretion
- hypoKalemia, alkalosis (hypoH+)
- hyperglycemia, hyperlipidemia
- gout exacerbation
- allergy (sulfa)

(D) Mannitol - osmotic diuretic

(E) Spironolactone - competitive aldosterone antagonist
- hyperKalemia
- antiandrogen (gynecomastia)

Q5

A 17-year-old man is brought to the emergency department with severe right lower quadrant pain that he first felt around his umbilicus. His white blood cell count is 12,000/mL of blood. He is taken to the operating room for emergent laparoscopic appendectomy. About an hour into the surgery, his body temperature spikes and CO2 production rises uncontrollably.

What is the next step in the treatment of this patient?

(A) Acetaminophen

(B) Bromocriptine

(C) Dantrolene

(D) Diazepam

(E) Naproxen

Q5

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What is going on?

(A) Acetaminophen

(B) Bromocriptine

(C) Dantrolene

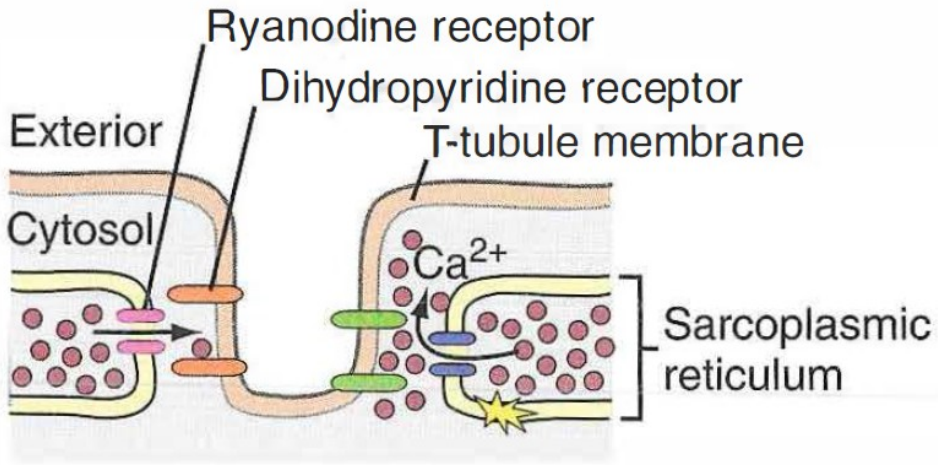
(D) Diazepam

(E) Naproxen

A5

This scenario describes a case of malignant hyperthermia. Malignant hyperthermia can be caused by any one of several genetic defects, most of which are autosomal dominant. Most cases involve a **mutated ryanodine receptor** and are triggered by **anesthetic** or **succinylcholine** use during surgery. The signs and symptoms appear to arise from a sudden increase in cellular metabolism. Dantrolene is the drug used to treat malignant hyperthermia. It is believed to inhibit calcium release from the sarcoplasmic reticulum. By paralyzing the muscle in this way, muscle cell metabolism is drastically decreased.

(A) Acetaminophen has antipyretic and analgesic effects. It can be used for mild pain and fevers but is not useful in malignant hyperthermia.
(B) Bromocriptine is a dopamine agonist that can be used to treat neuroleptic malignant syndrome. Neuroleptic malignant syndrome in some ways resembles malignant hyperthermia, but their pathophysiologies are very different. Bromocriptine is not useful for treating malignant hyperthermia.
(D) Diazepam is a benzodiazepine that can be used to treat serotonin syndrome. Serotonin syndrome in some ways resembles malignant hyperthermia, but their pathophysiologies are very different. Diazepam is not useful for treating malignant hyperthermia.
(E) Naproxen is a nonsteroidal antiinflammatory drug (NSAID). It can be used to decrease pain, inflammation, and fever, but these are not hallmarks of malignant hyperthermia.



Q6

A 59-year-old man with hypertension, gastroesophageal reflux disorder, AIDS, seizure disorder, tuberculosis and depression is currently maintained on multiple medications, including propranolol. He does not have his medication list at his current office visit with his primary care physician. His blood pressure is 180/100 mm Hg. The patient states that he is taking all of his medications as scheduled. Which of the following drugs is the most likely explanation of this finding?

(A) Cimetidine

(B) Fluoxetine

(C) Paroxetine

(D) Rifampin

(E) Ritonavir

Q - hints

A 59-year-old man with hypertension, gastroesophageal reflux disorder, AIDS, seizure disorder, tuberculosis and depression is currently maintained on multiple medications, including propranolol. He does not have his medication list at his current office visit with his primary care physician. His blood pressure is 180/100 mm Hg. The patient states that he is taking all of his medications as scheduled. Which of the following drugs is the most likely explanation of this finding?

(A) Cimetidine - H2 antagonist

(B) Fluoxetine - SSRI

(C) Paroxetine - SSRI

(D) Rifampin - RNA polymerase inhibitor

(E) Ritonavir - HIV protease inhibitor

A

Drugs that interfere with, or inhibit, the metabolism of propranolol, such as cimetidine, fluoxetine, paroxetine, and ritonavir, may potentiate its antihypertensive effects.

Conversely, those that stimulate or induce its metabolism, such as barbiturates, phenytoin, and rifampin, can decrease its effects. In this case, the patient is taking rifampin; and it is affecting the metabolism of propranolol and inducing rapid metabolism, which is minimizing its antihypertensive effects.

Cimetidine, Fluoxetine, Paroxetine, Ritonavir inhibit P450 enzymes and thus potentiates the antihypertensive effects of propranolol.

Review

P-450 interactions	Inducers (+)	Inhibitors (–)
	Quinidine*	Macrolides
	Barbiturates	Amiodarone
	St. John's wort	Grapefruit juice
	Phenytoin	Isoniazid
	Rifampin	Cimetidine
	Griseofulvin	Ritonavir
	Carbamazepine	Acute alcohol abuse
	Chronic alcohol use	Ciprofloxacin
		Ketoconazole
		Sulfonamides

*Quinidine can both induce and inhibit different isoforms of P-450. Induction is the more important effect.

Drugs metabolized by P450: many
most important: **warfarin**

Q7

A 63-year-old woman with history of atrial fibrilation treated with amiodarone presents to her primary care physician complaining of headache, productive cough, diarhoea. HR: 80/min, BP 110/70. Labs are significant for increased CRP, and hyponatremia. Sputum culture grew Legionella pneumophila. She is admitted and gives azithromycin. Which of the following sequelae could be problematic for this patient?

(A) Asystole

(B) Myocardial infarction

(C) Pulmonary edema

(D) Pulmonary embolism

(E) QT interval prolongation

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(A) Asystole

(B) Myocardial infarction

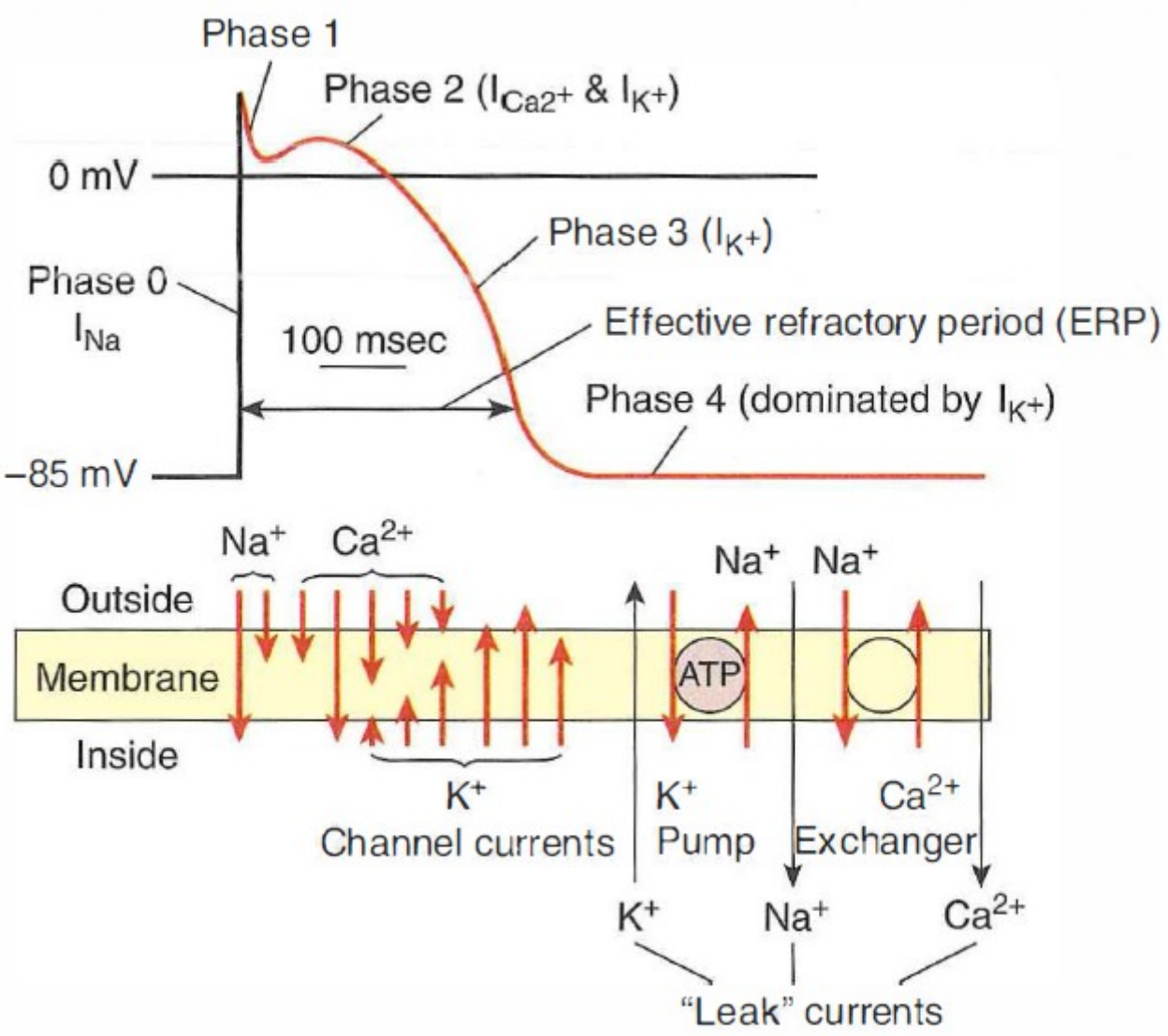
(C) Tendon rupture

(D) Pulmonary embolism

(E) QT interval prolongation

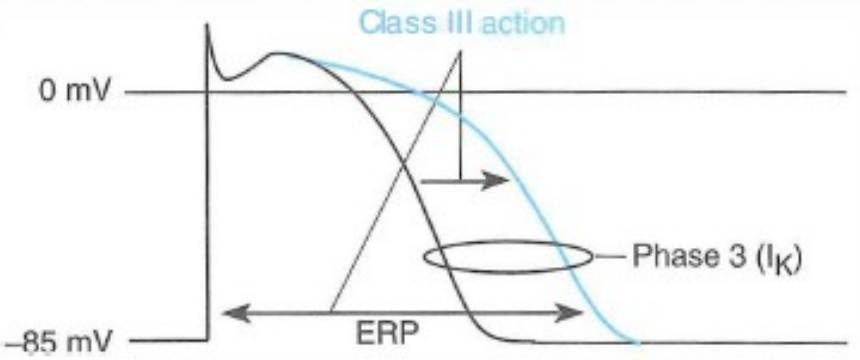
Q7

How does amiodarone work?



A7

Antiarrhythmics–K^+ channel blockers (class III)	**I**butilide, **S**otalol, **B**retylium, **A**miodarone, **D**ofetilide.	**"K IS BAD"**
Mechanism	↑ AP duration, ↑ ERP. Used when other antiarrhythmics fail. ↑ QT interval.	
Toxicity	Sotalol—torsades de pointes, excessive β block; ibutilide—torsades; bretylium—new arrhythmias, hypotension; amiodarone—**pulmonary fibrosis, hepatotoxicity, hypothyroidism/hyperthyroidism** (amiodarone is 40% iodine by weight), corneal deposits, skin deposits (blue/gray) resulting in photodermatitis, neurologic effects, constipation, cardiovascular effects (bradycardia, heart block, CHF). Amiodarone has class I, II, III, and IV effects because it alters the lipid membrane.	Remember to check **PFT**s, **LFT**s, and **TFT**s when using amiodarone.



(Adapted, with permission, from Katzung BG, Trevor AJ. *Pharmacology: Examination & Board Review*, 5th ed. Stamford, CT: Appleton & Lange, 1998: 120.)

A7

QT interval prolongation. Caution should be exerted when combining several **drugs with effects on the QT interval** (e.g., quinidine with azitrhomycin) or when giving these drugs combined with drugs known to **inhibit drug metabolism**, leading to large increases in plasma drug concentrations(-azole antifungals: fluconazole and itraconazole).

Macrolides may prolong QT via both mechanisms.

(A) Asystole is unlikely in this patient.

(B) The QT prolongation is more common than myocardial infarction

in this setting.

(C) Tendon rupture in adults is asociated with fluoroqiunolone use, not macrolide.

(D) Pulmonary embolism would not be expected in this patient.

Review

P-450 interactions	Inducers (+)	Inhibitors (–)
	Quinidine*	Macrolides
	Barbiturates	Amiodarone
	St. John's wort	Grapefruit juice
	Phenytoin	Isoniazid
	Rifampin	Cimetidine
	Griseofulvin	Ritonavir
	Carbamazepine	Acute alcohol abuse
	Chronic alcohol use	Ciprofloxacin
		Ketoconazole
		Sulfonamides

*Quinidine can both induce and inhibit different isoforms of P-450. Induction is the more important effect.

Drugs metabolized by P450: many
most important: **warfarin**

Q8

A 44-year-old, previously healthy man has experienced worsening exercise tolerance accompanied by marked shortness of breath for the past 6 months. On physical examination, he is afebrile. His pulse is 78/min, respirations are 22/min, and blood pressure is 110/70 mm Hg. He has diffuse rales in all lung fields and pitting edema to the knees. Laboratory studies show serum sodium, 130 mmol/L; potassium, 4 mmol/L; chloride, 102 mmol/L; CO2, 25 mmol/L; creatinine, 2 mg/dL; and glucose, 120 mg/dL (6,7mmol). A 100-mL urine sample is collected. There is 1.3 mmol of sodium and 40 mg of creatinine in the urine sample. A chest radiograph shows cardiomegaly and pulmonary edema with pleural effusions. An echocardiogram shows four-chamber cardiac dilation and mitral and tricuspid valvular regurgitation, with an ejection fraction of 30%. A coronary angiogram shows less than 10% narrowing of the major coronary arteries. Which of the following is the most likely diagnosis?

(A) Rheumatic heart disease

(B) Hereditary hemochromatosis

(C) Chagas disease

(D) Diabetes mellitus

(E) Idiopathic dilated cardiomyopathy

Q8

A 44-year-old, previously healthy man has experienced worsening exercise tolerance accompanied by marked shortness of breath for the past 6 months. On physical examination, he is afebrile. His pulse is 78/min, respirations are 22/min, and blood pressure is 110/70 mm Hg. He has diffuse rales in all lung fields and pitting edema to the knees. Laboratory studies show serum sodium, 130 mmol/L; potassium, 4 mmol/L; chloride, 102 mmol/L; CO2, 25 mmol/L; creatinine, 2 mg/dL; and glucose, 120 mg/dL (6,7mmol). A 100-mL urine sample is collected. There is 1.3 mmol of sodium and 40 mg of creatinine in the urine sample. A chest radiograph shows cardiomegaly and pulmonary edema with pleural effusions. An echocardiogram shows four-chamber cardiac dilation and mitral and tricuspid valvular regurgitation, with an ejection fraction of 30%. A coronary angiogram shows less than 10% narrowing of the major coronary arteries. Which of the following is the most likely diagnosis?

(A) Rheumatic heart disease

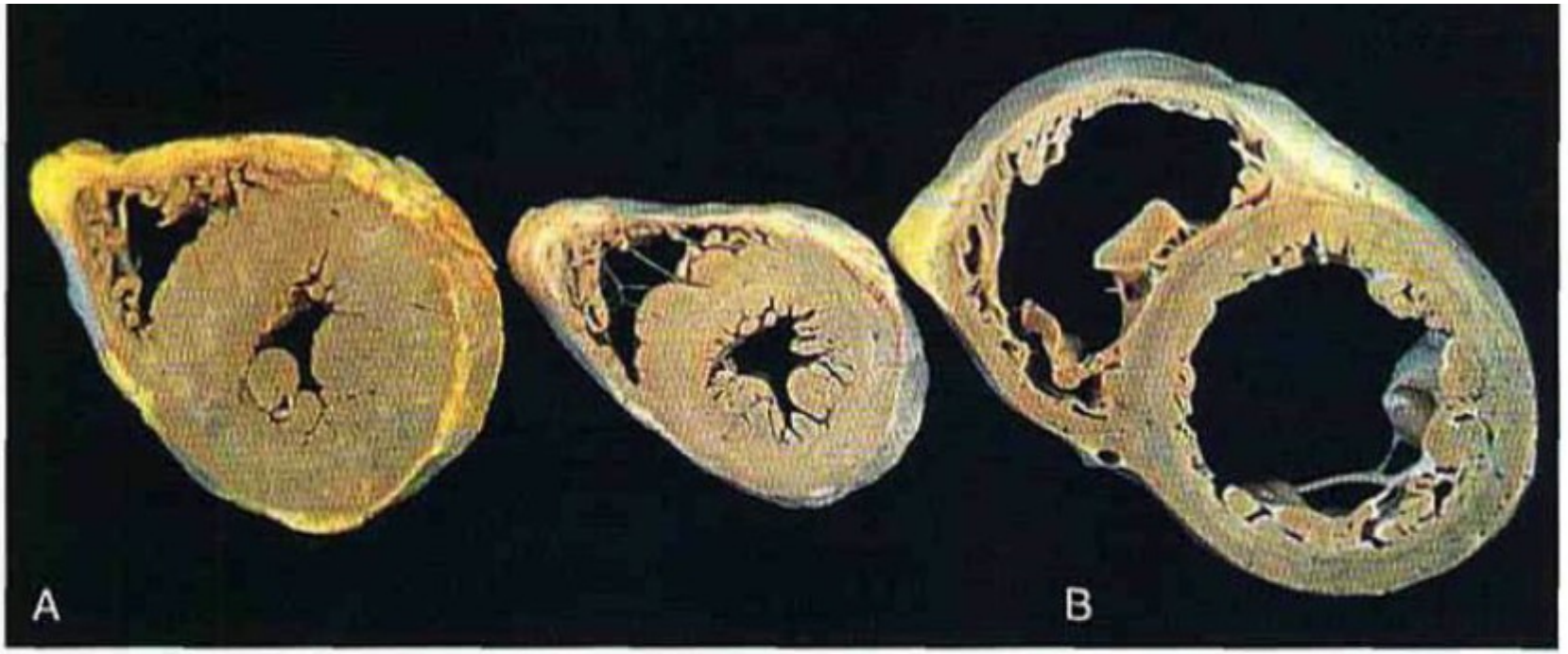
(B) Hereditary hemochromatosis

(C) Chagas disease

(D) Diabetes mellitus

(E) Idiopathic dilated cardiomyopathy

Q8



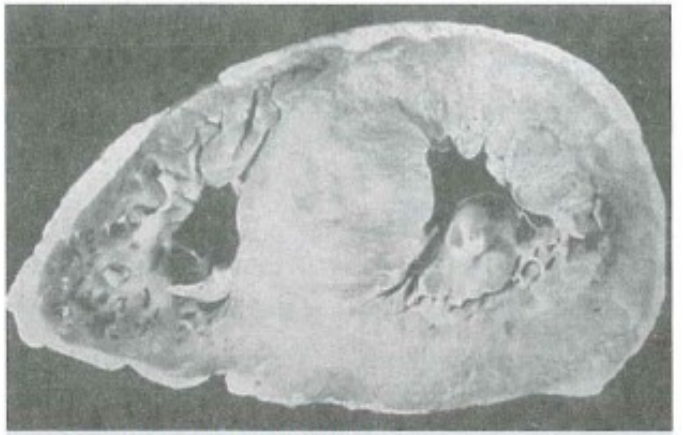
10-1: Left ventricular hypertrophy. The heart in the middle has a normal thickness of the left ventricle (LV). The heart on the left (**A**) has concentric hypertrophy of the LV, while the heart on the right (**B**) has eccentric hypertrophy of the LV. *(Reproduced with permission from Edwards WD: Cardiac anatomy and examination of cardiac specimens. In Emmanouilides GC, Riemenschneider TA, Allen HD, Gutgesell HP [eds]: Moss and Adams Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adults, 5th ed. Philadelphia, Williams & Wilkins, 1995. p 86.)*

2. Types of CHF
   a. Left-sided heart failure (most common type)
   b. Right-sided heart failure
   c. Biventricular heart failure (left- and right-sided heart failure)
   d. High-output heart failure (least common type)

Q8

Cardiomyopathies

Dilated (congestive) cardiomyopathy	Most common cardiomyopathy (90% of cases). Etiologies include chronic **A**lcohol abuse, wet **B**eriberi, **C**oxsackie B virus myocarditis, chronic **C**ocaine use, **C**hagas' disease, **D**oxorubicin toxicity, hemochromatosis, and peripartum cardiomyopathy. +genetic Findings: S3, dilated heart on ultrasound, balloon appearance on chest x-ray.	Systolic dysfunction ensues. Eccentric hypertrophy (sarcomeres added in series). **ABCCCD**.
Hypertrophic cardiomyopathy	Hypertrophied IV septum is "too close" to mitral valve leaflet, leading to outflow tract obstruction A. 50% of cases are familial, autosomal dominant. Associated with Friedreich's ataxia. Disoriented, tangled, hypertrophied myocardial fibers. Cause of sudden death in young athletes. Findings: normal-sized heart, S4, apical impulses, systolic murmur. Treat with β-blocker or non-dihydropyridine calcium channel blocker (e.g., verapamil).	Diastolic dysfunction ensues. Concentric hypertrophy (sarcomeres added in parallel). Proximity of hypertrophied IV septum to mitral leaflet obstructs outflow tract, resulting in systolic murmur and syncopal episodes.
Restrictive/ obliterative cardiomyopathy	Major causes include sarcoidosis, amyloidosis, postradiation fibrosis, endocardial fibroelastosis (thick fibroelastic tissue in endocardium of young children), Löffler's syndrome (endomyocardial fibrosis with a prominent eosinophilic infiltrate), and hemochromatosis (dilated cardiomyopathy can also occur).	Diastolic dysfunction ensues.



A **Hypertrophic cardiomyopathy.**

A8

Congestive heart failure with four-chamber dilation is suggestive of dilated cardiomyopathy; implicated in causation are myocarditis, alcohol abuse, and genetic factors (in 20% to 50% of cases). Many cases of dilated cardiomyopathy have no known cause. Dilation is more prominent than hypertrophy, although both are present, and all chambers are involved.

A/ Rheumatic heart disease would most often produce some degree of valvular stenosis, often with some regurgitation, and the course usually is more prolonged.

B/ Hemochromatosis produces restrictive cardiomyopathy.

C/ Chagas disease affects the right ventricle more often than the left

D/ Coronary artery narrowing would be worse in diabetes mellitus and accelerated atherosclerosis. Also, in DM, diastolic heart failure (a restrictive pattern) eould be expected, rather tham dilatation.

subQ8

A 44-year-old, previously healthy man has experienced worsening exercise tolerance accompanied by marked shortness of breath for the past 6 months. On physical examination, he is afebrile. His pulse is 78/min, respirations are 22/min, and blood pressure is 110/70 mm Hg. He has diffuse rales in all lung fields and pitting edema to the knees. Laboratory studies show serum sodium, 130 mmol/L; potassium, 4 mmol/L; chloride, 102 mmol/L; CO2, 25 mmol/L; **creatinine, 2 mg/dL** (= 177 umol/l); and glucose, 120 mg/dL (6,7mmol). A 100-mL urine sample is collected. There is 1.3 mmol of sodium and 40 mg of creatinine in the urine sample. A chest radiograph shows cardiomegaly and pulmonary edema with pleural effusions. An echocardiogram shows four-chamber cardiac dilation and mitral and tricuspid valvular regurgitation, with an ejection fraction of 30%. A coronary angiogram shows less than 10% narrowing of the major coronary arteries.

Why is the creatinine increased?

(ref. range: 0,6-1,2 mg/dL; 53-106 umol/l)

subQ8

Reason for azotemia?

- prerenal
- renal
- postrenal

TABLE 19-2. CAUSES OF INCREASED AND DECREASED SERUM BUN

CAUSE	DISCUSSION
Increased Serum BUN	
Decreased cardiac output	CHF, shock (e.g., hemorrhage) ↓ Cardiac output → ↓ GFR → ↑ proximal tubule reabsorption of urea → ↑ serum BUN
Increased protein intake	High-protein diet, blood in gastrointestinal tract ↑ Amino acid degradation → ↑ serum BUN
Increased tissue catabolism	Third-degree burns, postoperative state ↑ Amino acid degradation → ↑ serum BUN
Acute glomerulonephritis	Poststreptococcal glomerulonephritis ↓ GFR → ↑ serum BUN
Acute or chronic renal failure	Acute tubular necrosis, diabetic glomerulopathy ↓ GFR → ↑ serum BUN
Postrenal disease	Urinary tract obstruction (e.g., urinary stone, BPH) ↓ GFR back-diffusion of urea → ↑ serum BUN

subQ8: review of Renal failure

Acute renal failure (acute kidney injury)

In normal nephron, BUN is reabsorbed (for countercurrent multiplication), but creatinine is not. Acute renal failure is defined as an abrupt decline in renal function with ↑ creatinine and ↑ BUN over a period of several days.

1. Prerenal azotemia—due to ↓ RBF (e.g., hypotension) → ↓ GFR. Na^+/H_2O and urea retained by kidney in an attempt to conserve volume, so BUN/creatinine ratio ↑.
2. Intrinsic renal—generally due to acute tubular necrosis or ischemia/toxins; less commonly due to acute glomerulonephritis (e.g., RPGN). Patchy necrosis leads to debris obstructing tubule and fluid backflow across necrotic tubule → ↓ GFR. Urine has epithelial/granular casts. BUN reabsorption is impaired → ↓ BUN/creatinine ratio.
3. Postrenal—due to outflow obstruction (stones, BPH, neoplasia, congenital anomalies). Develops only with bilateral obstruction.

Variable	Prerenal	Renal	Postrenal
Urine osmolality	> 500	< 350	< 350
Urine Na	< 10	> 20	> 40
Fe_{Na}	< 1%	> 2%	> 4%
Serum BUN/Cr	> 20	< 15	> 15

sub-subQ8: What is Fractional Excretion of Na+ and when to use it?

You may calculate Fractional excretion of sodium (FE-Na) used in **oliguric** (<500ml/24h) patients to guide you in differentiating **prerenal vs. renal** failure.

sub-subQ8: What is Fractional Excretion of Na+ and when to use it?

You may calculate Fractional excretion of sodium (FE-Na) used in **oliguric** (<500ml/24h) patients to guide you in differentiating **prerenal vs. renal** failure.

The FE-Na represents the amount of sodium *excreted in the urine* divided by the amount of sodium that is *filtered by the kidneys*.

The calculation is as follows:

$$\text{FE-Na-} = [(\text{UNa} / \text{PNa}) / (\text{UCr} / \text{PCr})] \times 100$$

where
UNa- is a random urine sodium concentration,
PNa- is serum sodium,
UCr is random urine creatinine, and
PCr is plasma creatinine.

Creatinine is used in the formula, because the amount of sodium filtered is dependent on the glomerular filtration rate (CFR), which closely approximates the creatinine clearance (CCr).

An FE-Na < 1% indicates ... ?

.

An FE-Na > 2% indicates ... ?

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Creatinine is used in the formula, because the amount of sodium filtered is dependent on the glomerular filtration rate (CFR), which closely approximates the creatinine clearance (CCr).

An FENa < 1% indicates good tubular function and excludes acute tubular necrosis (ATN) as a cause of oliguria.
An FENa **> 2%** indicates **tubular dysfunction** and is highly predictive of **ATN** as the cause of oliguria.

sub-subQ8: What is Fractional Excretion of Na+ and when to use it?

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Are you sure it's prerenal azotemia? Could FE-Na help you?

(ref. range: 0,6-1,2 mg/dL; 53-106 umol/l)

sub-subQ8: What is Fractional Excretion of Na+ and when to use it?

Are you sure it's prerenal azotemia?

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Are you sure it's prerenal azotemia?

Calculation of FE-Na:

Serum: sodium 130 mmol/L; creatinine 2 mg/dL (= 177 umol/l);
A 100-mL urine sample: 1.3 mmol of sodium and 40 mg of creatinine.

$$FE\text{-}Na = [(UNa / PNa) / (UCr / PCr)] \times 100\ \%$$

$$FE\text{-}Na = [(1{,}3 / 130) / (40 / \mathbf{20})] \times 100\ \%$$

$$FE\text{-}Na = [(0{,}01) / (2)] \times 100\ \%$$

$$FE\text{-}Na = [(0{,}005)] \times 100\ \%$$

$$FE\text{-}Na = 0{,}5\%$$

So, is it prerenal azotemia?

subQ8: so, Does it make sense?

Acute renal failure (acute kidney injury)

In normal nephron, BUN is reabsorbed (for countercurrent multiplication), but creatinine is not. Acute renal failure is defined as an abrupt decline in renal function with ↑ creatinine and ↑ BUN over a period of several days.

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Thank you

Sources

- Lippincot's Q A pharm (http://www.amazon.co.uk/Lippincotts-Illustrated-Review-Pharmacology-Stanley/dp/1451182864/)
- First Aid for Step 1, 2012
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- Goljan: Rapid review pathology, 3rd
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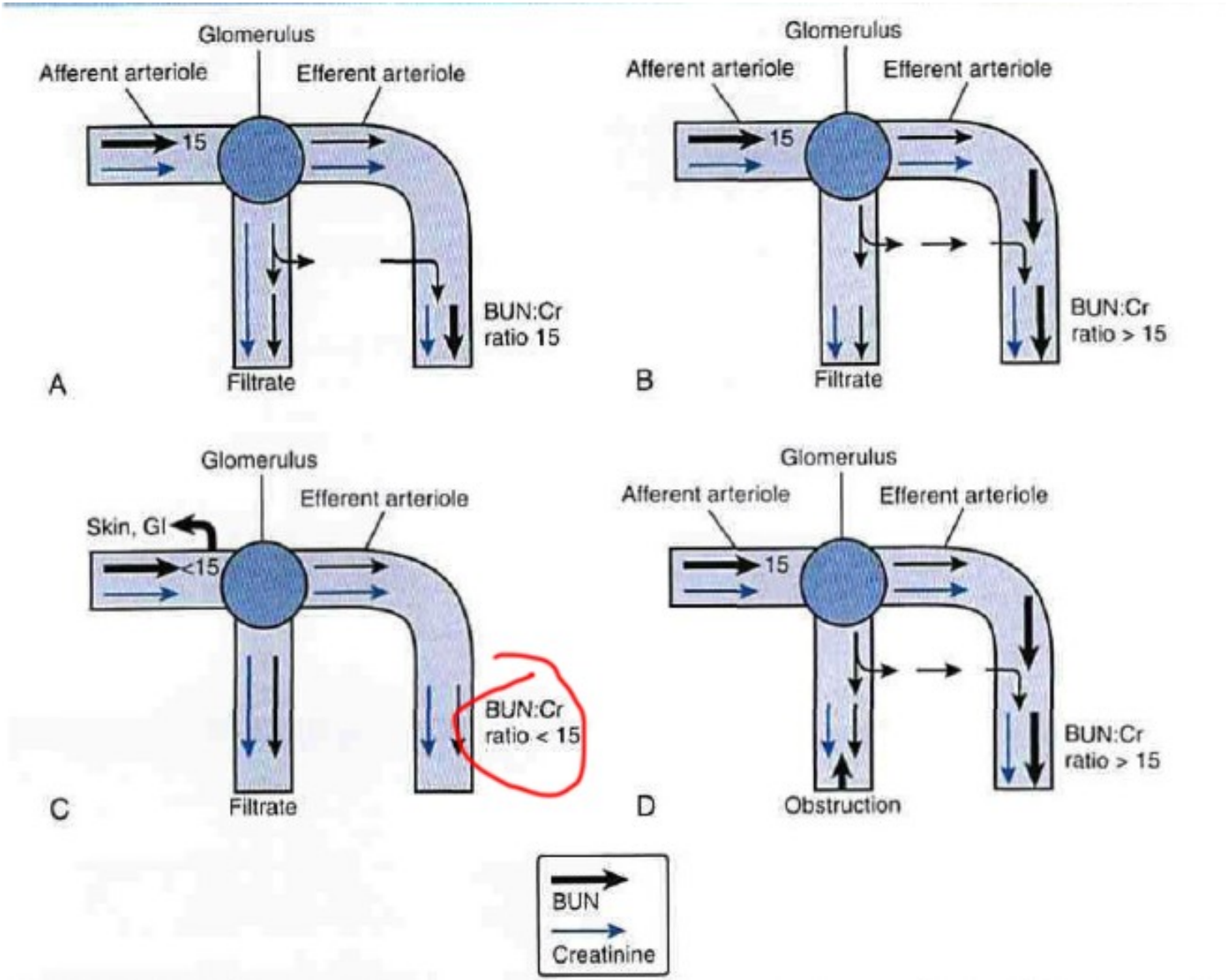
Q8

What precisely happens with BUN and Creatinine in acute renal failure?



19-1: Blood urea nitrogen (BUN) and creatinine (Cr) ratios in normal persons (A), and in prerenal (B), renal (C), and postrenal azotemia (D). See text for discussion. *(From Goljan EF, Sloka KI: Rapid Review Laboratory Testing in Clinical Medicine. St. Louis, Mosby Elsevier, 2008, p 102, Fig. 4-15.)*