

test questions PharmaCE™

To qualify for continuing education credit for this PharmaCE program, you must first enroll. An application form appears on page 586 of this issue. You may also register online at www.pharmace.com. Once enrolled, complete one or more of the tests below related to the articles in this issue. Mark clearly on the answer sheet the name of the article and the ACPE Universal Program number of the completed test. Send the completed answer sheet to the address below, or to expedite the grading process submit your answers online at www.pharmace.com.

Participants who successfully complete tests will receive credit hours and corresponding CEUs as designated above each test. A statement of credit will then be issued. Tests are valid for credit up to 3 years after the program is published.

Kim Whitney, PharmaCE Manager,
April Salyers, PharmaCE Assistant Manager,
PO Box 42696, Cincinnati, Ohio 45242-0696



PharmaCE is approved by the Accreditation Council for Pharmacy Education as a provider of continuing pharmaceutical education.

Educational Consultants

David A Riley EdD, Chairman, PharmaCE Panel, School of Pharmacy, West Virginia University, Morgantown, WV; Michael C Shannon PhD, Vice-Chairman, PharmaCE Panel, Nicholasville, KY; Ginger G Scott PhD, School of Pharmacy, West Virginia University, Morgantown, WV; Robert B Supernaw PharmD, School of Pharmacy, Wingate University, Wingate, NC.

ACPE Universal Program Number
407-000-05-007-H01
1.0 credit hour (0.1 CEU) Expires: 3/31/08

See page 460.

VALSARTAN IN HEART FAILURE

Goal

To review the pharmacology, pharmacokinetics, and clinical trial evidence for use of valsartan in heart failure and compare its efficacy and safety relative to other ARBs in heart failure.

Objectives

After reviewing this article, the reader should be able to:

1. state the pharmacology and pharmacokinetics of valsartan;
2. compare and contrast use of valsartan in heart failure with other ARBs in heart failure;
3. summarize the appropriate use of valsartan in heart failure.

Test Questions

1. Which of the following statements about chronic heart failure is true?

- (a) Cardiovascular interventions have reduced the predicted prevalence of heart failure cases.
- (b) Approximately 10 million patients are expected to have heart failure by 2037.
- (c) Cost of heart failure is likely to be reduced with the incorporation of implantable cardiac defibrillators and biventricular pacemakers.
- (d) Attenuation of the RAAS with ACE effectively reduces angiotensin II levels.

- (e) Blockade of the angiotensin receptor subtype 2 leads to bradykinin accumulation.

2. Stimulation of angiotensin receptor subtype 1 causes all of the following except:

- (a) vasoconstriction.
- (b) aldosterone release.
- (c) nitric oxide accumulation.
- (d) vascular hypertrophy.
- (e) norepinephrine release.

3. Blockade of angiotensin receptor subtype 1 causes unopposed stimulation of angiotensin receptor subtype 2, leading to all of the following effects except:

- (a) bradykinin synthesis.
- (b) nitric oxide accumulation.
- (c) vascular fibrosis.
- (d) cardiac hypertrophy.
- (e) vasoconstriction.

4. Which of the following statements about the pharmacologic/pharmacokinetic characteristics of valsartan is true?

- (a) Valsartan's elimination half-life is approximately 6 hours.
- (b) Valsartan is eliminated via urinary secretion.
- (c) Valsartan completely inhibits the binding of valsartan to the angiotensin II receptor subtype 2.
- (d) Valsartan accumulates in patients with heart failure.
- (e) Valsartan mildly inhibits CYP2C9.

5. A 63-year-old African American male is diagnosed with NYHA class III systolic heart failure, hypertension, diabetes, and osteoarthritis. His med-

ications include metoprolol extended-release 100 mg/day, amlodipine 10 mg/day, glipizide 10 mg twice daily, and acetaminophen 500 mg as needed for osteoarthritis pain. He did not tolerate lisinopril because of a severe cough. His blood pressure is 142/90 mm Hg, heart rate is 76 beats/min, sodium 136 mEq/L, potassium 4.2 mEq/L, serum creatinine 1.9 mg/dL, and blood urea nitrogen 22 mg/dL. Which of the following statements is the most correct about the use of valsartan in this patient?

- (a) Valsartan should be safe despite the renal dysfunction.
- (b) Valsartan will likely cause worsening renal function.
- (c) Valsartan will likely cause hypotension.
- (d) Valsartan has not been evaluated in patients with renal insufficiency and thus should be avoided.
- (e) Valsartan should be administered with food to maximize efficacy and minimize risk.

6. A 70-year-old white female is diagnosed with NYHA class II heart failure, coronary artery disease (status-post MI 3 y ago), hypertension, dyslipidemia, and hypothyroidism. She is currently treated with lisinopril 20 mg/day, carvedilol 12.5 mg twice daily, furosemide 40 mg twice daily, atorvastatin 10 mg/day, and levodopa 0.1 mg/day. Her blood pressure and heart rate are 138/90 mm Hg and 84 beats/min, respectively. Which of the following is the best treatment approach for this patient?

- (a) Initiate valsartan 40 mg twice daily.
- (b) Initiate diltiazem CD 120 mg/day.
- (c) Increase the dose of carvedilol to 25 mg twice daily.
- (d) Do not adjust any medications in this regimen.
- (e) Increase furosemide to 80 mg twice daily.

Questions 7–9 are based on the following case:

A 76-year-old African American male is diagnosed with NYHA class III, stage C heart failure, diabetes, dyslipidemia, hypertension, obesity, chronic renal insufficiency, and peripheral neuropathy. His drugs include metoprolol extended-release 100 mg/day, digoxin 0.125 mg/day, spironolactone 25 mg/day, furosemide 80 mg/day, metolazone 5 mg/day as needed, and gabapentin 300 mg twice daily. He is in acute discomfort, with pulmonary rales and an irregular heart beat. His electrocardiogram reveals new ST segment elevation. His blood pressure is 150/88 mm Hg and heart rate is 62 beats/min. He is admitted and diagnosed with an ST-segment elevation MI.

7. The physician wants to start a drug to attenuate the RAAS, but is concerned about the patient's chronic renal insufficiency (serum creatinine in the hospital 2.2 mg/dL; 4 wk prior to hospitalization, serum creatinine was 2.1 mg/dL). Which of the following is an accurate recommendation?

- (a) ACE inhibitors are less likely to cause worsening renal insufficiency.
- (b) ARBs are less likely to cause worsening renal insufficiency.
- (c) ACE inhibitors and ARBs should be avoided in patients with renal insufficiency.
- (d) Candesartan is the ARB that is least likely to cause worsening renal insufficiency based on CHARM-Added data.
- (e) Both ACE inhibitors and ARBs can cause worsening renal insufficiency, and treatment should be monitored closely.

8. Which of the following would be the best initial choice for attenuation of the RAAS for this patient?

- (a) Initiate telmisartan 20 mg/day.
- (b) Initiate captopril 6.25 mg 3 times daily plus valsartan 20 mg twice daily.
- (c) Initiate valsartan 20 mg twice daily.
- (d) Initiate candesartan 4 mg/day.
- (e) Initiate losartan 25 mg/day.

9. The physician incorporates your recommendation. The following drugs are also added to the patient's regimen while he is in the hospital: atorvastatin 40 mg/day, aspirin 160 mg/day, and potassium chloride 60 mEq twice daily. The furosemide dose is increased to 60 mg twice daily. Which of the following concerns should be addressed first?

- (a) A trial of an ACE inhibitor should be attempted prior to using an ARB.
- (b) Potassium supplementation may cause hyperkalemia.
- (c) Aspirin will counter the effects of the ARB and/or ACE inhibitor.
- (d) The patient is at high risk for experiencing hypotension and should be monitored closely.
- (e) ARBs have not been shown to be effective in African American patients with heart failure.

10. A 59-year-old white female is diagnosed with hypertrophic cardiomyopathy. Her EF is 55%. Which of the following represents an evidence-based justification for therapy?

- (a) Candesartan is the best choice.
- (b) Valsartan is the best choice.
- (c) An ACE inhibitor is the best choice.
- (d) Neither an ACE inhibitor nor an ARB has been shown to be effective in diastolic dysfunction.
- (e) Either an ACE inhibitor or an ARB would be an appropriate selection in diastolic dysfunction.

11. A physician asks you why valsartan is approved as an alternative to ACE inhibitors for ACE inhibitor-intolerant patients when the Val-HeFT trial showed that the combination of ACE inhibitors and valsartan improved the combination of morbidity and mortality. Which of the following is the most accurate response?

- (a) A subanalysis of the Val-HeFT data showed that the overall benefit was primarily due to the effect in the patients who were not taking an ACE inhibitor.
- (b) A subanalysis of the Val-HeFT data showed that there was increased mortality in patients taking the combination valsartan plus ACE inhibitor.
- (c) A subanalysis of the Val-HeFT data showed a trend toward improved outcomes in patients taking the combination, but it did not reach statistical significance.
- (d) The FDA would like to see confirmation of the effect of the combination in another clinical trial.
- (e) The FDA was being cautious—use of the combination is beneficial.

12. A 70-year-old African American male is diagnosed with NYHA class III heart failure, diabetes, hypertension, obesity, and emphysema. His drugs include enalapril 10 mg twice daily, valsartan 80 mg twice daily, carvedilol 25 mg twice daily, digoxin 0.25 mg/day, Lantus insulin 40 units at bedtime, and ipratropium bromide/albuterol 2 puffs every 6 hours. The physician is concerned about the use of an ACE inhibitor, an ARB, and a β -blocker. He recently was told that this combination was dangerous. Which of the following is a complete and accurate response to address this physician's concern?

- (a) A subgroup analysis of Val-HeFT showed that this triple therapy increased mortality.
- (b) The increased mortality observed in Val-HeFT was confirmed by the VALIANT, but not the CHARM data.
- (c) The increased mortality observed in Val-HeFT was confirmed by the CHARM, but not the VALIANT data.
- (d) The increased mortality observed in Val-HeFT was not confirmed by either the VALIANT or CHARM data.
- (e) There have been no trials suggesting that this combination is dangerous.

13. Which of following trials provides the best evidence of support for using the combination of an ACE inhibitor plus an ARB?

- (a) CHARM
- (b) Val-HeFT
- (c) VALIANT
- (d) ELITE
- (e) RESOLVD

14. In a patient who is intolerant of an ACE inhibitor due to renal dysfunction, what chance does that patient have of experiencing renal dysfunction while receiving an ARB?

- (a) 10%
- (b) 25%
- (c) 40%
- (d) 50%
- (e) 75%

15. The recommended starting dose of valsartan in a patient with heart failure and renal insufficiency is:

- (a) 20 mg twice daily.
- (b) 40 mg twice daily.
- (c) 60 mg twice daily.
- (d) 60 mg/day.
- (e) 80 mg/day.

<p>ACPE Universal Program Number 407-000-05-008-H01 1.0 credit hour (0.1 CEU) Expires: 3/31/08</p>

See page 470.

ANGIOTENSIN RECEPTOR BLOCKERS VERSUS ACE INHIBITORS

Goal

To review pertinent clinical trials evaluating ARBs in patients at high risk of cardiovascular events and compare this with the established efficacy of ACE inhibitors to provide clinicians with the evidence needed to make rational drug therapy decisions.

Objectives

After reviewing this article, the reader should be able to:

1. identify the pharmacologic differences between ACE inhibitors and ARBs;
2. understand how pharmacologic differences influence clinical outcomes (ie, tolerability, efficacy);
3. analyze pertinent clinical trials evaluating ACE inhibitors or ARBs in high-risk populations;
4. identify which agents prolong survival and prevent MI;
5. make evidence-based recommendations regarding drugs that block the RAS when these drugs are indicated.

Test Questions

1. One reason that clinicians might view ACE inhibitors and ARBs as interchangeable is because:

- (a) they have a similar adverse effect profile.
- (b) they were introduced to the marketplace simultaneously.
- (c) both classes have been shown to prevent MI.
- (d) both drugs inhibit the RAS.
- (e) their mechanism of action is the same.

2. Which of the following identifies an important pharmacologic difference between ACE inhibitors and ARBs?

- (a) ARBs exhibit complete blockade of the RAS because they block all angiotensin II receptor subtypes.
- (b) ACE inhibitors increase levels of bradykinin.
- (c) ARBs decrease levels of bradykinin.
- (d) The effectiveness of ARBs is limited because "non-ACE" pathways also produce angiotensin II.
- (e) ACE inhibitors promote unopposed activation of angiotensin II receptor AT₂.

3. Which of the following is *not* true regarding the effects of bradykinin?
- It is responsible for cross-reactivity with ARBs in patients who develop ACE inhibitor-induced angioedema.
 - It is thought to be responsible for cough associated with ACE inhibitors.
 - It is thought to contribute to the beneficial effects of ACE inhibitor therapy.
 - It may limit the size of MI due to ischemic preconditioning.
 - It is elevated in patients with heart failure and cardiac ischemia, and who are post-MI.
4. Studies of ventricular function in patients with heart failure who are post-MI suggest that:
- treatment with either losartan or captopril is expected to result in similar effects on ventricular function.
 - treatment with captopril is expected to result in greater benefit with respect to ventricular function.
 - treatment with losartan is expected to result in greater benefit with respect to ventricular function.
 - neither losartan nor captopril exert beneficial effects on ventricular function.
 - ventricular function has not been studied in these populations.
5. The ELITE II study compared losartan 50 mg/day with captopril 150 mg/day in patients with heart failure and concluded that:
- losartan is an equally effective alternative to captopril in patients with heart failure.
 - losartan and captopril are equally tolerated at these doses.
 - captopril was superior for preventing mortality.
 - MI was more likely to occur in patients receiving captopril.
 - there was a nonsignificant trend toward fewer episodes of sudden cardiac death or resuscitated cardiac arrest in patients treated with captopril.
6. The addition of valsartan to standard background therapy for heart failure in Val-HeFT appeared to benefit which group of patients the most?
- those with the lowest ejection fraction
 - those not receiving aspirin
 - those not receiving an ACE inhibitor
 - those receiving an ACE inhibitor, but not a β -blocker
 - those receiving both an ACE inhibitor and a β -blocker
7. A 65-year-old patient with newly diagnosed ischemic cardiomyopathy, hypertension, and angina reports that he cannot take ACE inhibitors. What is the most common cause for ACE inhibitor intolerance?
- hyperkalemia
 - cough
 - angioedema
 - increase in serum creatinine
 - rash
8. The same patient is started on candesartan and titrated to 64 mg. Based on studies in patients with heart failure, which of the following is a reasonable expectation?
- The expectations are similar to those in patients receiving ACE inhibitors.
 - The patient will be less likely to die from cardiovascular causes.
 - The likelihood of experiencing an MI will be reduced.
 - The patient will be hospitalized for heart failure less frequently.
 - The patient is unlikely to tolerate candesartan.
9. If the patient's intolerance to ACE inhibitors was due to angioedema, which of the following statements is true based on CHARM-Alternative?
- Candesartan could not be used since angioedema is likely to recur.
 - A second ACE inhibitor should be tried before abandoning the class.
 - The patient should be rechallenged with the same ACE inhibitor that provoked angioedema initially to document the reaction.
 - Candesartan should be used in combination with an ACE inhibitor for added afterload reduction.
 - Candesartan can be used cautiously.
10. Which of the following is *not* an important question that was raised by the ELITE and OPTIMAAL trials?
- Was the dose of losartan insufficient relative to the dose of captopril?
 - Can the results with losartan be generalized to other ARBs?
 - Would a higher dose of losartan sacrifice the improved tolerability?
 - Why was the combination of losartan, captopril, and a β -blocker harmful?
 - Why were the results of ELITE and ELITE II so different?
11. A 68-year-old woman recently experienced an anterior wall MI. An echocardiogram showed that the patient's ejection fraction is 30%. She was subsequently started on valsartan. Which of the following adverse effects is most likely to occur?
- hypotension
 - cough
 - angioedema
 - taste disturbance
 - rash
12. Based on results from the VALIANT trial, which of the following conclusions can be made?
- Valsartan was better tolerated than captopril.
 - Captopril was better tolerated than valsartan.
 - Valsartan is just as likely to cause cough as captopril when the highest dose of valsartan is considered.
 - Treatment with either valsartan or captopril resulted in similar outcomes.
 - Treatment with valsartan should be considered superior to captopril.
13. With regard to the LIFE trial, losartan was shown to:
- decrease the incidence of cardiovascular death without affecting overall mortality.
 - be less effective for preventing MI.
 - decrease the risk of stroke.
 - be equally effective compared with atenolol.
 - cause more adverse effects than atenolol.
14. A 48-year-old woman with a medical history significant for hypertension, type 2 diabetes, proteinuria, and obesity requires additional antihypertensive medication to control her blood pressure. She is currently receiving only hydrochlorothiazide. She has no known allergies. Which of the following statements is the best reason to initiate a drug that blocks the RAS?
- ACE inhibitors have been shown to decrease the risk of death and MI.
 - ARBs have been shown to decrease the risk of death and MI.
 - ARBs slow the progression to end-stage renal disease.
 - ACE inhibitors slow the progression to end-stage renal disease.
 - ARBs improve insulin sensitivity.
15. In IDNT and RENAAL, the most frequent clinical event was:
- end-stage renal disease.
 - cardiovascular disease.
 - amputation.
 - death.
 - worsening renal function.

ACEP Universal Program Number 407-000-05-009-H01 1.0 credit hour (0.1 CEU) Expires: 3/31/08

See page 481.

LMWHs IN ST-ELEVATION MI

Goal

To review available literature on the efficacy and safety of LMWH in the treatment of STEMI in patients treated with fibrinolytic therapy or conservative medical management.

Objectives

After reviewing this article, the reader should be able to:

- explain the rationale for the administration of an antithrombotic agent during STEMI;
- state the benefit of LMWH in patients receiving nonspecific fibrinolytic therapy;
- compare the effect of LMWH and UFH in patients receiving fibrin-specific fibrinolytic therapy;

4. list potential advantages and risks of using LMWH in the treatment of STEMI.

Test Questions

1. STEMI is different from other acute coronary syndromes because:

- (a) patients experience chest pain.
- (b) the coronary artery is completely occluded.
- (c) thrombin plays a key role.
- (d) platelets make up the majority of the thrombus.
- (e) fibrin plays only a minor role.

2. Which of the following statements about the usefulness of UFH in STEMI is true?

- (a) Its role is controversial in medically managed patients.
- (b) It has shown definitive benefit in combination with streptokinase.
- (c) It has been studied extensively in combination with aspirin.
- (d) It should be used subcutaneously in combination with fibrin-specific fibrinolytics.
- (e) The AHA/ACC guidelines recommend a 7-day course of heparin therapy.

3. According to the AHA/ACC guidelines, which patients could receive LMWH as an alternative to UFH?

- (a) those with heparin-induced thrombocytopenia
- (b) those >75 years of age
- (c) those <75 years of age without renal dysfunction
- (d) those receiving medical management
- (e) those with contraindications to heparin therapy

4. LMWHs have been studied in combination with streptokinase. How were the dalteparin studies different from the enoxaparin studies?

- (a) They were all placebo-controlled.
- (b) They used only subcutaneous dosing.
- (c) One showed significantly more bleeding.
- (d) They did not show decreased reinfarction or increased reperfusion.
- (e) All of the above are true.

5. Which of the following statements about the use of UFH in the studies presented is true?

- (a) All used weight-based dosing.
- (b) PTTs were not reported or were less than the therapeutic range 50% of the time.
- (c) It always increased risk of major bleeding.
- (d) Subcutaneous dosing was the most common.
- (e) It was the control in every study.

6. After evaluating the trials of enoxaparin in combination with streptokinase, which of the following conclusions is appropriate?

- (a) Enoxaparin should be given as an intravenous bolus, then 40 mg subcutaneously every 8 hours.
- (b) UFH was optimally dosed.
- (c) Enoxaparin does not increase the risk of major hemorrhage.

- (d) Enoxaparin should replace heparin in combination with streptokinase.
- (e) All of the above are true.

7. In the ASSENT PLUS study, dalteparin and UFH were compared in patients receiving fibrin-specific fibrinolytic therapy. Which of the following statements about that study is true?

- (a) Dalteparin is not more efficacious than UFH.
- (b) Weight-based heparin dosing was used.
- (c) Dalteparin was initiated as an intravenous dose.
- (d) Bleeding was greater with UFH.
- (e) None of the above is true.

8. Several studies compared UFH with enoxaparin in combination with fibrin-specific fibrinolytic therapy. The results of these studies suggest that:

- (a) enoxaparin is inferior to UFH.
- (b) the addition of abciximab to UFH significantly improves outcomes.
- (c) antithrombotic therapy should be continued for at least 7 days.
- (d) there is no difference in bleeding with enoxaparin.
- (e) All of the above are true.

9. A 65-year-old male is being treated by emergency medical services for chest pain in a rural area. An electrocardiogram is sent to the nearest medical center (a 45-min drive away) and the emergency department physician diagnoses a STEMI. He orders tenecteplase to be initiated in the ambulance. What do you recommend for antithrombotic therapy for this patient?

- (a) Start enoxaparin the next morning.
- (b) Start UFH with a 60-unit/kg bolus followed by an infusion.
- (c) Start a glycoprotein IIb/IIIa receptor antagonist.
- (d) No antithrombotic is needed until the patient reaches the hospital.
- (e) Give intravenous enoxaparin 30 mg immediately.

10. According to the ASSENT-3 trial, what conclusion regarding abciximab in combination with half-dose tenecteplase and UFH is accurate?

- (a) Abciximab decreases bleeding compared with enoxaparin.
- (b) UFH alone should clearly remain the standard of practice.
- (c) Abciximab decreases reinfarction rate compared with enoxaparin.
- (d) It results in greater bleeding than UFH and does not improve outcomes more than enoxaparin.
- (e) Abciximab should be used in combination with half-dose tenecteplase in patients planned for percutaneous coronary intervention.

11. What do the 2 meta-analyses of the LMWH with fibrinolytic studies have in common?

- (a) They reported the same risk of bleeding.
- (b) They reported a decrease in mortality with enoxaparin.
- (c) They did not include any studies with abciximab.

- (d) They reported increased bleeding with enoxaparin.
- (e) They looked only at studies of enoxaparin.

12. A 70-year-old male is diagnosed with STEMI and is being treated with tenecteplase. His creatinine clearance is 70 mL/min and he weighs 90 kg. You are consulted to dose enoxaparin in this man. Which of the following doses is most supported by the literature?

- (a) 30-mg intravenous bolus followed by 90 mg subcutaneously every 12 hours
- (b) 40-mg intravenous bolus followed by 40 mg subcutaneously every 8 hours
- (c) 1 mg/kg subcutaneously every 12 hours
- (d) 40 mg subcutaneously daily
- (e) Enoxaparin is contraindicated because of this man's age.

13. The benefit of enoxaparin added to fibrin-specific fibrinolytic therapy is most likely due to a reduction in:

- (a) bleeding.
- (b) renal dysfunction.
- (c) mortality.
- (d) reinfarction.
- (e) cardiogenic shock.

14. In patients who cannot receive fibrinolytic therapy, LMWH use results in:

- (a) decreased length of hospital stay.
- (b) reduction in reinfarction rates.
- (c) decreased mortality.
- (d) no increased risk of bleeding.
- (e) None of the above is true.

15. In the treatment of STEMI, enoxaparin offers the greatest evidence of benefit in:

- (a) combination with fibrin-specific fibrinolytic agents.
- (b) combination with nonspecific fibrinolytic agents.
- (c) combination with abciximab.
- (d) medical management.
- (e) patients with renal dysfunction.

ACPE Universal Program Number
407-000-05-010-H01
1.0 credit hour (0.1 CEU) Expires: 3/31/08

See page 492.

HYPERGLYCEMIA IN THE HOSPITAL

Goal

To review studies on the role of hyperglycemia in adult non-diabetic inpatients and the outcomes associated with strict glucose control allowing pharmacists to participate in glucose management efforts, regardless of diabetes diagnosis, in acutely ill patients with hyperglycemia.

Objectives

After reviewing this article, the reader should be able to:

1. identify diseases in which hyperglycemia has a negative impact on patient outcomes;

2. identify potential difficulties in comparing study results in the literature;
3. from a list of statements regarding current literature, distinguish which are true and which are false;
4. identify specific health outcomes that have been associated with hyperglycemia in non-diabetic patients;
5. given a case study of a hyperglycemic patient, select appropriate therapy actions from a list of options.

Test Questions

1. **A 50-year-old female patient is admitted to the critical care unit following head trauma. Her admission serum glucose level is 198 mg/dL, but she has no history of diabetes. Based on the literature, which of the following actions is most appropriate?**
 - (a) Monitor glucose levels during the hospital stay and initiate insulin therapy only if glucose reaches ≥ 250 mg/dL.
 - (b) Monitor glucose levels during the hospital stay, but do not provide insulin therapy since she is not diabetic.
 - (c) Monitor glucose levels during the hospital stay and initiate insulin therapy to lower the glucose level.
 - (d) Monitor glucose levels during the hospital stay, but do not provide insulin therapy unless the patient is diagnosed with diabetes during hospitalization.
 - (e) Monitor glucose levels in the critical care unit only; once the patient is transferred to the floor, discontinue glucose monitoring.
2. **A 75-year-old female is admitted to the medical ward with pneumonia. She has no known history of diabetes. On admission, her blood glucose level is 220 mg/dL. Which of the following statements is false?**
 - (a) She has an increased chance of hospital mortality compared with a known diabetic.
 - (b) She has an increased chance of ICU transfer compared with a known diabetic.
 - (c) She is more likely to be transferred to another facility at discharge compared with a known diabetic.
 - (d) She will likely have a decreased length of hospital stay compared with a known diabetic.
 - (e) She will likely not be treated for her hyperglycemia compared with a known diabetic.
3. **A 48-year-old male is admitted to the hospital with an acute neurologic event. His admission glucose level is 170 mg/dL. Compared with normoglycemic patients, studies have shown all of the following to be true except:**
 - (a) he is likely to have worse neurologic deficits in the first 24 hours after admission.
 - (b) he is likely to benefit more from alteplase.
 - (c) he is likely to demonstrate less neurologic improvement in 3 months.
 - (d) he has a greater risk of intracranial hemorrhage.
 - (e) he is likely to have increased length of stay and hospital charges.
4. **Which of the following statements is false? According to a study by Umpierrez et al.¹⁸ on hyperglycemic patients on a general medicine floor:**
 - (a) diabetic patients had a higher hospital mortality rate than non-diabetic hyperglycemic patients.
 - (b) diabetic patients were more likely to receive insulin therapy than non-diabetic hyperglycemic patients.
 - (c) non-diabetic hyperglycemic patients were more likely than diabetic patients to be admitted to critical care.
 - (d) 12% of patients had no previous history of diabetes, but were hyperglycemic at admission.
 - (e) hyperglycemia was defined as having an admission or in-hospital fasting glucose level >126 mg/dL or 2 random glucose levels >200 mg/dL.
5. **Which of the following statements regarding MI and hyperglycemia is true?**
 - (a) The percentage of persons with glucose dysregulation varies widely.
 - (b) Cardiac outcomes (eg, infarct segment lengths, wall motion scores, ejection fraction) are similar for both hyperglycemic and normoglycemic patients.
 - (c) When compared with the mortality rate of normoglycemic patients, mortality among hyperglycemic patients is significantly higher up to one year after admission.
 - (d) Both a and c are true.
 - (e) All of the above are correct.
6. **According to a study by van den Berghe et al.,⁵¹ critically ill patients who remained in the ICU for at least 5 days and received continuous insulin infusion to maintain tight glucose control demonstrated all of the following except:**
 - (a) increased bloodstream infections.
 - (b) decreased ICU mortality.
 - (c) decreased duration of ventilatory support.
 - (d) increased hospital survival.
 - (e) decreased ICU length of stay.
7. **Evidence in the literature suggests that the optimal glucose range in which to maintain ICU patients is:**
 - (a) 60–90 mg/dL.
 - (b) 80–110 mg/dL.
 - (c) 90–210 mg/dL.
 - (d) 100–300 mg/dL.
 - (e) 150–275 mg/dL.
8. **Negative outcomes of hyperglycemia have been demonstrated in which of the following in-patient populations?**
 - (a) diabetic
 - (b) trauma
 - (c) stroke
 - (d) cardiac
 - (e) All of the above are correct.
9. **Outcomes studied in recent research on hyperglycemia in hospitalized patients have included risk of:**
 - (a) intracranial hemorrhage following anti-thrombolytic therapy.
 - (b) mortality after acute MI.
 - (c) surgical site infections in patients undergoing CABG.
 - (d) Both b and c are correct.
 - (e) All of the above are correct.
10. **Which of the following statements regarding the need for assessing glucose levels in hospitalized patients is true?**
 - (a) Diabetes is often undetected and undiagnosed.
 - (b) Glucose levels tend to increase when patients are under stress.
 - (c) Patients with hyperglycemia have higher healthcare costs compared with those who do not.
 - (d) Only a and b are correct.
 - (e) All of the answers are correct.
11. **Which of the following statements regarding hyperglycemia research in the hospital setting is false?**
 - (a) Methods of glucose control vary across hospitals.
 - (b) Hyperglycemia traditionally goes untreated in non-diabetic patients.
 - (c) Most studies in the hospital setting have examined the impact of admission glucose levels on outcomes.
 - (d) Glucose control has been demonstrated to benefit outcomes only in known diabetics.
 - (e) Improved outcomes have been demonstrated with glucose control in randomized controlled trials.
12. **Which of the following statements regarding current literature on hyperglycemia in non-diabetic patients is false?**
 - (a) Hyperglycemia in patients with coronary illness is detrimental only among females.
 - (b) The definition of hyperglycemia differs across studies.
 - (c) The majority of studies have used observational cohort designs.
 - (d) Outcomes of interest differ across studies.
 - (e) Non-diabetics are less likely than diabetics to receive treatment for hyperglycemia.

ACPE Universal Program Number
407-000-05-011-H01
1.0 credit hour (0.1 CEU) Expires: 3/31/08

See page 502.

INSULIN DETEMIR

Goal

To present the rationale for basal insulin therapy, pharmacology and pharmacokinetics, comparative clinical trials, adverse drug reactions, and dosing of insulin detemir.

Objectives

After reviewing this article, the reader should be able to:

1. evaluate the efficacy and pharmacokinetics of insulin detemir compared with NPH and insulin glargine by utilizing the data from clinical trials;
2. given a case of a patient with type 1 or type 2 diabetes mellitus, choose appropriate dosing of insulin detemir;
3. given a case of a patient with type 1 or type 2 diabetes, convert doses of NPH, glargine, or premixed insulin to those corresponding to insulin detemir;
4. identify serious and common adverse drug reactions of insulin detemir.

Test Questions

1. Which of the following statements regarding insulin detemir's pharmacology is true?

- (a) Insulin detemir differs from human insulin, with the amino acid glycine replacing asparagine at the A21 position.
- (b) Insulin detemir differs from human insulin, with 2 arginine amino acids added to the C-terminus of the B-chain.
- (c) Insulin detemir relies on dissolution of the crystals formed following subcutaneous injection.
- (d) Insulin detemir binds reversibly to albumin because of the removal of threonine from position B30 and the addition of the fatty acid component.
- (e) Insulin detemir needs to dissolve microprecipitates that are formed after subcutaneous injection.

2. Using the available data, which of the following statements regarding how age affects the pharmacokinetics of insulin detemir is true?

- (a) The pharmacokinetic effects do not appear to be affected by age differences in patients with type 1 diabetes.
- (b) The pharmacokinetic effects do not appear to be affected by age differences in patients with type 2 diabetes.
- (c) The pharmacokinetic effects are affected by age differences in patients with type 1 diabetes.
- (d) The pharmacokinetic effects are affected by age differences in patients with type 2 diabetes.
- (e) The pharmacokinetic effects are affected by age only in patients >70 years of age.

Questions 3–6 pertain to the following case:

A 57-year-old male patient weighing 100 kg is diagnosed with type 2 diabetes mellitus, hypertension, hypercholesterolemia, and atrial fibrillation. He suffered a myocardial infarction 4 years ago. His medications include metformin 1000 mg twice daily, glipizide 10 mg once daily, rosiglitazone 8 mg once daily, quinapril 20 mg once daily, atenolol 100 mg once daily, and warfarin 5 mg once daily. Basal insulin therapy is to be started.

3. According to dosing recommendations for insulin detemir, which of the following would be the most appropriate starting dose?

- (a) 2 units at bedtime
- (b) 20 units at bedtime
- (c) 40 units at bedtime
- (d) 60 units at bedtime
- (e) 80 units at bedtime

4. Following 2 weeks of therapy with insulin detemir, the patient's blood glucose levels are improved, but not within goal. Fasting blood glucose levels range from 140 to 180 mg/dL. What would be the most appropriate recommendation for the dose at this time?

- (a) Double the current dose and monitor fasting blood glucose levels.
- (b) Increase insulin detemir doses by 20 units each day and monitor fasting blood glucose levels.
- (c) Increase insulin detemir doses by 50% and monitor fasting blood glucose levels.
- (d) Increase insulin detemir by 2 units every 7 days until fasting blood glucose levels are within goal.
- (e) Change treatment to NPH insulin at bedtime and monitor fasting blood glucose levels.

5. Four weeks have gone by, and the patient's fasting and premeal blood glucose levels are still not at goal with insulin detemir. According to insulin detemir dosing guidelines, what would be the most appropriate recommendation?

- (a) Increase insulin detemir by 10 units.
- (b) Split the insulin detemir dose in half, giving one-half in the morning and one-half in the evening.
- (c) Split the insulin detemir dose in thirds, giving one-third at each meal.
- (d) Switch the administration time from bedtime to every morning.
- (e) Add NPH insulin at bedtime.

6. After 6 additional weeks of therapy with insulin detemir, the patient's fasting and premeal blood glucose levels are within goal. However, his postprandial levels are not. Which of the following would be the most appropriate recommendation?

- (a) Discontinue insulin detemir and initiate insulin glargine.
- (b) Discontinue insulin detemir and initiate premixed insulin NPH/regular 70/30.
- (c) Initiate insulin glargine with meals.
- (d) Initiate NPH insulin with meals.
- (e) Initiate aspart or lispro insulin with meals.

7. A 48-year-old man has a history of type 2 diabetes mellitus, hypertension, and hypercholesterolemia. His medications include metformin 1000 mg twice daily, glipizide 10 mg once daily, pioglitazone 45 mg once daily, lisinopril 10 mg once daily, hydrochlorothiazide 25 mg once daily, atorvastatin 20 mg once daily, and

aspirin 81 mg once daily. His HbA_{1c} is above goal at 9.2%. The physician would like to start basal insulin therapy. Which of the following would be the most appropriate insulin to initiate as basal therapy?

- (a) ultralente
- (b) regular
- (c) detemir
- (d) glargine
- (e) either detemir or glargine

8. A 67-year-old woman with type 2 diabetes mellitus is taking metformin, glipizide, pioglitazone, and insulin glargine 40 units at bedtime. Her clinician would like to switch treatment from insulin glargine to insulin detemir. According to the insulin detemir dosing guidelines, what would be the most appropriate starting dose?

- (a) 20 units at bedtime
- (b) 20 units in the morning and 40 units in the evening
- (c) 32 units at bedtime
- (d) 40 units at bedtime
- (e) 80 units at bedtime

9. A 44-year-old male with type 1 diabetes mellitus is taking NPH/regular 70/30 insulin 40 units in the morning and 20 units in the evening. His physician would like to switch treatment to insulin detemir. What would be the most appropriate initial dose for the basal portion of therapy?

- (a) 30 units in the evening and titrate the dose as needed
- (b) 40 units in the morning and 20 units in the evening
- (c) 48 units in the evening
- (d) 60 units in the morning
- (e) 60 units in the evening

10. A 22-year-old female with type 1 diabetes mellitus is taking NPH insulin 35 units in the morning and 15 units in the evening plus lispro insulin 6–14 units with meals. Her clinician would like to switch treatment from NPH insulin to insulin detemir. What would be the most appropriate starting dose?

- (a) 15 units at bedtime
- (b) 40 units at bedtime
- (c) 50 units at bedtime
- (d) 80 units at bedtime
- (e) 35 units in the morning and 15 units in the evening

11. A 67-year-old male with type 2 diabetes mellitus is taking metformin, glyburide, rosiglitazone, and 32 units of NPH insulin at bedtime. His clinician would like to switch treatment from NPH insulin to insulin detemir. What would be the most appropriate starting dose?

- (a) 16 units at bedtime
- (b) 26 units at bedtime
- (c) 32 units at bedtime
- (d) 16 units in the morning and in the evening
- (e) 64 units at bedtime

12. A 53-year-old female with type 2 diabetes is taking metformin, glyburide, and

pioglitazone, and NPH insulin 20 units in the morning and 10 units in the evening. Her clinician would like to switch treatment from NPH insulin to insulin detemir. What would be the *most* appropriate starting dose?

- (a) 24 units at bedtime
- (b) 20 units in the morning and 10 units in the evening
- (c) 30 units at bedtime
- (d) 30 units in the morning and 30 units in the evening
- (e) 60 units at bedtime

Questions 13 and 14 refer to the following case:

A patient with type 2 diabetes who is insulin-naïve is going to begin insulin detemir therapy. Information on adverse effects should be explained to the patient.

13. Which of the following was the *most* common serious adverse reaction in clinical trials of insulin detemir?

- (a) Stevens–Johnson syndrome
- (b) acute myocardial infarction
- (c) severe hypoglycemia
- (d) renal failure
- (e) hepatic failure

14. Which of the following are common adverse effects of insulin detemir?

- (a) diarrhea
- (b) edema
- (c) abdominal pain
- (d) headache, dizziness
- (e) weight gain

15. Based on findings from insulin detemir comparison with NPH insulin in clinical trials, which of the following statements regarding hypoglycemia is *true*?

- (a) In several studies, insulin detemir was associated with a lower risk for nocturnal or overall hypoglycemia than NPH insulin.
- (b) In several studies, insulin detemir was associated with a lower risk

for nocturnal or overall hypoglycemia than insulin glargine.

- (c) In several studies, insulin detemir was associated with a higher risk for nocturnal or overall hypoglycemia than NPH insulin.
- (d) In several studies, insulin detemir and NPH insulin showed similar rates of hypoglycemia.
- (e) In several studies, it was shown that insulin detemir has little to no risk of hypoglycemia.