XV. HYPERTENSIVE EMERGENCY

Hypertensive emergency is a rare but life-threatening situation characterized by severe elevations in blood pressure (systolic greater than 180 mm Hg or diastolic greater than 120 mm Hg) with evidence of impending or progressive target organ damage (for example, stroke, myocardial infarction). [Note: A severe elevation in blood pressure without evidence of target organ damage is considered a hypertensive urgency.] Hypertensive emergencies require timely blood pressure reduction with treatment administered intravenously to prevent or limit target organ damage. A variety of medications are used, including calcium channel blockers (*nicardipine* and *clevidipine*), nitric oxide vasodilators (*nitroprusside* and *nitroglycerin*), adrenergic receptor antagonists (*phentolamine*, *esmolol*, and *labetalol*), the vasodilator *hydralazine*, and the dopamine agonist *fenoldopam*. Treatment is directed by the type of target organ damage present and/or comorbidities present.

XVI. RESISTANT HYPERTENSION

Resistant hypertension is defined as blood pressure that remains elevated (above goal) despite administration of an optimal three-drug regimen that includes a diuretic. The most common causes of resistant hypertension are poor compliance, excessive ethanol intake, concomitant conditions (diabetes, obesity, sleep apnea, hyperaldosteronism, high salt intake, and/or metabolic syndrome), concomitant medications (sympathomimetics, nonsteroidal anti-inflammatory drugs, or antidepressant medications), insufficient dose and/or drugs, and use of drugs with similar mechanisms of action.

XVII. COMBINATION THERAPY

Combination therapy with separate agents or a fixed-dose combination pill may lower blood pressure more quickly with minimal adverse effects. Initiating therapy with two antihypertensive drugs should be considered in patients with blood pressures that are more than 20/10 mm Hg above the goal. A variety of combination formulations of the various pharmacologic classes are available to increase ease of patient adherence to treatment regimens that require multiple medications to achieve the blood pressure goal.

Study Questions

Choose the ONE best answer.

17.1 A 45-year-old man was just started on therapy for hypertension and developed a persistent, dry cough. Which is most likely responsible for this side effect?

A. Enalapril.
B. Losartan.
C. Nifedipine.
D. Prazosin.
E. Propranolol.

Correct answer = A. The cough is most likely an adverse effect of the ACE inhibitor enalapril. Losartan is an ARB that has the same beneficial effects as an ACE inhibitor but is less likely to produce a cough. Nifedipine, prazosin, and propranolol do not cause this side effect.

17.2 Which may cause reflex tachycardia and/or postural hypotension on initial administration?

A. Atenolol.
B. Hydrochlorothiazide.
C. Metoprolol.
D. Prazosin.
E. Verapamil.

Correct answer = D. Prazosin produces first-dose hypotension, presumably by blocking α_1 receptors. This effect is minimized by initially giving the drug in small, divided doses. The other agents do not have this adverse effect.

17.3 Which can precipitate a hypertensive crisis following abrupt cessation of therapy?

A. Clonidine.
B. Diltiazem.
C. Enalapril.
D. Losartan.
E. Hydrochlorothiazide.

Correct answer = A. Increased sympathetic nervous system activity occurs if clonidine therapy is abruptly stopped after prolonged administration. Uncontrolled elevation in blood pressure can occur. Patients should be slowly weaned from clonidine while other antihypertensive medications are initiated. The other drugs on the list do not produce this phenomenon.

17.4 A 48-year-old hypertensive patient has been successfully treated with a thiazide diuretic for the last 5 years. Over the last 3 months, his diastolic pressure has steadily increased, and he was started on an additional antihypertensive agent. He complains of several instances of being unable to achieve an erection and not being able to complete three sets of tennis as he once did. Which is the likely second antihypertensive medication?

A. Captopril.
B. Losartan.
C. Metoprolol.
D. Minoxidil.
E. Nifedipine.

Correct answer = C. The side effect profile of β-blockers, such as metoprolol, is characterized by interference with sexual performance and decreased exercise tolerance. None of the other drugs is likely to produce this combination of side effects.

17.5 A 40-year-old male has recently been diagnosed with hypertension due to pressure readings of 163/102 and 165/100 mm Hg. He also has diabetes that is well controlled with oral hypoglycemic medications. Which is the best initial treatment regimen for treatment of hypertension in this patient?

A. Felodipine.
B. Furosemide.
C. Lisinopril.
D. Lisinopril and hydrochlorothiazide.
E. Metoprolol.

Correct answer = D. Because the systolic blood pressure is more than 20 mm Hg above goal (10 mm Hg above goal diastolic), treatment with two different medications is preferred. Because the patient is diabetic, he also has a compelling indication for an ACE inhibitor or ARB.

17.6 A 60-year-old white female has not reached her blood pressure goal after 1 month of treatment with a low dose of lisinopril. All of the following would be appropriate next steps in the treatment of her hypertension except:

A. Increase dose of lisinopril.
B. Add a diuretic medication.
C. Add on a calcium channel blocker medication.
D. Add on an ARB medication.

Correct answer = D. Increasing the dose of lisinopril or adding a second medication from a different class (such as a calcium channel blocker or diuretic) would be appropriate steps to control the blood pressure. Adding an ARB as the second medication is not recommended. ARBs have a similar mechanism of action to ACE inhibitors, and combination therapy may increase the risk of adverse effects.

17.7 A patient returns to her health care provider for routine monitoring 3 months after her hypertension regimen was modified. Labs reveal elevated serum potassium. Which is likely responsible for this hyperkalemia?

A. Chlorthalidone.
B. Clonidine.
C. Furosemide.
D. Losartan.
E. Nifedipine.

Correct answer = D. Losartan, an ARB, can cause an increase in serum potassium similar to ACE inhibitors. Furosemide and chlorthalidone can cause a decrease in serum potassium. Nifedipine and clonidine do not affect potassium levels.

17.8 A 58-year-old female reports that she recently stopped taking her blood pressure medications because of swelling in her feet that began shortly after she started treatment. Which is most likely to cause peripheral edema?

A. Atenolol.
B. Clonidine.
C. Felodipine.
D. Hydralazine.
E. Prazosin.

Correct answer = C. Peripheral edema is one of the most common side effects of calcium channel blockers. None of the other agents commonly cause peripheral edema.

17.9 Which is an appropriate choice for hypertension treatment during pregnancy?

A. Aliskiren.
B. Fosinopril.
C. Hydralazine.
D. Valsartan.

Correct answer = C. Hydralazine is an appropriate choice for a hypertensive pregnant patient. ACE inhibitors, ARBs, and the direct renin inhibitor, aliskiren, are all contraindicated in pregnancy due to their potential for fetal harm.

17.10 DD is a 50-year-old male with newly diagnosed hypertension. His comorbidities include diabetes and chronic hepatitis C infection with moderate liver impairment. He requires two drugs for initial treatment of his hypertension. Which should be prescribed in combination with a thiazide diuretic?

A. Lisinopril.
B. Spironolactone.
C. Fosinopril.
D. Furosemide.
E. Hydralazine.

Correct answer = A. Because DD has diabetes, he has a compelling indication for an ACE inhibitor or ARB for the treatment of his hypertension and prevention of diabetic nephropathy. However, most ACE inhibitors undergo hepatic conversion to active metabolites, so his hepatic impairment is of concern. Because lisinopril is one of the two ACE inhibitors that does not undergo hepatic conversion to active metabolites, it is the best choice. Fosinopril is the only ACE inhibitor that is not eliminated primarily by the kidneys but does undergo hepatic conversion. An additional diuretic like spironolactone or furosemide is not indicated. DD does not have a compelling indication for hydralazine.

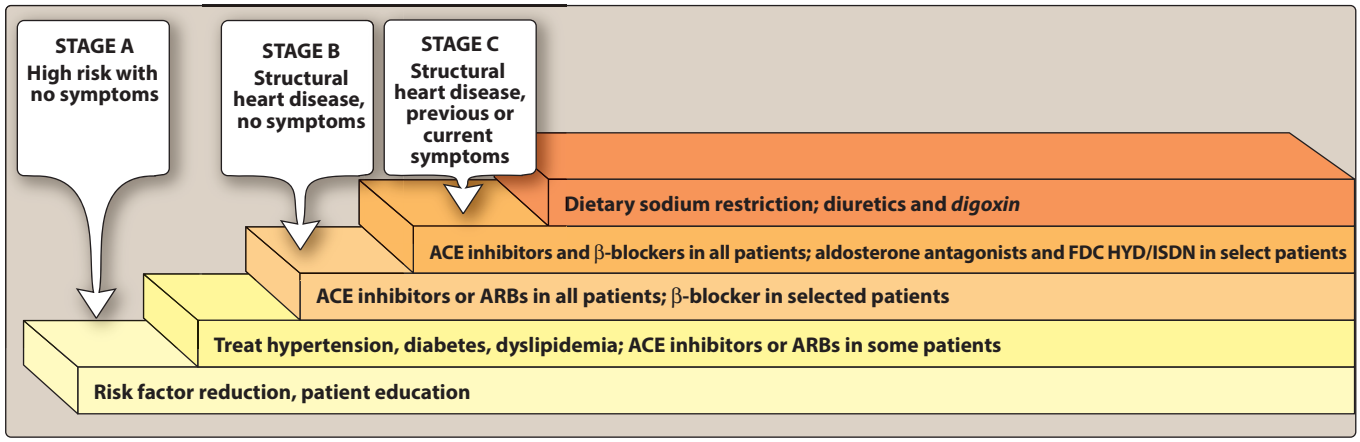

Figure 19.11
Treatment options for various stages of HF. ACE = angiotensin-converting enzyme; ARBs = angiotensin receptor blockers; FDC = fixed dose combination; HYD = hydralazine; ISDN = isosorbide dinitrate. Stage D (refractory symptoms requiring special interventions) is not shown.

however, most patients newly diagnosed with HFrEF are initiated on both low doses of an ACE inhibitor and β-blocker after initial stabilization. These agents are slowly titrated to optimal levels to increase tolerability. *Digoxin*, aldosterone antagonists, and fixed-dose *hydralazine* and *isosorbide dinitrate* are initiated in patients who continue to have HF symptoms despite optimal doses of an ACE inhibitor and β-blocker.

Study Questions

Choose the ONE best answer.

19.1 Which drug may exacerbate HF?

A. Acetaminophen.
B. Cetirizine.
C. Chlorthalidone.
D. Ibuprofen.

Correct answer = D. NSAIDs, such as ibuprofen, lead to increased fluid retention and increased blood pressure. If possible, NSAIDs should be avoided in HF patients in order to avoid exacerbations of HF.

19.2 Which best describes the action of ACE inhibitors on the failing heart?

A. ACE inhibitors increase vascular resistance.
B. ACE inhibitors decrease cardiac output.
C. ACE inhibitors reduce preload.
D. ACE inhibitors increase aldosterone.

Correct answer = C. ACE inhibitors decrease vascular resistance, decrease preload, decrease afterload, and increase cardiac output. In addition, ACE inhibitors blunt aldosterone release.

19.3 What makes losartan different from other ARBs?

A. Losartan is renally eliminated.
B. Losartan has an active metabolite.
C. Losartan has the shortest half-life.
D. Losartan has a small volume of distribution.

Correct answer = B. Losartan is the only ARB that undergoes first-pass metabolism to convert to its active metabolite. Most ARBs have once-daily dosing, and all (except candesartan) have large volumes of distribution.

19.4 How do β-blockers improve cardiac function in HF?

A. By decreasing cardiac remodeling.
B. By increasing heart rate.
C. By increasing renin release.
D. By activating norepinephrine.

Correct answer = A. Although it seems counterintuitive to decrease heart rate in HF, β-blockers improve cardiac functioning by slowing heart rate, decreasing renin release, and preventing the direct effects of norepinephrine on cardiac muscle to decrease remodeling.

19.5 BC is a 70-year-old female who is diagnosed with HFrEF. Her past medical history is significant for hypertension and atrial fibrillation. She is taking hydrochlorothiazide, lisinopril, metoprolol tartrate, and warfarin. BC says she is feeling "good" and has no cough, shortness of breath, or edema. Which is the most appropriate medication change to make?

A. Discontinue hydrochlorothiazide.
B. Change lisinopril to losartan.
C. Decrease warfarin dose.
D. Change metoprolol tartrate to metoprolol succinate.

Correct answer = D. Metoprolol succinate should be used in HF, given that there is mortality benefit shown with metoprolol succinate in landmark HF trials. Hydrochlorothiazide and warfarin are appropriate based on the information given; there is no reason to change to an ARB since the patient has no cough or history of angioedema.

19.6 SC is a 75-year-old white male who has HF. He is seen in clinic today, reporting shortness of breath, increased pitting edema, and a 5-pound weight gain over the last 2 days. His current medication regimen includes losartan and metoprolol succinate. SC has no chest pain and is deemed stable for outpatient treatment. Which of the following is the best recommendation?

A. Increase the dose of metoprolol succinate.
B. Start hydrochlorothiazide.
C. Start furosemide.
D. Discontinue losartan.

Correct answer = C. As it is possible that SC is having a HF exacerbation, increasing the dose of the β-blocker is not indicated at this time. There is no reason to stop losartan, based on the information we have. Loop diuretics are preferred over thiazide diuretics when patients require diuresis immediately.

19.7 How is spironolactone beneficial in HF?

A. Promotes potassium secretion.
B. Agonizes aldosterone.
C. Prevents cardiac hypertrophy.
D. Decreases blood glucose.

Correct answer = C. Spironolactone antagonizes aldosterone, which in turn prevents salt/water retention, cardiac hypertrophy, and hypokalemia. Spironolactone has endocrine effects on hormones but not on glucose.

19.8 Which is important to monitor in patients taking digoxin?

A. Chloride.
B. Potassium.
C. Sodium.
D. Zinc.

Correct answer = B. Hypokalemia can lead to life-threatening arrhythmias and increases the potential of cardiac toxicity with digoxin.

19.9 Which describes the mechanism of action of milrinone in HF?

A. Decreases intracellular calcium.
B. Increases cardiac contractility.
C. Decreases cAMP.
D. Activates phosphodiesterase.

Correct answer = B. Milrinone is a phosphodiesterase inhibitor that leads to increased cAMP, increased intracellular calcium, and therefore increased contractility.

19.10 What is the most common adverse effect associated with fixed-dose hydralazine/isosorbide dinitrate?

A. Diarrhea.
B. Drug-induced lupus.
C. Headache.
D. Heartburn.

Correct answer = C. While drug-induced lupus is a possibility with hydralazine, headache is the most common adverse effect.

velocity in the AV node. *Digoxin* is used to control ventricular response rate in atrial fibrillation and flutter; however, sympathetic stimulation easily overcomes the inhibitory effects of *digoxin*. At toxic concentrations, *digoxin* causes ectopic ventricular beats that may result in VT and fibrillation. [Note: Serum trough concentrations of 1.0 to 2.0 ng/mL are desirable for atrial fibrillation or flutter, whereas lower concentrations of 0.5 to 0.8 ng/mL are targeted for systolic heart failure.]

B. Adenosine

Adenosine [ah-DEN-oh-zeen] is a naturally occurring nucleoside, but at high doses, the drug decreases conduction velocity, prolongs the refractory period, and decreases automaticity in the AV node. Intravenous *adenosine* is the drug of choice for abolishing acute supraventricular tachycardia. It has low toxicity but causes flushing, chest pain, and hypotension. *Adenosine* has an extremely short duration of action (approximately 10 to 15 seconds) due to rapid uptake by erythrocytes and endothelial cells.

C. Magnesium sulfate

Magnesium is necessary for the transport of sodium, calcium, and potassium across cell membranes. It slows the rate of SA node impulse formation and prolongs conduction time along the myocardial tissue. Intravenous *magnesium sulfate* is the salt used to treat arrhythmias, as oral *magnesium* is not effective in the setting of arrhythmia. Most notably, *magnesium* is the drug of choice for treating the potentially fatal arrhythmia torsades de pointes and *digoxin*-induced arrhythmias.

Study Questions

Choose the ONE best answer.

20.1 A 60-year-old woman had a myocardial infarction. Which of the following should be used to prevent life-threatening arrhythmias that can occur post–myocardial infarction in this patient?

A. Digoxin.
B. Flecainide.
C. Metoprolol.
D. Procainamide.
E. Quinidine.

Correct answer = C. β-Blockers such as metoprolol prevent arrhythmias that occur subsequent to a myocardial infarction. None of the other drugs has been shown to be effective in preventing postinfarct arrhythmias. Flecainide should be avoided in patients with structural heart disease.

20.2 Suppression of arrhythmias resulting from a reentry focus is most likely to occur if the drug:

A. Has vagomimetic effects on the AV node.
B. Is a β-blocker.
C. Converts a unidirectional block to a bidirectional block.
D. Slows conduction through the atria.
E. Has atropine-like effects on the AV node.

Correct answer = C. Current theory holds that a reentrant arrhythmia is caused by damaged heart muscle, so that conduction is slowed through the damaged area in only one direction. A drug that prevents conduction in either direction through the damaged area interrupts the reentrant arrhythmia. Class I antiarrhythmics, such as lidocaine, are capable of producing bidirectional block. The other choices do not have any direct effects on the direction of blockade of conduction through damaged cardiac muscle.

20.3 A 57-year-old man is being treated for an atrial arrhythmia. He complains of dry mouth, blurred vision, and urinary hesitancy. Which antiarrhythmic drug is he mostly like taking?

A. Metoprolol.
B. Disopyramide.
C. Dronedarone.
D. Sotalol.

Correct answer = B. The clustered symptoms of dry mouth, blurred vision, and urinary hesitancy are characteristic of anticholinergic adverse effects which are caused by class IA agents (in this case, disopyramide). The other drugs do not cause anticholinergic effects.

20.4 A 58-year-old woman is being treated for chronic suppression of a ventricular arrhythmia. After 1 week of therapy, she complains about feeling severe upset stomach and heartburn. Which antiarrhythmic drug is the likely cause of these symptoms?

A. Amiodarone.
B. Digoxin.
C. Mexiletine.
D. Propranolol.
E. Quinidine.

Correct answer = C. The patient is exhibiting a classic adverse effect of mexiletine. None of the other agents listed are likely to cause dyspepsia.

20.5 A 78-year-old woman has been newly diagnosed with atrial fibrillation. She is not currently having symptoms of palpitations or fatigue. Which is appropriate to initiate for rate control as an outpatient?

A. Amiodarone.
B. Dronedarone.
C. Esmolol.
D. Flecainide.
E. Metoprolol.

Correct answer = E. Only C and E are options to control rate. The other options are used for rhythm control in patients with atrial fibrillation. Since esmolol is IV only, the only option to start as an outpatient is metoprolol.

20.6 Which of the following is correct regarding digoxin when used for atrial fibrillation?

A. Digoxin works by blocking voltage-sensitive calcium channels.
B. Digoxin is used for rhythm control in patients with atrial fibrillation.
C. Digoxin increases conduction velocity through the AV node.
D. Digoxin levels of 1 to 2 ng/mL are desirable in the treatment of atrial fibrillation.

Correct answer = D. Digoxin works by inhibiting the Na^+/K^+-ATPase pump. It decreases conduction velocity through the AV node and is used for rate control in atrial fibrillation (not rhythm control). Digoxin levels between 1 and 2 ng/mL are more likely to exhibit negative chronotropic effects desired in atrial fibrillation or flutter. A serum drug concentration between 0.5 and 0.8 ng/mL is for symptomatic management of heart failure.

20.7 All of the following are adverse effects of amiodarone except:

A. Cinchonism.
B. Hypothyroidism.
C. Hyperthyroidism.
D. Pulmonary fibrosis.
E. Blue skin discoloration.

Correct answer = A. Cinchonism is a constellation of symptoms (blurred vision, tinnitus, headache, psychosis) that is known to occur with quinidine. All other options are adverse effects with amiodarone that require close monitoring.

20.8 Which arrhythmia can be treated with lidocaine?

A. Paroxysmal supraventricular ventricular tachycardia.
B. Atrial fibrillation.
C. Atrial flutter.
D. Ventricular tachycardia.

Correct answer = D. Lidocaine has little effect on atrial or AV nodal tissue; thus, it used for ventricular arrhythmias such as ventricular tachycardia.

20.9 A clinician would like to initiate a drug for rhythm control of atrial fibrillation. Which of the following coexisting conditions would allow for initiation of flecainide?

A. Hypertension.
B. Left ventricular hypertrophy.
C. Coronary artery disease.
D. Heart failure.

Correct answer = A. Since flecainide can increase the risk of sudden cardiac death in those with a history of structural heart disease, only A will allow for flecainide initiation. Structural heart disease includes left ventricular hypertrophy, heart failure, and atherosclerotic heart disease.

20.10 Which statement regarding dronedarone is correct?

A. Dronedarone is more effective than amiodarone.
B. QT interval prolongation is not a risk with dronedarone.
C. Dronedarone increases the risk of death in patients with permanent atrial fibrillation or symptomatic heart failure.
D. There is no need to monitor liver function with dronedarone.

Correct answer = C. Dronedarone is not as effective as amiodarone, QT prolongation is a risk with this drug, and liver function should be monitored when taking dronedarone since it increases the risk of liver failure. The drug is contraindicated in those with symptomatic heart failure or permanent atrial fibrillation due to an increased risk of death.

DRUG CLASS	COMMON ADVERSE EFFECTS	DRUG INTERACTIONS	NOTES
β-blockers ***atenolol*** ***metoprolol*** ***propranolol***	**Bradycardia, worsening peripheral vascular disease, fatigue, sleep disturbance, depression, blunt hypoglycemia awareness, inhibit β_2-mediated bronchodilation in asthmatics**	**β_2 agonists (blunted effect); non-dihydropyridine calcium-channel blockers (additive effects)**	**β_1-selective agents preferred (*atenolol, metoprolol*). Avoid agents with ISA for angina therapy (*pindolol*).**
Dihydropyridine calcium-channel blockers ***amlodipine*** ***felodipine*** ***nifedipine***	**Peripheral edema, headache, flushing, rebound tachycardia (immediate release formulations), hypotension**	**CYP 3A4 substrates (will increase drug concentrations)**	**Avoid short-acting agents as they can worsen angina (may use extended-release formulations)**
Non-dihydropyridine calcium-channel blockers ***diltiazem*** ***verapamil***	**Bradycardia, constipation, heart failure exacerbations, gingival hyperplasia (*verapamil*), edema (*diltiazem*)**	**CYP 3A4 substrates (will increase drug concentrations); increase *digoxin* levels; β-blockers and other drugs affecting AV node conduction (additive effects)**	**Avoid in patients with heart failure** **Adjust dose of both agents in patients with hepatic dysfunction**
Organic nitrates ***isosorbide dinitrate*** ***isosorbide mononitrate*** ***nitroglycerin***	**Headache, hypotension, flushing, tachycardia**	**Contraindicated with PDE5 inhibitors (*sildenafil* and others)**	**Ensure nitrate-free interval to prevent tolerance**
Sodium-channel inhibitor ***ranolazine***	**Constipation, headache, edema, dizziness, QT interval prolongation**	**Avoid use with CYP 3A4 inducers (*phenytoin, carbamazepine, St. John's wort*) and strong inhibitors (*clarithromycin*, azole antifungals) and agents that prolong QT interval (*citalopram, quetiapine*, others)**	**No effect on hemodynamic parameters**

CYP = cytochrome P450; ISA = intrinsic sympathomimetic activity; PDE5 = phosphodiesterase type 5

Figure 21.7
Summary of characteristics of antianginal drugs.

Study Questions

Choose the ONE best answer.

21.1 What is the clinical term for angina caused by coronary vasospasm?

A. Classic angina.
B. Myocardial infarction.
C. Prinzmetal angina.
D. Unstable angina.

Correct answer = C. Prinzmetal angina is angina caused by vasospasm of the coronary arteries. It is also known as vasospastic or variant angina. The other answers refer to angina (with varying levels of severity) caused by atherosclerosis.

21.2 All of the following medications can be useful for managing stable angina in a patient with coronary artery disease except:

A. Amlodipine.
B. Atenolol.
C. Immediate-release nifedipine.
D. Isosorbide dinitrate.

Correct answer = C. The short-acting dihydropyridine calcium channel blocker nifedipine should be avoided in CAD patients as this can worsen angina; however, the extended-release formulation can be used.

21.3 A 72-year-old male presents to the primary care clinic complaining of chest tightness and pressure that is increasing in severity and frequency. His current medications include atenolol, lisinopril, and nitroglycerin. Which intervention is most appropriate at this time?

A. Add amlodipine.
B. Initiate isosorbide mononitrate.
C. Initiate ranolazine.
D. Refer the patient to the nearest emergency room for evaluation.

Correct answer = D. Crescendo angina is indicative of unstable angina that requires further workup.

21.4 A 62-year-old patient with a history of asthma and vasospastic angina states that he gets chest pain both with exertion and at rest, about ten times per week. One sublingual nitroglycerin tablet always relieves his symptoms, but this medication gives him an awful headache every time he takes it. Which is the best option for improving his angina?

A. Change to sublingual nitroglycerin spray.
B. Add amlodipine.
C. Add propranolol.
D. Replace nitroglycerin with ranolazine.

Correct answer = B. Calcium channel blockers are preferred for vasospastic angina. β-Blockers can actually worsen vasospastic angina; furthermore, nonselective β-blockers should be avoided in patients with asthma. The nitroglycerin spray would also be expected to cause headache, so this is not the best choice. Ranolazine is not indicated for immediate relief of an angina attack, nor is it a first-line option.

21.5 Which side effect is associated with amlodipine?

A. Bradycardia.
B. Cough.
C. Edema.
D. QT prolongation.

Correct answer = C. Edema is the correct answer. The other answers are incorrect.

21.6 Which medication should be prescribed to all anginal patients to treat an acute attack?

A. Isosorbide dinitrate.
B. Nitroglycerin patch.
C. Nitroglycerin sublingual tablet or spray.
D. Ranolazine.

Correct answer = C. The other options will not provide prompt relief of angina and should not be used to treat an acute attack.

21.7 A 65-year-old male experiences uncontrolled angina attacks that limit his ability to do household chores. He is adherent to a maximized dose of β-blocker with a low heart rate and low blood pressure. He was unable to tolerate an increase in isosorbide mononitrate due to headache. Which is the most appropriate addition to his antianginal therapy?

A. Amlodipine.
B. Aspirin.
C. Ranolazine.
D. Verapamil.

Correct answer = C. Ranolazine is the best answer. The patient's blood pressure is low, so verapamil and amlodipine may drop blood pressure further. Verapamil may also decrease heart rate. Ranolazine can be used when other agents are maximized, especially when blood pressure is well controlled. The patient will need a baseline ECG and lab work to ensure safe use of this medication.

21.8 A 68-year-old male with a history of angina had a MI last month, and an echocardiogram reveals heart failure with reduced ejection fraction. He was continued on his previous home medications (diltiazem, enalapril, and nitroglycerin), and atenolol was added at discharge. He has only had a few sporadic episodes of stable angina that are relieved with nitroglycerin or rest. What are eventual goals for optimizing this medication regimen?

A. Add isosorbide mononitrate.
B. Increase atenolol.
C. Stop atenolol and increase diltiazem.
D. Stop diltiazem and change atenolol to bisoprolol.

Correct answer = D. Nondihydropyridine calcium channel blockers such as diltiazem should be avoided in patients with heart failure with reduced ejection fraction. Patients should be treated with one of three β-blockers approved for heart failure with reduced ejection fraction (bisoprolol, metoprolol succinate, or carvedilol). It sounds like his angina symptoms are well managed with his current therapy so adding isosorbide mononitrate would not be necessary. These symptoms may become even less frequent as his new β-blocker is titrated.

21.9 Which of the following medications would be safe to use in a patient taking ranolazine?

A. Carbamazepine.
B. Clarithromycin.
C. Enalapril.
D. Quetiapine.

Correct answer = C. All other medications should be avoided due to potential drug–drug interactions.

21.10 A patient whose angina was previously well controlled with once-daily isosorbide mononitrate states that recently he has been taking isosorbide mononitrate twice a day to control angina symptoms that are occurring more frequently during early morning hours. Which of the following is the best option for this patient?

A. Continue once-daily administration of isosorbide mononitrate but advise the patient to take this medication in the evening.
B. Advise continuation of isosorbide mononitrate twice daily for full 24-hour coverage of anginal symptoms.
C. Switch to isosorbide dinitrate, as this has a longer duration of action than the mononitrate.
D. Switch to nitroglycerin patch for consistent drug delivery and advise him to wear the patch around the clock.

Correct answer = A. It is important to maintain a nitrate-free period to prevent the development of tolerance to nitrate therapy. The mononitrate formulation has the longer half-life. The nitroglycerin patch should be taken off for 10 to 12 hours daily to allow for nitrate-free interval.

Study Questions

Choose the ONE best answer.

23.1 Which one of the following is the most common side effect of antihyperlipidemic drug therapy?

A. Elevated blood pressure.
B. Gastrointestinal disturbance.
C. Neurologic problems.
D. Heart palpitations.
E. Migraine headaches.

Correct answer = B. Gastrointestinal disturbances frequently occur as a side effect of antihyperlipidemic drug therapy. The other choices are not seen as commonly.

23.2 Which one of the following hyperlipidemias is characterized by elevated plasma levels of chylomicrons and has no drug therapy available to lower the plasma lipoprotein levels?

A. Type I.
B. Type II.
C. Type III.
D. Type IV.
E. Type V.

Correct answer = A. Type I hyperlipidemia (hyperchylomicronemia) is treated with a low-fat diet. No drug therapy is effective for this disorder.

23.3 Which one of the following drugs decreases cholesterol synthesis by inhibiting the enzyme 3-hydroxy-3-methylglutaryl coenzyme A reductase?

A. Fenofibrate.
B. Niacin.
C. Cholestyramine.
D. Lovastatin.
E. Gemfibrozil.

Correct answer = D. Lovastatin decreases cholesterol synthesis by inhibiting HMG CoA reductase. Fenofibrate and gemfibrozil increase the activity of lipoprotein lipase, thereby increasing the removal of VLDL from plasma. Niacin inhibits lipolysis in adipose tissue, thus eliminating the building blocks needed by the liver to produce triglycerides and, therefore, VLDL. Cholestyramine lowers the amount of bile acids returning to the liver via the enterohepatic circulation.

23.4 Which one of the following drugs causes a decrease in liver triglyceride synthesis by limiting available free fatty acids needed as building blocks for this pathway?

A. Niacin.
B. Fenofibrate.
C. Cholestyramine.
D. Gemfibrozil.
E. Lovastatin.

Correct answer = A. At gram doses, niacin strongly inhibits lipolysis in adipose tissue—the primary producer of circulating free fatty acids. The liver normally utilizes these circulating fatty acids as a major precursor for triglyceride synthesis. Thus, niacin causes a decrease in liver triglyceride synthesis, which is required for VLDL production. The other choices do not inhibit lipolysis in adipose tissue.

23.5 Which one of the following drugs binds bile acids in the intestine, thus preventing their return to the liver via the enterohepatic circulation?

A. Niacin.
B. Fenofibrate.
C. Cholestyramine.
D. Fluvastatin.
E. Lovastatin.

Correct answer = C. Cholestyramine is an anion-exchange resin that binds negatively charged bile acids and bile salts in the small intestine. The resin/bile acid complex is excreted in the feces, thus preventing the bile acids from returning to the liver by the enterohepatic circulation. The other choices do not bind intestinal bile acids.

23.6 JS is a 65-year-old man who presents to his physician for management of hyperlipidemia. His most recent lipid panel reveals an LDL cholesterol level of 165 mg/dL. His physician wishes to begin treatment to lower his LDL cholesterol levels. Which of the following therapies is the best option to lower JS's LDL cholesterol levels?

A. Fenofibrate.
B. Colesevelam.
C. Niacin.
D. Simvastatin.
E. Ezetimibe.

Correct answer = D. Simvastatin, an HMG CoA reductase inhibitor (statin), is the most effective option for lowering LDL cholesterol, achieving reductions of 30% to 41% from baseline levels. Fenofibrate and niacin are more effective at lowering triglyceride levels or raising HDL levels (niacin). Colesevelam can reduce LDL levels but not as effectively as statins. Ezetimibe lowers LDL levels modestly compared to the LDL reduction achieved by statins.

23.7 WW is a 62-year-old female with hyperlipidemia and hypothyroidism. Her current medications include cholestyramine and levothyroxine (thyroid hormone). What advice would you give to WW to avoid a drug interaction between her cholestyramine and levothyroxine?

A. Stop taking the levothyroxine as it can interact with cholestyramine.
B. Take levothyroxine 1 hour before cholestyramine on an empty stomach.
C. Switch cholestyramine to colesevelam as this will eliminate the interaction.
D. Switch cholestyramine to colestipol as this will eliminate the interaction.
E. Take levothyroxine and cholestyramine at the same time to minimize the interaction.

Correct answer = B. Cholestyramine and the bile acid resins can bind several medications causing decreased absorption. Cholestyramine can decrease absorption of medications such as levothyroxine. Taking levothyroxine 1 hour before or 4 to 6 hours after cholestyramine can help to avoid this interaction. Choices C and D are incorrect, as all bile acid resins cause this interaction. Choice A is incorrect, as this patient should not stop her thyroid medication. Choice E will worsen this drug interaction.

23.8 AJ is a 42-year-old man who was started on niacin sustained-release tablets 2 weeks ago for elevated triglycerides and low HDL levels. He is complaining of an uncomfortable flushing and itchy feeling that he thinks is related to the niacin. Which of the following options can help AJ manage this adverse effect of niacin therapy?

A. Administer aspirin 30 minutes prior to taking niacin.
B. Administer aspirin 30 minutes after taking niacin.
C. Increase the dose of niacin SR to 1000 mg.
D. Continue the current dose of niacin.
E. Change the sustained-release niacin to immediate-release niacin.

Correct answer = A. Flushing associated with niacin is prostaglandin mediated; therefore, use of aspirin (a prostaglandin inhibitor) can help to minimize this adverse effect. It must be administered 30 minutes prior to the dose of the niacin; therefore, choice B is incorrect. Increasing the dose of niacin is likely to increase these complaints; therefore, choice C is incorrect. Continuing the current dose is unlikely to relieve these complaints, which are bothersome to AJ. The sustained-release formulation of niacin has less incidence of flushing versus that of the immediate release; therefore, choice E is incorrect.

23.9 CN is a 72-year-old male who is treated for hyperlipidemia with high-dose atorvastatin for the past 6 months. He also has a history of renal insufficiency. His most recent lipid panel shows an LDL cholesterol level of 131 mg/dL, triglycerides of 510 mg/dL, and HDL cholesterol of 32 mg/dL. His physician wishes to add an additional agent for his hyperlipidemia. Which of the following choices is the best option to address CN's dyslipidemia?

A. Fenofibrate.
B. Niacin.
C. Colesevelam.
D. Gemfibrozil.
E. Ezetimibe.

Correct answer = B. This patient has significantly elevated triglycerides and low HDL. Niacin can lower triglycerides by 35% to 50% and also raise HDL levels. The fibrates (fenofibrate and gemfibrozil) should not be used due to CN's history of renal insufficiency. Use of colesevelam is contraindicated because triglycerides are greater than 400 mg/dL. Ezetimibe can further lower LDL cholesterol but has modest effects on triglycerides versus niacin.

23.10 Which of the following patient populations is more likely to experience myalgia (muscle pain) or myopathy with use of HMG CoA reductase inhibitors?

A. Patients with diabetes mellitus.
B. Patients with renal insufficiency.
C. Patients with gout.
D. Patients with hypertriglyceridemia.
E. Patients taking warfarin (blood thinner).

Correct answer = B. Patients with a history of renal insufficiency have a higher incidence of developing myalgias, myopathy, and rhabdomyolysis with use of HMG CoA reductase inhibitors (statins), especially with those that are renally eliminated as drug accumulation can occur. The other populations have not been reported to have a higher incidence of this adverse effect with HMG CoA reductase inhibitors.