Learning Objectives
After reading this article, the reader should be able to:

• Describe the role of treatment guidelines for treating hypertension.
• Identify the importance and long-term benefits of vascular protection.
• Discuss the various considerations when using angiotensin-converting enzyme inhibitors as first-line agents for the treatment of hypertension.
• Review the best available evidence-based treatment options used to provide vascular protection and to reduce the risk of future cardiovascular complications.

RATIONALE
Many therapies currently exist for hypertension. The concept of vascular protection has been recognized in recent years as an important factor for consideration in reducing global cardiovascular risk. The complex cellular mechanisms responsible for vascular injury help to explain how different risk factors contribute to the development of cardiovascular disease and how different treatment strategies can impact these risk factors.

Hypertension is one of the most common and most significant risk factors for cardiovascular disease. Physicians make drug therapy choices for their patients with hypertension on a daily basis. However, the goal of reducing global cardiovascular risk requires an evidence-based choice of an antihypertensive agent that provides vascular protection in addition to blood pressure reduction. The objective of this educational program is to provide the audience with an overview of the cardiovascular benefits of specific antihypertensive therapies that provide vascular protection in addition to simply lowering blood pressure.

Case 1
Treating Hypertension: Drug Selection to Improve Patient Outcomes

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Hypertension
Cardiovascular disease (CVD) is the number one killer of men and women in the United States. Nearly 2500 Americans die of CVD every day—approximately 1 death every 35 seconds. CVD claims more lives each year than the next 4 leading causes of
death combined. Multiple well-known risk factors, such as obesity, hypertension, diabetes, smoking, and dyslipidemia, contribute to the development of CVD. Hypertension, the most common form of CVD, is estimated to affect approximately 65 million people or nearly 1 in 3 American adults. Data from the Framingham Heart Study suggest that persons who are normotensive at age 55 have a 90% lifetime risk for developing hypertension. About 69% of people who have a first heart attack, 77% of people who have a first stroke, and 74% of people who have heart failure have blood pressure (BP) higher than 140/90 mm Hg. The presence of each additional risk factor for CVD compounds the risk from hypertension.

According to data from the Framingham Heart Study, the 10-year rate of developing coronary heart disease increases almost linearly with the addition of each cardiovascular (CV) risk factor (hypertension, dyslipidemia, diabetes, and smoking). The overall number of CV deaths have decreased. However, from 1993 to 2003, the age-adjusted death rate from high BP increased 29.3%, and the actual number of deaths rose 56.1%. Vascular Protection

In recent years, the renin-angiotensin-aldosterone system (RAAS) has emerged as a major factor in the pathogenesis of CVD. The complex interrelationship of tissue and/or circulating angiotensin-converting enzyme (ACE) and angiotensin II with various biologically active mediators contributes to the vascular disease process through multiple pathobiologic mechanisms.

The vascular endothelium is at the center of these complex mechanisms. The normal vascular endothelium maintains equilibrium between vasodilation and vasoconstriction, and between inhibition versus promotion of cell growth, thrombotic events, inflammatory processes, and oxidative damage. Endothelial damage or dysfunction may disturb this equilibrium, resulting in increased vasoconstriction, platelet and leukocyte adhesion, lipid deposition, increased macrophage activity, and increased invasion by and growth of vascular smooth muscle cells. In addition, it should be noted that there are also important endogenous mechanisms to protect against these atherogenic processes. These protective mechanisms, mediated by molecules such as bradykinin and nitric oxide (NO), include vasodilation, inhibition of smooth muscle cell proliferation, inhibition of platelet aggregation, fibrinolysis, and contraction of smooth muscle cells.

**Figure 1**

**Progression of Cardiovascular Disease—The Cardiovascular Continuum**

According to data from the Framingham Heart Study, the 10-year rate of developing coronary heart disease increases almost linearly with the addition of each cardiovascular (CV) risk factor (hypertension, dyslipidemia, diabetes, and smoking). The overall number of CV deaths have decreased. However, from 1993 to 2003, the age-adjusted death rate from high BP increased 29.3%, and the actual number of deaths rose 56.1%.

Vascular Protection

In recent years, the renin-angiotensin-aldosterone system (RAAS) has emerged as a major factor in the pathogenesis of CVD. The complex interrelationship of tissue and/or circulating angiotensin-converting enzyme (ACE) and angiotensin II with various biologically active mediators contributes to the vascular disease process through multiple pathobiologic mechanisms. The effects of biologically active mediators produced in the vessel wall are long-term, which may contribute to the progressive nature of vascular disease.

The vascular endothelium is at the center of these complex mechanisms. The normal vascular endothelium maintains equilibrium between vasodilation and vasoconstriction, and between inhibition versus promotion of cell growth, thrombotic events, inflammatory processes, and oxidative damage. Endothelial damage or dysfunction may disturb this equilibrium, resulting in increased vasoconstriction, platelet and leukocyte adhesion, lipid deposition, increased macrophage activity, and increased invasion by and growth of vascular smooth muscle cells. In addition, it should be noted that there are also important endogenous mechanisms to protect against these atherogenic processes. These protective mechanisms, mediated by molecules such as bradykinin and nitric oxide (NO), include vasodilation, inhibition of smooth muscle cell proliferation, inhibition of platelet aggregation, fibrinolysis, and contraction of smooth muscle cells.
Oxidative stress is a common mechanism by which CV risk factors initiate endothelial injury. Hypertension, for example, produces oxidative stress at the cellular level through the formation of reactive oxygen species that lead to endothelial injury (Figure 2). Endothelial injury triggers a cascade of events, including activation of the RAAS system, resulting in an increase in angiotensin II. This initiates a positive feedback mechanism involving increased angiotensin II production and decreased NO production and inactivation of bradykinin (endogenous protective mechanisms), causing further endothelial damage. Angiotensin II has pronounced atherogenic and proinflammatory properties and contributes to the processes leading to plaque rupture.

Because the RAAS is one of the key pathways activated by endothelial injury and plays an important role in the activation of the cascade that leads to further endothelial injury, therapies that inhibit the RAAS may play an important role in reducing vascular injury and decreasing the risk of CV events.

**DRUG THERAPY FOR HYPERTENSION: NAVIGATING THE CHOICES**

Physicians are faced with a myriad of drug therapy options for the treatment of hypertension. The ultimate goal of therapy is easy to understand: controlling hypertension to reduce morbidity and mortality from CVD. However, our growing understanding of the role of endothelial injury in the progression of CVD challenges us to select therapeutic strategies that provide vascular protection in addition to BP reduction.

Unfortunately, selection of an optimal drug therapy regimen to achieve this goal can be difficult. Results from large, international clinical trials comparing antihypertensive drugs are often difficult to translate into day-to-day clinical practice. Differences in patient populations, primary end points, drug dosing, or...
other methodology make comparison of trials difficult, if not impossible. Treatment guidelines from national organizations or professional societies attempt to summarize available evidence into a more user-friendly format to help guide clinical decision making. However, a basic understanding of the pathophysiology of hypertension is necessary to understand that treatment of hypertension involves much more than simply reducing BP. In other words, hypertension is part of a disease process of which elevated BP is merely 1 manifestation. Modern treatment of hypertension should focus on assessing patients’ global risk for CVD and choosing treatment regimens accordingly.

Reduction of elevated BP is a primary strategy to reduce CV morbidity and mortality. Control of hypertension is associated with significant reduction in CV events. The end points of the most recent trials for the treatment of hypertension primarily focus on reduction of clinical events as surrogates for end-organ damage. Injury from elevated BP starts at the level of the vasculature, with progression of atherosclerosis and end-organ injury. When selecting antihypertensive medications, the first principle should be to choose a medication or a combination of medications that will reduce the BP into the desired range. The second principle is to choose antihypertensive medications that, through their effects on concurrent risk factors, and possibly by acting directly on vascular mechanisms intrinsic to hypertension, provide benefits beyond BP lowering.

The following case discussion was developed as an example of an evidence-based approach to choosing antihypertensive therapy while assessing and addressing global CV risk.

Adoption of a healthy lifestyle is an essential part of the management of patients with hypertension.

**PATIENT CASE**

- 58-year-old white man
- Non–insulin-dependent diabetes for 10 years
- Nonsmoker
- Body mass index 36 kg/m²
- BP 160/102 mm Hg
- Heart rate 83 bpm
- Normal sinus rhythm on electrocardiogram
- Serum creatinine 1.1 mg/dL

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**FIGURE 3**

**JNC 7 Guidelines**

**Lifestyle modifications**

- Not at goal BP (<140/90 mm Hg or <130/80 mm Hg for diabetes or chronic renal disease)
- With compelling indications

**Stage 1 hypertension**

(Systolic BP 140-159 mm Hg or diastolic BP 90-99 mm Hg)

- Thiazide-type diuretics for most
- May consider ACEI, ARB, BB, CCB, or combination

**Stage 2 hypertension**

(Systolic BP ≥160 mm Hg)

- 2-drug combination for most (usually thiazide-type diuretic and ACEI, or ARB, or BB, or CCB)

- Not at goal BP

- Optimize dosages or add additional drugs until goal BP is achieved.

- Consider consultation with hypertension specialist.

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JNC 7 = Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; BP = blood pressure; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BB = β-blocker; CCB = calcium channel blocker.

• Microalbuminuria 200 mg/dL
• Fasting lipid profile: total cholesterol, 255 mg/dL; low-density lipoprotein, 178 mg/dL; high-density lipoprotein, 39 mg/dL; triglycerides, 190 mg/dL.
• Family history of coronary artery disease (CAD); his father died of heart attack at age 60.

How would you approach the treatment of hypertension in this patient?

**THE JNC 7 GUIDELINES**

Patients With Compelling Indications Versus Patients Without Compelling Indications

The well-known Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) algorithm for the treatment of hypertension is a useful, evidence-based tool for guiding initial drug therapy choices (Figure 3).

In addition to pharmacologic therapy, adoption of a healthy lifestyle is an essential part of the management of patients with hypertension. Weight loss, smoking cessation, dietary modifications, limiting alcohol intake, and increased aerobic exercise should be part of any treatment regimen. One important distinction in the drug therapy recommendation criteria is the identification of patients with compelling indications versus patients without compelling indications. The compelling indications are comorbid conditions where specific classes of antihypertensive drugs are recommended to decrease morbidity and mortality associated with the comorbid condition.

In patients without compelling indications, a thiazide diuretic is recommended as first-line therapy for most patients due to results from landmark trials. However, any class of agents may be considered as first-line therapy depending on the individual patient situation. ACE inhibitors, β-blockers, calcium channel blockers, and angiotensin receptor blockers (ARBs) should be considered as alternative antihypertensive drugs for patients with contraindications to treatment with thiazide diuretics. All 5 of these drug classes are considered primary antihypertensive agents, and all 5 classes have outcome data demonstrating reduced CV events.

JNC 7 also provides direction for patients with compelling indications. These compelling indications include chronic kidney disease, diabetes, history of stroke, coronary disease, history of myocardial infarction (MI), and heart failure. The antihypertensive drug therapy recommendation is based on the compelling indication present.

**The Need for Combination Therapy**

The JNC 7 guidelines recommend that combinations of antihypertensive drugs be used to initiate therapy in the large proportion of patients in whom single agents are unlikely to achieve needed BP targets (ie, those with BP >20 mm Hg above systolic goal or 10 mm Hg above diastolic goal). In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), which compared a thiazide diuretic versus a calcium channel blocker versus an ACE inhibitor, only 40% of patients had their BP controlled on 1 antihypertensive drug. Most patients will require combination therapy for the successful treatment of hypertension. Patients, like the one in the case, who present with stage 2 hypertension (systolic BP ≥160 mm Hg or diastolic BP ≥100 mm Hg), should be considered as candidates for combination therapy with 2 or more drugs. Reductions in BP with drugs in combination are additive and/or synergistic and increase efficacy, and may result in a more rapid achievement of BP goals. The JNC 7 guidelines recommend a BP goal of <140 mm Hg systolic and <90 mm Hg diastolic.
and <90 mm Hg diastolic. However, the JNC 7 guidelines and the American Diabetes Association (ADA) are consistent in recommending that patients with diabetes should be treated to a systolic BP of <130 mm Hg and a diastolic BP <80 mm Hg. JNC 7 also recommends a goal of <130/80 mm Hg for patients with chronic renal disease.

### Addressing Global CV Risk

Unfortunately, the majority of patients with hypertension have other CAD risk factors. A cluster of 2 or more risk factors occurs in more than half of hypertensive persons (Figure 4). A state-based US health survey found that the prevalence of adults with 2 or more risk factors increased from 23.6% in 1991 to 27.9% in 1999. Hypertension is an independent contributor to the risk of CV events, but its impact is greatly influenced by associated risk factors. This underscores a need for a comprehensive approach to the treatment of hypertension that addresses a patient’s overall risk for CVD, in addition to simply decreasing BP.

### Drug Therapy for Hypertension: Selection Considerations

As stated previously, there is no question that reduction of BP by all 5 major classes of antihypertensive agents reduces CV complications related to hypertension. However, certain classes of antihypertensive agents have emerged in providing CV risk reduction beyond what would be expected by their BP-lowering effects alone. The following sections explain how the ACE inhibitors studied in large clinical trials should be considered as first-line agents for the treatment of hypertension in patients with other CV risk factors to reduce the risk of CV events.

Treatment guidelines recommend that in patients who have concomitant conditions (compelling indications) for which a specific antihypertensive has proven beneficial, therapy should be directed at both the compelling indication and BP reduction (Figure 3). For example, the majority of patients with diabetes will require 2 or more drugs for BP control. According to the ADA, initial therapy for diabetic patients with a BP >140/90 mm Hg should be with a drug class shown to reduce CVD events in patients with diabetes. This includes ACE inhibitors, ARBs, β-blockers, diuretics, and calcium channel blockers. However, the guidelines also state that patients with diabetes and hypertension should be treated with a regimen that includes either an ACE inhibitor or an ARB. With that said, if no contraindications to ACE inhibitor therapy are present, it makes sense to choose an ACE inhibitor as initial therapy for hypertension in a patient with diabetes, such as the one presented in the case. If an additional agent is needed to achieve BP control (which is required in the majority of patients), a thiazide diuretic should be added. Diuretics have long been considered a first-line choice for the treatment of hypertension. They are generally well tolerated, have proved to decrease mortality, and are relatively inexpensive. However, in a patient with diabetes, there is concern with using an “unprotected” diuretic or a diuretic as a single agent. ACE inhibitors can prevent the countervailing effects of stimulation of the RAAS that is commonly produced by diuretics.

Given their documented benefits in conditions that can be direct sequelae of hypertension (heart failure, chronic renal disease, recurrent stroke, ischemic heart disease) and those that are commonly associated with hypertension (diabetes, high coronary heart disease risk), ACE inhibitors are considered appropriate first-line antihypertensives for patients with any of these compelling indications.

### CV Risk Reduction: Beyond Reducing BP

The choice of an ACE inhibitor for initial therapy of hypertension in patients at high risk for CV events is also supported by the results from one of the largest prospective, randomized, double-blind trials evaluating the impact of antihypertensive therapy on CV events. The Heart Outcomes Prevention Evaluation (HOPE) study enrolled 9297 high-risk patients 55 years of age or older who had evidence of vascular disease or diabetes plus 1 other CV risk factor and who were not known to have a low ejection fraction or heart failure. Patients were treated with the ACE inhibitor ramipril 10 mg

### Table

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ACEIs = angiotensin-converting enzyme inhibitors; LV = left ventricular.
Adapted from Reference 22.
once daily or placebo for a mean of 5 years. Treatment with ramipril significantly reduced the rates of death, MI, and stroke in a broad range of high-risk patients.

The mean initial BP in patients enrolled in the HOPE study was 139/79 mm Hg in both groups. The BP reduction observed with ramipril therapy was 3/2 mm Hg. Most experts believe that the degree of CV risk reduction achieved with ramipril was unlikely to be explained solely by the degree of BP reduction observed in the study. Analysis of predefined subgroups in the HOPE study showed that CV benefits were observed in patients both with and without hypertension at baseline. Further analysis of the relationship between the observed benefit and baseline BP and the degree of BP reduction in the HOPE study data indicated that the benefits of ACE inhibition with ramipril were independent of, and additive to, those from other proven hypertension therapies, including β-blockers, diuretics, or calcium channel blockers.

Despite the overwhelming reduction in CV events observed in the HOPE study, the relatively minimal reduction in BP by ramipril has resulted in questions surrounding its antihypertensive efficacy. One possible explanation is that the HOPE study protocol required ramipril dosing once daily at bedtime. Study visits for office BP measurements were performed during the day, usually 10 to 18 hours after the dose. This may have resulted in an underestimation of the 24-hour BP reduction. To address this question further, another HOPE substudy assessed the effect of ramipril on 24-hour BP patterns using ambulatory BP monitoring. Twenty-four-hour ambulatory BP was significantly reduced (10/4 mm Hg; \( P = .03 \)), mainly because of a more pronounced BP-lowering effect during the nighttime (17/8 mm Hg; \( P < .001 \)). The ambulatory BP monitoring showed a greater fall in BP than with office BP monitoring during treatment with ramipril given once daily at bedtime.

The Microalbuminuria, Cardiovascular, and Renal Outcomes Heart Outcomes Prevention Evaluation (MICRO-HOPE) substudy of the HOPE trial examined CV and microvascular outcomes in 3577 diabetic patients with a history of a previous CV event or at least 1 other CV risk factor. Compared with placebo, ramipril significantly lowered the risk of overt nephropathy in patients with diabetes who did and did not have baseline microalbuminuria by 24% \( (P = .027) \), MI by 22% \( (P = .01) \), stroke by 33% \( (P = .007) \), CV death by 37% \( (P = .0001) \), and total mortality by 24% \( (P = .004) \). The observed reduction in microalbuminuria in the trial may be representative of the favorable effect of ramipril on endothelial function.

Other ACE inhibitors have also been studied for vascular protective effects. The European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease (EUROPA) assessed the effects of the ACE inhibitor perindopril versus placebo on CV outcomes in a relatively low-risk population of 12,218 patients with stable CAD and without clinical evidence of heart failure. The majority of these patients were taking platelet inhibitors (92%), β-blockers (62%), and lipid-lowering agents (58%). Perindopril 8 mg once daily significantly reduced the primary end point (a composite of CV mortality, nonfatal MI, plus resuscitated cardiac arrest) by 19% \( (P = .0003) \); CV mortality plus MI by 19%; fatal plus nonfatal MI by 24%; and hospitalization for heart failure by 39%. Note that these benefits were observed across all subgroups regardless of comorbidities or other therapies for CAD. In the Perindopril Substudy in Coronary Artery Disease and Diabetes (PERSUADE) of

![Angiotensin II Plays a Central Role in Organ Damage](image-url)

**Figure 5**

Angiotensin II Plays a Central Role in Organ Damage

MI = myocardial infarction; LVH = left ventricular hypertrophy.

EUROPA, perindopril reduced CV events in 1502 patients with CAD and diabetes.26 Although not statistically significant in the diabetic population, the relative risk reduction in the primary outcome was similar to that observed in the main EUROPA population. The results of PERSUADE extend the benefit of ACE inhibitors shown in MICROHOPE to a lower-risk population with diabetes and CAD.26

**ACE Inhibitors: Mechanisms of Vascular Protection**

Endothelial dysfunction is the end of a cascade of processes in which CV risk factors contribute to inflammation and atherogenesis.6 ACE inhibitors improve endothelial function by blocking the formation of angiotensin II and preventing the degradation of bradykinin.27 ACE inhibitors may also act on other peptides of the RAAS, thereby potentially providing cardiac and vascular protection (see Table).22 ACE inhibitors may prevent damaging effects on endothelial function, vascular smooth muscle cells, and inflammatory vascular processes by inhibiting the formation of angiotensin II (Figure 5).6,28-39 An increase in the release of NO as a result of ACE inhibition may contribute to the CV protective effect of these agents.6

More than 90% of ACE is located in the tissues, rather than the plasma. The antiatherosclerotic effects of an ACE inhibitor may partially depend on its affinity for tissue ACE and partially on its lipophilicity, which determines how readily it can penetrate into atherosclerotic plaques.27 Perindopril, quinapril, and ramipril all have relatively high affin-
ity for tissue ACE and have been studied in trials for vascular protection.\textsuperscript{19,24-26,46}

**ACE Inhibitors Versus ARBs for Vascular Protection in High-risk Patients**

ARBs\textsuperscript{37,38} and ACE inhibitors\textsuperscript{19,24} have both been shown to delay the progression of nephropathy, but current evidence supports a better global CV risk reduction with ACE inhibitors.\textsuperscript{19,24} The results of these trials support the use of ACE inhibitors versus ARBs as first-line choices for a broader range of high-risk conditions. ACE inhibitors have also been shown to improve CV outcomes in high-risk patients with or without hypertension.\textsuperscript{19,24,25}

**Goals of therapy for hypertension need to focus on reducing overall CV risk.**

The Losartan Intervention For Endpoint reduction (LIFE) study, a randomized double-blind trial comparing the ARB losartan with atenolol, showed a similar decrease in BP with the 2 treatments. There was an adjusted relative risk reduction of 13\% in the primary composite end point (CV death, MI, and stroke) in the losartan group ($P = .021$); this was driven by a 25\% relative risk reduction in fatal and nonfatal stroke ($P = .001$), with no significant differences between losartan and atenolol in CV mortality or in fatal and nonfatal MI.\textsuperscript{41}

The Valsartan Antihypertensive Long-term Use Evaluation (VALUE) study tested the hypothesis that in hypertensive patients at high CV risk and with the same level of BP control, a valsartan-based regimen would reduce cardiovascular mortality and morbidity more than an amlodipine-based regimen. There was no difference between the 2 treatment groups on the primary outcome, a composite of CV mortality and morbidity, although BP was significantly lower with amlodipine at every time point.\textsuperscript{42}

**ANTIHYPERTENSIVE TREATMENT FOR THE CASE PRESENTATION**

The patient in our case presented with stage II hypertension. In addition to diet and lifestyle modifications, the JNC 7 guidelines\textsuperscript{1} would support initiating therapy with 2 antihypertensive drugs in combination for patients with stage II hypertension. The patient also has diabetes, a compelling indication that should be considered for drug selection. Based on the longstanding evidence of beneficial effects of ACE inhibitors in patients with hypertension and other CV risk factors such as diabetes (HOPE study), we selected the ACE inhibitor ramipril in combination with a thiazide diuretic for initial therapy. This has been demonstrated to be an effective combination for reducing BP. Our patient also matches the profile of a patient at high risk for a CV event who may benefit from the vascular protective effects associated with ACE inhibitor therapy beyond reduction of BP.

**CONCLUSION**

CV mortality related to high BP continues to increase. Goals of therapy for hypertension need to focus on reducing overall CV risk. Patients should be assessed and managed according to their global CV risk, not just their BP numbers. Evidence-based selection of antihypertensive agents is a critical consideration in developing a management strategy. Although concerns have been raised regarding only modest reduction in BP observed with ACE inhibitor therapy, it is likely that most patients will require combination therapy to achieve BP goals regardless of initial agent selection. A drug or a combination of drugs that has demonstrated effectiveness for the particular high-risk conditions (compelling indications) present in the individual patient should be selected. JNC 7 guidelines recommend the use of ACE inhibitors as an option for all 6 of the compelling indications (heart failure, post-MI, high coronary disease risk, diabetes, chronic kidney disease, and recurrent stroke prevention). Evidence from large clinical trials supports the use of the ACE inhibitors for CV protection beyond BP control.

**REFERENCES**


10. Jamerson KA, Bakris GL, Wun CC, et al. Rationale and design of the Avoiding Cardiovascular Events Through Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) trial: the first randomized controlled trial to compare the clinical outcome effects of first-line combination therapy.


**Professional classification:**

1. What is your professional classification?
   - [ ] MD  [ ] DO  [ ] PharmD  [ ] PA  [ ] NP
   - [ ] RN  [ ] Other ________________

2. What is your specialty?
   - [ ] Cardiology  [ ] Internal medicine
   - [ ] Family medicine  [ ] Other ________________

3. What best describes your practice setting?
   - [ ] private  [ ] group  [ ] hospital
   - [ ] rural community clinic  [ ] urban community clinic
   - [ ] Other ________________

**Educational value:**

1. Did the newsletter meet each of the following objectives?
   a. Describe the role of treatment guidelines for treating hypertension.
      - [ ] Yes  [ ] No  [ ]
   b. Identify the importance and long-term benefits of vascular protection.
      - [ ] Yes  [ ] No  [ ]
   c. Discuss the various considerations when using angiotensin-converting enzyme inhibitors as first-line agents for the treatment of hypertension.
      - [ ] Yes  [ ] No  [ ]
   d. Review the best available evidence-based treatment options used to provide vascular protection and to reduce the risk of future cardiovascular complications.
      - [ ] Yes  [ ] No  [ ]

2. The content level was:
   - [ ] Too easy  [ ] About right  [ ] Too difficult

3. After reading this newsletter, do you feel more confident about
   a. Evaluating risk in a patient with cardiovascular disease?
      - [ ] Yes  [ ] No  [ ]
   b. Making decisions about treatment of cardiovascular disease?
      - [ ] Yes  [ ] No  [ ]

4. What is the most important thing you learned from this newsletter?

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1. Do you plan to read future issues of this newsletter?
   - [ ] Yes  [ ] No  [ ]

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   - [ ] Yes  [ ] No  [ ]

3. Would you be willing to participate in follow-up research to evaluate the long-term impact of the newsletter on your practice? (CME credit will be provided for participating in the follow-up survey.)
   - [ ] Yes  [ ] No  [ ]

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   - [ ] E-mail  [ ] Phone  [ ] Web site  [ ] Fax

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   - [ ] Print newsletter or journal article  [ ] Internet
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What change(s) (if any) do you plan to make in your practice as a result of reading this newsletter?_________________________

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**Cases in Vascular Protection: Reducing Risk Factors: MEN08014-01**

Release Date: June 2007  Expiration Date: June 30, 2008
No Charge for This CME
JUNE 2007

Posttest Questions

1. What is the most common form of cardiovascular disease (CVD)?
   a. diabetes mellitus
   b. hypertension
   c. heart failure
   d. dyslipidemia

2. The renin-angiotensin-aldosterone system (RAAS) has emerged as playing a major role in the pathogenesis of CVD.
   a. True
   b. False

3. The normal vascular endothelium __________.
   a. maintains equilibrium between vasodilation and vasoconstriction
   b. maintains equilibrium between inhibition and promotion of cell growth
   c. protects from thrombotic events, inflammatory processes, and oxidative damage
   d. All of the above

4. Endothelial dysfunction may result in __________.
   a. lipid deposition
   b. platelet and leukocyte adhesion
   c. increased vasoconstriction
   d. All of the above

5. It is thought that therapies which inhibit the RAAS may play an important role in reducing vascular injury and decreasing the risk of cardiovascular events.
   a. True
   b. False

6. In the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) guidelines, the compelling indications or comorbid conditions where specific classes of antihypertensive drugs are recommended include __________.
   a. chronic kidney disease
   b. diabetes mellitus
   c. history of stroke
   d. heart failure
   e. coronary disease or history of myocardial infarction
   f. All of the above

7. The JNC 7 report recommends that combinations of antihypertensive drugs be used to initiate therapy in the large proportion of patients in whom single agents are unlikely to achieve needed blood pressure (BP) targets.
   a. True
   b. False

8. Nearly half of all patients with hypertension have 2 or more other risk factors for coronary artery disease.
   a. True
   b. False

9. According to the American Diabetes Association Standards of Medical Care in Diabetes (2006), __________.
   a. patients with diabetes should be treated to a systolic BP <130 mm Hg
   b. patients with diabetes should be treated to a diastolic BP of <80 mm Hg
   c. patients with diabetes and hypertension should be treated with a regimen that includes either an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker
   d. All of the above

10. Potential vascular protective effects of ACE inhibitors beyond reduction of BP have been observed in which of the following large clinical trials?
   a. Heart Outcomes Prevention Evaluation (HOPE) study
   b. European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease (EUROPA)
   c. Both a and b
   d. None of the above

Answer Form  ☑  Circle the correct answer.

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Statement of completion: I attest to having completed this CME activity.

Signature _______________________ Date ____________

Name ____________________________
Street ____________________________
City __________________ State ______ Zip _______
Daytime phone ____________________
Fax ____________________________
E-mail _______________________________