## CASES IN CARDIOVASCULAR MEDICINE<sup>\*</sup>

## **CASE 1-1**

#### Alice Blankenship

Mrs. Blankenship is an 69-year-old African American female who presents for follow-up on her blood pressure (BP). At her regular visit 1 month ago, it was slightly elevated at 138/88 mm Hg. Her only other known medical problem is type 2 diabetes mellitus of 3 years' duration. It is currently well controlled with metformin and lifestyle modifications. However, she admits to not following her diet "as close as I could" and not exercising regularly.

She did have her daughter, who is a nurse, check her BP at home in the interim. The first reading, approximately 3 weeks ago, was 134/80 mm Hg. The second reading roughly 1 week later was 138/82 mm Hg. Her daughter rechecked it last week and it was 136/84 mm Hg.

She has regular health maintenance check-ups with screening diagnostic testing and immunizations as well as regular disease-specific visits and diagnostic evaluations. She has only been hospitalized for childbirth and has never had surgery. Mrs. Blankenship is not taking any other prescription medications. She is not allergic to any medications.

**1.** Based on this information, which of the following questions are essential to ask Mrs. Blankenship and why?

- **A.** Has she been experiencing vertigo, presyncope, syncope, palpitations, unusual fatigue, or headaches?
- B. Has she been experiencing weakness in one or more of her extremities, weakness of her facial muscles, difficulty talking, dysphagia, or transient monocular blindness?
- **C.** Has she noticed any tachycardia, bradycardia, palpitations, changes in her hair or nails, skin rashes or discoloration, diaphoresis, tremor, snoring, or excessive sleepiness?
- **D.** Is she taking any over-the-counter (OTC) medications, vitamins, supplements, or herbal products?
- E. Does she have a family history of diabetes mellitus?

#### **Patient Responses**

She denies vertigo, presyncope, syncope, palpitations, fatigue, headaches, weakness in her extremities, weakness of her facial muscles, difficulty talking, dysphagia, transient monocular blindness, tachycardia, bradycardia, palpitations, changes in her hair or nails, skin rashes or discoloration, diaphoresis, tremor, snoring, or excessive sleepiness.

Mrs. Blankenship admits to daily usage of OTC ibuprofen 100 mg one pill twice a day for "arthritis" in her knees. She states that it controls her pain and stiffness. She denies taking other OTC medications, vitamins, supplements, or herbal products. Her mother and her older sister have hypertension; otherwise, her family history is negative.

**2.** Based on this information, which of the following components of a physical examination are essential to perform on Mrs. Blankenship and why?

- **A.** BP and pulse measurements in both arms in lying, sitting, and standing positions as well as BP measurement in both legs with Doppler
- B. Funduscopic examination
- C. Heart and lung examination
- D. Evaluation of all pulses
- E. Rectal examination

#### **Physical Examination Findings**

Mrs. Blankenship is 5'3" tall and weighs 165 lb (body mass index [BMI] = 29). Other vital signs are pulse, 86 beats per minute (BPM) and regular; respiratory rate, 12/min and regular; and oral temperature, 98.2°F. Her blood pressure is 134/84 mm Hg in her right arm and 136/82 mm Hg in her left arm lying supine; sitting, it is 134/86 mm Hg in her right arm and 134/88 mm Hg in her right arm and 134/86 mm Hg in her left arm. The BP is 144/86 mm Hg in

<sup>\*</sup>Remember, for each question, none to all of the answers could be correct/essential or incorrect/nonessential. See page 14 for Chapter 1 answers.

her right leg and 144/84 mm Hg in her left leg. Her pulse is 82 BPM lying, 86 BPM sitting, and 90 BPM standing.

Her bilateral funduscopic examination does not reveal any opacities of her lenses. Her discs have distinct margins and a normal cup:disc ratio. There is no evidence of papilledema. Her arteries, veins, and arteriovenous crossings appear normal. Her macular area and retina are normal in color and without any abnormal lesions.

Mrs. Blankenship's heart is regular in rate and rhythm and without any murmurs, gallops, or rubs. Her apical impulse is nondisplaced and without any thrills. Her lungs are clear.

Her knees do not demonstrate any decreased range of motion, deformities, effusions, crepitus, warmth, discoloration, or tenderness.

Her carotid, subclavian, renal, and femoral pulses are normal and equal bilaterally and without bruits. Her brachial, ulnar, radial, popiteal, dorsalis pedis, and posterior tibial pulses are normal and equal bilaterally. Her abdominal aorta is normal in size and pulsation and without bruits.

Her rectal examination is normal.

**3.** Based on this information, which of the following diagnostic studies are essential to conduct on Mrs. Blankenship and why?

- **A.** Bilateral magnetic resonance imaging (MRI) of her knees
- **B.** Urinalysis
- **C.** Fasting lipid profile
- **D.** Electrocardiogram (ECG)
- E. Ambulatory BP monitoring

#### **Diagnostic Results**

Mrs. Blankenship's MRI, lipid panel, and ambulatory BP monitoring are pending. Her urinalysis was normal except for 1+ glucose. Her hematocrit was 42% (normal for women: 37–47). Her ECG revealed normal sinus rhythm with a rate of 80 BPM, normal axis, and no waveform or segmental changes.

**4.** Based on this information, in addition to her type 2 diabetes mellitus and obesity, which one of the following is Mrs. Blankenship's most likely diagnosis and why?

- A. White coat syndrome producing pseudo-hypertension
- B. Prehypertension
- **C.** Hypertension, stage 1
- **D.** Hypertension, stage 2
- **E.** Diabetic nephropathy-induced hypertension

**5.** Based on this diagnosis, which of the following are appropriate components of a treatment plan for Mrs. Blankenship and why?

- **A.** Dietary modification including low-sodium, low-fat, Dietary Approaches to Stop Hypertension (DASH) eating plan
- **B.** Start a regular aerobic exercise program, with a goal of 30 minutes daily
- **C.** Start triamterene 37.5 mg with hydrochlorothiazide 50 mg once every morning
- D. Start valsartan 80 mg once a day
- **E.** Substitute ibuprofen with acetaminophen 500 mg two pills twice a day

#### **CASE 1-2**

#### **Betty Crane**

Betty is a 15-year-old white female who presents for a preparticipation sports physical for basketball. Her permission slip has been signed by her mother; however, neither of her parents accompanies her today. She has played for the previous 2 years without difficulty. She denies having any complaints, symptoms, or concerns.

Her only known medical problem is myopia, which is corrected to 20/20 with glasses. She denies any hospitalizations or surgeries. She is not taking any prescription or overthe-counter medications, vitamins, supplements, or herbal preparations. She does not have regular health maintenance examinations; however, her immunizations are up to date. Her menarche began at the age of 13 years. She has been having regular monthly menses since, and her last one was 3 weeks ago. She is not sexually active.

**1.** Based on this information, which of the following questions are essential to ask Betty and why?

- **A.** Has she ever experienced chest pain, pressure, or discomfort; presyncope or syncope; dyspnea; or fatigue with exercise?
- **B.** Has she ever been diagnosed with hypertension or a heart murmur?
- **C.** Is there a family history of cardiac death or cardiac disability before the age of 50 years?
- D. Is there any known heart disease in the family?
- E. When does she plan on becoming sexually active?

#### **Patient Responses**

Betty denies chest pain, pressure, or discomfort; presyncope or syncope; dyspnea; fatigue with exercise; a history of hypertension or a heart murmur; a family history of cardiac death or cardiac disability before the age of 50 years; or heart disease in the family. She does not know when she plans on becoming sexually active.

**2.** Based on this information, which of the following components of a physical examination are essential to perform on Betty and why?

- **A.** Funduscopic examination (or preferably slit-lamp examination if available)
- B. Ear and hearing examination
- C. Heart evaluation
- D. Examination of femoral pulse and abdominal aorta
- **E.** Measurement of arm span from tip of left middle finger to tip of right middle finger and evaluation for arachnodactyly, joint hyperextensibility, joint laxity, and scoliosis

#### **Physical Examination Findings**

Betty is 5'11" tall and weighs 120 lb. Other vital signs are BP, 106/56 mm Hg in her right arm and 102/52 mm Hg in her left arm; pulse, 80 BPM and regular; respirations, 10/min and regular; and oral temperature, 97.9°F.

Her bilateral funduscopic examination does not reveal any opacities. Her discs have distinct margins and her cup:disc ratio is normal. There is no evidence of papilledema. Her arteries, veins, and arteriovenous crossings appear normal. Her macular area and retina are normal in color and without any abnormal lesions. Her lenses do not appear to be displaced. However, she does have an incidental finding of a bilaterally elongated ocular globe.

Her ear canals are normal in color and without lesions or abnormal discharge. Her tympanic membranes are normal in color, without any gross lesions; intact; and freely mobile. Her hearing is grossly normal to whisper and watch ticking at appropriate lengths.

Betty's heart is regular in rate and rhythm with a grade 3/6 systolic ejection murmur in her mitral area that radiates to her left axilla and that increases with expiration, standing up, and performing a Valsalva maneuver; however, it softens when she squats or performs isometric exercises. It is unchanged by lying in the left lateral decubitus position. She also has a grade 2/6 diastolic murmur with a click in her aortic area that increases with expiration, squatting, and isometric exercise; however, it decreases with standing upright and with performing a Valsalva maneuver. She does not have any gallops or rubs. Her apical impulse is nondisplaced and not associated with a thrill. Incidentally, pectus excavatum is noted.

Her femoral pulses are normal bilaterally. Her aortic pulse is somewhat bounding, but her aorta is normal in size. There is no bruit.

Her arm span is 6' and she has arachnodactyly as well as hyperextensible, lax joints. Her spinal examination reveals a 15° thoracic scoliosis with curvature to the right as well as a compensatory 10° lumbar scoliosis to the left and mild thoracic kyphosis.

**3.** Based on this information, which of the following diagnostic studies are essential to conduct on Betty and why?

- **A.** Electrocardiogram (ECG)
- B. Echocardiogram
- C. Chest x-ray (CXR)
- **D.** Abdominal ultrasound
- E. Cardiac-specific troponin T and I

#### **Diagnostic Results**

Her ECG revealed normal sinus rhythm (NSR) with a rate of 80 BPM. Her echocardiogram is pending. Her CXR revealed pectus excavatum and confirmed the scoliosis and kyphosis. No other abnormalities were noted. Abdominal ultrasound revealed a normal-sized aorta without abnormal calcifications and/or aneurysms of the walls. Her cardiac troponin T was 0 ng/ml (normal: < 0.2) and her cardiac troponin I was 0 ng/ml (normal: < 0.03).

**4.** Based on this information, which one of the following is Betty's most likely diagnosis and why?

- A. Loeys-Dietz aneurysm syndrome (LDAS)
- B. Klinefelter syndrome
- C. Marfan syndrome (MFS)
- **D.** Ehlers-Danlos syndrome (EDS)
- E. Congenital contractural arachnodactyly (CCA)

**5.** Based on this diagnosis, which of the following are appropriate components of a treatment plan for Betty and why?

- A. Annual echocardiogram
- **B.** Annual eye examination, including a slit lamp, by an ophthalmologist
- **C.** Subacute bacterial endocarditis (SBE) prophylaxis for dental procedures
- D. Annual orthopedic evaluation
- **E.** Propranolol 10 to 20 mg twice a day initially; then, titrate every 1 to 2 weeks (to a maximum daily dose of 240 mg) to maintain exercise heart rate below 100 BPM

## **CASE 1-3**

#### **Carl Diaz**

Carl is a 15-year-old Hispanic male who presents with his mother for follow-up on an elevated cholesterol level obtained at a free community screening approximately 1 month ago. Carl's level was 237 and his father's was 240. According to Carl's mother, the nurse who performed the test told her Carl's cholesterol was "nothing to worry about because he is still a child"; however, the nurse recommended that Carl's father have a full lipid panel as soon as possible.

His father saw his regular health care provider (HCP) last week for the lipid panel. When the HCP diagnosed her husband with "dangerously high cholesterol," she asked about Carl's test. According to her, the HCP stated, "You might want to get it rechecked," hence prompting this visit.

Carl states (and his mother confirmed) that he has no known medical problems and has never had surgery nor been hospitalized. He is not taking any prescription or over-thecounter medications, vitamins, supplements, or herbal preparations. He is not allergic to any medications. He states that he does not smoke, drink alcohol, or do illicit drugs. He has regular health maintenance check-ups with his pediatrician and his immunizations are up to date.

Carl denies headaches, dizziness, vertigo, presyncope, syncope, palpations, tachycardia, bradycardia, chest pain/pressure, heartburn, gastrointestinal upset, arm or shoulder pain, problems with gait, difficulties with walking, problems using his hands or feet, difficulties talking, problems swallowing, fatigue, diaphoresis, changes in his skin, differences in the texture of his hair and nails, polyuria, polydipsia, and recent weight change.

**1.** Based on this information, which of the following questions are essential to ask Carl and/or his mother and why?

- A. Has Carl ever had his BP checked?
- **B.** Was Carl's cholesterol test done while he was fasting or nonfasting?
- C. What is Carl's mother's cholesterol level?
- **D.** Has either of Carl's parents and/or grandparents been diagnosed with a myocardial infarction (MI), coronary artery disease (CAD), sudden cardiac death (SCD), a cerebral vascular accident (CVA), or peripheral vessel disease (PVD) prior to the age of 55 years?
- **E.** Have his parents and/or grandparents been diagnosed with diabetes mellitus (including gestational diabetes) or any other serious medical condition(s)?

#### **Patient Responses**

According to Carl's mother, he had his BP checked at his last well-child visit with his pediatrician and was told it was "a little high" and "to lose some weight and get some exercise and it would not be a problem." He has done neither and has not had his BP checked since. When Carl had his cholesterol checked, he was nonfasting. However, he is fasting today.

His father's repeat total cholesterol was 245 mg/dl and he was started on medication. Carl's mother knows he had a lipoprotein panel in addition to the total cholesterol level but cannot remember the exact values. She has never had her cholesterol checked.

Carl's paternal grandfather had a nonfatal MI at the age of 62 years. His maternal grandfather was diagnosed with angina and PVD when he was 58 years old. His paternal grandmother had a CVA at the age of 70 years. All four of his grandparents and both of his parents are obese and hypertensive. His maternal grandfather has type 2 diabetes mellitus.

**2.** Based on this information, which of the following components of a physical examination are essential to perform on Carl and why?

- A. Ears, nose, and throat (ENT) examination
- B. Thyroid palpation
- C. Heart examination
- **D.** Abdominal examination
- E. Assessment of pulses

#### **Physical Examination Findings**

Carl is 5'5" tall and weighs 225 lb. His BP is 138/86 mm Hg in his right arm and 138/88 mm Hg in his left arm while seated; repeat BP in 5 minutes is 136/86 mm Hg in his right arm and 138/86 mm Hg in his left arm. Other vital signs are pulse, 96 BPM and regular; respirations, 12/min and regular; and oral temperature, 98.7°F.

His ENT and thyroid examinations are normal.

His heart is regular in rate (98 BPM) and rhythm with no murmurs, gallops, or rubs. His apical impulse is nondisplaced and without a thrill.

His abdomen reveals normoactive and equal bowel sounds in all four quadrants. There is no tenderness, masses, or organomegaly. His renal and aortic pulses are normal and without bruits.

His carotid pulses are normal bilaterally and without bruit. His brachial, ulnar, radial, femoral, popiteal, dorsalis pedis, and posterior tibial pulses are normal bilaterally. His feet are normal in color and temperature. His capillary refill is good.

**3.** Based on this information, which of the following diagnostic studies are essential to conduct on Carl and why?

- A. Fasting blood lipoprotein analysis
- ${\bf B.}$  Total cholesterol only
- C. Fasting plasma glucose (FPG)
- **D.** C-reactive protein (CRP)
- E. Glycosylated hemoglobin (Hgb A1C)

#### **Diagnostic Results**

Carl's total cholesterol was 222 mg/dl (normal child: 120–200); his low-density lipoproteins (LDLs) were 160 mg/dl (normal: 60–180); his high-density lipoproteins (HDLs) were 30 mg/dl (normal male: > 45); his very low-density lipoproteins (VLDLs) were 32 mg/dl (normal: 7–32); and his triglycerides were 250 mg/dl (normal male, 12–15 years old: 36–138). His FBS was 94 mg/dl (normal child older than 2 years of age to adult: 70–110) and his CRP was 2 mg/dl (normal: < 1.0). His Hgb A1C was 5.0% (nondiabetics and children: < 4).

**4.** Based on this information, which one of the following is Carl's most likely diagnosis and why?

- **A.** Hyperlipidemia, hypertension, and type 1 diabetes mellitus
- **B.** Hyperlipidemia, hypertension, and type 2 diabetes mellitus
- **C.** Hyperlipidemia, hypertension, obesity, and type 2 diabetes mellitus
- D. Hyperlipidemia, hypotension, and obesity
- E. Hyperlipidemia, hypertension, and overweight for age

**5.** Based on this diagnosis, which of the following are appropriate components of a treatment plan for Carl and why?

- **A.** Repeat total lipoprotein analysis in 1 month to obtain LDL average to utilize for monitoring and treatment
- **B.** Initiate a program of lifestyle modification with a lowfat, low-cholesterol, low-sodium diet; decreased caloric diet; and regular exercise program with goal of 30 minutes of aerobic exercise on most days of the week
- **C.** Start niacin 500 mg once a day for 2 weeks; then increase to 500 mg twice a day
- **D.** Thyroid stimulation test (TSH), liver function studies (LFTs), creatinine, and urine protein
- **E.** Start triamterene 37.5 mg with hydrochlorothiazide 50 mg once every morning

## CASE 1-4

#### **Dale Elliott**

Mr. Elliott is a 22-year-old white male who presents with the chief complaint, "I've got to get something for this flu—it is killing me." Further questioning reveals that he has been experiencing a moderate-grade fever, chills, malaise, wide-spread myalgias, generalized arthralgias, cough, and chest pain for approximately 1.5 weeks. The arthralgias involve "all my joints." He feels that all his symptoms are progressively getting worse.

The cough was nonproductive until last night, when he experienced his first episode of hemoptysis, described as a small amount of blood-streaked, clear, thick sputum. Since then, he has had three or four more episodes that are preceded by "coughing hard" and are followed by dyspnea. He has not noticed any stridor, "barking" sounds, wheezing, or rhonchi at any time. He does not have orthopnea. He has also experienced anorexia and has lost 5 or 6 lb since the onset of his illness.

He denies rhinorrhea; sore throat; ear pain; sinus pressure; headache; stiff neck; nausea; vomiting; diarrhea; other changes in his bowel movements; abdominal pain; penile discharge; dysuria; urinary urgency; urinary frequency; hematuria; confusion; problems using his arms, legs, or facial muscles; dysphagia; difficulty talking; drooling; or abnormalities of gait.

His medical history is negative for any medical conditions, previous surgeries, or hospitalizations. He does not take any prescription or over-the-counter medications, vitamins, supplements, or herbal preparations. He is allergic to penicillin and experienced urticaria, angioedema, dyspnea, and wheezing with last exposure. He has smoked half a pack of cigarettes a day for 6 years. He drinks three beers on Friday and Saturday evenings every week. He denies illicit drug usage. His family history is negative.

**1.** Based on this information, which of the following questions are essential to ask Mr. Elliott and why?

- **A.** Where is the chest pain located, does it radiate, what is its nature, what is its intensity, is it constant or intermittent, is it worsening, and are there any known aggravating or alleviating factors?
- **B.** Has he checked his temperature with a thermometer?
- C. Has he noticed any skin lesions or rash?
- **D.** Has he experienced any visual abnormalities?
- E. Does he have any pet rabbits at home?

#### **Patient Responses**

The chest pain is left anterior in location without radiation. It is sharp in nature and worsens with inspiration. It also appears to be somewhat worse when he lies down. He describes it as 8 out of 10 on the pain scale. He gets moderate relief from the pain when he takes oxycodone that one of his friends gave to him.

He has not checked his temperature with a thermometer. He denies any problem with his vision. He does not own rabbits.

He has noticed some painful, especially if touched or bumped, raised purplish-red lesions on the dorsal surface of some of his fingers; some nontender "red spots" on his palms and soles; and some "red dots" under his nails and in his eyes. He is uncertain how long they have been present. However, they have not changed since he first noticed them.

**2.** Based on this information, which of the following components of a physical examination are essential to perform on Mr. Elliott and why?

- **A.** General appearance
- B. Heart examination
- **C.** Lung auscultation
- D. Digital rectal examination (DRE)
- **E.** Skin and nail examination

#### **Physical Examination Results**

Mr. Elliott is 5'11" tall and weighs 150 lb (BMI = 21). Other vital signs are oral temperature,  $100.8^{\circ}$ F; BP, 92/62 mm Hg; pulse, 108 BPM and slightly irregular, respirations, 28/min and regular. He looks very ill, and toxic appearing.

His heart is slightly irregular in rhythm and rate (110 BPM) with a grade 1/6 systolic ejection murmur over the tricuspid area, which is unchanged with a Valsalva maneuver. He does

not have any gallops or rubs. His apical impulse is not displaced and he does not have a thrill.

His lungs have occasional inspiratory rhonchi in the bases bilaterally which do not resolve when Mr. Elliott coughs. His lungs are normal to percussion.

His rectal examination reveals good tone and no internal or external lesions.

He has nontender, 1 to 2 mm in diameter, petechial lesions on his conjunctiva surfaces and underneath all of his fingernails. With the exception of his right thumbnail, all his other nails reveal between three and five longitudinal, dark purplish-red to black-colored, enlongated triangular-shaped (tapering proximally), subungual lesions of approximately 2 to 5 mm in length, near the distal ends of his nails (splinter hemorrhages).

His skin reveals irregular, painless, erythematous macular lesions on his palms and fingertips (Janeway lesions) and painful, purplish papules on the dorsal aspect of his fingers (Osler nodes). He refuses to remove his socks to permit visualization of his feet because "my feet get too cold and I've already gotten the chills." He states that his "feet look just like his hands."

**3.** Based on this information, which of the following diagnostic studies are essential to conduct on Mr. Elliott and why?

- A. Complete blood count with differential (CBC w/diff)
- **B.** Chest x-ray (CXR)
- **C.** A minimum of 2 blood cultures with sensitivities and Gram stains drawn at least 1 hour apart
- D. Electrocardiogram (ECG)
- **E.** Transesophageal echocardiography (TEE)
- F. Urinary drug screen for illicit substances and narcotics

#### **Diagnostic Results**

His CBC revealed a red blood cell (RBC) count of  $4.8 \times 10^{6}/\mu$ l (normal male: 4.7-6.1) with a mean corpuscular volume (MCV) of 82.3 µm<sup>3</sup> (normal adult: 80–95), a mean corpuscular hemoglobin (MCH) of 26.7 pg (normal adult: 27-31), a mean corpuscular hemoglobin concentration (MCHC) of 32.2 g/dl (normal adult: 32-36), and a red blood cell distribution width (RDW) of 12.5% (normal adult: 11-14.5). His white blood cell (WBC) count was 25,500/mm3 (normal adult: 5000-10,000) with 82% neutrophils (normal: 55-70), 10% lymphocytes (normal: 20-40), 4% monocytes (normal: 2-8), 3% eosinophils (normal: 1-4), and 1% basophils (normal: 0.5-1). His hemoglobin (Hgb) was 12.8 g/dl (normal adult male: 14-18) and his hematocrit (HCT) was 39.5% (normal male: 42-52). His platelet (thrombocyte) count was 150,000/mm<sup>3</sup> (normal adult: 150,000-400,000) and his mean platelet volume (MPV) was 7.9 fl (normal: 7.4-10.4). His smear was consistent with the aforementioned and revealed no cellular abnormalities except multiple bands.

His CXR revealed no abnormalities.

His blood cultures are pending; however, both of the specimens' Gram stains revealed gram-positive cocci in clusters.

His ECG revealed a sinus tachycardia of 110 BPM with rare unifocal premature ventricular contractions (PVCs). There were no other waveform abnormalities, arrhythmias, or segmental changes present. His TEE was normal except for a small vegetation on his tricuspid valve with mild to moderate regurgitation.

His urinary drug screen is pending.

**4.** Based on this information, which one of the following is Mr. Elliott's most likely diagnosis and why?

- A. Lymphocytic leukemia
- B. Rocky Mountain spotted fever
- C. Acute influenza and tricuspid regurgitation
- **D.** Infective endocarditis (IE)
- E. Disseminated gonococcal infection (DGI)

**5.** Based on this diagnosis, which of the following are appropriate components of a treatment plan for Mr. Elliott and why?

- A. Cefazolin 2 g IV every 8 hours and gentamicin 70 mg IV every 8 hours until blood cultures and sensitivities are available
- **B.** Vancomycin 1 g IV every 12 hours and gentamicin 70 mg IV every 8 hours until blood cultures and sensitivities are available
- **C.** Hospitalize and observe closely for additional complications
- D. Refer for substance abuse treatment
- E. Bone marrow biopsy

## **CASE 1-5**

#### **Eric Floyd**

Mr. Floyd is a 53-year-old African American male who presents with the chief complaint of chest pain that began when he crashed his all terrain vehicle (ATV) "head-on" into a tree approximately 3 to 4 hours ago. He states that he hit his chest "really hard" against the area between the ATV's handle bars, causing it to dent on the vehicle on the left side.

Currently, he describes his chest pain as a 6 out of 10 on the pain scale, sharp in nature, and located over the left anterior chest wall. It radiates to his left arm and shoulder but does not involve his neck. It is aggravated by breathing, coughing, and lying flat on his back. It feels best when he is sitting up and bending forward. The pain started immediately after impact as an ache that he would have rated as a 3 out of 10 on the pain scale. He assumed it was just "a bad bruise"; however, as it progressively worsened to its current state, he became concerned.

He has been experiencing some exertional fatigue, exertion dyspnea, and orthopnea for approximately the last hour. He denies lightheadedness, vertigo, presyncope, syncope, headache, confusion, chest pressure/tightness, neck pain, nausea, vomiting, hemoptysis, cough, wheezing, stridor, rales, fever, pedal edema, and palpitations.

His only known medical problem is hypertension, which is controlled with triamterene 37.5 mg/hydrochlorothiazide 25 mg every morning, nadolol 40 mg twice a day, and controlledrelease dihydropyridine 10 mg every night. He does not take any other prescription or over-the-counter medications, vitamins, supplements, or herbal preparations. He is not allergic to any medications. He has never had any surgery nor been hospitalized. He has regular health maintenance visits and age-appropriate diagnostic testing, and his immunizations are up to date. He quit smoking 2 years ago after smoking approximately one pack per day since he was 15 years old. He denies drinking alcohol.

**1.** Based on this information, which of the following questions are essential to ask Mr. Floyd and why?

- A. Did he sustain a head injury or loss of consciousness?
- B. Is his helmet intact?
- **C.** Did he injure or is he experiencing pain elsewhere in his body?
- **D.** What is his "usual" BP?
- **E.** Does he have a family history of coronary artery disease (CAD)?

#### **Patient Responses**

He did not sustain a head injury or loss of consciousness. His helmet was intact after the incident. He denies pain anywhere else in his body or any other type of injury. His "usual" BP is "around" 140/90 mm Hg. His father had a fatal MI at the age of 52 years.

**2.** Based on this information, which of the following components of a physical examination are essential to perform on Mr. Floyd and why?

- A. Heart examination
- **B.** Evaluate for the presence of an elevated jugular venous pressure (JVP), jugular venous distension (JVD), Kussmaul sign, pulsus alternans, pulsus bigeminus, and pulsus paradoxicum
- C. Lung evaluation
- D. Chest wall examination
- E. Cranial nerve evaluation

#### **Physical Examination Findings**

Mr. Floyd is 5'8" tall and weighs 250 lb (BMI = 41.6). Other vital signs are pulse, 120 BPM and regular; respirations, 28/min and regular; BP, 96/62 mm Hg, decreases to 80/58 mm Hg with inspiration; and oral temperature,  $99.2^{\circ}$ F.

At a 30° angle, his right internal jugular vein reveals an estimated central venous pressure of 10 cm. It also shows a prominent x descent but no detectable y descent. It does not change with inspiration (negative Kussmaul sign). Compression of the lower portion of his right external jugular vein results in distension, or JVD.

His carotid pulses are normal bilaterally and without bruits. However, checking his carotid pulse for a full 2 minutes reveals a regular tachycardic rhythm that is unchanged with inspiration. No abnormal beats or PVCs are noted.

His heart reveals distant heart sounds throughout and a regular tachycardia at 120 BPM. He has no murmurs or gallops; however, he has a pericardial friction rub by his left sternal border. It is most pronounced when he sits up and bends forward. His apical impulse is displaced inferiorly and laterally to the seventh intercostal space midway between the midclavicular line and the anterior axillary line. It is slightly increased in size, duration, and amplitude. His lung sounds are slightly decreased and dull sounding in his left base; tactile fremitus, vocal fremitus, and egophony are detected below the angle of the left scapula (positive Ewart sign). The remainder of the left lung and his right lung are clear to auscultation. His chest wall is tender to palpation from ribs 2 to 8 in an area approximately 2.5 inches wide that centered over his midclavicular line with no flailing or laxity.

His cranial nerves are grossly intact.

**3.** Based on this information, which of the following diagnostic studies are essential to conduct on Mr. Floyd and why?

- A. Chest x-ray (CXR) with rib enhancement
- B. Serial cardiac troponin I and T
- C. Electrocardiogram (ECG) and cardiac monitoring
- D. Echocardiography
- E. Tuberculosis skin test (TST)

#### **Diagnostic Results**

Mr. Floyd's CXR revealed an enlarged "water bottle shaped" cardiac silhouette and a small pleural effusion in the left base; no other abnormalities were noted.

His cardiac troponin I was slightly elevated at 0.05 ng/ml (normal: < 0.03 ng/ml) and his troponin T was 0.25 ng/ml (normal: < 0.2).

His ECG revealed a sinus tachycardia (rate 110 BPM); diffuse ST-segment elevation of 2 mm in leads I, II, aVF, and  $V_2$ to  $V_6$ ; PR-segment depression in III, aVR, aVL, and  $V_1$ ; upright P waves; overall low voltage; and a change in the height of the P, QRS, and/or T waves that occurred at regular intervals (electrical alternans). No Q waves were seen.

His echocardiogram revealed a large pericardial effusion (estimated size ~800 ml) with a moderate decrease of the size of his right ventricle and associated diastolic and right atrial collapse. No myocardial or pericardial thickening or calcifications were observed. His tuberculosis skin test is pending.

**4.** Based on this information, in addition to his underlying hypertension and his class 3 (extreme) obesity, which one of the following is Mr. Floyd's most likely diagnosis and why?

- A. Constrictive pericarditis
- B. Cardiac tamponade secondary to a pericardial effusion
- **C.** Tension pneumothorax
- **D.** Restrictive cardiomyopathy
- E. Right ventricular myocardial infarction (RVMI)

**5.** Based on this diagnosis, which of the following are appropriate components of a treatment plan for Mr. Floyd and why?

- A. Hospitalize for arterial pressure, venous pressure, and cardiac monitoring; IV fluids; oxygen; further testing; and treatment
- **B.** Pericardiocentesis via subxiphoid approach under echocardiography guidance
- **C.** Evaluation of fluid from tap for cytology, microscopy, bacterial culture and sensitivity, and polymerase chain reaction (PCR) test of DNA of *Mycobacterium tuberculosis*
- **D.** Consultation with a cardiac surgeon
- **E.** Continue his current blood pressure medicines at half strength

#### **CASE 1-6**

#### **Frank Gee**

Mr. Gee is a 79-year-old Asian American male who presents with the chief complaint of chest pain of 2 hours' duration. He rates it as a 5 out of 10 on the pain scale. He describes it as a substernal ache, but not a true heaviness or pressure. It radiates to both his shoulders and his intrascapular area. It is associated with nausea (without vomiting), weakness, lightheadedness (but no true vertigo), mild diaphoresis, and dyspnea on exertion. It is alleviated some, but does not completely resolve, if he "sits down and rests." It is aggravated by most any form of exertion, including walking. He knows of no other aggravating or alleviating factors.

He states that the sensation feels identical to the pain he was experiencing with his gallstones; however, he knows they cannot be causing the problem because his gallbladder was removed 2 weeks ago. Nevertheless, as with the previous episodes, his chest pain began while he was eating breakfast. Unlike previous episodes, this one did not resolve within a maximum of half an hour. His daughter convinced him to come and have it evaluated because it is not only persisting but also appearing to be worsening.

He has a history of hypertension and hyperlipidemia, which is being treated with herbal therapy by a traditional Chinese physician. He does not know the name of the medication being prescribed; he just makes it into a tea and drinks it four times a day. He has no other known medical problems. His only surgery has been a laparoscopic cholecystectomy. That was his only hospitalization as well. He doesn't take any prescription or over-the-counter medications, vitamins, or supplements. He has no known drug allergies. He is a widower of 20 years and lives with his father. He does the cooking for the two of them and feels it is "healthy."

His father is 102 years old and does not have any medical problems. His family history is positive for cardiac disease. His mother is deceased as a result of a myocardial infarction at the age of 53 years. One of his brothers had a nonfatal MI at the age of 54 years. To his knowledge, there is no other family history of cardiac disease or serious illnesses.

**1.** Based on this information, which of the following questions are essential to ask Mr. Gee and why?

- **A.** Has he ever tried any Western (i.e., nitroglycerine) or traditional Chinese medications for his chest pain? If yes, what were the treatments and results?
- **B.** Does he smoke, and if so, what is his smoking history?
- **C.** When was his cholesterol last checked and what were the results?
- **D.** What is his "usual" BP?
- **E.** Does he use sildenafil, vardenafil, or tadalafil for his erectile dysfunction (ED)?

#### **Patient Responses**

He has not tried any medicines, Western or traditional Chinese, for his chest pain.

He is a smoker and has been smoking one pack of cigarettes per day for the last 65 years.

He had his cholesterol checked before his surgery (~3 weeks ago). According to Mr. Gee, his total cholesterol was 180, his "good" (HDL) cholesterol was 40, his "bad" (LDL) cholesterol was 130, and his triglycerides were 150. His BP generally runs from 130/70 to 140/80.

He denies having ED and being sexually active since his wife died 20 years ago.

**2.** Based on this information, which of the following components of a physical examination are essential to perform on Mr. Gee and why?

- A. General appearance
- **B.** Oral examination
- C. Heart auscultation
- **D.** Lung auscultation
- **E.** All his pulses

#### **Physical Examination Findings**

Mr. Gee is 5'3" tall and weighs 175 lb (BMI = 31). Other vital signs are BP, 164/96 mm Hg in his right arm and 162/98 mm Hg in his left arm; pulse, 112 BPM and regular; respirations, 20/min and regular; and oral temperature, 99.1°F. He appears to be in moderate distress and is slightly diaphoretic. Otherwise, his general appearance is normal.

His oral examination is unremarkable.

His heart is tachycardic at a rate of 112 BPM but regular. He has a faint systolic ejection murmur of his mitral valve that can be heard best in the left lateral decubitus position. Otherwise, no murmurs, rubs, or gallops are heard. His point of maximum intensity is stronger and larger than normal but not displaced. There is not a thrill.

His breath sounds are slightly harsh throughout but clear to auscultation except for bilateral rales in his bases. They are unchanged by coughing or position. Percussion, fremitus, and egophony are normal.

His carotid, renal, and aortic pulses are normal and without bruit. His aorta is not dilated. His brachial, ulnar, radial, femoral, popiteal, dorsalis pedis, and posterior tibial pulses are normal and equal bilaterally. His feet are normal in color and temperature. His capillary refill is good. He has no pedal edema.

**3.** Based on this information, which of the following diagnostic studies are essential to conduct on Mr. Gee and why?

- A. Cardiac telemetry followed by 12-lead electrocardiogram (ECG)
- **B.** Oxygen saturation followed by oxygen at 2 L/min via nasal cannula (NC)
- C. Echocardiogram
- D. Gallbladder ultrasound
- **E.** Cardiac troponin I and T (cTn-I and cTn-T) stat; then repeat in 4 and 8 hours

#### **Diagnostic Results**

His cardiac telemetry revealed a sinus tachycardia with a slight downward convexity to his ST segment and an elevation of approximately 2 mm above baseline. His 12-lead ECG also revealed a sinus tachycardia and the same type of STsegment convexity in all of the peripheral leads but in none of the chest leads; however, the elevation of the ST segment was only apparent in II, III, and aVF. It was approximately 2 mm in all three leads. These three leads also revealed what appeared to be the formation of early Q waves.

His  $O_2$  saturation was 94% on room air but increased to 98% on oxygen at 2 L/min via NC.

His echocardiogram revealed a small area of inferior wall immobility as well as sinus tachycardia. His valves appeared normal. His estimated ejection fraction was greater than 40%.

His gallbladder ultrasound was normal.

His cTn-I was 0.075 ng/ml (normal: < 0.03) and his cTn-T was 0.19 ng/ml (normal: < 0.2).

**4.** Based on this information, in addition to hypertension, hyperlipidemia, obesity, and current smoker, which one of the following is Mr. Gee's most likely diagnosis and why?

- **A.** Unstable angina
- B. Old anterior myocardial infarction
- C. Acute anteroseptal myocardial infarction
- **D.** Choledocholithiasis
- E. Acute inferior myocardial infarction

**5.** Based on this diagnosis, which of the following are appropriate components of a treatment plan for Mr. Gee and why?

- **A.** Admit to intensive care unit (ICU), continue telemetry, vital sign monitoring, IV fluids, and oxygen
- **B.** IV nitroglycerine 2 to 200 μg/min at a dose sufficient enough to alleviate the patient's pain but not so high as to cause adverse effects. If this titration cannot be achieved or maximum dosage fails to alleviate the patient's pain, then give morphine sulfate at 2 to 8 mg IV every 15 minutes as needed, provided no signs of respiratory depression are present
- **C.** Aspirin 160 to 325 mg stat; then 81 mg enteric-coated aspirin daily with food
- **D.** Acebutolol 200 mg once a day orally
- E. Fibrinolysis with tissue plasma activator (tPA)
- **F.** Percutaneous transluminal coronary angiography (PTCA) with stent placement if indicated

## **CASE 1-7**

#### **George Harris**

Mr. Harris is a 58-year-old Asian American male who presents with the chief complaint of "coughing up blood" for approximately 2 to 3 weeks. He estimates it to be "less than a teaspoon" and to occur no more frequently than every 3 or 4 hours; however, it does occur "around the clock." It is bright red in color and not associated with sputum, mucus, stomach acid/contents, or "coffee grounds"-looking material. It is unchanged since its onset.

He has been experiencing a nonproductive cough for approximately the last 5 or 6 years. It does not appear to be any different now than it was at its onset. His cough had been nonproductive until the hemoptysis began. He sleeps on three pillows and has paroxysmal nocturnal dyspnea (PND) less than once a week. He admits to occasionally feeling his heart rate increase with exertion; however, he denies noting any other irregularities regarding his heart's rate/beat.

He denies chest pain or pressure, vertigo, lightheadedness, presyncope, syncope, tinnitus, fever, chills, wheezing, stridor, rhonchi, rales, nausea, or vomiting.

He has no known medical problems. He was hospitalized at the age of 16 years for rheumatic fever; however, he denies cardiac involvement and/or long-term antibiotics following the episode. He has never had any surgery. He does not take any OTC or prescription medications, vitamins, supplements, or herbal preparations. He smokes two packs of cigarettes per day and has done so for the past 30 years. He drinks two glasses of red wine every evening. He denies any other alcohol intake. His family history is noncontributory.

**1.** Based on this information, which of the following questions are essential to ask Mr. Harris and why?

- **A.** Has he experienced any epistaxis, nasal or oral lesions, or gingival or dental problems recently?
- **B.** Has he experienced any abdominal pain or change in his bowel movements?
- **C.** Has he experienced any fatigue, malaise, weight loss, hoarseness, or night sweats?
- D. Has he experienced any dyspnea?
- E. Has he experienced any hallucinations?

#### **Patient Responses**

Mr. Harris denies any epistaxis, nasal or oral lesions, gingival or dental problems, abdominal pain, change in bowel movements, nausea, vomiting, heartburn, fatigue, malaise, weight loss, hoarseness, night sweats, or hallucinations.

He has had some dyspnea on exertion daily for several months but denies it worsening. He can climb a flight of steps at a normal pace without having any problems; however, if he tries to do it "too fast," he experiences the dyspnea and occasionally the tachycardia. He can walk more than two blocks, without symptoms, if the ground is level.

**2.** Based on this information, which of the following components of a physical examination are essential to perform on Mr. Harris and why?

- A. Skin examination
- B. Heart examination
- **C.** Lung auscultation
- **D.** Evaluation of jugular venous pressure (JVP), of pulses, and for pedal edema
- E. Joint evaluation

#### **Physical Examination Findings**

Mr. Harris is 5'8" tall and weighs 195 lb (BMI = 29.6). Other vital signs are BP, 120/76 mm Hg; pulse, 92 BPM and regular; respiratory rate, 24/min and regular; and oral temperature, 97.9°F. He is overweight and in moderate respiratory distress, bending forward with his hands on his thighs to breathe. He has a bluish discoloration to his face with a malar flushing on his cheeks.

His heart is regular in rate and rhythm. He has a loud opening snap that is more prominent in expiration and with a significant time lapse from the closure of the aortic valve. He has a grade II/VI diastolic murmur and rumble at his apex that is best heard when he is lying on his left side. He has no gallops or rubs. He does not have a thrill but does have a "tapping" sensation over his apical impulse, which is located in the firth intercostal margin approximately 8 cm from his midsternal line. He also has a grade I/VI diastolic murmur in his tricuspid area that increases with inspiration.

His breath sounds are harsh throughout but symmetric. He does not have any wheezing, rales, rhonchi, or stridor. Percussion, fremitus, and egophony are normal.

At 30° of head elevation, his JVP is 8.5 cm and he has an elevated  $\alpha$  wave.

His carotid and renal pulses are normal, equal bilaterally, and without bruits. His aortic pulsation is normal and does not reveal any evidence of enlargement or a bruit. His brachial, ulnar, femoral, popiteal, dorsalis pedis, and posterior tibial pulses are normal and equal bilaterally. His feet are normal in color and temperature and equal bilaterally. His capillary refill is good. He does not have any pedal edema.

**3.** Based on this information, which of the following diagnostic studies are essential to conduct on Mr. Harris and why?

- **A.** Oxygen saturation ( $O_2$  sat) and chest x-ray (CXR)
- **B.** Electrocardiogram (ECG) and echocardiogram with Doppler
- C. D-dimer
- **D.** First morning sputum for cytology  $\times 3$
- E. Antinuclear antibodies (ANAs); erythrocyte sedimentation rate (ESR); antinative DNA; anticardiolipin antibodies, including lupus anticoagulant; C<sub>3</sub> and C<sub>4</sub> complement assay; systemic lupus erythematosus preparation (SLE prep); and CBC w/diff

#### **Diagnostic Results**

Mr. Harris's  $O_2$  sat was 88% (normal adult:  $\geq$  95). His CXR did not reveal any effusions, lesions, consolidations, or infiltrates. However, it did reveal a cardiac silhouette with a straight left heart border, a large left atrial appendage, and a calcified mitral valve.

His ECG revealed normal sinus rhythm, with large P waves throughout. They were tall and peaked in II and upright in  $V_1$ . No other abnormalities were noted.

His echocardiogram confirmed a thickened, immobile, calcified, stenotic mitral valve with left atrial enlargement. His mitral valvular diameter was 0.8 cm<sup>2</sup> (normal: 4–6 cm<sup>2</sup>). His tricuspid valve was also slightly stenotic but with a normal valvular diameter. Ejection fraction was estimated to be approximately 35%.

His D-dimer, ANA, ESR, antinative DNA, anticardiolipin antibodies, lupus anticoagulant,  $C_3$  and  $C_4$  complement assay, SLE prep, and CBC w/diff were negative. His sputum cytologies are pending.

**4.** Based on this information, in addition to his being overweight and a current smoker, which one of the following is Mr. Harris's most likely diagnosis and why?

- A. Lung cancer
- **B.** Pulmonary embolism
- **C.** Atypical vertucous endocarditis of Libman-Sacks secondary to systemic lupus erythematous
- **D.** Left atrial myxoma
- E. Mitral stenosis with associated tricuspid stenosis

**5.** Based on this diagnosis, which of the following are appropriate components of a treatment plan for Mr. Harris and why?

- **A.** Hospitalization with oxygen therapy starting at 2 L/min after arterial blood gases and then adjusted accordingly, cardiac monitoring, and IV line to keep vein open (KVO)
- **B.** Refer to thoracic surgeon and oncologist for evaluation and treatment of lung cancer
- **C.** Refer to cardiac surgeon for possible cardiac catheterization, possible balloon valvuloplasty, or other interventions
- **D.** Start on warfarin therapy
- E. Encourage smoking cessation

## **CASE 1-8**

#### Harriet Issac

Mrs. Issac is a 54-year-old white female who presents with the chief complaint of chest pain and shortness of breath. She describes the chest pain as a "swollen, pressure-like" sensation that is substernal in location and radiates to her left shoulder and arm. It is minimally alleviated by rest and markedly aggravated by activity. She rates it as a 9 out of 10 on the pain scale. It started abruptly approximately 4 hours ago and appears to be getting progressively worse. Her dyspnea started shortly after the chest pain and has been constant since.

She has some mild nausea without vomiting. She has not had any bowel changes, fever, malaise, arthralgias, cough, wheezing, stridor, rhonchi, rales, headache, vertigo, presyncope, syncope, loss of consciousness, visual changes, or edema.

She saw her family physician approximately 1 hour after her pain began and he assured her it was caused by "stress" because she had been involved in a motor vehicle accident (MVA) the previous night. The car she was driving was "T-boned" by a large truck on the passenger side when she drove through an intersection. The accident resulted in the death of her husband and grandson. At this point, she became tearful and stated the police at the scene "said it was all my fault." She admits to being "upset," "crying a lot," and unable to sleep since the incident ~14 hours ago. She feels guilty over her family members' deaths, but she denies thoughts of suicide.

Her only known medical problems are a history of chronic anxiety and depression dating back to her adolescence and problems related to the previous day's MVA consisting of contusions to her left arm, ribs, and thigh; a few minor abrasions and a small laceration to the right side of her face, which was repaired in the emergency department last night; and some mild ecchymosis under both her eyes from the airbag's deployment. None of these symptoms have changed since their onset. She denies any surgery. Her only hospitalizations were for childbirth.

She is taking fluoxetine 40 mg once a day and acetaminophen 500 mg two tablets every 6 to 8 hours as needed for pain. The acetaminophen alleviates all her pain except her chest pain.

She is not taking any other prescription or overthe-counter medications, vitamins, supplements, or herbal preparations. She is allergic to meperidine (it causes generalized hives but no dyspnea). She has never smoked cigarettes or drank alcohol. She has a family history of coronary artery disease (mother: nonfatal myocardial infarction at the age of 70 years).

**1.** Based on this information, which of the following questions are essential to ask Mrs. Issac and why?

- A. Has she ever experienced similar symptoms in the past?
- **B.** Is she aware of any other aggravating or alleviating factors?
- **C.** What type of evaluation and diagnostic tests were performed on her in the emergency department following her MVA, and what were the results?
- **D.** Has she been experiencing any diaphoresis, palpitations, tachycardia, anxiety, or shakiness?
- **E.** Does she have any other grandchildren to replace the one she lost?

#### **Patient Responses**

Mrs. Issac has never experienced any chest pain or shortness of breath in the past. Her only other known aggravating factor is breathing deeply; and, her only other known alleviating factor is shallow breathing. According to the patient, she had a comprehensive physical examination; radiographs of her neck, back, chest, and left hip; an MRI of her head; an electrocardiogram; and a urinalysis in the ED following her MVA last night. She states she was informed that all the tests were negative and she was "just bruised badly." She denies diaphoresis. She has had some intermittent anxiety, palpations, and shakiness "mostly when I think about my husband and grandson" since the MVA. She has not had any increased stress except for the MVA. She does not have any other grandchildren.

**2.** Based on this information, which of the following components of a physical examination are essential to perform on Mrs. Issac and why?

- A. Heart examination
- **B.** Lung auscultation
- C. Palpation of ribs
- **D.** Evaluation of jugular venous pressure (JVP) and ankles/ feet for edema
- E. Visual acuity

#### **Physical Examination Findings**

Mrs. Issac is 5'1" tall and weighs 150 lb (BMI = 29.2). Other vital signs are BP, 162/98 mm Hg in her right arm and 166/100 mm Hg in her left arm; pulse, 96 BPM and regular; respirations, 20/min and regular; and oral temperature, 99.2°F.

Her heart is regular in rate and rhythm. There is a midsystolic click followed by a grade 1/6 late systolic murmur in her mitral area that increases in intensity and length with a Valsalva maneuver and standing, and decreases with squatting. She also has an S4 gallop, but no rub. Point of maximal impulse (PMI) is located 15 cm from the left sternal border, in the 8th to 10th intercostal spaces (ICSs), and is 4.5 cm in size. Her lungs are clear to auscultation and breath sounds are present in all fields. She does not have any chest wall tenderness except from her anterior-axillary line to her midaxillary line over ribs 8 to 10. There is some minor ecchymosis developing on the skin in this area.

Her JVP is not visualized, even with her lying as high as 90° and after performing the abdominojugular reflux test. Her carotid and renal pulses are normal and equal bilaterally; they did not reveal any bruits. Her aorta pulsation is normal, nonenlarged, and without a bruit. Her brachial, ulnar, femoral, popiteal, dorsalis pedis, and posterior tibial pulses are normal and equal bilaterally. Her feet are normal in color and temperature. Her capillary refill is good. She does not have any pedal edema.

Distance vision is 20/25 wearing her corrective lenses.

**3.** Based on this information, which of the following diagnostic studies are essential to conduct on Mrs. Issac and why?

- A. Brain natriuretic peptide (BNP)
- **B.** Serial cardiac troponin levels (cTn-I and cTn-T)
- C. Electrocardiogram (ECG) and echocardiogram
- D. Chest x-ray (CXR)
- **E.** 24-Hour urine vanillylmandelic acid (VMA) and catecholamine levels

#### **Diagnostic Results**

Mrs. Issac's BNP was 125 pg/ml (normal: < 100). Her cTn-I was slightly elevated at 0.035 ng/ml (normal: < 0.03), as was her cTn-I at 0.205 ng/ml (normal: < 0.2).

Her ECG revealed ST-segment elevations of 1 mm and deep T-wave inversion in leads  $V_1$  through  $V_5$ . Her echocardiogram revealed left ventricular apical ballooning that had a round ampulla shape similar to an "octopus pot" with dyskinesia and mild mitral valve prolapse with mild regurgitation.

Her CXR showed a cardiac silhouette revealing a rounded ampulla of the left ventricle similar to an "octopus pot."

Her VMA level was 8.0 mg/24 hr (normal: < 6.8). Her free catecholamine level was 142  $\mu$ g/24 hr (normal: < 100) with a dopamine level of 350  $\mu$ g/24 hr (normal: 65–400), an epinephrine level of 50  $\mu$ g/24 hr (normal: < 20), a metanephrine level of 1.0 mg/24 hr (normal: < 1.3), a norepinephrine level of 145  $\mu$ g/24 hr (normal: < 100), and a normetanephrine level of 100  $\mu$ g/24 hr (normal: 15–80).

**4.** Based on this information, in addition to her being overweight, which one of the following is Mrs. Issac's most likely diagnosis and why?

- A. Pheochromocytoma
- **B.** Acute inferior myocardial infarction (AIMI)
- C. Heart failure
- D. Takotsubo cardiomyopathy
- E. Chest pain secondary to stress reaction

**5.** Based on this diagnosis, which of the following are appropriate components of a treatment plan for Mrs. Issac and why?

- **A.** Hospitalize with telemetry and close monitoring of vital signs
- B. Repeat cTn-I and cTn-T in 4 and 8 hours

- C. Cardiac catheterization
- **D.** Meperidine 50 mg IM every 3 to 4 hours as needed
- E. Nebivolol 10 mg orally once a day

## **CASE 1-9**

#### Ira Jackson

Mr. Jackson is a 78-year-old white male who presents with the chief complaint of "not being able to keep my blood level in the right range, so I keep getting those irregular heartbeats." Upon further questioning, he is referring to his international normalized ratio (INR) for his warfarin, which he started taking approximately 5 years ago when he was diagnosed with atrial fibrillation (AF). His heart rate had been regular and his INR within the desired range since the time of diagnosis until approximately 2 months ago, when he began experiencing palpitations of his heart and fluctuations of his INR.

He states that the palpitations begin without provocation, occur two or three times a day, last for approximately 10 to 15 minutes, and then resolve spontaneously. He is unaware of any aggravating or alleviating factors. They are not associated with weakness, fatigue, tiredness, lightheadedness, vertigo, presyncope, syncope, tinnitus, chest pains, chest pressure, nausea, dyspnea, problems with gait, other difficulties using extremities, abnormalities of speech, lack of coordination, confusion, loss of consciousness, seizures, tremors, anxiety, hunger, or eating.

He has not had any episodes of epistaxis, gingival bleeding with brushing his teeth, vomiting blood or "coffee grounds"appearing substances, gross hematuria, rectal bleeding, passing dark tarry-appearing stools, or bruising more easily.

According to Mr. Jackson, his INR can be high, low, or, rarely, normal without him doing anything different. He claims his regular physician has not adjusted his warfarin dosage but has just been checking it every week and encouraging him "to take his medication regularly." However, he is unequivocally certain that he takes the same dose of his medication at the same time every day, never missing a dose or taking an extra dose.

His only known medical problems are atrial fibrillation (AF) and hypertension (HTN). His HTN was diagnosed approximately 25 years ago and has always been well controlled with propranolol. His current medications include warfarin 2.5 mg/day and long-acting propranolol 120 mg/day. He is not allergic to any medications. He does not take any other prescription or over-the-counter medications, vitamins, supplements, or herbal preparations. He has never had surgery. His only hospitalization occurred when the AF was first diagnosed. He has never smoked or drank alcohol. His family history is positive for his father and two brothers having AF.

**1.** Based on this information, which of the following questions are important to ask Mr. Jackson and why?

- A. Were there any changes in his medical condition, medication list (including medications used on an as-needed basis), or life when he began reexperiencing palpitations and having fluctuations of his INR?
- **B.** Do his medications look different since he started experiencing problems?

- C. Does he consume caffeine?
- **D.** Does he alter the amounts of "greens" that he consumes daily?
- **E.** Does he alter the amount of orange juice that he drinks daily?

#### **Patient Responses**

Mr. Jackson did not experience any changes in his life/stress level, medical conditions, medications (including over-thecounter drugs, vitamins, supplements, herbal preparations, short-term-usage medications, or as-needed medications), or appearance of his pill. He does not drink caffeine regularly; however, he will have a couple of glasses of iced tea when eating out. This could vary from every day for a couple of days to every couple of weeks. He has never noticed any relationship between the occurrence of the palpitations and the tea consumption; however, he cannot be certain it does not exist. He does vary the amount of "greens" in his diet from no servings a day to four or five servings per day when "fresh" ones are available. He drinks one glass of orange juice each morning for breakfast.

**2.** Based on this information, which of the following components of a physical examination are essential to perform on Mr. Jackson and why?

- A. Nasal and pharyngeal examination
- B. Heart examination
- C. Lung auscultation
- **D.** Evaluation of jugular venous pulse (JVP)
- E. Check for pedal edema

#### **Physical Examination Findings**

Mr. Jackson is 5'11" tall and weighs 165 lb (BMI = 23). Other vital signs are pulse, 80 BPM and irregularly irregular; respirations, 10/min and regular; BP, 118/76 mm Hg lying, 124/76 mm Hg sitting, and 128/74 mm Hg standing; and oral temperature,  $98.8^{\circ}$ F.

His nose and throat examination is unremarkable.

His heart is irregularly irregular in rhythm and its ventricular rate is 78 BPM. There are no murmurs, gallops, or rubs; however, his first heart sound appears to be louder than normal and his fourth heart sound cannot be identified. His apical impulse is located in the third intracostal space approximately 7 cm from his left sternal border. There are no thrills.

His lungs are clear to auscultation. His JVP is also irregularly irregular. He does not have any pedal edema.

**3.** Based on this information, which of the following diagnostic studies are essential to conduct on Mr. Jackson and why?

- A. International normalized ratio (INR)
- B. Hematocrit (HCT) and hemoglobin (Hgb), or H&H
- **C.** Electrocardiogram (ECG) and echocardiogram, preferably transesophageal (TEE)
- **D.** Thyroid panel, hepatic function, and renal function
- E. Holter monitor (outpatient telemetry)

#### **Diagnostic Results**

His INR was 1.6 (patient's goal: 2–3), his HCT was 48% (normal adult male: 42–52), and his Hgb was 16 g/dl (normal adult male: 14–18). His ECG revealed AF with an average ventricular response rate of 72 BPM (see **Figure 1-1**). No other abnormalities were noted. His TEE revealed no areas of myocardial dyskinesis, cardiomegaly, hypertrophy, abnormal chamber sizes, valvular abnormalities, or emboli. His ejection fraction was normal.

His thyroid-stimulating hormone was 5.0  $\mu$ U/ml (normal adult: 2–10), free thyroxine (FT<sub>4</sub>) was 1.3 ng/dl (normal adult: 0.8–2.8), and triiodothyronine by radioimmunoassay (T<sub>3</sub> by RIA) was 60 ng/dl (normal adult older than 50 years: 40–180).

His alkaline phosphatase (ALP) was 50 units/L (normal adult: 30-120), aspartate aminotransferase (AST) was 20 units/L (normal adult: 0-35), alanine aminotransferase (ALT) was 7.5 units/L (normal adult: 4-36), and  $\gamma$ -glutamyl transferase (GTT) was 9.5 units/L (normal adult male: 8-38).

His blood urea nitrogen (BUN) was 12.0 mg/dl (normal adult: 10–20) and his creatinine was 0.8 mg/dl (normal male: 0.6–1.2).

His Holter monitor revealed intermittent bursts of AF lasting 10 to 15 minutes occurring on average three times per day with an average resting ventricular heart rate of 72 BPM and an average ventricular heart rate with exertion of 88 BPM.



**Figure 1-1** ECG strip (lead II) revealing atrial fibrillation. *Source:* From Garcia, T.B., and Holtz, N.E. 2003. *Introduction to 12-Lead ECG*. Boston: Jones & Bartlett Learning.

**4.** Based on this information, which one of the following is Mr. Jackson's most likely diagnosis and why?

- **A.** Recurrent paroxysmal atrial fibrillation with fluctuations in INR as a result of inconsistent dietary vitamin K intake
- B. Atrial fibrillation with poor medical compliance
- **C.** Familial atrial fibrillation with fluctuations in INR as a result of inadequate vitamin C in diet
- **D.** Atrial fibrillation with normal INR
- **E.** Atrial flutter with excessive propranolol dosage responsible for palpitations and INR fluctuations

**5.** Based on this diagnosis, which of the following are appropriate components of a treatment plan for Mr. Jackson and why?

- A. Add digoxin 0.125 mg once a day
- **B.** Schedule for nodal ablation
- **C.** Schedule for pacemaker implantation
- D. Schedule for cardioversion
- **E.** Advise patient to consume the same amount of "greens" daily and adjust warfarin dose accordingly

#### CHAPTER

# 1

# CASES IN CARDIOVASCULAR MEDICINE

## **RESPONSES AND DISCUSSION**

## CASE 1-1 Alice Blankenship 1. History

**A.** Has she been experiencing vertigo, presyncope, syncope, palpitations, unusual fatigue, or headaches? ESSENTIAL

Hypertension is known as the "silent killer" because the majority of individuals afflicted with the condition are asymptomatic. However, some individuals do have symptoms associated with their hypertension. The most common ones include vertigo, presyncope, syncope, palpitations, unusual fatigue, or headaches. Therefore, it is essential to inquire whether Mrs. Blankenship has been experiencing any of these symptoms. However, it is theorized that these symptoms are not caused by the hypertension itself but reflect symptomatology that is associated with hypertensive cardiovascular disease or, in some cases, a secondary hypertension.

Cardiovascular disease (CVD), including coronary artery disease (CAD), peripheral arterial disease (PAD), renovascular disease (RVD), and heart failure, is seen at twice the rate in individuals who have hypertension compared to those who do not. Some experts estimate the risk of CVD to be doubled with every 20-mm Hg increase in systolic blood pressure (BP) and/or every 10-mm Hg increase in diastolic BP starting with a BP of 115/75. This is significant for Mrs. Blankenship because both diabetes mellitus and obesity can also increase the incidence of these conditions as well. Furthermore, the risks of these three conditions are cumulative.

**B.** Has she been experiencing weakness in one or more of her extremities, weakness of her facial muscles, difficulty talking, dysphagia, or transient monocular blindness? ESSENTIAL

These are major signs that are associated with a cerebral vascular accident (CVA) or transient ischemic attack (TIA). Having hypertension doubles a patient's risk of a CVA. Obesity and diabetes mellitus are also associated with an increased risk of CVA. These risks are cumulative.

The length of time the patient experiences these symptoms assists in determining whether they are a TIA or CVA. The current definition of a TIA includes that focal neurologic defects be completely resolved within 24 hours (the majority are resolved in 1–2 hours). However, because approximately 30 to 50% of all individuals with these symptoms have a positive neuroimaging study for a CVA within 24 hours, the American Heart Association and the American Stroke Association Collaborative Guidelines Committee recommends decreasing the length of time that the symptoms could represent a TIA (instead of a CVA) to 1 hour.

A TIA increases a patient's risk of having a CVA within the next 3 months by approximately 10 to 15%. This risk is greatest in the first 48 hours following the TIA. The first month following the TIA is associated with a greater risk than in the subsequent 2 months. Therefore, it is important to inquire whether individuals who are at risk for a CVA are experiencing symptoms suspicious for a TIA and evaluate and treat them promptly, if present.

Transient monocular blindness, or amaurosis fugax, is a TIA symptom that requires immediate evaluation because it is caused by an embolus to the central retinal artery of the ipsilateral eye. This could be from carotid stenosis or local ophthalmic artery disease.

**C.** Has she noticed any tachycardia, bradycardia, palpitations, changes in her hair or nails, skin rashes or discoloration, diaphoresis, tremor, snoring, or excessive sleepiness? ESSENTIAL

It is estimated that anywhere from 80 to 95% of all cases of hypertension are essential hypertension, otherwise known as idiopathic or primary hypertension (no identifiable cause). An estimated 5 to 20% of all cases of hypertension are secondary, meaning that they are caused by some other medical condition. Some of the more common of these conditions include fever, aortic regurgitation, aortic insufficiency, calcified arteriosclerosis, arteriolovenous shunt, hyperkinetic heart syndrome, coarctation of the aorta, renovascular disease, hypothyroidism, hyperthyroidism, parathyroid disease, hypercalcemia, acromegaly, primary aldosteronism, pheochromocytoma, Cushing syndrome, Gordon syndrome, obstructive sleep apnea, familial dysautonomia, certain types of polyneuritis, increased intracranial pressure, eclampsia, preeclampsia, excessive alcohol intake, and certain medications.

**D.** Is she taking any over-the-counter (OTC) medications, vitamins, supplements, or herbal products? ESSENTIAL

It is essential to specifically inquire about nonprescription products because many patients do not consider these medications and won't list them when asked. Some medications can cause secondary hypertension. The primary ones include oral contraceptives, estrogens, corticosteroids, nasal decongestants, tricyclic antidepressants (TCAs), monamine oxidase inhibitors (MAOIs), and nonsteroidal anti-inflammatory drugs (NSAIDs).

**E.** Does she have a family history of diabetes mellitus? NONESSENTIAL

Although a family history of type 1 diabetes mellitus is associated with an increased risk of acquiring type 1 diabetes mellitus, the risk is not as defined when it comes to type 2 diabetes mellitus. Regardless, because Mrs. Blankenship has already been diagnosed with diabetes mellitus, the question of risk factors for the disease is moot.

#### 2. Physical Examination

**A.** BP and pulse measurements in both arms in lying, sitting, and standing positions as well as BP measurement in both legs with Doppler ESSENTIAL

In evaluating a patient who has an elevated BP, it is essential to evaluate the BP in the contralateral arm as well to determine if there is a significant difference (defined as  $\geq$  10 mm Hg of the systolic and/or the diastolic BP) in the readings. The most serious cause of this degree of discrepancy is aortic dissection. It could also be representative of an arterial obstruction or compression on the ipsilateral side of the lower BP.

Although the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) utilizes the sitting BP as the reading to determine the presence of an elevated blood pressure and its category, if the BP is elevated, the JNC 7 report recommends that measurements be done in both arms lying, standing, and sitting to ensure that there are no signs of orthostatic hypotension (defined as a  $\geq$  20-mm Hg drop in systolic blood pressure [SBP] or  $a \ge 10$ -mm Hg drop in diastolic blood pressure [DBP] when measured within 3 minutes of going from supine to standing). If orthostasis is present, then the pulse should be utilized to determine if it is more likely a neurologic or peripheral process causing the condition. If the pulse increased more than 15 beats per minute (BPM), the cause is more likely to be peripheral (e.g., dehydration and/or anemia). However, if it does not increase more than 15 BPM, the cause is more likely to be neurologic (e.g., Shy-Dragger syndrome or familial dysautonomia).

Furthermore, the JNC 7 report recommends the measurement of blood pressure in at least one, but preferably both, lower extremities. The systolic values of ankle BP and the sitting BP are useful in determining the ankle-brachial index (ABI). The ABI is the SBP divided by the higher systolic arm value while sitting. Therefore, Mrs. Blankenship's ABI would be 1.1 (144 [her ankle SBP] / 136 [her highest sitting arm SBP]). Any value below 0.9 is considered abnormal and significant for PAD; if below 0.3, it generally indicates the presence of ischemia secondary to severe PAD. Essentially, the lower the ABI is, the more severe the disease.

#### B. Funduscopic examination ESSENTIAL

The fundus of the eye is the only place on the body where direct visualization of the arteries and veins is possible. The arterioles on funduscopic examination can reveal changes that are often associated with the length of time the patient has had hypertension. For example, early in the course of hypertension, the arterioles could reveal either focal or complete spasms resulting in segmental or generalized narrowing of the vessel, respectively. As the disease progresses, the arterial walls begin to thicken and the column of blood that is normally visible in the center of the arterioles changes to a narrow yellowish-red discoloration. This condition is known as "copper wiring." As the disease continues to worsen, the thickening of the walls becomes so severe that the blood column cannot be visualized; this change is referred to as "silver wiring." Arteriovenous (A-V) nicking, AV concealment, and small infarcts of the distal arteriole (called soft exudates or "cotton wool" patches because of their white, fluffy appearance) are other vascular changes from hypertension that can be visualized funduscopically. Retinal changes seen with hypertension include small hemorrhages, flame-shaped hemorrhages, and hard exudates (which are well-demarked creamy to yellowish-colored lesions).

Changes from diabetes mellitus can also be visualized in the fundus; they include deep hemorrhages, microaneurysms of the macular area, and preretinal hemorrhages.

#### C. Heart and lung examination ESSENTIAL

The heart examination is important in the evaluation of hypertension to identify signs that could be associated with secondary hypertension (e.g., cardiomegaly, splitting of the heart sounds, cardiac murmurs, an opening snap, or fourth heart sounds). The lungs need to be auscultated for signs suspicious of heart failure.

#### **D.** Evaluation of all pulses ESSENTIAL

Evaluation of the pulses can reveal secondary causes of hypertension. For example, decreased or absent peripheral pulses could indicate PAD or calcified arteriosclerosis. A renal bruit could indicate that a renovascular abnormality is the cause of the secondary hypertension. And a widened pulse pressure could be from aortic regurgitation, aortic insufficiency, fever, arteriovenous shunts, thyrotoxicosis, or hyperkinetic heart syndrome.

E. Rectal examination NONESSENTIAL

#### 3. Diagnostic Studies

**A.** Bilateral magnetic resonance imaging (MRI) of her knees NONESSENTIAL

Mrs. Blankenship's knee pain is currently controlled with an OTC agent. Therefore, she does not require further evaluation for this condition at this time. Furthermore, an MRI is not the initial imaging study of choice; it is a knee radiograph.

#### B. Urinalysis ESSENTIAL

A urinalysis is indicated to assist in ruling out any renal disease that could be responsible for Mrs. Blankenship's

hypertension. This is especially important because her diabetes places her at a greater risk for a nephropathy. A microalbumin on Mrs. Blankenship's urine should also be considered; it has not been done in the past year because of her diabetes.

#### C. Fasting lipid profile ESSENTIAL

A lipid profile is indicated not only because of her BP level but also for her other risk factors for CVD (e.g., diabetes, obesity, and age). Elevated lipids can further contribute to her risk of CVD. If they are elevated, they also need to be treated promptly and to appropriate levels.

#### D. Electrocardiogram (ECG) ESSENTIAL

An ECG is indicated to look for signs that are suspicious for ventricular hypertrophy, which is associated with hypertension; silent ischemia caused by her risk factors; or other findings associated with CVD and hypertension (e.g., arrhythmias, hyperkalemia, or hypokalemia).

The JNC 7 also recommends that the initial evaluation of a hypertensive patient include hematocrit, fasting blood glucose, serum potassium, sodium, calcium, blood urea nitrogen and/or creatinine. Additionally, they recommend a urinary albumin:creatinine ratio and a thyroid-stimulating hormone (TSH) as optional tests.

#### E. Ambulatory BP monitoring NONESSENTIAL

Currently, the primary indication for ambulatory BP monitoring is when it is suspected that the patient is experiencing "white coat syndrome" (the patient's BP is elevated while in the clinical setting but is normal in all other situations). Because Mrs. Blankenship's daughter checked it at home and it was essentially the same as it was during her clinical visits, this condition is unlikely.

The JNC 7 recommends the use of ambulatory monitoring in other situations as well (e.g., treatment-resistant hypertension, symptomatic hypotension, orthostatic hypotension, autonomic failure, and episodic hypertension). Because it does not appear that Mrs. Blankenship is afflicted by any of these conditions at this time, ambulatory BP monitoring is not currently indicated for her.

#### 4. Diagnosis

Mrs. Blankenship's type 2 diabetes mellitus was diagnosed via her history and her mild glucosuria. Her obesity was diagnosed on the basis of her body mass index (BMI). Genderspecific tables are available that can quickly provide the patient's BMI by plotting height against weight. However, these tables generally represent the height in centimeters and the weight in kilograms. Because in the United States patients are generally measured in inches and weighed in pounds, conversions to metric measurements must be completed before one can utilize the table. Even when these tables are in inches and pounds, these tables must be readily accessible if they are going to be used to determine the patient's BMI. Therefore, utilizing the following formula might be the quickest method to calculate the patient's BMI when using weight in pounds and height in inches:

 $\frac{\text{Patient's weight (in pounds)} \times 703}{\text{Patient's height (in inches)}^2}$ 

An even quicker method to make this calculation in the clinical setting is:

#### [(Patient's weight in pounds × 703) ÷ Patient's height in inches] ÷ Patient's height in inches

For example, Mrs. Blankenship is 5'3" (63") tall and weighs 165 lb. Her BMI would be:

#### [(165 × 703) ÷ 63] ÷ 63 = 29

This would place her BMI in the upper end of the obese category as defined by the National Institutes of Health (NIH). The NIH classification system for obesity according to BMI can be found in **Table 1-1**.

**A.** White coat syndrome producing pseudo-hypertension INCORRECT

This condition was essentially ruled out because her athome blood pressure measurements are fundamentally equivalent to her measurements taken in the clinic.

#### B. Prehypertension CORRECT

According to the JNC 7, the BP readings listed in **Table 1-2** correspond to the diagnostic category for BP. Because all of Mrs. Blankenship's sitting brachial SBPs and DBPs were in the prehypertension range, this is her most likely diagnosis. If the SBP and the DBP values are found in different categories, the higher level is utilized. For example, a BP of 122/90 would be considered hypertension, stage 1.

#### C. Hypertension, stage 1 INCORRECT

According to the JNC 7 classification scheme, Mrs. Blankenship does not meet the diagnostic criteria for hypertension, stage 1, as defined in Table 1-2.

#### D. Hypertension, stage 2 INCORRECT

According to the JNC 7 classification scheme, Mrs. Blankenship does not meet the diagnostic criteria for hypertension, stage 2, as defined in Table 1-2.

#### E. Diabetic nephropathy-induced hypertension INCORRECT

She does have type 2 diabetes mellitus and, as outlined earlier, prehypertension because her BP has consistently been between 120 and 139 mm Hg systolic and/or 80 and 89 mm Hg diastolic. However, it is unlikely that it has a renovascular cause because her physical examination does not reveal a renal bruit and her urinalysis is negative for protein.

**Table 1-1**National Institutes of Health ClassificationSystem for Obesity According to Body Mass Index

Body Mass Index	Classification
18.5–24.9	Normal
25.0–29.9	Overweight
30.0–34.9	Class 1 obesity
35.0–39.9	Class 2 obesity
≥ 40	Class 3 (extreme) obesity

**Table 1-2** Blood Pressure (BP) Readings and Diagnostic

 Categories
 Pressure (BP) Readings and Diagnostic

Category	Systolic BP (mm Hg)		Diastolic BP (mm Hg)
Normal	< 120	and	< 80
Prehypertension	120–139	or	80–89
Hypertension, stage 1	140–159	or	90–99
Hypertension, stage 2	≥ 160	or	≥ 100

#### 5. Treatment Plan

**A.** Dietary modification including low-sodium, low-fat, Dietary Approaches to Stop Hypertension (DASH) eating plan CORRECT

With a history of either diabetes mellitus or chronic kidney disease, the JNC 7 recommends treating patients with prehypertension as well as hypertension. The goal of treatment is BP less than 140/90 mm Hg, unless the aforementioned conditions are present—then the goal is BP less than 130/80 mm Hg. The first step in the treatment of a patient with prehypertension and stage 1 hypertension is lifestyle modification, including dietary restrictions such as following the DASH diet, restricting sodium, restricting caffeine, and limiting or eliminating alcohol. Furthermore, dietary modification is essential in addition to exercise and pharmacological interventions in stage 2 hypertension and other treatments of secondary causes of hypertension. Finally, dietary modification should be continued if a patient who has prehypertension or stage 1 hypertension requires medication therapy.

**B.** Start a regular aerobic exercise program, with a goal of 30 minutes daily CORRECT

This recommendation comes from the JNC 7 for the initial treatment of and as an adjunct to medication in all patients being treated for prehypertension and hypertension.

**C.** Start triamterene 37.5 mg with hydrochlorothiazide 50 mg once every morning INCORRECT

A diuretic is recommended as a first-line agent for the medical management of hypertension. However, the hydrochlorothiazide dose should never exceed 25 mg/day.

#### D. Start valsartan 80 mg once a day INCORRECT

If Mrs. Blankenship required medication at this time for her BP, this would be an excellent choice. Angiotensin receptor blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors are good first-line choices, especially in patients with diabetes because they offer some degree of renal protection (however, this indication is not approved by the US Food and Drug Administration [FDA]). ARBs tend to be a better choice than ACE inhibitors because there is a lower incidence of angioedema and cough.

Regardless, with prehypertension, a trial of 1 to 3 months of lifestyle modifications via diet/exercise and frequent athome and in-office BP measurements are the most appropriate treatment and are approved by the JNC 7. However, if this is not effective or her BP is elevating despite these lifestyle changes, then a medication should be instituted. According to the JNC 7, appropriate first-line agents for patients with diabetes and hypertension include thiazide diuretics, ACE inhibitors, ARBs, calcium channel blockers (CCBs), and beta-blockers.

**E.** Substitute ibuprofen with acetaminophen 500 mg two pills twice a day CORRECT

Although she is on a very small dose of ibuprofen, it could be enough to adversely affect her BP. Furthermore, this is a nonselective NSAID. If continuation of this medication is indicated, she should probably be on a proton pump inhibitor (PPI) for gastrointestinal protection because she is likely to require long-term usage. Treating hypertension to goal results in a decreased risk of CVA of 35 to 40%, MI of 20 to 24%, and heart failure of 50%. Most patients require at least two medications to reach goal.

## **Epidemiologic and Other Data**

Estimates of the number of individuals with hypertension in the United States (defined as a systolic BP of  $\geq$  140 and/or a diastolic BP of  $\geq$  90) range from approximately 55.4 million to 66 million. The overall incidence is increasing in the United States; experts attribute this to the increasing number of obese individuals and the advancing age of our population, which are well-known risk factors for hypertension. It is estimated that normotensive individuals at the age of 55 years have a 90% lifetime risk for the development of hypertension. It appears that the acquisition of hypertension is a combination of genetic and lifestyle factors. By race, non-Hispanic blacks have the highest incidence, followed by non-Hispanic whites, and then Mexican Americans.

## CASE 1-2 Betty Crane 1. History

**A.** Has she ever experienced chest pain, pressure, or discomfort; presyncope or syncope; dyspnea; or fatigue with exercise? ESSENTIAL

The American Heart Association (AHA) has developed a consensus statement regarding the preparticipation cardiovascular screening for competitive athletes because of the increasing number of sudden cardiac death in athletes. Its purpose is to screen for individuals who might be at risk for sudden cardiac death and perform additional cardiac testing before making the recommendation that the patient should be able to compete or not. This 12-component screening tool consists of four questions regarding potential symptoms, two questions regarding the patient's personal medical history, and two questions regarding the patient's family history, and defines four essential components required on the physical examination. Additionally, the AHA recommends that for middle and high school students the history be verified with a parent. All positive responses would need to be discussed in detail. This choice asks about these four symptoms.

**B.** Has she ever been diagnosed with hypertension or a heart murmur? ESSENTIAL

These are the two personal medical history questions on the AHA screening guideline.

**C.** Is there a family history of cardiac death or cardiac disability before the age of 50 years? ESSENTIAL

This is one of the two questions pertaining to family history recommended by the AHA consensus statement.

D. Is there any known heart disease in the family? ESSENTIAL

This is the second question recommended by the AHA consensus statement regarding the patient's family history. Additionally, it would probably be useful to inquire not only about cardiac disease in the family but also about specific conditions (e.g., hypertrophic or dilated cardiomyopathy, prolonged QT syndromes, other ion channelopathies, significant arrhythmias, sudden cardiac death, and Marfan syndrome).

**E.** When does she plan on becoming sexually active? NONESSENTIAL

This question does not have anything to do with the patient's ability to participate in sports and is inappropriate as it implies she should be sexually active.

#### 2. Physical Examination

**A.** Funduscopic examination (or preferably slit-lamp examination if available) ESSENTIAL

The four essential components of the physical examination, as recommended in the AHA consensus statement regarding the cardiovascular preparticipation evaluation for competitive athletes, include seated blood pressure in both arms; auscultation of the heart supine, standing, and with vagal maneuver; bilateral femoral pulse evaluation; and observation for any signs or symptoms suspicious of Marfan syndrome (MFS).

Therefore, a funduscopic (or the better procedure, a slitlamp) examination is indicated to look for optical signs that could be consistent with MFS. The most common finding is ectopia lentis (the downward displacement of the lens of the eye). Although generally not progressive, it is associated with the development of cataracts. Other ophthalmologic findings could include retinal detachment, retinal tears, lattice degeneration, optical globe elongation, and myopia.

B. Ear and hearing examination NONESSENTIAL

#### C. Heart evaluation ESSENTIAL

This is one of the areas that the AHA recommends be very carefully evaluated. During the cardiac examination, attention must be focused not only in trying to hear cardiac murmurs but also in attempting to identify other signs suggestive of valvular disease, cardiomegaly, cardiac arrhythmias, extra heart sounds, abnormal splitting of heart sounds, clicks, thrills, parasternal lifts, and changes in heart sounds and/or murmurs (if present). The AHA recommends that the patient's heart be examined supine, standing, squatting, and with a Valsalva maneuver (which increases the intrathoracic pressure). The heart should also be auscultated during respiration and in the left lateral decubitus position (if an abnormal mitral sound is heard or mitral stenosis is suspected). These different maneuvers will enhance or decrease certain heart sounds and cardiac murmurs.

For example, when the patient stands upright or performs a Valsalva maneuver, murmurs tend to lessen in intensity and duration, except for those caused by mitral valve prolapse (it generally becomes louder and longer) and hypertrophic cardiomyopathy (it generally becomes louder).

However, when the patient squats or raises his or her legs while supine, the majority of cardiac murmurs become louder, except for those caused by mitral valve prolapse and hypertrophic cardiomyopathy (these become much softer and can even disappear completely). Isotonic and isometric exercise tends to cause murmurs associated with valvular stenosis (especially mitral and pulmonic) to worsen; however, isometric exercise will only cause regurgitation murmurs to worsen (especially mitral and aortic). A murmur caused by hypertrophic cardiomyopathy will only worsen with hand-grip exercise when maximum exertion is nearly achieved.

Inspiration often intensifies the sound and duration of systolic murmurs caused by tricuspid regurgitation and pulmonary stenosis and diastolic murmurs caused by tricuspid stenosis and pulmonary regurgitation. Expiration often intensifies the sound and duration of systolic murmurs caused by mitral regurgitation and aortic stenosis and diastolic murmurs caused by mitral stenosis and aortic regurgitation.

Bilateral BP measurements are required to determine if they are equivalent. If they are greater than 10 mm Hg, either systolic or diastolic, between the arms, the patient requires additional evaluation to determine the cause (e.g., aortic dissection, arterial obstruction, or arterial compression on the ipsilateral side of the lower BP).

**D.** Examination of femoral pulse and abdominal aorta ESSENTIAL

Evaluation of the femoral pulse is also indicated by the AHA guidelines. Decreased pulses could indicate peripheral artery disease and occlusions or obstructions to the arteries in the legs. Comparison of the radial pulse with the ipsilateral femoral pulse evaluates primarily for possible coarctation of the aorta. Femoral pulses are weaker than the radials in this condition.

The aorta needs to be evaluated if the patient has abnormal aortic valvular sounds or is suspected of having Marfan syndrome.

**E.** Measurement of arm span from tip of left middle finger to tip of right middle finger and evaluation for arachnodactyly, joint hyperextensibility, joint laxity, and scoliosis ESSENTIAL

Since Betty's physical appearance is suspicious for Marfan syndrome, these additional components should be performed. An arm span greater than the patient's height, arachnodactyly, joint hypermobility, and scoliosis are all signs that could indicate the presence of Marfan syndrome.

Other findings that could be associated with MFS include skin laxity, striae atrophicae (especially on the buttocks and shoulders), pes planus or high pedal arches, high-arched palate, kyphosis, anterior chest asymmetry (such as pectus excavatum or pectus carinatum), spontaneous pneumothorax, dural ectasis, inguinal hernias, incisional hernias, abnormal mitral and/or aortic heart valve leaflets, elongated chordae tendineae, aortic root dilation with dissection and/or rupture, and ocular abnormalities as described earlier.

#### 3. Diagnostic Studies

#### A. Electrocardiogram (ECG) ESSENTIAL

An ECG provides information regarding the presence of an arrhythmia, left ventricle hypertrophy, atrial hypertrophy, electrolyte abnormalities, conductive system defects, ischemia, acute infarction, and old infarction(s), with the latter three being extremely rare in adolescents.

#### B. Echocardiogram ESSENTIAL

The echocardiogram provides greater detail regarding the valvular components, the aortic root, and wall thickness. It is indicated by Betty's mitral and aortic murmurs.

#### C. Chest x-ray (CXR) ESSENTIAL

A CXR is indicated because Betty had findings on her physical examination suspicious for MFS. It will provide information regarding the presence of cardiomegaly, pectus excavatum, pectus carinatum, kyphosis, and thoracic scoliosis, which can be features of the disease.

#### D. Abdominal ultrasound ESSENTIAL

The abdominal ultrasound is indicated because Betty has an aortic murmur. Its primary purpose is to evaluate her abdominal aorta for calcification, aneurysm, and/or early dissection.

#### E. Cardiac-specific troponin T and I NONESSENTIAL

Cardiac-specific troponin T and I are biochemical markers that are utilized to detect cardiac ischemia. Because Betty does not have any signs or symptoms suspicious for angina or MI, these tests are not indicated.

#### 4. Diagnosis

A. Loeys-Dietz aneurysm syndrome (LDAS) INCORRECT

This syndrome is considered to be one of the heritable disorders of connective tissue. Like Marfan syndrome, LDAS is associated with a mutation of chromosome 15, but instead of it involving a mutation of the fibrillin-1 (FBN1) gene, it affects the transforming growth factor- $\beta$  receptor 1 (TGFB1) and the transforming growth factor- $\beta$  receptor 2 (TGFB2) genes. Although it is associated with the formation of abdominal aneurysms, it affects the ascending aorta more than the descending aorta, as seen in MFS. Additionally, it can be associated with tortuous arteries, hypertelorism, and a cleft palate. Hence, it can be eliminated as Betty's most likely diagnosis.

#### B. Klinefelter syndrome INCORRECT

Klinefelter syndrome occurs exclusively in males and is also known as "the extra X-chromosome disease" because its karyotype is typically 47,XXY. Boys with Klinefelter syndrome appear to be typical males until puberty. At that time, they start to grow very long arms and legs, giving them an appearance similar to individuals with MFS. However, they do not exhibit the characteristic cardiovascular and ocular abnormalities. They do tend to have gynecomastia, a feminine pattern of hair distribution, hypogonadism, small testes, and infertility. Because Klinefelter syndrome only affects males, this is not Betty's most likely diagnosis.

#### C. Marfan syndrome (MFS) CORRECT

Marfan syndrome is a connective tissue disease. It is characterized by abnormalities of the cardiovascular, musculoskeletal, and ocular systems. Traditionally, if there is a known family history of Marfan syndrome, the diagnosis can be made when an individual has at least two of the three systems involved with typical signs and symptoms as described earlier. However, if there is no family history, then the patient must have characteristic signs and symptoms of musculoskeletal involvement plus ocular and cardiovascular symptoms, with one of the following major criteria: aortic root dilation, aortic dissection, or ectopia lentis. Thus, this is Betty's most likely diagnosis.

Because specific mutations in the FBN1 gene on chromosome 15 are not always present and the symptomatology of other heritable disorders of connective tissue syndromes/diseases can meet these limited criteria, there is an international movement recommending only the Ghent criteria be utilized to diagnose MFS. It emphasizes the major criteria—the presence of a minimum of four skeletal abnormalities, ectopia lentis, dilation of the ascending aorta, dural ectasia, and a blood relative who also has these abnormalities; however, it is balanced with a combination of minor criteria as well to establish the diagnosis of MFS. Still, other experts in the field feel that if the FBN1 gene abnormality is not present, the patient has another condition (e.g., type II Marfan or Loeys-Dietz aneurysm syndrome).

#### **D.** Ehlers-Danlos syndrome (EDS) INCORRECT

EDS is another heritable disorder of connective tissue. It is characterized by hyperelasticity of the skin and hypermobility of the joints, both of which can be seen with MFS. Additionally, mitral valve prolapse, aortic aneurysms, kyphosis, scoliosis, and hernias are frequently seen. However, unlike MFS, the predominate ocular defect is dependent upon the form of disease the patient has—for example, patients with ocular-scoliotic EDS can have complete eye rupture with very little trauma, and individuals with EDS associated with respiratory impairment can have blue-colored sclerae. Additionally, patients with EDS tend to have bleeding abnormalities. Therefore, this can be eliminated as Betty's most likely diagnosis.

#### E. Congenital contractural arachnodactyly (CCA) INCORRECT

CCA is another heritable disorder of connective tissue. It has symptoms that are partially consistent with MFS and partially consistent with osteogenesis imperfecta (OI) but does not completely fulfill the criteria for either. It can be ruled out as Betty's most likely diagnosis because she does not have any joint contractures, which are always associated with CCA.

#### 5. Treatment Plan

#### A. Annual echocardiogram CORRECT

An annual echocardiogram is important to monitor the progression of Betty's mitral and/or aortic regurgitation as

well as the diameter of her aortic root. In some cases, more frequent echocardiograms may be required.

**B.** Annual eye examination, including a slit lamp, by an oph-thalmologist CORRECT

An annual eye examination by an ophthalmologist primarily monitors for ectopic lentis, retinal detachment, retinal hemorrhages, amblyopia, and other ocular abnormalities caused by MFS.

**C.** Subacute bacterial endocarditis (SBE) prophylaxis for dental procedures INCORRECT

Unless something unusual appears on Betty's subsequent echocardiogram or she requires a valve replacement, she will not require antibiotic prophylaxis for dental procedures.

When the latest American Heart Association's guidelines for SBE prophylaxis were released in 2007, the indications for dental procedures included: history of infective endocarditis, presence of a prosthetic heart valve or a prosthetic material utilized to repair a heart valve, cardiac transplant patients who develop a valvulopathy, and the following congenital heart diseases (CHDs): unrepaired CHD with cyanosis, including palliative shunts and conduits; 6 months following completely repaired CHD when a prosthetic material or device is utilized regardless of procedure used for the intervention; and repaired CHD with residual defects at the site or adjacent to the site inhibiting endothelialization.

These guidelines have subsequently been modified, but not re-written, to state that the only requirement for SBE prophylaxis for dental procedures is for those that could involve manipulation and/or perforation of the gingiva, oral mucosa, and/or periapical areas of the teeth in individuals whose underlying cardiac abnormality places him or her at the highest risk of developing adverse outcomes if infectious endocarditis occurred.

#### D. Annual orthopedic evaluation CORRECT

The annual orthopedic examination provides for the monitoring of scoliosis and permits appropriate interventions to prevent deformities. In general, bracing and physical therapy are begun if the degree of scoliosis reaches 20°; surgery is generally required if it reaches 45°.

**E.** Propranolol 10 to 20 mg twice a day initially; then, titrate every 1 to 2 weeks (to a maximum daily dose of 240 mg) to maintain exercise heart rate below 100 BPM CORRECT

A beta-blocker, like propranolol, should be given to Betty as it appears to slow the progression of the aortic dilation and hence the need for cardiac surgery.

#### **Epidemiologic and Other Data**

Type I Marfan syndrome is a genetic disorder that is generally associated with a mutation of the FBN1 gene on chromosome 15. Approximately 75% of the cases are inherited via autosomal dominant traits. The remainder of the cases consist of new sporadic mutations. The incidence is estimated to be approximately 1 per 3000 to 5000 individuals in the United States. There does not appear to be an increased incidence in any particular race.

## **CASE 1-3**

## Carl Diaz

## 1. History

A. Has Carl ever had his BP checked? ESSENTIAL

It is important to inquire about Carl's previous BP readings because of his elevated value today. An elevated BP on two occasions is considered to be diagnostic for hypertension.

This is important because having hypertension doubles the patient's risk for CAD, CVA, PAD, heart failure, and renal failure. Multiple clinical trials have proven that normalizing the BP level reduces the risk of developing these complications.

Although it is the standard of care to check the BP of all children at every visit after the age of 3 years, the only organization that makes that recommendation is the National Heart, Lung and Blood Institute (NHLBI). The American Academy of Family Physicians (AAFP) believes that there is insufficient evidence available to make a recommendation for or against routine BP measurements in children to screen for hypertension. However, they recommend checking BP every other year if normal, annually if prehypertensive, and as required if hypertensive. The U.S. Preventative Services Task Force (USP-STF) recommends screening for hypertension beginning at the age of 18 years; however, they do not make a recommendation for frequency.

**B.** Was Carl's cholesterol test done while he was fasting or nonfasting? NONESSENTIAL

Total cholesterol levels do not vary significantly regardless of whether they are done in the fasting or nonfasting state. However, it is generally recommended that the patient fast for 8 to 12 hours before having a "cholesterol test" because that term (although technically incorrect) generally involves obtaining an entire lipid panel, which measures not only total cholesterol but also its various components (i.e., high-density lipoproteins [HDLs], low-density lipoproteins [LDLs], very low-density lipoproteins [VLDLs], and non-HDL cholesterol), plus the triglycerides. For an accurate triglyceride measurement, the test must be performed in the fasting state because triglyceride levels can fluctuate significantly during the day.

#### C. What is Carl's mother's cholesterol level? NONESSENTIAL

The AHA expanded upon the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults and developed recommendations for screening children and adolescents (ages 2–18) for hyperlipidemia based on personal and family history. One of the criteria is either parent having a total serum cholesterol measurement of greater than or equal to 240 mg/dl. Because Carl requires screening based on his father's level, his mother's findings are not relevant at this time.

The other criteria are a positive family history of CAD and a personal risk for CAD without any parental risks, defined as one having one or more of the following: hypertension, obesity, diseases known to be associated with hyperlipidemia (e.g., pancreatitis, hepatitis, diabetes mellitus, or Cushing syndrome), medications known to produce hyperlipidemia (e.g., carbamazepine,

#### Case 1-3 Responses and Discussion

beta-blockers, glucocorticoids, growth hormone, or isotretinoin), or detrimental lifestyle habits (e.g., smoking cigarettes, drinking alcohol, or sedentary lifestyle).

The USPSTF believes that there is not sufficient evidence to recommend for or against routine screening of children and adolescents, regardless of risk factors. However, they do support the screening of high-risk men who are 20 and 35 years old and high-risk women who are 20 to 45 years old; they do not make any recommendations regarding screening frequency if normal. After 35 years of age in men and 45 years of age in women, they recommend "periodic" screening depending on risk factors.

The NCEP III recommends routine screening every 5 years, if normal, beginning at the age of 20 years for both men and women. The AAFP recommends screening at undetermined intervals beginning at the age of 35 years for men and 45 years for women.

**D.** Has either of Carl's parents and/or grandparents been diagnosed with a myocardial infarction (MI), coronary artery disease (CAD), sudden cardiac death (SCD), a cerebral vascular accident (CVA), or peripheral vessel disease (PVD) prior to the age of 55 years? ESSENTIAL

According to the AHA, a child or adolescent should have a fasting blood lipoprotein analysis if his or her parents and/or grandparents have had a premature MI, CAD, SCD, CVA, and/or PVD (defined as occurring before the age of 55 years).

Furthermore, even if they are not premature, the presence of any of these conditions in a blood relative increases the later risk of these diseases and should be noted.

**E.** Have his parents and/or grandparents been diagnosed with diabetes mellitus (including gestational diabetes) or any other serious medical condition(s)? ESSENTIAL

This is important because the American Diabetes Association recommends routine screening for diabetes mellitus every other year for children starting at the age of 10 years (or the onset of puberty if before the age of 10 years) if overweight (defined as a BMI > 85th percentile for either age and gender or weight for height OR weight > 120% of ideal height) PLUS the presence of two additional risk factors: type 1 or type 2 diabetes mellitus in any first- or second-degree blood relative (genetic risk is greatest with type 1 diabetes mellitus), maternal gestational diabetes mellitus (GDM), high-risk race (Native American, African American, Hispanic American, Asian American, or Pacific Islander), or any signs, symptoms, or conditions associated with insulin resistance (e.g., hypertension, hyperlipidemia, significantly elevated triglyceride levels, polycystic ovarian disease, and visceral distribution obesity).

No other organization makes a recommendation to routinely screen children or adults. However, the AAFP and the USPSTF do make the recommendation to screen all adults with hypertension with fasting plasma glucose (FPG) measurements for type 2 diabetes mellitus.

#### 2. Physical Examination

A. Ears, nose, and throat (ENT) examination NONESSENTIAL

B. Thyroid palpation ESSENTIAL

Even though a child or adolescent does not require an evaluation for a secondary cause of hyperlipidemia unless he

or she has failed 6 to 12 months of lifestyle modification or is symptomatic, Carl still needs his thyroid palpated because of the association of thyroid disease and hypertension.

#### C. Heart examination ESSENTIAL

A careful heart examination looking for the abnormalities outlined in Case 1-2 is indicated for Carl because of his weight, BP, cholesterol level, and family history.

#### D. Abdominal examination ESSENTIAL

Carl should have an abdominal examination primarily because of his elevated BP. In addition to the routine abdominal examination, particular attention should be directed to the aorta (to ensure normal pulsation and size), the renal arteries (to assess for bruits, which could indicate renovascular disease), the kidney and adrenal area (to assess for abnormal sizes and/or masses, which could indicate renal failure, adrenal tumors/masses, or pheochromocytoma), and the bladder (to assess for enlargement, as would be seen with an obstructive uropathy) because these are just a few of the potential causes of secondary hypertension.

#### E. Assessment of pulses ESSENTIAL

Assessment of the pulses would help ensure Carl is getting good and equal blood flow to all parts of his body. However, it is important to remember that bruits generally disappear when the degree of vascular occlusion becomes greater than 70%; hence, the lack of this abnormality does not necessarily equate with the lack of disease.

Additionally, the strength of the femoral pulses needs to be compared to that of the ipsilateral radial pulse to evaluate for coarctation of the aorta, as discussed in the previous case.

#### 3. Diagnostic Studies

#### A. Fasting blood lipoprotein analysis ESSENTIAL

The American Heart Association Guidelines recommends that if the initial total cholesterol is greater than 200 mg/dl, then a lipoprotein analysis should be conducted.

#### B. Total cholesterol only NONESSENTIAL

According to the AHA guidelines, a high-risk adolescent should be screened with a total cholesterol level. However, because Carl already had an elevated screening total cholesterol, an additional one is not indicated (he requires a fasting lipoprotein analysis which includes a total cholesterol).

#### C. Fasting plasma glucose (FPG) ESSENTIAL

Because Carl is older than the age of 10 years, his weight is greater than 120% for his ideal height and above the 85th percentile of BMI for height (however, the use of BMI in individuals younger than 18 years of age is discouraged by the Centers for Disease Control and Prevention [CDC] to prevent "labeling" a child as "obese"), and his maternal grandfather has diabetes, he meets the criteria set forth by the American Diabetes Association to be screened with an FPG.

#### D. C-reactive protein (CRP) NONESSENTIAL

CRP is a nonspecific measurement of inflammation in the body, including that associated with endothelium dysfunction. Therefore, it can be utilized in conjunction with the patient's cholesterol and cardiovascular risk factors to provide additional information of a patient's future potential of a

cardiovascular event. However, the ideal test is the highsensitivity CRP (hs-CRP), not just a CRP, because it can detect much smaller levels of inflammation. Nevertheless, neither is indicated as a part of the cardiovascular risk determination in the assessment of children and/or adolescents.

E. Glycosylated hemoglobin (Hgb A1C) NONESSENTIAL

The Hgb A1C test is a diabetes treatment management tool that is used to monitor the patient's blood sugar level, and hence control, over the past 3 months. It is not indicated as a screening tool at this time; however, there is an ongoing discussion for its potential use as such.

#### 4. Diagnosis

**A.** Hyperlipidemia, hypertension, and type 1 diabetes mellitus INCORRECT

Carl's total cholesterol was 222 mg/dl, his LDL 160 mg/dl; his HDL 30 mg/dl, his VLDL 32 mg/dl, and his triglycerides 250 mg/dl. Because this was his second total cholesterol measurement, he can be considered to be hyperlipidemic by adult and more appropriately adolescent standards. The AHA and NCEP developed the levels listed in **Table 1-3** regarding hyperlipidemia in children and adolescents (ages 2–18 years).

In adolescents, hypertension is defined as a BP being greater than the 95th percentile for height on at least two occasions. Carl's maximum BP at the 95th percentile would be 135/85 mm Hg; therefore, he can be considered hypertensive.

Prehypertension is defined in adolescents as being between the 90th and 95th percentile for height OR greater than 120/80 mm Hg on two or more occasions for Carl.

Carl's FPG was normal; therefore, he cannot be considered to be diabetic. Hence, this choice is not his most likely diagnosis.

**B.** Hyperlipidemia, hypertension, and type 2 diabetes mellitus INCORRECT

Carl does meet the diagnostic criteria for hyperlipidemia and hypertension in an adolescent. However, his FPG is not of a sufficient level to diagnose him as having diabetes mellitus. In addition, with his other coexisting medical conditions and a lack of a family history of type 1 diabetes mellitus, if he did have diabetes, he would more than likely have premature type 2. Nevertheless, per the aforementioned definitions, this is also not Carl's most likely diagnosis.

**C.** Hyperlipidemia, hypertension, obesity, and type 2 diabetes mellitus INCORRECT

Carl's diagnoses consist of hyperlipidemia and hypertension as defined earlier.

**Table 1-3**Hyperlipidemia in Children and Adolescents(Ages 2 to 18 Years)

	Total Cholesterol	Low-Density Lipoprotein Cholesterol
Acceptable	< 170	< 110
Borderline	170–199	110–129
High	≥ 200	≥ 130

Regarding the diagnosis of obesity, many organizations now consider obesity in adolescents to be a BMI for age and gender that is greater than or equal to the 95th percentile. Carl's BMI of 37.4 falls significantly above his projected 95th percentile of BMI for age of 26.5; therefore, it would be appropriate to diagnose him as obese. Additionally, he meets the criteria of obesity defined in individuals younger than the age of 18 years as being greater than 120% of weight for ideal height.

Overweight is classified by most as a BMI for age and gender that is greater than or equal to the 85th percentile but less than the 95th percentile. However, as stated previously, the CDC prefers utilizing the terminology in individuals younger than the age of 20 years as "overweight" if their BMI for age and gender is greater than or equal to the 95th percentile and "at risk of overweight" if their BMI for age and gender is greater than or equal to the 85th percentile but less than the 95th percentile. Currently the Expert Committee on the Assessment, Prevention, and Treatment of Childhood and Adolescent Overweight and Obesity is working with the CDC to develop consistent terminology. Therefore, the more appropriate diagnosis would be overweight for age.

Regardless, he has a normal FPG; hence, he does not meet the diagnostic criteria for diabetes mellitus. Therefore, this is not his most likely diagnosis.

**D.** Hyperlipidemia, hypotension, and obesity INCORRECT

For the aforementioned reasons regarding obesity, and Carl's BP being high, not low, this is not his most likely diagnosis.

E. Hyperlipidemia, hypertension, and overweight for age CORRECT

By the aforementioned definitions, this is Carl's most likely diagnosis.

#### 5. Treatment Plan

**A.** Repeat total lipoprotein analysis in 1 month to obtain LDL average to utilize for monitoring and treatment CORRECT

According to the AHA guidelines, if the total cholesterol is greater than 200 on the initial screening, then a lipoprotein analysis should be conducted. That analysis should then be repeated in approximately 1 month to obtain the patient's average LDL value. The average LDL value from these two measurements is what his treatment will be based on. His current LDL goal is less than 110 mg/dl or a minimum of less than 130 mg/dl.

**B.** Initiate a program of lifestyle modification with a low-fat, low-cholesterol, low-sodium diet; decreased caloric diet; and regular exercise program with goal of 30 minutes of aerobic exercise on most days of the week CORRECT

Lifestyle modification is the cornerstone of treatment for all of Carl's current conditions: overweight for height, hyperlipidemia, and hypertension. Even if lifestyle modifications alone fail to meet his treatment goals, they are still going to be an essential component of any treatment plan for any of these conditions.

**C.** Start niacin 500 mg once a day for 2 weeks; then increase to 500 mg twice a day INCORRECT

Medication management for children and adolescents with hyperlipidemia is not indicated until a minimum of 6 to 12 months of dietary modification has failed to be effective. Then, it is only indicated if the LDL is greater than or equal to 190 mg/dl OR the LDL is greater than or equal to 160 mg/dl AND there is a positive family history of premature CAD AND the patient has at least two other risk factors present (hypertension, smoking, diabetes, male gender, sedentary lifestyle, or the suspicion of familial hyperlipidemia). The ideal treatment goal would be an LDL of less than 110 mg/dl; however, less than 130 mg/dl would be acceptable. Statins are currently considered to be the first-line drug and should never be used unless the child is older than 10 years. Other appropriate choices include niacin and bile acid sequestrants. One of these latter two options might soon be the drug of choice as more and more adverse effects are being linked to the statins. However, most would be considered "off-label" usage as few are FDA approved for use in individuals younger than the ages of 18 to 21 years. Those with current FDA approval to be used in children 10 years of age or older include atorvastatin, lovastatin, pravastatin (indication starting at 8 years old), cholestyramine, ezetimibe, and simvastatin.

**D.** Thyroid stimulation test (TSH), liver function studies (LFTs), creatinine, and urine protein INCORRECT

These tests are indicated in adults to determine if there is a coexisting medical condition that could be responsible for or contributing to the elevated cholesterol level. The TSH is to screen for hypothyroidism. The LFT will evaluate for hepatic conditions (e.g., hepatitis and cholestasis). The serum creatinine and the urine protein will assist in determining whether chronic renal failure or nephrotic syndrome is present. If the triglycerides are elevated, then an FPG is also indicated to rule out type 2 diabetes mellitus.

However, according to the AHA guidelines, children do not need to be screened for any secondary cause of hyperlipidemia unless they have failed to respond to 6 to 12 months of lifestyle modifications or were symptomatic. Therefore, these tests are not currently indicated for Carl.

**E.** Start triamterene 37.5 mg with hydrochlorothiazide 50 mg once every morning INCORRECT

Medical management of hypertension in adolescents (and children) is only indicated if lifestyle modifications fail to decrease the BP to acceptable levels, the adolescent has coexisting type 1 or type 2 diabetes mellitus, the hypertension is caused by another condition (secondary hypertension), the patient has evidence of end-organ damage, or the patient is symptomatic. Because Carl does not fall into any of these groups, he does not require medication at this time.

Additionally, the dosage of hydrochlorothiazide should not exceed 25 mg, because studies indicate that beyond that dosage the BP-lowering effects are negated or reversed. Therefore, instead of increasing hydrochlorothiazide to 50 mg, starting a second agent with an alternative pathway of action is preferable.

#### **Epidemiologic and Other Data**

Lipoprotein levels, especially triglycerides, do not remain constant over time. This partially explains the discrepancies between the recommendations of the various organizations as to the optimal time to initiate screening and the appropriate screening interval in adults who have normal levels. Furthermore, it is the justification that some organizations use to never screen a child or adolescent, regardless of levels.

The exact incidence of hypertension in children and adolescents is unknown. Even though the majority of the cases are caused by secondary hypertension, the incidence of essential (or primary) hypertension is increasing in children and adolescents in the United States. This is believed to be associated with the increased rates of overweight and obesity in these groups. African American children, as well as adults, are the racial group with the greatest incidence in the United States.

As with hypertension, the exact incidence of type 2 diabetes mellitus in adolescents is unknown. However, it is also increasing, and it is theorized that that increase is related to the increased rate of overweight and obesity among US teens.

It is estimated that approximately 17% of children and adolescents are overweight in the United States. This equates to approximately 4.2 million children between the ages of 6 and 11 years (with 1.9 million of these being girls) and 5.7 million adolescents (of which 2.6 million are female).

In the last 40 years, the incidence in grade school–aged children being overweight has increased nearly 350%. In the past 35 years, the incidence of overweight adolescents has increased nearly 300%. It is estimated that if these trends continue, by the year 2015, one out of every four children in the United States will be overweight.

## CASE 1-4 Dale Elliott 1. History

**A.** Where is the chest pain located, does it radiate, what is its nature, what is its intensity, is it constant or intermittent, is it worsening, and are there any known aggravating or alleviating factors? ESSENTIAL

Chest pain can occur with a vast array of cardiac, pulmonary, gastrointestinal, musculoskeletal, dermatologic, metabolic, neurologic, and psychological conditions. They can range from mild problems (e.g., Tietze syndrome or flatulence) to potentially fatal conditions (e.g., myocardial infarction, pneumothorax, or pulmonary embolism). Although certain symptoms are suspicious for some conditions, they are generally not specific (e.g., crushing substernal chest pain alleviated with nitroglycerine could be an esophageal spasm or an acute myocardial infarction, and lateral chest pain aggravated by inspiration could range from a muscle strain to pneumonia). Therefore, the more details that can be obtained regarding Mr. Elliott's chest pain, the more likely an accurate differential diagnosis list will be established to narrow this wide array of possibilities.

**B.** Has he checked his temperature with a thermometer? ESSENTIAL

Many patients (and parents) base the presence of a fever on whether the skin, especially over the forehead, feels warm or hot. The hotter it feels, the higher they assume the fever. This is not an accurate method of determining core body temperature.

In fact, when the core body temperature is significantly elevated, the patient's skin can feel cool secondary to the vasoconstriction mechanism of the body to dissipate the excessive heat. All patients who feel febrile should have their temperature checked with a thermometer that the user knows how to correctly operate.

C. Has he noticed any skin lesions or rash? ESSENTIAL

The presence of a rash narrows the list of potential diagnoses for many complaints, especially chest pain. Although it will likely eliminate the possibility of an acute myocardial infarction, it still does not limit the potential diagnoses to benign conditions only. For example, a contusion to the chest wall could cause pain from local tissue trauma or it could represent a serious underlying condition such as cardiac tamponade, ventricular aneurysm, constrictive pericarditis, hemothorax, or diaphragm rupture. Other rashes associated with chest pain are characteristic for specific conditions (e.g., herpes zoster has a dermatomal distribution).

**D.** Has he experienced any visual abnormalities? ESSENTIAL Several viral syndromes (e.g., influenza, herpes zoster, measles, and mumps) can be associated with the visual disturbances of Devic disease (neuromyelitis optica). In view of Mr. Elliott's flulike symptoms, this is an appropriate question to ask. Additionally, chest pain–associated visual abnormality and the presence of Roth spots (exudative lesions of the retina) are frequently associated with acute infectious endocarditis (IE) or SBE.

E. Does he have any pet rabbits at home? NONESSENTIAL

The concern with constitutional symptoms and rabbits is tularemia. However, Mr. Elliott's other symptoms are not consistent with this diagnosis. Tularemia generally consists of a sudden-onset headache associated with fever, nausea, and a papule at the site of inoculation. This papule quickly ulcerates and is associated with marked regional lymphadenopathy. Additionally, it is rare to acquire the infection by having a rabbit for a pet; generally it takes direct inoculation of the infected tissue (e.g., cutting oneself with the knife while skinning a wild rabbit).

#### 2. Physical Examination

A. General appearance ESSENTIAL

The patient's general appearance and demeanor is an essential component of the physical examination of each and every patient encounter. It provides a gross assessment of both the patient's physical and psychological condition. However, unless something is grossly abnormal, these finding are rarely recorded in the patient's chart.

The most common elements that should be observed include the patient's overall physical condition (e.g., malnourished, obese, or disheveled), appearance of being seriously ill (e.g., signs of toxicity, acute distress, or altered consciousness), general mental state (e.g., depressed, euphoric, apathetic, or indifferent), other signs of a mental disorder (e.g., poor hygiene, inappropriate dress, or inappropriate affect), incongruency between appearance and chief complaint, and discordance of verbal and body languages. It is important for the HCP not to permit his or her own biases, beliefs, values, and personality to taint this assessment.

#### **B.** Heart examination ESSENTIAL

A careful heart examination looking for the abnormalities outlined in Case 1-2 is indicated because of Mr. Elliott's complaint of left-sided anterior chest pain.

#### C. Lung auscultation ESSENTIAL

Auscultation of Mr. Elliott's lung is important to assess that his breath sounds are present and symmetric throughout his lungs, to determine the presence of abnormal breath sounds (e.g., wheezing, rhonchi, rales, and/or stridor), and to evaluate depth and length of inspiration and expiration and their relationship to his pain since he has been experiencing respiratory symptoms.

D. Digital rectal examination (DRE) NONESSENTIAL

#### E. Skin and nail examination ESSENTIAL

Skin and nail changes can be associated with a wide variety of medical conditions. For example, the splinter hemorrhages noted on Mr. Elliott's nails can result from something as simple as trauma to something as severe as SBE. They can also occur without being associated with any specific medical condition in 10 to 20% of all hospitalized patients. Regardless, because Mr. Elliott has dermatologic and nail complaints, these areas need to be evaluated.

#### 3. Diagnostic Studies

**A.** Complete blood count with differential (CBC w/diff) ESSENTIAL

A CBC w/diff is essential to perform on Mr. Elliott because it provides a lot of information regarding the patient. The primary function of white blood cells (WBCs) is to fight infection and foreign bodies. When they are elevated (leukocytosis), they are associated with infection, inflammation, severe stress (both physical and psychological), severe trauma, tissue necrosis, and some forms of leukemia. A low WBC count (leukopenia) is seen with conditions such as viral infections, some autoimmune diseases, and poor nutrition. The total WBC count is composed of five different types of cells, each one having its own significance: neutrophils, lymphocytes, eosinophils, basocytes, and monocytes. Because the total always has to equal 100%, if one or more types are elevated, then one or more types have to be decreased to compensate. Some of the more common causes for these differential counts to be either elevated or decreased are as follows:

Neutrophil elevations are generally associated with acute bacterial processes, severe inflammation, trauma, metabolic abnormalities, and stress (both physical and psychological). Additionally, if immature neutrophils (bands or stabs) are seen, it is usually indicative of a significant stimulation of the neutrophils and hence a more severe infection or inflammatory process. Neutropenia can be seen with dietary deficiencies, viral infections, overwhelming bacterial infections, and aplastic anemia.

Monocytes are generally elevated in acute viral infections, in inflammatory conditions, and with nongastrointestinal parasites. Monocytopenia is rare and frequently found in patients taking chronic oral corticosteroids and/or chemotherapy.

Eosinophilia is frequently associated with allergic conditions, parasitic infections (primarily gastrointestinal), and autoimmune diseases. They tend to only be decreased when there is abnormal adrenocorticosteroid production.

Basophils tend to be elevated in myeloproliferative diseases and leukemia; basopenia can be found in acute physical or emotional stress or an acute allergic reaction.

Lymphocytosis is generally affiliated with acute viral infections, chronic bacterial infections, and some carcinomas; they are decreased in sepsis, leukemia, immunodeficiency syndromes, and some autoimmune diseases.

The red blood cell (RBC) count, its indices, the hemoglobin, and the hematocrit provide information regarding possible anemia. A patient is considered anemic when his or her hemoglobin and/or hematocrit are decreased. However, early in acute hemorrhage, these values could be normal and the patient could still have significant blood loss.

Anemias are further classified based on the size and hemoglobin concentrations obtained from the RBC indices to assist in determining the most likely type of anemia the patient has. The mean corpuscular volume (MCV) is the average size of a single RBC; from this, an anemia is classified as normocytic, macrocytic, or microcytic. The mean corpuscular hemoglobin (MCH) is a measurement of the average amount of hemoglobin found in a single RBC. It is not a major determinant of the type of anemia the patient is experiencing; however, it tends to match the mean corpuscular hemoglobin concentration (MCHC), which is a measurement of the average percentage of hemoglobin in an RBC. It is this latter value that determines whether the patient's anemia is hypochromic, normochromic, or hyperchromic.

Platelets are necessary for blood to clot properly. The lower the platelet count (thrombocytopenia) is, the more severe the bleeding diathesis tends to be.

#### B. Chest x-ray (CXR) ESSENTIAL

Because of the minimal findings on his physical examination, a CXR would not have been generally indicated for Mr. Elliott. However, because he is experiencing hemoptysis, it is recommended to attempt to identify any potential abnormalities that might reveal the cause (e.g., a mass with lung cancer, nodular infiltrates with septic pulmonary infarcts, infiltrates with pneumonia, nodules with tuberculosis [especially in the upper lobes], and left ventricular failure with an enlargement of the ventricular portion of the cardiac shadow).

It is assumed that Mr. Elliott's hemoptysis is secondary to breaking superficial blood vessels in the trachea or bronchi as a result of his severe coughing. However, it could also represent early septic pulmonary infarcts or a malignancy. In theory, his hemoptysis should resolve when his infection resolves. If not, he will probably require a bronchoscopy and/or computed tomography (CT) scan to identify the cause, especially because he is a smoker.

**C.** A minimum of 2 blood cultures with sensitivities and Gram stains drawn at least 1 hour apart ESSENTIAL

These are definitely indicated because Mr. Elliott is toxic appearing. It is important to remember to collect the blood for the blood culture BEFORE instituting the empiric antibiotic therapy.

Blood cultures and sensitivities often take up to 72 hours for growth, identification, and sensitivity testing of the organism. Therefore, the Gram stain performed on the specimen to determine whether the sputum is adequate for culture can be utilized to attempt to determine the most likely pathogen (and its empiric treatment) based on its characteristics.

#### D. Electrocardiogram (ECG) ESSENTIAL

An ECG is indicated because he has tachycardia, an irregular pulse, and chest pain.

E. Transesophageal echocardiography (TEE) ESSENTIAL

Because Mr. Elliott's symptoms could represent a heart valve infection, a TEE is indicated. TEE is superior to transthoracic echocardiography (TTE) in attempting to find evidence to diagnose IE because TTE is limited by obesity, large breasts, and/or chronic lung disease. Furthermore, it is less accurate in determining the overall structure and function of the valves. The sensitivity of TTE in determining findings consistent with IE is estimated to be approximately 65% vs approximately 90% with TEE.

F. Urinary drug screen for illicit substances and narcotics ESSENTIAL

Considering that several of the potential conditions on Mr. Elliott's list of differential diagnoses could be associated with or caused by illicit drug use, his admitting to taking oxycodone that was not prescribed for him, and his refusing a foot examination (possibly due to "track marks" being seen) raise suspicions enough to warrant a drug screen. If he has a substance abuse problem that caused, or in addition to, his current condition, it also needs to be addressed and treated.

#### 4. Diagnosis

A. Lymphocytic leukemia INCORRECT

Mr. Elliott's positive Gram stains for bacteria and his CBC abnormalities of mild leukocytosis with neutrophilia and lymphopenia make lymphocytic leukemia very unlikely to be his most likely diagnosis because the hallmark of lymphocytic leukemia is noninfectious lymphocytosis.

#### B. Rocky Mountain spotted fever INCORRECT

Rocky Mountain spotted fever is a serious systemic infection that includes, among other symptoms, a rash on the palms of the hands and the soles of the feet. However, it is a rickettsial infection (hence, it should not be associated with a positive Gram stain) transmitted by ticks (*Dermacentor andersoni* and *variabilis*). Because this is inconsistent with his findings, this is not Mr. Elliott's most likely diagnosis.

C. Acute influenza and tricuspid regurgitation INCORRECT

Although some of Mr. Elliott's symptoms are consistent with influenza, many of them are not. Uncomplicated acute influenza should be improving, not worsening, after 1.5 weeks of illness. His WBC count and Gram stain indicate a bacterial, not a viral, pathogen is responsible for his illness. And, although his echocardiogram does reveal tricuspid regurgitation, it also reveals vegetation on the tricuspid valve which is inconsistent with uncomplicated tricuspid regurgitation. Hence, this is not his most likely diagnosis.

#### D. Infective endocarditis (IE) CORRECT

The Duke criteria have been established to assist in making the clinical diagnosis of IE. It is composed of two major and five minor criteria. The diagnosis of IE can be made by

having both major criteria OR one major and three minor criteria OR all five minor criteria.

The major criteria are two separate positive blood cultures for organisms that typically cause IE and echocardiographic evidence of IE. The minor criteria consist of (1) fever of greater than or equal to 38° C (Temperature conversion equations to and from Fahrenheit can be found in **Table 1-4**.), (2) predisposing cardiac condition or IV drug use/abuse, (3) vascular phenomena (e.g., major arterial emboli, septic pulmonary infarctions, intracranial hemorrhage, conjunctival hemorrhages, and/or Janeway lesions), (4) immunologic phenomena (e.g., Osler nodes, Roth spots, or positive rheumatoid factor), and (5) a positive blood culture that did not meet the major criteria's standard OR serologic evidence of an organism associated with IE.

Because Mr. Elliott has one major criterion (perhaps two, if his cultures are positive) and three minor criteria (perhaps four, if he abuses IV drugs), he can be diagnosed with IE. Thus, from the list provided, IE is his most likely diagnosis.

E. Disseminated gonococcal infection (DGI) INCORRECT

DGI, or gonococcal bacteremia, has some symptoms that are consistent with Mr. Elliott's presentation; however, DGI has other characteristic symptoms that he is not experiencing (i.e., monoarticular arthritis [or occasionally two or three joints maximum] and a sparse macular-papular, pustular, or hemorrhagic rash that is peripherally located). Finally, gonorrhea is a gram-negative intracellular diplococcus. Because of these inconsistencies, this is not his most likely diagnosis.

#### 5. Treatment Plan

**A.** Cefazolin 2 g IV every 8 hours and gentamicin 70 mg IV every 8 hours until blood cultures and sensitivities are available INCORRECT

Considering Mr. Elliott's Gram stain reveals gram-positive cocci in clusters; the organisms that most commonly cause infective endocarditis are *Streptococcus viridans, Staphylococcus aureus,* and *Enterococcus*; his tricuspid valve is affected (60% incidence of being due to *S. aureus*); and the suspicion that he uses/abuses IV drugs (which increases the incidence of *S. aureus* even higher), his most likely pathogen is *S. aureus.* However, the offending organism cannot be positively identified until the culture results are available.

Cefazolin would be an acceptable empiric antibiotic treatment regimen for IE caused by *S. aureus* if there were no concerns regarding methicillin-resistant *S. aureus* (MRSA). However, because of the increasing incidence of MRSA in most areas of the United States and the serious nature of his infection, this is not an acceptable empiric choice.

#### Table 1-4 Temperature Conversions

From Fahrenheit to Celsius:
[(Degrees in Fahrenheit – 32) $\times$ 5] $\div$ 9 = Degrees in Celsius
From Celsius to Fahrenheit:
[(Degrees in Celsius $\times$ 9) ÷ 5] + 32 = Degrees in Fahrenheit

Furthermore, cephalosporins have been known to have a cross-sensitivity to the penicillins; hence, Mr. Elliott could experience a similar (or worse) allergic reaction from the cephalosporins than he did with the penicillin. Thus, this is not an appropriate treatment option for him.

**B.** Vancomycin 1g IV every 12 hours and gentamicin 70 mg IV every 8 hours until blood cultures and sensitivities are available CORRECT

Vancomycin alone should cover *S. aureus*, even if it is methicillin resistant. However, until the culture results are available to confirm this suspected pathogen, gentamicin should be added to cover other possible pathogens. Once the cultures' and sensitivities' results are available, his antibiotics can be adjusted accordingly.

**C.** Hospitalize and observe closely for additional complications CORRECT

Based on Mr. Elliott's appearance, vital signs, and diagnostic tests, he is considered to be septic. Therefore, hospitalization is indicated for IV fluids, IV antibiotics, additional diagnostic procedures, vital sign monitoring, cardiac monitoring, and close observation.

#### D. Refer for substance abuse treatment CORRECT

When the tricuspid valve is involved in IE, it is estimated that 80 to 95% of the cases are secondary to IV drug use/abuse. This combined with the aforementioned reasons for ordering a drug screen is concerning. However, a referral for treatment is not indicated unless his drug screen returns positive, he goes into withdrawal, or he admits to a problem.

#### E. Bone marrow biopsy INCORRECT

This painful procedure is not currently indicated for Mr. Elliott. His CBC changes are consistent with his diagnosis; therefore, they should normalize after his IE has responded to therapy. If not, an evaluation is indicated, which may or may not include a bone marrow biopsy.

#### **Epidemiologic and Other Data**

It is estimated that there are anywhere from 2 to 7 cases per 100,000 persons of IE in the United States annually. The incidence caused by rheumatic heart disease has been decreasing in recent years; however, the incidence from degenerative valvular disease, prosthetic valves, other implanted intracardiac devices, intra- or post-operative contamination, invasive cardiac procedures, and IV drug use/abuse has been increasing. It is currently estimated that 10 to 30% of all cases of infective endocarditis occur in patients with prosthetic heart valves, with the greatest incidence during the first six months post-operatively. The majority of infections that occur within two months of the surgery is more than likely due to an intraor post-operative complication. Despite the revised prophylaxis guidelines by the AHA, an estimated 55 to 75% of all cases of IE are associated with an underlying cardiac valvular abnormality (this number includes prosthetic heart valves).

Increased incidence is seen in patients who are male, are immunocompromised (e.g., human immunodeficiency virus [HIV] infection, diabetes, or renal dialysis), are IV drug users/abusers, have a history of rheumatic heart disease (even when SBE prophylaxis is employed), have a history of congenital heart disease (regardless of repair status), have mitral valve prolapse syndrome, or have poor dental hygiene.

## CASE 1-5

#### **Eric Floyd**

#### 1. History

**A.** Did he sustain a head injury or loss of consciousness? ESSENTIAL

From the description of his injury, it is apparent that his body was propelled forward, forcing his head over/between the handlebars of the ATV. Because the front of the vehicle directly impacted with the tree, there is a question of whether his head did also. Furthermore, following any type of an impact injury, it is imperative to inquire regarding whether a head injury and/or a loss of consciousness occurred.

B. Is his helmet intact? ESSENTIAL

If a head injury occurred, a helmet that is relatively unscathed is generally associated with a low incidence of a serious head injury. However, a significantly damaged helmet is not as predictive because this could represent protection of the head or the impact being so severe, both were significantly damaged. Even without a head injury, this question is important because it provides an opportunity to discuss helmet safety.

**C.** Did he injure, or is he experiencing pain elsewhere in his body? ESSENTIAL

Inquiring about pain elsewhere in the body enables the full spectrum of potential injuries to be identified instead of focusing on the most obvious symptom. For example, abdominal pain in this patient's case could be the result of a splenic injury and his hypotension could be secondary to acute internal hemorrhage. Obviously, disastrous outcomes could occur if this type of injury was overlooked.

#### D. What is his "usual" BP? ESSENTIAL

As discussed in Case 1-1, "normal" BP is essentially defined as less than 120/80 mm Hg. Currently, studies indicate that the better the BP control is, the less the likelihood of developing complications from the disease. Furthermore, some experts believe that BP cannot be decreased "too low" unless the patient becomes symptomatic from the treatment. Although Mr Floyd's current measurement is unlikely to represent his current targeted treatment goal or his "typical" BP, it is therefore essential to obtain his "usual" (or general range) to compare with today's slightly hypotensive reading as part of the assessment of his hemodyanamic stability. This is especially important because Mr. Floyd has a history of hypertension that requires three medications to control.

**E.** Does he have a family history of coronary artery disease (CAD) ESSENTIAL

Because he is experiencing chest pain and has several risk factors for CAD (male gender, older age, obesity, previous smoker, and hypertensive), inquiring about additional risk factors for CAD (i.e., family history) is appropriate. If his family history is positive for blood relative(s) with premature CAD (i.e., before the age of 55 years) or for a first-degree relative (i.e., mother, father, or children) with CAD regardless of age, Mr. Floyd's risk of CAD further increases.

#### 2. Physical Examination

#### A. Heart examination ESSENTIAL

Because Mr. Floyd is experiencing chest pain, it is important to do a complete heart evaluation looking for the findings as outlined in Case 1-2.

The pericardial friction rub found on his examination can be distinguished from a pleural friction rub because the pleural rub is absent when the patient is not breathing (e.g., between breaths or with breath holding). However, a pericardial rub is present in all stages of the respiratory cycle.

**B.** Evaluate for the presence of an elevated jugular venous pressure (JVP), jugular venous distension (JVD), Kussmaul sign, pulsus alternans, pulsus bigeminus, and pulsus paradoxicum ESSENTIAL

The primary purpose of evaluating the internal JVP is to obtain a noninvasive estimate of the patient's central venous pressure (CVP). Less than or equal to 8 cm of blood is considered to be normal. Elevation of the right ventricular diastolic pressure is the main cause of an elevated JVP.

If the JVP is normal but there is still concern regarding the possibility of right ventricular failure, then an abdominojugular (or hepatojugular) reflex test is often helpful. The test is considered to be positive if 10 or more seconds of pressure applied to the midabdomen results in an elevation of the CVP AND a 4-cm or greater quick decrease of the pressure.

Another sign of right ventricular failure is the Kussmaul sign. It is an observable increase in the CVP during inspiration (CVP should normally decrease with inspiration).

Pulsus alternans (PA) is a decrease in the intensity or strength of the pulse associated with inspiration, despite an underlying regular cardiac rhythm. It is seen primarily following an episode of paroxysmal supraventricular tachycardia (PSVT) or premature ventricular contraction (PVC). Pulsus bigeminus (PB) is the same type of alterations in the pulse amplitude as seen with PA, except it is observed following a PVC after a regular beat (bigeminy).

Pulsus paradoxicum is a decrease of greater than or equal to 10 to 15 mm Hg in the SBP during inspiration while at the same time, the peripheral pulses decrease or disappear completely. It is associated with pericardial tamponade, airway obstruction, and superior vena cava obstruction.

#### C. Lung evaluation ESSENTIAL

Careful lung auscultation is required to identify any increases or decreases in breath sounds that are either localized or generalized through all the lung fields—posteriorly, anteriorly, and laterally. Decreased breath sounds are generally associated with an air-, fluid-, or blood-filled sac compressing normal lung tissue or consolidation of the lungs, as would be the case with severe pneumonia. The presence of wheezing, stridor, rhonchi, and rales indicates that there is an obstruction to airflow in the phase of respiration during which the abnormality is heard. All of these findings can indicate a pulmonary and/or a cardiac disease process. Pleural friction rubs are created when opposing pulmonary serous surfaces are "roughened" acutely by inflammation or chronically by fibrosis.

The presence of intracostal retractions or bulging tends to be associated with severe respiratory distress. Evaluation for symmetry of chest wall movement is essential as it can

represent a chest wall abnormality (e.g., rib fracture or severe contusion) or an internal pulmonary process (e.g., pneumothorax or hemithorax). Percussion is sometimes required to distinguish between fluid-/tissue-/air-filled areas. Additionally, vocal and/or tactile fremitus, egophony, bronchophony, and/or whispered pectoriloquy can also be utilized to make this determination.

#### D. Chest wall examination ESSENTIAL

Visualization of his chest wall is to evaluate for potential injuries (e.g., contusions, gross deformities or compound rib fractures, lacerations, puncture wounds, and abrasions). His ribs need to be palpated for laxity and tenderness, indicating potential fractured rib(s).

#### E. Cranial nerve evaluation NONESSENTIAL

A cranial nerve evaluation is not indicated because Mr. Floyd did not experience a head injury or loss of consciousness with his accident. Furthermore, he has not had nor currently does he have any signs or symptoms suspicious of a neurologic abnormality. However, if his symptoms change or his condition deteriorates, one might be necessary at that time.

#### 3. Diagnostic Studies

A. Chest x-ray (CXR) with rib enhancement ESSENTIAL

Because Mr. Floyd is experiencing chest wall tenderness, rib pain, and other signs and symptoms that are consistent with musculoskeletal, cardiac and pulmonary disorders, a CXR with rib enhancement is indicated. It can assist in identifying abnormalities such as rib fractures; pleural effusions, contusions, and/or pneumothoraxes; and cardiac conditions such as heart failure, cardiomegaly, and other conditions that could result in abnormal cardiac shadows.

#### B. Serial cardiac troponin I and T ESSENTIAL

Serial cardiac troponin levels are biochemical markers that assist in the identification of the presence (or absence) of myocardial ischemia or infarction. Because the cardiac troponins (I and T) can be separated from the troponin found in skeletal muscle by monoclonal antibodies or enzyme-linked immunosorbent assay techniques, they are able to identify myocardial damage with a much higher specificity and sensitivity than even the fractionated creatinine phosphokinase (CPK) levels. Minor elevations of the cardiac troponins can occasionally occur with musculoskeletal trauma; however, the levels tend to be much lower.

Troponin I levels begin to rise in approximately 3 hours from the onset of chest pain and they persist for 7 to 10 days post-MI. Troponin T can actually be elevated for 10 to 14 days post-MI. This is important in attempting to evaluate individuals who delay seeking treatment following an episode of chest pain. Additionally, it appears that the cardiac troponin levels also have prognostic properties in assisting with determining the likelihood of the event being fatal.

## **C.** Electrocardiogram (ECG) and cardiac monitoring ESSENTIAL

Because the patient is experiencing chest pain, it is important that an ECG be performed. Abnormal ST segments and Q waves are suspicious for cardiac ischemia and/or

infarction (especially in conjunction with elevated cardiac troponin levels). Cardiomegaly, atrioventricular (AV), bundle branch blocks, chamber enlargements, arrhythmias, and some electrolyte abnormalities can also be identified based on ECG findings.

#### D. Echocardiography ESSENTIAL

Echocardiography is considered to be the "gold standard" for evaluating cardiac structures and identifying areas of ischemia and/infarction. Furthermore, it permits evaluation for any signs of valvular abnormalities, chamber sizes, thickness of the myocardium, thickness of the pericardium, presence of effusions, and other structural blood flow abnormalities. Additionally, it can provide an estimate of the patient's ejection fraction.

#### E. Tuberculosis skin test (TST) NONESSENTIAL

Even though TB is a leading cause of cardiac tamponade secondary to a pericardial effusion, with Mr. Floyd's history of trauma, makes an infectious process unlikely. Therefore, this test is not indicated at this time to evaluate his complaint.

#### 4. Diagnosis

#### A. Constrictive pericarditis INCORRECT

Constrictive pericarditis is an inflammatory process that is almost always associated with a thickened and frequently scarred pericardium with or without calcifications that produces the "constriction" on the heart. On evaluation, the JVP has both a prominent x and y descent and a positive Kussmaul sign. Because of the absence of a thickened scarred pericardium and a prominent x descent (but no y) constrictive pericarditis is not Mr. Floyd's most likely diagnosis.

**B.** Cardiac tamponade secondary to a pericardial effusion CORRECT

Cardiac tamponade's primary diagnostic criteria are known as "Beck's triad." It is a combination of (1) hypotension, (2) diminished or absent heart sounds on auscultation, and (3) JVD with an elevated JVP exhibiting a prominent x descent but an absent y descent.

The presence of a pericardial effusion is confirmed echographically. Additionally, Mr. Floyd's ECG monitoring revealed what is known as electrical alternans. When present, it is considered pathognomonic for a pericardial effusion. It results from the movement of the heart back and forth within a large effusion. Hence, this fulfills the second half of this diagnosis, making cardiac tamponade secondary to a pericardial effusion Mr. Floyd's most likely diagnosis.

Small, slow bleeds are better tolerated than large, massive bleeds because a slow bleed can gradually stretch the pericardial sac, whereas a large bleed cannot be accommodated. Hence, large, fast bleeds are associated with a much greater morbidity and mortality.

#### C. Tension pneumothorax INCORRECT

A tension pneumothorax is air (or other gases) trapped between the pleural layers lining the lungs that causes "tension" or pressure on the remaining lung tissue, causing it not to be able to expand and ventilate the body efficiently. Although common with blunt chest trauma, this can be eliminated as Mr. Floyd's most likely diagnosis because there was no evidence of a loss of lung parenchymal tissue markings or a mediastinal shift on his CXR or physical examination.

#### D. Restrictive cardiomyopathy INCORRECT

The most striking difference between restrictive cardiomyopathy and cardiac tamponade is the presence of fluid accumulation in the pericardial sac and the small right ventricular size seen with tamponade. Furthermore, restrictive cardiomyopathy is also associated with myocardial thickness; in view of Mr. Floyd's diagnostic studies, this is not his most likely diagnosis.

E. Right ventricular myocardial infarction (RVMI) INCORRECT

An RVMI is generally associated with an enlarged right ventricle and evidence of infarction on ECG and echocardiography. These findings would be associated with elevated cardiac troponin levels consistent with a myocardial infarction because it has been longer than 3 hours since Mr. Floyd's injury and pain onset. Furthermore, with an RVMI there is no evidence of right atrial collapse, a large pericardial effusion, an *x* descent with JVP measurement, and pulsus paradoxicum. Therefore, RVMI is not Mr. Floyd's most likely diagnosis.

#### 5. Treatment Plan

**A.** Hospitalize for arterial pressure, venous pressure, and cardiac monitoring; IV fluids; oxygen; further testing; and treatment CORRECT

With the size of his effusion and the presence of shock (or at least impending shock), Mr. Floyd definitely needs to be hospitalized for more definitive evaluation, monitoring, and treatment.

**B.** Pericardiocentesis via subxiphoid approach under echocardiography guidance CORRECT

Because of the rapid accumulation of his effusion and the development of symptoms suggesting an inadequate pumping ability of the heart, he definitely requires pericardiocentesis to alleviate the pressure the effusion is placing on his heart. Because the subxiphoid approach is the easiest method, it is the technique of choice, especially for noncardiac providers.

**C.** Evaluation of fluid from tap for cytology, microscopy, bacterial culture and sensitivity, polymerase chain reaction (PCR) test of DNA of *Mycobacterium tuberculosis* CORRECT

A bloody tap is the typical finding with a traumatic pericardial tamponade; however, accepted treatment guidelines include having the fluid analyzed cytologically for malignancy and microscopically for WBC and bacteria counts (which if positive, indicates an infectious process); bacterial cultures and sensitivities to identify the offending agent if a bacterial infection is present; and PCR testing for *M. tuberculosis* (as it is the number one cause of infectious cardiac tamponade). Hence, these tests should be done despite Mr. Floyd's history of trauma and his tap being bloody.

#### D. Consultation with a cardiac surgeon CORRECT

In the case of trauma, the pericardiocentesis is highly unlikely to be definitive treatment for this condition because there is a very high likelihood that it will reaccumulate until the underlying pathology is corrected. A cardiac surgeon will likely order either an MRI or a CT scan to determine the exact cause; then, treat it appropriately and hopefully permanently.

**E.** Continue his current blood pressure medicines at half strength INCORRECT

CCBs, such as dihydropyridine, and beta-blockers (BBs), such as nadolol, are contraindicated in patients with cardiac tamponade because they can alter the reflex tachycardia, which compensates for the decreased cardiac output. Furthermore, Mr. Floyd is already hypotensive and the medications are likely to drop his blood pressure even further.

#### **Epidemiologic and Other Data**

Over 50% of all cases of cardiac tamponade are secondary to a malignancy. The next most common causes, each accounting for approximately 14% of the cases, are idiopathic pericarditis and renal failure–induced cardiac effusion. Other conditions that can be seen with cardiac tamponade include acute myocardial infarctions (especially if the patient is anticoagulated), adverse events resulting from cardiac surgery or invasive procedures, purulent pericarditis, TB pericarditis, dissected aortic aneurysms, myxedema, and trauma.

## CASE 1-6 Frank Gee

#### 1. History

**A.** Has he ever tried any Western (i.e., nitroglycerine) or traditional Chinese medications for his chest pain? If yes, what were the treatments and results? ESSENTIAL

From his symptoms description, until proven otherwise, ischemic heart disease has to be his current working diagnosis. Therefore, it is important to know the response of his pain to nitroglycerine. However, it is essential to remember that even though chest pain that resolves with nitroglycerine does not confirm a cardiac cause for the pain. Other conditions, most notably esophageal spasms, are also alleviated by the vasodilatory effects of nitroglycerine.

Additionally, because he is treating his hypertension and hyperlipidemia with a traditional Chinese herbal therapy, it is important to know if he has been utilizing any alternative medications for his chest pain, and if so, what results, if any, occurred.

Attempting to make an accurate diagnosis for his past episodes of chest pain is also important because if he has a history of angina, he already has some degree of CAD. Furthermore, it is estimated that approximately 50% of all patients who develop acute myocardial infarctions (AMIs) have a history of stable angina. The AMI rates among patients with unstable angina are even greater.

**B.** Does he smoke, and if so, what is his smoking history? ESSENTIAL

There are many risk factors associated with CAD. Because these tend to be cumulative, the greater number of risk factors a patient possesses, the greater risk he or she has of acquiring CAD. Because Mr. Gee already has several risk factors (hypertension, hyperlipidemia, and obesity), it is important to

identify how many of the other ones he possesses. Because smoking is a common (and potentially correctable) risk factor as well as a "significant" comorbid conditions, it is essential to inquire about. In fact, a better question is, "What is your smoking history?"

Studies have found that the significant risk factors for CAD include the presence of the following comorbid conditions: diabetes mellitus, hypertension, hyperlipidemia, prior CAD, obesity, and current smoker. Not as significant, but still important, are the additional risk factors of a positive family history, especially in a first-degree relative or any blood relative who was experienced a fatal MI younger than the age of 55 years; advancing age; male gender until approximately 50 years old, then female gender; sedentary lifestyle; former smokes (especially if recent) poor nutritional habits, especially a diet that is high in saturated fats, salts, and excessive alcohol; elevated homocysteine levels; and elevated levels of highly sensitive C-reactive protein.

It is estimated that as many as 80% of individuals with unstable angina and 87 to 100% of individuals with fatal coronary events have at least one or more risk factors present.

**C.** When was his cholesterol last checked and what were the results? ESSENTIAL

In general, the higher the lipoprotein levels are, the greater is the risk of CAD. The exception to this is HDL cholesterol as they appear to be cardioprotective; therefore, higher HDL levels are associated with lower CAD risk. Knowing what Mr. Gee's levels were (and how long ago they were tested) provides additional information regarding his current risk of CAD and its likelihood of being responsible for his current episode of chest pain.

#### D. What is his "usual" BP? ESSENTIAL

This is important information to obtain from Mr. Gee because his BP is elevated at this visit. It is important to know if this represents his "usual" BP or if it is resulting from pain or another underlying cause. The associated tachycardia makes pain the more likely culprit.

Furthermore, by knowing the exact numbers for his "usual" BP (and his lipid values from the previous response), his estimated 10-year cardiac risk can be calculated. A high value would provide additional support that his chest pain might be cardiovascular in nature.

The most commonly used 10-year estimation scale is based on data from the Framingham Study and was established by the U.S. Department of Health and Human Services (USDHHS), Public Health Service (PHS), NIH, and NHLBI. There are two separate scales, one for men and one for women. The factors it evaluates are age, total cholesterol level for age, smoking status for age, HDL, systolic BP, and whether or not the patient is on antihypertensive medications. Numerical values are assigned to each of these areas. The total sum of these values is then placed on a scale to determine the individual patient's risk of having a coronary event within the next 10 years. Utilizing this scale, Mr. Gee's 10-year cardiac risk is greater than or equal to 30%.

Higher points are assigned for greater risk; for example, men who are between the ages of 20 and 34 years receive –9 points for age and men between the ages of 75 and 79 receive +13 points. However, with other risk factors such as smoking and elevated total cholesterol, the younger the patient is, the higher the score assigned. For example, if a man is 20 years old and had a total cholesterol above 280, he would be given +11 points; however, if a man 79 years old had the same cholesterol level, he would only be assigned +1 point. HDL and systolic blood pressure values are assigned without an age status. However, an elevated BP under treatment receives a higher score than the same BP level not being treated for hypertension (the complete tool can be found online at http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype=pub).

**E.** Does he use sildenafil, vardenafil, or tadalafil for his erectile dysfunction (ED)? NONESSENTIAL

This question as stated does not provide much useful information because it is based on two assumptions (both of which are incorrect in Mr. Gee's case): first is that he is sexually active and second that he suffers from ED. Furthermore, it could be considered "insulting" to the patient and could have an adverse impact on the patient–provider relationship.

The information that this question is attempting to ascertain is whether the patient is taking a phosphodiesterase type 5 inhibitor because they can produce tachyarrhythmias and inhibit autonomic regulation of BP. A better approach to obtain this information is to specifically ask about these agents when obtaining his medication list.

#### 2. Physical Examination

#### A. General appearance ESSENTIAL

When the patient is presenting with a painful condition, his or her general appearance is useful because it provides an overall impression of the relationship between the complaint and its severity by how the patient looks and acts. Additionally, it provides clues that could support a diagnosis (e.g., diaphoresis is frequently associated with chest pain caused by ischemia).

#### B. Oral examination NONESSENTIAL

**C.** Heart auscultation ESSENTIAL

Because Mr. Gee is complaining of chest pain, it is essential to conduct a comprehensive heart examination, paying particular attention to the areas outlined in Case 1-2.

#### D. Lung auscultation ESSENTIAL

Because Mr. Gee is complaining of chest pain, it is essential to perform a comprehensive lung examination as outlined in Case 1-5.

#### E. All his pulses ESSENTIAL

Reduced pulses or a bruit in an artery generally indicates the presence of atherosclerotic vessel disease. Additionally, skin color, skin temperature, and capillary refill are essential components in the evaluation of the patient's pulses; if abnormal, they can indicate reduced circulation even in the presence of a normal pulse. The presence of atherosclerosis would increase the likelihood that Mr. Gee's chest pain is caused by CAD.

However, it is essential to remember than when a blood vessel is more than ~70% occluded, the bruit generally disappears, so significant vessel disease can occur without a bruit. Likewise, up to 30% of bruits are found in normal blood vessels with normal blood flow.

#### **3. Diagnostic Studies**

**A.** Cardiac telemetry followed by 12-lead electrocardiogram (ECG) ESSENTIAL

Telemetry provides a continuous view of the patient's heart rate and underlying rhythm. Additionally, it permits evaluation of the wave formations, the segment lengths, and their relationship. Furthermore, it is beneficial because any changes in rate and rhythm can be identified quickly; then, any required treatments can be instituted and monitored immediately.

However, it does not provide a complete view of the heart because it is generally conducted in just one lead (usually lead II). Hence, a full 12-lead ECG also needs to be performed. It will provide an overall "snapshot" of the electrical activity of the heart to identify patterns of ischemia, infarction, conduction defects, and other conditions that take more than one lead to correctly diagnose.

**B.** Oxygen saturation followed by oxygen at 2 L/min via nasal cannula (NC) ESSENTIAL

Because Mr. Gee has dyspnea (and a strong smoking history), an oxygen saturation ( $O_2$  sat) is required to provide an estimate of the patient's oxygenation status. Regardless of the oxygenation status, any patient with suspected myocardial ischemia should receive oxygen therapy starting at 2 L/min to assist with myocardial perfusion. The amount of oxygen can be increased based on the patient' symptoms,  $O_2$  sat, and arterial blood gases (when indicated).

#### C. Echocardiogram ESSENTIAL

If the ECG looks suspicious for ischemia, an echocardiogram (echo) can assist in further determining the area and extent of involvement because it will reveal abnormal motion of the affected area of the myocardium. Furthermore, it can provide a gross estimation of the function of the left ventricle, or the ejection fraction. This additional information can be useful in determining the most appropriate intervention for that individual patient.

However, it is important to remember that segmental wall dysfunction does not necessarily mean that the patient is having an AMI. It can also be seen with scarring from a previous MI, a resolved or mild constrictive pericarditis, or severe ischemia without infarction.

#### D. Gallbladder ultrasound NONESSENTIAL

Because the patient had a cholecystectomy, he does not have a gallbladder on which to perform an ultrasound. Therefore, this is not an appropriate diagnostic option for Mr. Gee. However, evaluation of his common bile duct for the presence of a retained gallstone would be appropriate, once more urgent and life-threatening conditions were eliminated, because this would explain why his pain felt like the pain he experienced that was caused by cholelithiasis, and the postoperative window is appropriate for this complication to become symptomatic.

**E.** Cardiac troponin I and T (cTn-I and cTn-T) stat; then repeat in 4 and 8 hours ESSENTIAL

Serum cardiac troponin I and T have essentially replaced CPK and/or CPK fractionation as the method of choice for determining myocardial injury because they are more cardiac specific and produce fewer false-positives caused by skeletal muscle damage. They are estimated to be 84 to 96% sensitive and 80 to 95% specific. (For further discussion, please see Case 1-5.)

It is important to remember that a single elevated troponin level is not diagnostic of an AMI, just as a single normal value does not rule out an AMI. Cardiac troponins also elevate in response to any damage to the myocardial muscle; however, the elevation is not nearly as extreme and the increase over time not nearly as significant as is seen with infarction.

Furthermore, if the patient presents early in the course of an AMI, the cardiac troponin levels can still be negative because cardiac troponin levels do not begin to elevate until approximately 3 hours postinjury. Therefore, repeat testing of the levels in 4 hours should reveal a rise in the levels if the chest pain is truly from myocardial ischemia and/or infarction.

Once cardiac troponins are elevated, the cardiac troponin I can still be detected in the serum of the patient for 7 to 10 days and the cardiac troponin T for up to 10 to 14 days.

If the patient is at low risk for an AMI, some experts feel that only two, not three, sets of troponins are adequate to determine chest pain as nonmyocardial in origin (provided the second set is also negative). However, there is a caveat that a minimum of 8 hours must have elapsed since the patient last experienced any chest pain for this to be accurate. Therefore, most HCPs opt for continued monitoring and performing a third set of troponin levels.

#### 4. Diagnosis

A. Unstable angina INCORRECT

Unstable angina is characterized by ischemic chest discomfort (or equivalent symptoms) with at least one of the following three characteristics: (1) occurs at rest and generally lasts for more than 10 minutes, (2) is described as severe and never experienced before 6 weeks previous, and (3) is a worsening of previous angina (e.g., occurring at more frequent intervals, lasting longer, or increasing in severity of pain [and/or other symptoms]. Although it is considered to be an acute coronary syndrome and associated with myocardial ischemia, infarction is not part of the picture. If tissue death does occur, then the diagnosis is changed to myocardia infarction.

In unstable angina, the typical ST-T-segment change is depression, not elevation, and there are no Q-wave formations as are evident on Mr. Gee's ECG; therefore, despite his first set of cardiac troponin levels being negative, unstable angina is not his most likely diagnosis.

#### B. Old anterior myocardial infarction INCORRECT

ST-segment elevation and the beginning of Q waves are characteristic of an AMI. Q waves with resolving ST-segment changes are seen in recent or subacute MIs. Q waves without any ST-segment changes are associated with old or indeterminate-age MIs. Because Mr. Gee's ECG reveals the former, this is not his most likely diagnosis. Furthermore, anterior MIs affect ECG leads  $V_1$  through  $V_5$ ; Mr. Gee's involvement is currently in II, III, and aVF.

#### C. Acute anteroseptal myocardial infarction INCORRECT

This answer would be consistent with Mr. Gee's Q-wave and ST-segment elevations; however, anteroseptal MIs have

the affected ST segments in leads  $V_1$  through  $V_3$ , not II, III, and aVF as Mr. Gee does. Therefore, this is also not his most likely diagnosis.

#### D. Choledocholithiasis INCORRECT

Choledocholithiasis is the presence of a cholelith in the common bile duct. His symptoms and ECG findings prevent this from being his most likely diagnosis.

If there is a high index of suspicion that this is Mr. Gee's diagnosis, then an endoscopic ultrasonography or an endoscopic retrograde cholangiography is indicated.

#### E. Acute inferior myocardial infarction CORRECT

As previously stated, Mr. Gee's ECG findings of evolving Q waves and ST-segment elevations are consistent with an AMI. The ST-segmental abnormalities occurring in II, III, and aVF are consistent with an acute inferior myocardial infarction. Despite the negative cardiac troponin levels (which are probably resulting from his early presentation as discussed previously), this is his most likely diagnosis.

It would be appropriate at this time to consider performing some type of assessment to further determine the patient's risk of death from ST-segment elevation MI with negative troponin antibodies (although his are likely to be elevated upon repeat testing).

One such tool developed by Thrombolysis In Myocardial Infarction (TIMI) is the Unstable Angina and ST-segment Elevated MI (UA/STEMI). It provides a numerical score ranging from 0 (lowest risk) to 6 (highest risk) that estimates the likelihood of cardiac death cause by either unstable angina or an ST-segment-elevated MI. The scores are divided as follows: 0 to 2, low risk; 3 to 4, moderate risk; and 5 to 6, high risk. It is based on assigning 1 point each to the following six factors: age 65 years or older, history of previous stenosis of 50% or greater, two or more episodes of angina in the past 24 hours, three or more risk factors for CAD, current elevation of cardiac biomarkers, and current ST segment deviations of more than 0.5 mm. CAD risk factors were defined as hypertension, hyperlipidemia, diabetes, current smoke, and positive family history. Mr. Gee's UA/STEMI score is 4, or moderate risk.

The TIMI group has developed 12 different clinical tools for the evaluation of possible cardiac death based on various factors/medications that are available to clinicians to use in appropriate situations. They are based on over 50 clinical trials (all the tools [and trials] can be found at http://timi.org).

#### 5. Treatment Plan

**A.** Admit to intensive care unit (ICU), continue telemetry, vital sign monitoring, IV fluids, and oxygen CORRECT

With his symptoms and most likely diagnosis, Mr. Gee needs to be hospitalized for continued telemetry, vital sign monitoring, observation, IV fluids, oxygen, and evaluation.

**B.** IV nitroglycerine 2 to 200  $\mu$ g/min at a dose sufficient enough to alleviate the patient's pain but not so high as to cause adverse effects. If this titration cannot be achieved or maximum dosage fails to alleviate the patient's pain, then give morphine sulfate at 2 to 8 mg IV every 15 minutes as needed, provided no signs of respiratory depression are present CORRECT IV nitroglycerine is generally very effective in alleviating myocardial pain. Nevertheless, regardless of the patient's response to it, it is not diagnostic in either ruling in or ruling out an AMI. If nitroglycerine is ineffective in alleviating the pain, then morphine sulfate IV should be utilized next. In theory, the only ceiling to the maximum dosage is respiratory depression.

**C.** Aspirin 160 to 325 mg stat; then 81 mg enteric-coated aspirin daily with food CORRECT

Mr. Gee needs to be given a full-strength aspirin now because he is a candidate for thrombolysis, it will already be "on board." Furthermore, he will need to take low-dose aspirin daily for the rest of his life in hopes of preventing platelet aggravation and clot formation.

#### D. Acebutolol 200 mg once a day orally CORRECT

Beta-blockers are indicated immediately in a post-MI patient and also to be continued indefinitely because they are associated with a lower first-year mortality rate from AMIs.

Ideally, the chosen beta-blocker should be one that is  $\beta_1$  selective because there is less chance of pulmonary complications. With Mr. Gee's smoking history, it would not be unreasonable for him to have chronic bronchitis that could be adversely affected by a beta-blocker. Because he is hospitalized, this complication could be quickly identified and treated.

Furthermore, the beta-blocker should have good membrane-stabilizing activity. Some studies have found it to be advantageous in assisting with the prevention of cardiac arrhythmias. Additionally, it would be preferable for it to possess intrinsic sympathomimetic activity because recent studies indicate this might partially reduce cardiac depression.

Additionally, his herbal products need to be identified and evaluated for efficacy and safety. If that is not possible, then they should be tapered off and replaced with appropriate medications to ensure the best possible outcome and to avoid possible drug-herb interactions.

E. Fibrinolysis with tissue plasma activator (tPA) INCORRECT

Fibrinolysis therapy, regardless of agent (tPA, streptokinase, tenecteplase [TNK], and reteplase [rPA]) employed, is theoretically contraindicated in Mr. Gee because of his age. In patients between the ages of 76 and 86, studies have failed to reveal any benefit in providing the therapy. However, elderly patients without any other contraindications to fibrinolysis who have a significant amount of myocardium in danger from the AMI need to be individually evaluated as the benefits of fibrinolysis might outweigh the risks.

Regardless, Mr. Gee would not be an acceptable candidate for fibrinolysis therapy because he has a relative contraindication to the treatment—a cholecystectomy 2 weeks ago (relative contraindication is major surgery in the last 3 weeks). Additionally, because the exact details of his surgery are unknown, it is possible that he has another relative contraindication (internal bleeding within the past 2 to 4 weeks) secondary to the surgery. Other relative contraindications include traumatic cardiopulmonary resuscitation (CPR) or CPR that lasted for longer than 10 minutes; bleeding that does not respond appropriately to pressure; ischemic stroke more than 3 months ago; active stomach or duodenal peptic ulcer disease; hypertension, defined a SBP that is greater than 180 and/or as DBP that is greater than 100 at presentation; pregnancy; and currently on anticoagulant therapy.

#### Case 1-7 Responses and Discussion

Absolute contraindications include ischemic CVA longer than 3 hours ago but less than 3 months ago (some experts recommend 1 year), previous intracranial hemorrhage, known structural cerebral vascular lesion (e.g., aneurysm or AV malformation), significant head injury/trauma (including closed) within the past 3 months, brain tumor, known or suspected aortic dissection, or any active internal bleeding. Some experts consider the aforementioned BP criteria as an absolute, not relative, contraindication.

Fibrinolysis therapy is indicated in patients who have STsegment elevation of greater than 1 mm in two or more contiguous leads, have been symptomatic for less than 12 hours (with an ideal goal of within the first 30 minutes of presentation or within 3 hours of symptom onset), have a true posterior MI, or have appeared to experience an AMI but a bundle branch block (BBB) makes it impossible to determine because of the secondary ST-segment changes from the BBB.

**F.** Percutaneous transluminal coronary angiography (PTCA) with stent placement if indicated CORRECT

PTCA with stent placement is a possible option for Mr. Gee. However, he must be at a facility where it and a qualified HCP is available to perform the procedure within 12 hours from the onset of his symptoms. It is indicated in patients who have contraindications to fibrinolysis but have heart failure, recurrent ischemia, a previous MI, and cardiogenic shock.

Interestingly, a meta-analysis was performed on 23 trials with almost 8000 patients and the authors concluded that PTCA for AMI was superior to fibrinolysis therapy. Furthermore, a retrospective analysis of patients who failed to reperfuse with fibrinolysis therapy indicated rescue PTCA to be just as safe and effective as primary PTCA.

#### **Epidemiologic and Other Data**

In the United States, there are over 1,000,000 AMIs occurring annually. Approximately 650,000 individuals experience their first AMI annually, and 350,000 AMIs occur in individuals who have had at least one previous AMI.

There appears to be a seasonal relationship to fatal myocardial infarctions. The two months of December and January have 33% more fatal myocardial infarctions than are seen in the 4-month time span from June to September.

In the 30 days after an AMI, the death rate is approximately 30%. Unfortunately, over 50% of this number includes patients who never make it to an emergency department before they die from an AMI. One in every 25 patients who are discharged from the hospital following an AMI is dead at the end of 1 year. In patients older than the age of 75 years, the risk of dying from an AMI is 400% greater compared to individuals experiencing an AMI before the age of 75 years.

## **CASE 1-7**

#### **George Harris**

#### 1. History

**A.** Has he experienced any epistaxis, nasal or oral lesions, or gingival or dental problems recently? ESSENTIAL

Inquiring about bleeding elsewhere in the body is important because if it is present, it could indicate a bleeding disorder, thrombocytopenia, vitamin K deficiency, disseminated intravascular coagulation, or unknown ingestion of anticoagulants.

However, if he is experiencing a true hemoptysis, then the major causes include pulmonary infections; carcinomas; abnormalities of the pulmonary vasculature; pulmonary venous hypertension; AV malformations; pulmonary embolism; gastroesophageal reflux disease (GERD), especially with Barrett esophagitis; and some autoimmune diseases.

In the past it was believed that if the hemoptysis was associated with sputum or some other fluid production, it was less serious than if it was just blood alone. However, this has not been proven in any evidenced-based fashion.

**B.** Has he experienced any abdominal pain or change in his bowel movements? ESSENTIAL

Knowing if he is experiencing any gastrointestinal bleeding is important to evaluate not only for potential sources for the hemoptysis (e.g., esophageal varices caused by portal hypertension, Barrett esophagitis, and GERD can cause blood to be expelled with coughing as well as dark tarry stools) but also for other sources of bleeding (e.g., bleeding peptic ulcers and inflammatory bowel disease can cause both bleeding and abdominal pain, whereas colon cancer and polyps tend to cause painless bleeding).

**C.** Has he experienced any fatigue, malaise, weight loss, hoarseness, or night sweats? ESSENTIAL

The presence of these symptoms is suspicious for a carcinoma. With the hemoptysis, the most likely possibilities would be a lung carcinoma, lung metastasis, or esophageal cancer. However, an acute or chronic pulmonary infection can also present as hemoptysis with these symptoms. In view of the lack of fever and sputum production, an acute lung infection is less likely; however, it certainly cannot be completely ruled out.

D. Has he experienced any dyspnea? ESSENTIAL

The presence of dyspnea makes a pulmonary abnormality the most likely cause for Mr. Harris's hemoptysis. However, if dyspnea occurs in conjunction with constitutional symptoms, a carcinoma becomes a very likely probability. Poor physical conditioning, medical fragility, psychiatric disorders (e.g., panic attacks, somatization disorders, and malingering), cardiac conditions (e.g., heart failure, arrhythmias, myocardial ischemia, aortic stenosis, and constrictive pericarditis), neurologic conditions (e.g., Guillain-Barré syndrome, amyotrophic lateral sclerosis, and muscular dystrophy), musculoskeletal disorders (kyphoscoliosis or rib fractures), or other conditions (e.g., anemia, hyperthyroidism, and metabolic acidosis) can cause dyspnea, which may be unrelated to his chief complaint.

E. Has he experienced any hallucinations? NONESSENTIAL

This question would only be relative if he was experiencing neurologic or psychological symptoms, was acting bizarrely, or suddenly ceased drinking alcohol.

#### 2. Physical Examination

A. Skin examination ESSENTIAL

The skin is important to examine in patients who are experiencing dyspnea to observe for evidence of cyanosis, erythema, and/or pallor. Furthermore, if an infection is suspected,

the presence of associated skin lesions can be very helpful in establishing the correct diagnosis. Finally, in patients where there is a suspicion of a metastatic process without an obvious cause, the skin should be examined thoroughly for the presence of a malignant melanoma.

As a general rule, central cyanosis has a pulmonary cause, whereas peripheral cyanosis is related to a cardiovascular condition. Obviously, these are not absolutes and frequently cardiac and pulmonary conditions coexist. For example, congenital cardiac conditions that result in right-to-left shunts can produce central cyanosis. Methemoglobinemia produces central cyanosis without either a cardiovascular or pulmonary cause; conditions like these are generally recognized by the patient's cyanosis failing to improve with oxygen therapy.

#### B. Heart examination ESSENTIAL

A careful heart examination following the criteria outlined in Case 1-2 is essential to determine whether Mr. Harris has any cardiac abnormalities that could account for his symptoms.

#### C. Lung auscultation ESSENTIAL

Because of Mr. Harris's hemoptysis and dyspnea, a thorough lung examination as outlined in Case 1-5 is essential.

**D.** Evaluation of jugular venous pressure (JVP), of pulses, and for pedal edema ESSENTIAL

As stated previously, the primary purpose of evaluating the JVP is to obtain a noninvasive estimate of the patient's CVP. An elevated *a* wave is generally caused by a very forceful right atrial systole.

Normal pulses provide some reassurance that the patient has adequate circulation and perfusion. Bilaterally decreased pulses are generally associated with decreased perfusion or atherosclerosis, whereas a unilaterally decreased pulse is most frequently caused by an obstruction.

The most common cause of bilateral pedal edema is heart failure. However, other conditions can also cause the problem (e.g., hepatic problems, azotemia and/or renal failure, ascites, pleural effusions, and malignancies).

Pedal edema is more accurately dependent edema. Therefore, it is important to remember that when evaluating a patient, the edema is located in the most dependent part of the body. Patients who are bedridden often have presacral edema instead of ankle and foot edema.

E. Joint evaluation NONESSENTIAL

#### **3. Diagnostic Studies**

**A.** Oxygen saturation ( $O_2$  sat) and chest x-ray (CXR) ESSENTIAL

Because Mr. Harris is experiencing dyspnea, orthopnea, cyanosis, harsh breath sounds, and abnormal cardiac sounds and has a long-standing history of smoking, both an  $O_2$  sat and a CXR are indicated. Although a normal  $O_2$  sat is considered to be 95% or higher, "critical values" are not defined until the level has fallen to 75% or less. However, it is generally accepted to recommend arterial blood gases (ABGs) and oxygen therapy when the  $O_2$  sat falls below 90%, when there is a compelling reason to suspect the reading is incorrect (e.g., poor peripheral circulation, Raynaud disease and/or phenomenon, or dark-colored fingernail polish that cannot be removed), or

when other values identified by the ABGs would provide useful information for managing the case.

**B.** Electrocardiogram (ECG) and echocardiogram with Doppler ESSENTIAL

Because two different cardiac murmurs, an abnormal opening snap, and an elevated JVP were discovered during Mr. Harris's physical examination, both an ECG and an echocardiogram with Doppler ultrasound are indicated as part of his evaluation.

An ECG can provide confirmation of the patient's pulse rate; determine his or her current heart rhythm; confirm conduction defects; and provide signs suggestive of ischemia, infarction, chamber enlargement, cardiomegaly, and electrolyte abnormalities.

The echocardiogram is an ultrasound of the heart. It can determine the presence of abnormalities in the motion and/or structure of the heart's chambers, valves, septum, walls, and other components. Furthermore, it can evaluate the valves of the heart for prolapse, regurgitation, stenosis, calcification, vegetation, and other abnormalities; it can also identify cardiomegaly, aneurysms, effusions, tumors, lesions, and emboli. The Doppler component can better visualize the flow and/or turbulence of the blood through the valves and chambers of the heart; hence, it makes it much easier to identify regurgitation and shunts.

#### C. D-dimer NONESSENTIAL

D-dimer results from the breakdown of cross-linked fibrin; therefore, values below the established "cut-off" are unlikely to occur in patients with a thromboembolic phenomenon (e.g., deep vein thrombosis or pulmonary embolism). Although some of Mr. Harris's symptoms can be found in patients with a pulmonary embolism, the duration alone of his nonprogressive symptoms essentially rules out this condition. Thus, a D-dimer is not indicated.

#### **D.** First morning sputum for cytology $\times$ 3 ESSENTIAL

This test is indicated because of Mr. Harris's history of hemoptysis and dyspnea in conjunction with his long-standing smoker status to rule out a primary lung malignancy as the cause of his hemoptysis. Despite the fact that the majority of the other findings of his history and physical examination are not very consistent with this diagnosis, these three symptoms alone justify the testing.

**E.** Antinuclear antibodies (ANA); erythrocyte sedimentation rate (ESR); antinative DNA; anticardiolipin antibodies, including lupus anticoagulant;  $C_3$  and  $C_4$  complement assay; systemic lupus erythematosus preparation (SLE prep); and CBC w/diff NONESSENTIAL

Although an autoimmune inflammatory disease could be responsible for Mr. Harris's condition, he lacks sufficient symptomatology to justify an evaluation at this time.

#### 4. Diagnosis

#### A. Lung cancer INCORRECT

Even though his sputum cytologies are pending, Mr. Harris's lack of identifiable masses/lesions on CXR, no significant constitutional symptoms, and identified cardiac abnormalities make other diagnoses more likely than lung cancer at this time.

#### **B.** Pulmonary embolism INCORRECT

Even though a pulmonary embolism shares some of the symptoms that Mr. Harris is complaining about, it can be ruled out because of the length of time he has been experiencing his symptoms without progression. Furthermore, he lacks history of unilateral leg edema, leg or pelvic trauma (including surgery), recent immobilization, recent air travel, or other signs, symptoms, and risks consistent with a deep vein thrombosis (DVT), which is nearly universally responsible for a PE.

#### **C.** Atypical vertucous endocarditis of Libman-Sacks secondary to systemic lupus erythematous INCORRECT

Regardless of the cause, the vertucous endocardial growths associated with Libman-Sacks syndrome are almost always apparent on echocardiogram. Furthermore, the other common cardiac manifestations of this condition (e.g., left atrial emboli and mitral regurgitation) are also generally apparent on an echocardiogram. Because Mr. Harris's echocardiogram did not reveal any of these findings (and in fact revealed mitral stenosis), this is not his most likely diagnosis.

#### D. Left atrial myxoma INCORRECT

A left atrial myxoma is a benign growth arising from connective tissue of the myocardium that intrudes into the cavity of the left atrium and obstructs the proper emptying of the chamber, producing a diastolic murmur, dyspnea, and several of the hemodynamic findings similar to what Mr. Harris is experiencing. However, a left atrial myxoma is generally associated with systemic symptoms that he denied (e.g., fatigue, weight loss, and fever) as well as some that were not evaluated for (i.e., anemia). Normally they are visible as a mass in the left atrium on echocardiography. In view of this information, a left atrial myxoma is not Mr. Harris's most likely diagnosis.

#### E. Mitral stenosis with associated tricuspid stenosis CORRECT

The murmurs identified on Mr. Harris's physical examination and confirmed by echocardiography are typical for both mitral stenosis with regurgitation and tricuspid stenosis with regurgitation.

Furthermore, the opening snap from the mitral valve is normally heard almost immediately following the sound created by the closure of the aortic valve. However, in conditions such as mitral stenosis, these two sounds become more separate and distinct. In fact, the severity of the mitral stenosis is proportional to the length of time between the two sounds. The size of the mitral valve opening on his echocardiogram further confirms the consistency of this finding.

Normal orifice size for the mitral valve is 4 to 6 cm<sup>2</sup>. The opening can get as small as 1 to  $1.5 \text{ cm}^2$  and still produce a relatively normal cardiac output; however, with exercise, it tends to have a subnormal rise. This degree of stenosis is referred to as moderate. Severe mitral stenosis is associated with a valvular orifice of less than 1 cm<sup>2</sup>. If the pulmonary vascular resistance is significantly increased when the orifice is this small, the cardiac output is subnormal at rest and often does not increase but declines further during activity.

His hemoptysis is most likely caused by an elevated pulmonary vascular resistance from rupture of pulmonary–bronchial venous communications and/or a secondary pulmonary venous hypertension. Therefore, from the information that has been gathered thus far, this is his most likely diagnosis. Additional support is provided for this diagnosis per his ECG findings, facial discoloration, and rash. The large P waves identified are most likely caused by an atrial enlargement. When these are also accompanied by tall, peaked P waves in II and upright P waves in V<sub>1</sub>, they are generally caused by a combination of mitral stenosis and tricuspid stenosis and/or pulmonary hypertension. A blue face and malar rash like Mr. Harris has can be attributed to cardiopulmonary conditions (e.g., mitral stenosis associated with tricuspid stenosis and mitral stenosis associated with pulmonary hypertension) or cardiac medications (e.g., amiodarone).

#### 5. Treatment Plan

**A.** Hospitalization with oxygen therapy starting at 2 L/min after arterial blood gases and then adjusted accordingly, cardiac monitoring, and IV line to keep vein open (KVO) CORRECT

The seriousness of Mr. Harris's condition, his hypoxia and dyspnea, and the fact that he will require additional cardiac monitoring and interventions support him being hospitalized.

**B.** Refer to thoracic surgeon and oncologist for evaluation and treatment of lung cancer INCORRECT

Because there is no current evidence to suggest that Mr. Harris has either a primary or secondary lung cancer, there is no need for these consultations at this time.

If his sputum cytologies come back positive, then this would be appropriate after obtaining a chest CT, with and without contrast, to evaluate for lesions and hilar lymphadenopathy that were too small or "hidden" on his CXR. Ideally, the CT should be performed even if his cytology is negative.

**C.** Refer to cardiac surgeon for possible cardiac catheterization, possible balloon valvuloplasty, or other interventions CORRECT

Mr. Harris is going to require cardiac catheterization to assess for any evidence of mitral regurgitation that was not identified on the echocardiogram and to provide more accurate and direct measurements of his pulmonary artery, left atrium, and left ventricle. These findings along with his history, physical, and diagnostic studies thus far obtained will permit the cardiac surgeon to determine the most appropriate intervention/treatment for his condition.

Cardiac catheterizations are also indicated if there is discordance between echocardiographic findings and the patient's symptoms, especially if the patient is symptomatic or the pulmonary arteries and the left atrium pressures during exercise don't correlate.

For symptomatic patients with significant disease (in mitral stenosis defined as a valve area of less than 1.5 cm<sup>2</sup> and in tricupsid stenosis defined as a effective orifice of less than 1.5 to 2.0 cm<sup>2</sup> and a diastolic pressure gradient of greater than 4 mm Hg), unless contraindicated, the treatment of choice is valvotomy. This can be accomplished by balloon valvuloplasty or "open" surgical repair for the mitral valve and by surgical correction alone for the tricuspid valve. In asymptomatic patients who meet the aforementioned mitral valvular area criteria PLUS have severe pulmonary hypertension or recurrent embolization (systemic), a valvotomy is also indicated.

In patients who have contraindications to a valvotomy or had a failed valvotomy, valvular replacement is indicated.

Valvotomy patients must be a New York Heart Association (NYHA) II, III, or IV. Valvular replacement patients must be a NYHA III or IV. A class I patient has no impairment and can perform normal activities. A class II patient has some mild limitations in performing activities of daily living (e.g., cannot walk up a flight of steps rapidly, in the cold, after a meal, or carrying objects of minimal weight). Class III individuals have marked physical limitation (e.g., cannot walk one to two blocks on level ground and cannot ascend steps rapidly); however, they are comfortable at rest. Class IV patients have significant difficulty in carrying out activities of daily living and become symptomatic from mild exertion; they often experience symptoms at rest.

#### D. Start on warfarin therapy INCORRECT

The primary reason to start patients with tricuspid and mitral regurgitation on warfarin therapy is a coexisting atrial fibrillation, endocarditis, or thromboembolus (which he does not have). However, if he requires a valvular replacement, he will be required to initiate warfarin at that time.

#### E. Encourage smoking cessation CORRECT

Mr. Harris needs to be encouraged to quit smoking. Although the number one reason people stop smoking is because their HCP told them to do so, he is not going to be successful until he decides it is a priority. Therefore, utilizing the five A's developed by the Agency for Health Care Policy and Research—Ask, Advise, Attempt, Assist, and Arrange—is an appropriate plan. Furthermore, smoking cessation should be discussed during each visit with patients who smoke.

#### **Epidemiologic and Other Data**

Rheumatic fever is the main cause of both mitral (approximately 40%) and tricuspid stenosis. Typically, the symptoms do not occur until approximately 15 to 20 years after the episode of rheumatic fever beginning with the mitral valve: Then, they tend to be gradual in onset and worse over a 3- to 4-year period. Approximately 66% of all cases occur in women.

The majority of cases (60 to 70%) of hemoptysis that present in the outpatient setting are caused by some type of pulmonary infection (e.g., bronchitis, pneumonia, or tuberculosis).

## **CASE 1-8**

#### **Harriett Issac**

#### 1. History

**A.** Has she ever experienced similar symptoms in the past? ESSENTIAL

This is an excellent question to ask virtually all patients, especially if they are complaining of acute pain. If positive, it provides information regarding prior circumstances, recurrence, progression, and previous diagnosis and suggests a chronic condition.

**B.** Is she aware of any other aggravating or alleviating factors? ESSENTIAL

Although important with any complaint, knowledge of aggravating and alleviating factors is even more significant when the patient is experiencing pain because the more information that is available regarding the condition, the more likely it is that the correct diagnosis will be established.

**C.** What type of evaluation and diagnostic tests were performed on her in the emergency department following her MVA, and what were the results? ESSENTIAL

Knowing which components of a physical exam and which diagnostic studies were previously performed and their findings are important when evaluating a patient for continuation of a problem. This provides a baseline assessment from which to work and to compare results while attempting to diagnose the multitude of conditions that could be responsible for Mrs. Issac's chest pain and dyspnea, especially because it is compounded by trauma, depression, and anxiety.

The most common serious conditions that must be included on Mrs. Issac's differential diagnosis list include aortic dissection, aortic root dissection, cardiac contusion, cardiac effusion and/or tamponade, myocardial ischemia, myocardial infarction, cardiomyopathy, ruptured papillary muscles, pneumothorax, and hemithorax.

**D.** Has she been experiencing any diaphoresis, palpitations, tachycardia, anxiety, or shakiness? ESSENTIAL

Although virtually any of the aforementioned conditions could be associated with these symptoms, they could also be caused by an excess catecholamine release and/or anxiety. Nevertheless, knowing if she is experiencing them can assist in determining her correct diagnosis.

**E.** Does she have any other grandchildren to replace the one she lost? NONESSENTIAL

In attempting to establish good rapport with a patient, especially in nonemergent situations, it is appropriate to inquire about one's family. However, it is inappropriate to even suggest that you can replace a recently deceased person with another. This is especially distasteful given the circumstances surrounding her grandson's death.

#### 2. Physical Examination

A. Heart examination ESSENTIAL

Because Mrs. Issac is complaining of chest pain, it is essential to perform a careful heart examination as outlined in Case 1-2.

#### B. Lung auscultation ESSENTIAL

Because she is experiencing dyspnea, it is essential to perform a comprehensive lung examination as outlined in Case 1-5. In dealing with the combination of chest pain, dyspnea, and trauma, it is important to remember when performing the physical examination and reviewing the CXRs that the apexes of the lungs extend above the clavicles. A small pneumothorax in that area can easily be missed if it is not being diligently sought.

#### C. Palpation of ribs ESSENTIAL

Even though Mrs. Issac had rib radiographs the previous evening that were reported as normal, it is still good medical practice to palpate the ribs for tenderness, crepitus, flailness, dislocations, and other signs of rib fracture because rib fractures are notoriously difficult to identify on CXR, especially if rib enhancement films were not performed. The sharp point of a progressing dislocated rib fracture could result in a

#### Case 1-8 Responses and Discussion

pneumothorax or a hemothorax, which would produce symptoms very similar to Mrs. Issac's.

Complete rib fractures have also been known to rupture spleens, perforate stomachs, and cause other intra-abdominal trauma resulting in peritoneal hemorrhage. However, if that were the case, Mrs. Issac should be complaining of abdominal pain, experiencing hypotensive and tachycardic episodes, and suffering from lightheadedness, vertigo, presyncope, or syncope. Furthermore, all of these symptoms should be getting progressively worse since their onset.

**D.** Evaluation of jugular venous pressure (JVP) and ankles/feet for edema ESSENTIAL

Because cardiomegaly is suggested by her heart examination, it is important to also evaluate her JVP to obtain a quick estimation of her CVP and evidence of right atrium involvement as well as evaluate her feet/ankles for edema, which could suggest the presence of heart failure.

E. Visual acuity NONESSENTIAL

Because Mrs. Issac did not lose consciousness and has not experienced a headache, visual disturbances, and/or signs or symptoms of an intracranial or cranial nerve injury during or since her accident, checking her visual acuity is not necessary at this time.

#### 3. Diagnostic Studies

A. Brain natriuretic peptide (BNP) ESSENTIAL

Because Mrs. Issac has abnormal heart sounds, a murmur, and cardiomegaly evident on her physical examination, a BNP is indicated to rule out heart failure. Although it is rare for this condition to exist without the presence of pedal edema, she might regularly wear support/compression stockings and/or sit with her feet supported, which would minimize pedal edema, or she could be spending more time supine and would have presacral edema instead.

Although trauma is not a significant cause of heart failure, traumatic pericardial effusions, hemopericardium, and cardiac tamponade can produce it. Still, it is unlikely to develop this quickly after injury. Nevertheless, there is no guarantee that Mrs. Issac's complaint is related to her accident, so heart failure must be ruled out.

B. Serial cardiac troponin levels (cTn-I and cTn-T) ESSENTIAL

Any patient who presents with severe, pressurelike chest pain with radiation into their left shoulder and arm (especially if associated with dyspnea) is considered to be having a myocardial infarction until proven otherwise. Hence, it is essential to do serial cardiac troponin levels on Mrs. Issac.

Even though cardiac troponins are very sensitive for myocardial damage, it is not impossible to get a small elevation from myocardial injury without infarction and/or severe or extensive skeletal muscle injury. Furthermore, cardiac troponins can elevate in response to cardiac ischemia as well. However, the rise due to myocardial and skeletal muscle ischemia and contusions is generally not going to be nearly as significant or as predictive as that with myocardial infarction.

**C.** Electrocardiogram (ECG) and echocardiogram ESSENTIAL The presence of pressure-like chest pain, left shoulder and arm pain, dyspnea, trauma, cardiomegaly, and abnormal heart sounds, justifies the performance of both of these tests to further assess Mrs. Issac's cardiac status. The ECG will provide, among other things, information regarding her heart rate, rhythm, conduction, and myocardial oxygenation status.

The echocardiogram can further evaluate for the presence of myocardial dyskinesis, papillary muscle and/or valvular rupture, other valvular abnormalities, the presence of emboli, pericardial effusions, and pericardial and myocardial tissue trauma/damage, as well as provide better estimates of chamber size and volume, overall cardiac size and shape, and an estimation of her ejection fraction.

#### D. Chest x-ray (CXR) ESSENTIAL

A CXR is indicated not only to obtain a view of the cardiac shadow but also to look for signs of heart failure that are not yet evident on physical examination, hemothoraxes, pneumothoraxes, and other pulmonary complications or problems.

**E.** 24-Hour urine vanillylmandelic acid (VMA) and catecholamine levels ESSENTIAL

Although these tests would likely not be ordered until Mrs. Issac's CXR is viewed, 24-hour urine VMA and catecholamine levels are essential in determining her most likely diagnosis. They are indicated to evaluate for a severe stress reaction with catecholamine release causing the abnormal ballooning pattern of her left ventricle evident on CXR.

The most common indications for these tests is to assist in the diagnosis of pheochromocytoma, a rare cause of secondary hypertension. They are also helpful in diagnosing neuroblastomas and rare adrenal tumors. However, the values can also be elevated with a ganglioneuroma, a ganglioneuroblastoma, some forms of cardiomegaly, strenuous exercise, and acute anxiety.

There is the potential for both false-positives and falsenegatives as the levels are affected by strenuous exercise, stress, starvation, some foods (e.g., caffeine, chocolate, and vanilla), and some medications (e.g., aminophylline, clonidine, erythromycin, imipramine, levodopa, lithium, methyldopa, nicotinic acid, nitroglycerine, phenelzine, quinidine, reserpine, salicylates, tetracycline, and tranylcypromine). Hence, multiple factors must be taken into account and caution utilized in interpreting the results of these tests.

#### 4. Diagnosis

#### A. Pheochromocytoma INCORRECT

A pheochromocytoma is a functional chromaffinoma that is most commonly derived from adrenal medullary tissue that secretes catecholamines, which results in hypertension and distinct episodes of headaches, nausea (generally without vomiting), palpitations, dyspnea, severe perspiration, and other signs of autonomic dysfunction. Even though Mrs. Issac's BP is elevated, she does not have a history of hypertension, which would be unusual for a pheochromocytoma advanced enough to produce her current symptoms. Furthermore, despite her total free catecholamines being elevated, her metanephrine level, the catecholamine most commonly elevated in pheochromocytoma, is not. Thus, pheochromocytoma is not her most likely diagnosis.

**B.** Acute inferior myocardial infarction (AIMI) INCORRECT An AIMI would not be an unlikely diagnosis for Mrs. Issac because of her symptoms, slightly elevated cardiac troponin

levels, ECG findings, and echocardiography results. However, if she were having an MI, based on the location of the ST-segment elevations, it would most likely be in the anterior portion of her heart because that is the area of the heart reflected in precordial leads  $V_1$  through  $V_5$ . An AIMI would be expected to show the ST changes in leads II, III, and aVF. Hence, this is not her most likely diagnosis.

#### C. Heart failure INCORRECT

Even though she has dyspnea associated with cardiomegaly, heart failure is not her most likely diagnosis because she does not have an elevated BNP or other signs on her physical examination or CXR to support this diagnosis.

#### D. Takotsubo cardiomyopathy CORRECT

Takotsubo cardiomyopathy, or apical ballooning syndrome, is a rare form of dilated cardiomyopathy that begins with an abrupt onset of severe chest pain. It generally presents with ECG changes that are consistent with an acute anterior MI; however, the coronary vessels are angiographically normal and the left ventricle exhibits the typical "octopus (or Takotsubo) pot" ballooning. It almost always follows a major release of catecholamines caused by severe physical or emotional stress, surgery, alcohol withdrawal, and certain medical conditions (e.g., hypoglycemia and hyperthyroidism). Thus, this is Mrs. Issac's most likely diagnosis from the list provided.

#### E. Chest pain secondary to stress reaction INCORRECT

Chest pain secondary to stress reaction implies that no actual physical damage and/or objective findings are present to account for the pain. Therefore, in view of her physical examination and diagnostic studies, this cannot be her most likely diagnosis.

#### 5. Treatment Plan

**A.** Hospitalize with telemetry and close monitoring of vital signs CORRECT

With Mrs. Issac's degree of cardiomegaly and ventricular abnormality as well as slightly elevated troponin level, hospitalization is definitely indicated for close monitoring, further diagnostic evaluation, and treatment.

**B.** Repeat cTn-I and cTn-T in 4 and 8 hours CORRECT

Repeating her cardiac troponins in 4 and 8 hours is going to permit an indirect assessment of the oxygenation status of her myocardium. A decreasing, plateauing, or insignificantly elevating level is more likely caused by ischemia secondary to the catecholamine storm effect on the epicardial vessels and/or coronary microcirculation or from skeletal muscle trauma. A significant elevation is more suggestive of an acute myocardial infarction.

#### C. Cardiac catheterization CORRECT

Although Takotsubo cardiomyopathy is not associated with an obstruction of the epicardial arteries, her symptoms mandate that her coronary vasculature be evaluated to ensure that she does not have significant atherosclerosis, obstruction, or emboli. If a significant abnormality is present, then early treatment can also be instituted for that problem.

**D.** Meperidine 50 mg IM every 3 to 4 hours as needed INCORRECT

Mrs. Issac should not receive meperidine for her pain because she has a history of an allergic reaction to it in the form of urticaria.

#### E. Nebivolol 10 mg orally once a day INCORRECT

Beta-blockers reduce the symptoms in approximately one-third to one-half of patients with Takotsubo cardiomyopathy; however, there are no evidence-based studies or firm clinical information confirming this. Furthermore, they do not appear to be protective against sudden cardiac death. Nevertheless, because there are essentially no other treatment options available, one could be tried if her intraventricular pressure gradient is relatively normal. However, it should not be nebivolol. Nebivolol, as well as fluoxetine, is metabolized by the P-450 CYP2D6 pathway; hence, a serious adverse interaction could occur. In fact, the FDA issued a letter of warning to the manufacturers of nebivolol in November 2008 because it felt an ad in a professional journal omitted and minimized this risk. A recent study was conducted on healthy patients who had been taking fluoxetine 20 mg once a day took a single dose of nebivolol 10 mg. The combination led to an area-under-curve (AUC) increase of eightfold and a maximum concentration (C<sub>max</sub>) of threefold for d-nebivolol. Hence, hypotension and syncope could occur and produce very serious, and potentially fatal, consequences because of this interaction. This is an excellent example of the importance of obtaining FULL prescribing information and weigh the potential benefits of treatment against the potential adverse effects before initiating any drug therapy.

#### **Epidemiologic and Other Data**

Takotsubo cardiomyopathy is also known as Tako-Tsubo cardiomyopathy, stress cardiomyopathy, and apical ballooning syndrome. It occurs predominately in women over the age of 50 years. It is thought to be caused by an adrenergic surge resulting from severe physical and/or emotional stress that causes the release of catecholamines. The catecholamines then attack the epicardial vessels and/or coronary microcirculation. In the majority of cases, all the symptoms are resolved in 3 to 7 days without any residual effects.

## CASE 1-9

#### Ira Jackson

#### 1. History

**A.** Were there any changes in his medical condition, medication list (including medications used on an as-needed basis), or life when he began reexperiencing palpitations and having fluctuations of his INR? ESSENTIAL

Mr. Jackson actually has two potentially unrelated complaints—a fluctuating INR and cardiac palpitations—plus he has confusion regarding the purpose of his medications. Although he takes the warfarin for his atrial fibrillation (AF), it is to prevent him from having a CVA caused by an embolus that formed in his poorly contracting and emptying atrium. His warfarin does nothing to control his ventricular response. However, it is possible that the propranolol he takes for his hypertension suppresses his ventricular rate and enables him to remain relatively asymptomatic and hemodynamically stable.

#### Case 1-9 Responses and Discussion

The INR is a standardized reporting mechanism to ensure better correlation and quality between prothrombin time (PT) levels, especially when the specimens are tested at different facilities. The INR is essentially the patient's measured PT divided by the mean normal PT. In Mr. Jackson's case, it is being utilized to monitor the anticoagulant effect of his warfarin.

Warfarin produces its anticoagulant effect by interfering with the body's vitamin K (which is required for the carboxylation of glutamine) conversion cycle, which in turn causes the liver to produce partially decarboxylated proteins that have decreased anticoagulant abilities.

Hence, any medication that can prevent or reduce the production of, increase the excretion of, or prevent the absorption of vitamin K can interfere with warfarin's anticoagulant properties. Such medications include second-generation cephalosporins, third-generation cephalosporins, erythromycin, penicillin, metronidazole, moxalactam, trimethoprim-sulfamethoxazole, rifampicin, sulfonamides, thyroxine, clofibrate, cholestyramine, phenylbutazone, salicylates, nonsteroidal anti-inflammatory drugs, acetaminophen, cimetidine, omeprazole, barbiturates, carbamazepine, and alcohol. Mutations/alterations in or medications metabolized by either the P-450 hepatic CYP2C9 or the VKORC1 enzyme pathways in the liver can also alter the warfarin level upward or downward. For these reasons, it is important to inquire about new medical conditions and new medications, with an emphasis on those bought without a prescription (including vitamins, supplements, and herbal preparations), which might be taken on an as-needed basis (e.g., cimetidine, acetaminophen, or ibuprofen) or taken for short periods of time (e.g., antibiotics, antifungals, and analgesics), because the effect of the combination of the medications could either elevate or decrease his warfarin level.

Even though there are significantly fewer medications that can potentially adversely affect his propranolol level, it is still important to consider this as a possible cause of his palpitations. For example, propranolol can be potentiated by medications that contain alcohol, other antihypertensives, cimetidine, chlorpromazine, central nervous system (CNS) depressants, and thyroid hormone replacement therapy. It can also be antagonized by medications such as barbiturates, NSAIDs, phenytoin, and rifampin.

Furthermore, warfarin and propranolol can adversely affect the levels of other drugs (e.g., antiarrhythmics, anticonvulsants, calcium channel blockers, digitalis, diuretics, hypoglycemics, lidocaine, and theophylline), providing them the opportunity to produce palpitations.

Other adverse influences on the regularity of the ventricle response and hence the ability to produce palpitations in some patients include, but are not limited to, individual metabolic factors, genetic factors, neurologic (especially vagal nerve) factors, NYHA functional status classification, presence of heart failure, and length of time the arrhythmia has persisted.

**B.** Do his medications look different since he started experiencing problems? ESSENTIAL

The FDA permits generic drugs to be classified as "equivalent" if the amount of active ingredient is within 25% of the brand-name product. Therefore, if he was on a generic formulation that had 25% more of the active ingredients than the brand and was changed to a different company's generic that contained 25% less of the active ingredients, then, at least theoretically, it is possible that his medication dosage was cut in half. This could account for a change in his symptom control and result in a lower INR. Conversely, going in the opposite direction could potentially result in an elevated INR. Additionally, if he was being provided a different company's generic every time he had his prescription refilled, this could also produce intermittent INR fluctuations and palpitations.

Furthermore, there is always the concern regarding human error (that the wrong medication was dispensed) when the appearance of the medication suddenly changes. Hence, it is essential to know if there was any change, and if so, to discuss it with his pharmacist to determine if he is getting the right medications in the proper dosages. Even in cases where brand-name medications cannot be justified (or afforded by the patient), requesting that the pharmacist refill the patient's medication with a generic from the same company is helpful in eliminating the problem of dosage fluctuations that could potentially occur when changed from company to company.

C. Does he consume caffeine? ESSENTIAL

In caffeine-sensitive individuals, consuming a single serving of a caffeinated beverage is enough to incite an episode of paroxysmal AF with a variable ventricle response and palpitations like Mr. Jackson is experiencing. Excessive caffeine, even in patients who are not caffeine sensitive, can cause palpitations. Therefore, it is important to inquire regarding his caffeine intake and its relationship to his symptoms.

**D.** Does he alter the amounts of "greens" that he consumes daily? ESSENTIAL

Because warfarin itself is essentially a vitamin K analog, fluctuating levels of vitamin K intake can cause fluctuating levels of the INR. Additionally, it appears that the individuals who have the most difficulty with this problem are the patients who have been on warfarin for extended periods of time. The greatest food source of vitamin K is greens (e.g., spinach, lettuce, and kale). It is theorized that this occurs because essentially all vitamin K is derived from phylloquinone. Phylloquinone is then metabolized to vitamin KH<sub>2</sub>, which prohibits the anticoagulant effect of the warfarin, hence altering the patient's INR, especially if the daily amount consumed is altered significantly.

Furthermore, if the patient was taking vitamins, supplements, or herbal preparations with large amounts of vitamin K, or only taking them "sometimes," the same problem could occur. This underscores the importance of a drug history that specifically inquires about over-the-counter medications, supplements, and herbal preparations because many patients frequently do not consider these to be medications and will not list to taking them unless specifically asked.

**E.** Does he alter the amount of orange juice that he drinks daily? NONESSENTIAL

Orange juice has not been implicated as a substance that can interfere with the vitamin K synthesis pathway or the liver metabolism associated with the use of warfarin or propranolol.

#### 2. Physical Examination

A. Nasal and pharyngeal examination NONESSENTIAL

B. Heart examination ESSENTIAL

Because Mr. Jackson has a history of AF and palpitations and the majority of AF is associated with underlying cardiac disease, it is very important to perform a careful heart examination as outlined in Case 1-2 not only to evaluate the AF but also to search for associated cardiac conditions that could be responsible for his intermittent palpitations.

#### C. Lung auscultation ESSENTIAL

A careful lung examination as outlined in Case 1-5 is also essential to identify any pulmonary changes caused by the AF or another underlying cardiac problem (e.g., rales from heart failure) or an associated pulmonary condition that could be causing hypoxia and precipitate the AF (e.g., wheezing secondary to asthma).

#### **D.** Evaluation of JVP ESSENTIAL

As previously stated, the height of the JVP provides a rough estimate of central venous pressure and evaluates for the presence of right atrium involvement (i.e., enlargement) which is important with his current symptoms.

#### E. Check for pedal edema ESSENTIAL

Mr. Jackson should also have his feet, ankles, and lower legs examined for pedal edema. It can result from cardiac, hepatic, or renal failure as well as some cancers. However, in Mr. Jackson's case, the greatest concern would be heart failure from a poorly controlled ventricular rate caused by the AF or from an underlying cardiac disease (e.g., myocardial ischemia, acute or old silent myocardial infarction, other arrhythmia, cardiomyopathies, or valvular heart disease).

#### 3. Diagnostic Studies

#### A. International normalized ratio (INR) ESSENTIAL

Because one of Mr. Jackson's main complaints is the inability to stabilize and maintain his INR at its goal, it is important to know what his current INR and INR goal are. Essentially, unless he has a prosthetic heart valve, his INR range would be somewhere between 2 and 3, with a goal of 2.5. With a mechanical heart valve, the patient's goal would be at least 2.5.

However, as medical treatments continue to evolve and a greater emphasis is placed on evidence-based medicine, equally (if not more) important is to determine whether Mr. Jackson is still an appropriate candidate for warfarin therapy. Numerous studies have been conducted with a multitude of stroke risk assessment tools to assist in determining which AF patients are most likely to have a CVA.

The American College of Cardiology (ACC), the AHA Task Force on Practice Guidelines, and the European Society of Cardiology (ESC) Committee for Practice Guidelines all agree that based on the currently available evidence, all patients with AF require some type of anticoagulation therapy; however, it might not be warfarin.

These organizations recommend utilizing a risk stratification system in which the patient's demographics and comorbidities are placed into one of three risk categories (invalidated/very weak, moderate, and high) to determine the likelihood of an embolic phenomenon occurring from their AF and resulting in a CVA. In other words, are the benefits relative to the prevention of an ischemic stroke with warfarin going to outweigh the risks of a potential hemorrhagic stroke, intracranial bleed or other serious bleed from the medication? The invalidated or very weak-risk factors include being female, being between the ages of 65 and 75 years, having coronary artery disease, and having thyroid disease. Moderaterisk factors are considered being age 75 years or older, being diabetic (type 1 or type 2), having hypertension, having heart failure, and having a left ventricle ejection of 35 or less. Highrisk factors are a history of a previous CVA, TIA, or embolism; the presence of mitral stenosis; and the presence of a mechanical heart valve.

Obviously, many patients are going to have characteristics that fall into more than one of these three categories. When that occurs, the higher-level risk is considered to be the category in which the patient is placed. For example, if a patient had all four invalid/very weak-risk factors, then he or she would be placed into the no-risk category; however, if another patient had only one of those same invalid/very weakrisk factors but also had one high-risk factor, then that patient would be categorized as high risk despite possessing a total of only two risk factors.

Regarding treatment, if the patient is in the no-risk (very low) group, the most appropriate anticoagulant is aspirin 81 to 325 mg once a day. However, if the patient has one moderaterisk factor and falls into the moderate-risk category, then the patient and the HCP together would make the determination as to which was better for that individual patient—one aspirin 81 to 325 mg once a day or warfarin with an INR target as defined previously. However, if the patient has one or more high-risk factors (categorized as high risk) OR two or more moderate-risk factors (still categorized as moderate risk), the treatment choice would be warfarin.

The consensus group also supported utilizing a riskonly-based approach, which is also supported by current studies. This evidence-based approach is considered to be a class 1 (highest rating) recommendation. If the patient has any of the following comorbidities, regardless of age (except where noted), he or she is considered at high risk for a CVA and should be placed on warfarin with an INR goal of between 2 and 3: presence of a mechanical heart valve; prior thromboembolic event; mitral stenosis from rheumatic heart disease; heart failure and a minimum age of 65 years; and the triad of a left ventricular ejection fraction of less than 35%, fractional shortening of less than 25%, and hypertension.

After these AF patients are eliminated, then, age plays a significant role in this model. If the patient is younger than the age of 60 years and does not have any of the aforementioned conditions, regardless of whether or not any other cardiac conditions or risks exist, antithrombotic therapy is recommended with aspirin 81 to 325 mg once a day. If the patient is between the ages of 60 and 75 years and has no other risk factors, then aspirin is also the recommended therapy. However, if a patient in this age group has either diabetes or CAD, it is recommended that he or she begin warfarin. If the patient is female and older than the age of 75 years regardless of other risk factors OR is male with any other risk factors, then warfarin is again recommended. If the patient is older than the age of 75 years, is male, and has no other risk factors, then both warfarin and aspirin are considered to be appropriate treatment options.

Another risk assessment tool to determine whether the patient with AF requires warfarin therapy is a lot easier to

remember because it provides a mnemonic,  $CHADS_2$  (cardiac failure, **h**ypertension, **a**ge older than 75 years, **d**iabetes, and previous **s**troke). For each characteristic the patient is assigned 1 point (except for stroke, which is given 2 points), for a maximum total of 6 points. A score of 0 to 2 is considered low risk and the patient should be anticoagulated with aspirin alone. A score of 3 or 4 is considered to be moderate risk and the patient and the HCP need to discuss the risks vs benefits and together determine whether aspirin or warfarin anticoagulation is more appropriate for that individual patient. A score of 5 or 6 is considered to be high risk and the patient should be instituted on warfarin therapy unless there is a contraindication.

There is a direct correlation between the numerical score and the risk of stroke with this simple system; however, the ACC, AHA, and ESC do not support it at this time because they believe it provides warfarin at too low of a risk of stroke and results in too many unnecessary adverse events, including hemorrhagic strokes.

In general, patients who have a stroke risk of less than 2% per year tend to have more adverse effects than benefits from warfarin therapy. Hence, it is not recommended for these individuals to take it. Individuals with an annual stroke risk of greater than 6% definitely benefit from warfarin therapy. It is most difficult to determine the risk vs benefit ratio for moderate-risk individuals; that is what all of these studies and guidelines are trying to accomplish. However, it is important to remember that these are not absolutes but guidelines, and need to be treated as such. Sound clinical judgment must go into the decision-making process to treat or not to treat with warfarin on an individualized basis, including the patient preference as part of that decision.

According to the initial risk assessment supported by the ACC, AHA, and ESC, Mr. Jackson would be considered moderate risk because he has two moderate-risk factors, an age older than 75 years and hypertension; therefore, he should continue his warfarin.

**B.** Hematocrit (HCT) and hemoglobin (Hgb), or H&H ESSENTIAL

The H&H provides confirmation of the history and physical findings that Mr. Jackson is not experiencing any bleeding.

**C.** Electrocardiogram (ECG) and echocardiogram, preferably transesophageal (TEE) ESSENTIAL

The ECG is essential because it permits evaluation of not only the ventricular response rate but also the atrial rate. Although no standards have been set regarding the goals of heart rate therapy, the accepted criteria are a ventricular rate between 60 and 80 BPM at rest and 90 and 115 BPM with moderately intense exercise. Additionally, the ECG is important for Mr. Jackson as it assists in searching for other causes of his palpitations in addition to his AF.

A TEE not only provides a clear picture of all the structural and functional details of the heart as outlined in Case 1-5, but also permits an evaluation for underlying cardiac abnormalities that are associated with AF. Furthermore, if using the aforementioned risk assessment stratification system as approved by the ACC, AHA, and ECS, a accurate measurement of the left ventricular ejection fraction is necessary. **D.** Thyroid panel, hepatic function, and renal function ESSENTIAL

These tests are also recommended by the ACC, AHA, and EUS as essential in evaluating AF. They are beneficial in ruling in or ruling out some of the correctable causes of AF (e.g., hyperthyroidism or hepatic damage/cirrhosis caused by excessive alcohol intake) as well as in ensuring adequate hepatic and renal functioning before instituting any medications.

E. Holter monitor (outpatient telemetry) ESSENTIAL

According to the ACC/AHA/ECS, a Holter monitor is not indicated as part of the initial evaluation of AF. However, the ACC/AHA/ECS guidelines would support utilizing this diagnostic test for Mr. Jackson because their main recommendations in confirming AF include determining whether the ventricular response rates (at rest and with exercise) are within the recommended ranges, evaluating further the patient who fails to respond to appropriate antiarrhythmic therapy, and/or evaluating for a second arrhythmia.

#### 4. Diagnosis

**A.** Recurrent paroxysmal atrial fibrillation with fluctuations in INR as a result of inconsistent dietary vitamin K intake CORRECT

AF is relatively easy to diagnose if the patient is experiencing the abnormal rhythm during evaluation. Its diagnostic criteria consist of a suspicious history, an irregularly irregular pulse on physical examination, and the identification of the abnormality on ECG.

However, because he has good rate control at rest with the propranolol and appears hemodynamically stable, but is still complaining of palpitations, an additional cause should be sought. His Holter monitoring reveals that his AF only occurs in bursts, or spasms; hence, the diagnosis of recurrent paroxysmal atrial fibrillation can be confirmed by this diagnostic test.

Regarding his INR control, the pharmacodynamics of warfarin vary significantly from one individual to another; however, usually by frequent dosage adjusting and laboratory monitoring, one can generally achieve the desired INR goal in almost all individuals. If not, attention needs to be directed towards not only other medications that utilize the P-450 hepatic CYP2C9 or the VKORC1 enzyme pathways but also of medications and foods that can have an effect on metabolism of vitamin K (which can lower the INR level, as warfarin is a vitamin K analog). In Mr. Jackson's case, the problem appears to be a significant variation in the amount of "greens" he consumes from one day to the next. Thus, this is Mr. Jackson's most likely diagnosis.

**B.** Atrial fibrillation with poor medical compliance INCORRECT

In general, patients who are noncompliant with their medication regimen tend to miss doses of their medication and/or take it irregularly, which would result in Mr. Jackson's INR fluctuating from low (when noncompliant) to normal (when compliant) However, there are a few patients who take more medication than prescribed, either trying to "catch up" on doses before they are due to have their INR checked, thinking it will normalize it, or when they remember they missed several doses. Additionally, some patients hold the belief that "if one is good, two is better"; therefore, they will

take extra medication if they "feel like" they need it. This latter practice could result in an INR that is high, low, or normal. Regardless, this is not Mr. Jackson's most likely diagnosis because a potential food–drug interaction was identified and he denies poor compliance with his medications.

Consultation with the patient's pharmacist to see if refills are obtained on schedule can sometimes add support to the suspicion of medication noncompliance. For example, if the patient is "late" in refilling his or her medication, he or she could be taking less than prescribed. Conversely, if the patient is consistently requiring his or her medication before the refill is technically available, he or she may be taking more than prescribed. However, it is important to remember that even though the patient might obtain the prescribed medication, he or she is not necessarily taking it as directed.

**C.** Familial atrial fibrillation with fluctuations in INR as a result of inadequate vitamin C in diet INCORRECT

Mr. Jackson's AF is probably a familial form because of his strong family history of AF and his lack of any other apparent cardiac abnormalities or associated conditions. Because vitamin C is not known to have a significant effect on warfarin metabolism and his daily intake of vitamin C is consistent, this is not his most likely diagnosis.

D. Atrial fibrillation with normal INR INCORRECT

Although Mr. Jackson has AF, he does not have a normal INR (patient, 1.6; treatment goal, 2.5 [or range between 2 and 3]). Thus, this is not his most likely diagnosis.

**E.** Atrial flutter with excessive propranolol dosage responsible for palpitations and INR fluctuations INCORRECT

Atrial fibrillation, not atrial flutter, was identified on Mr. Jackson's ECG. Atrial fibrillation tends to be the faster of the two arrhythmias and is characterized by the inability to visualize the P wave and an irregularly irregular rate. Atrial flutter is characterized as an atrial rate between 250 and 350 BPM and exhibits the pathognomonic flutter (or "sawtooth") appearance.

Propranolol is metabolized through one of the same pathways as warfarin. Therefore, it is possible for them to alter one another's dosage either positively or negatively depending on whichever medication binds to the most receptor sites. However, if he is on the same dose of propranolol daily and does not miss any of the doses, another factor should account for the fluctuating INR and his warfarin dosage should be able to be regulated accordingly. Thus, this is not his most likely diagnosis.

#### 5. Treatment Plan

A. Add digoxin 0.125 mg once a day CORRECT

When treating a patient with AF, there are three primary treatment goals: (1) rate control, (2) rhythm control, and (3) prevention of thromboembolism. Initial management of a patient who is hemodynamically stable and not in the acute phase of the onset of the illness can be either a rate-control or a rhythm-control strategy. The goal of rate control is to manage the ventricular response without any concern regarding the underlying rhythm disturbance. Rhythm control not only attempts to restore the patient to normal sinus rhythm but also assists in controlling the rate. According the ACC/AHA/ECS guidelines, rate control is generally accomplished with a beta-blocker or a nondihydropyridine CCB. In the past, when patients failed to respond to the medication, the dosage was increased until the desired results were achieved or the patient quit taking it because of adverse events. This practice is no longer recommended.

Because Mr. Jackson does not appear to be having any difficulty with his current dosage of propranolol, it would be logical to add a medication that worked via another pathway to complement his propranolol instead of pushing the medication to the point where he discontinues it because of adverse effects. This is currently the accepted recommendation. Therefore, he should be tried on a medication for rate control. The drug of choice for this is digoxin. The combination of digoxin and either a beta-blocker (or a CCB) should control the rate during both exercise and at rest. Caution must be taken to keep from causing a bradycardia with this combination. Additionally, digoxin should not be utilized as monotherapy to achieve rate control in paroxysmal AF.

#### B. Schedule for nodal ablation INCORRECT

Nodal ablation is only indicated in chronic, stable patients when they do not respond to or are intolerant of pharmacologic therapy with a combination of digoxin and a beta-blocker or a CCB. It can be done either by medication or laser ablation. The agent of choice for this procedure is IV amiodarone. Other acceptable agents include IV procainamide, disopyramide, and ibutilide. An alternative to pharmacologic ablation in a hemodynamically stable patient would be to add oral amiodarone to his current regimen.

If medications fail to control the ventricular rate or the sustained tachyarrhythmia caused a cardiomyopathy, a catheter-directed ablation is indicated. Radiofrequency ablation is the first-line choice for AV nodal ablation in very young and/or very symptomatic patients.

#### C. Schedule for pacemaker implantation INCORRECT

As long as the patient with AF remains hemodynamically stable, a pacemaker is not indicated until an adequate trial of an antiarrhythmic and/or a negative chronotropic agent has been unsuccessfully tried. The patient population that appears to benefit most from the combination of AV nodal ablation and permanent pacemaker insertion is again those who have developed a cardiomyopathy from the sustained tachyarrhythmia. The combination of a permanent pacemaker following AV nodal ablation is a very effective technique to improve symptomatic tachycardia in some patients.

#### D. Schedule for cardioversion INCORRECT

Cardioversion would only be recommended for Mr. Jackson if all available pharmacologic regimens and other techniques have failed to improve his ventricular rate. The main reason to avoid it with Mr. Jackson, if at all possible, is because it significantly increases the risk of thrombolic events despite pretreatment with an anticoagulant when AF has been present for more than 48 hours.

However, there are instances when a patient will require that his or her rhythm be restored to normal sinus rhythm immediately. This is most frequently done to prevent worsening of ischemia and/or angina, when hypotension and/or syncope are present, and/or for acute-onset heart failure. Anticoagulants should always be administered preprocedurally if at all possible.

Chemical cardioversion can generally be accomplished utilizing one of the following agents IV: flecainide, dofetilide, propafenone, or ibutilide. Amiodarone is a reasonable secondline option. Electrical cardioversion is usually the preferred method when the situation is acute. Interestingly, therapy with a statin, via an unknown mechanism, has significantly worked in maintaining the patient in normal sinus rhythm once conversion has been successful.

**E.** Advise patient to consume the same amount of "greens" daily and adjust warfarin dose accordingly CORRECT

If the fluctuations of Mr. Jackson's INR are caused by the significant variability of the quantity of "greens" he consumes on a daily basis, eliminating this irregularity should permit dosage adjustments that will successfully maintain his INR within the correct range of 2 to 3.

#### **Epidemiologic and Other Data**

Atrial fibrillation is considered to be the most common sustained cardiac arrhythmia. It is estimated that it will affect approximately 25% of the U.S. population older than the age of 40 years, with the vast majority (over 19%) of these patients being older than the age of 65 years. It occurs much more often in males than in females. This gender difference increases with advancing age and is approximately doubled after the age of 75 years. It generally occurs in patients with underlying cardiac disease.

It is estimated that the initial presentation of AF will be an atrial thrombus in approximately 15% of the cases. The annual CVA rate is 45% for uncoagulated patients and 14% for coagulated patients. According to the Framingham data, the risk of CVA also increases with advancing age.

There are six types of AF recognized by the American Heart Association: (1) AF without associated heart disease, (2) AF with associated heart disease, (3) familial (genetic) AF, (4) AF associated with other medical conditions, (5) AF associated with autonomic influences, and (6) reversible AF. It is important for the patient to be knowledgeable of his or her type because in some instances, medical treatments commonly used in AF are contraindicated.

AF without associated heart disease, also known as "lone AF," is most generally found in younger patients. It is estimated that 30 to 45% of paroxysmal AF and 20 to 25% of persistent AF in younger patients are idiopathic. However, as time passes, an underlying cause may identify itself in many of these cases. This is much rarer to see in the elderly because of the normal effects of aging on the heart.

AF with heart disease is the most common type. It has definitely been linked with certain cardiac conditions including mitral stenosis and/or regurgitation, heart failure, coronary artery disease, and hypertensive heart disease with left ventricular hypertrophy. It has been strongly associated with many other primary cardiac diseases such as congenital defects, hypertrophic cardiomyopathies, and dilated cardiomyopathies. Other potential comorbid diseases include pure cardiac conditions (e.g., restrictive cardiomyopathies, constrictive pericarditis, mitral valve prolapse with regurgitation, mitral valve prolapse without regurgitation, calcification of the mitral annulus, right atrial dilation, and cardiac tumors). Cardiopulmonary conditions associated with AF include cor pulmonale, right ventricular dilation, and arrhythmias produced by hypoxia.

Familial, or genetic, AF is a "lone AF" that tends to be found in family clusters. The exact cause is unknown, but patients with idiopathic AF tend to have a first-degree family member with AF. Additionally, just as a family history of AF increases the incidence of AF, so too does a family history of hypertension, diabetes mellitus, and heart failure. Work is currently under way to identify this genetic malfunction.

The next group consists of those individuals who have AF associated with other medical conditions. This group could probably be included in the reversible causes of AF because the primary one is obesity. Long-term obesity is related to left atrial dilation. Weight reduction has recently been shown to decrease the size of the left atrium; hence, it is possible that this could reduce or eliminate this form of AF and its subsequent risk of CVA.

AF associated with autonomic influences is another classification. The autonomic nervous system appears to have a significant role in the development of AF. It appears that either vagal or sympathetic predominance must exist before AF can occur. Vagal-mediated AF appears to be much more common and occurs after activities such as eating a large meal or during sleep. Adrenergically induced AF typically happens in the daytime and is often seen in patients who have organic cardiac disease. One of the primary differences between a vagally mediated AF and a nonvagally induced AF is the fact that normal medications used in AF (e.g., adrenergic blocking agents and digitalis) can worsen the symptoms; however, anticholinergic drugs (e.g., disopyramide) are often helpful to reduce the frequency or completely eliminate the AF. Betablockers are considered to be the treatment of choice in these neurologic-mediated cases of AF.

The final category is reversible AF. Examples include hyperthyroidism, excessive alcohol intake during a "binge," sleep apnea, myocardial infarctions, pericarditis, myocarditis, pulmonary embolism, surgery (especially pulmonary or cardiac), and electrocution.

## **REFERENCES/ADDITIONAL READING**

- The Agency for Health Care Policy and Research. Smoking cessation clinical practice guidelines. *JAMA*. 1996;275(16): 1270–1280.
- Aghababian RV, ed. *Essentials of Emergency Medicine*. Sudbury, MA: Jones & Bartlett Publishers; 2006.
  - Aghababian RV Diop D. Acute Coronary Syndrome (ACS). 97–116.

Anderson III HL. Chest Injuries. 920-929.

Gough J. Rodriguez L. Endocarditis and Myocarditis. 127–128.

Gough JE, Allison EJ, Jr. Dysrhythmias. 134-147.

Gough JE, Rodriguez LE. Cardiomyopathies. 129–130. Lai MW. Methemoglobinemia. 870–872.

Setnik G. Khan A. Hypertension. 148–155.

American Heart Association. Correction. (Additions to AHA guidelines for prevention of infective endocarditis *Circulation*. 2007;116:1736–1754.) *Circulation*. 2007;116:e376– e377.

- Antman EM, Anbe DT, Armstrong PW. et al. (writing on behalf of the American Heart Association 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction Committee). ACC/AHA Guidelines for the Management of Patients with ST-segment Elevation Myocardial Infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction. J Am Coll Cardiol. 2004:44(3):e1–e211.
- Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA 2006 Guidelines for the Management of Patients with Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients with Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *Circulation*. 2006;114:e84–e231.
- Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289(19):2560–2572.
- Duke Jr JR, Good Jr JT, Hudson LD, et al. Hemoptysis. In: Duke JR Jr, Good JT Jr, Hudson LD, et al. Frontline Assessment of Common Pulmonary Presentations. Denver, CO: Snowdrift Pulmonary Foundation, Inc; 2000. http:// www.nlhep.org/books/pul\_Pre/hemoptysis.htlm. Accessed September 6, 2008.
- Easton JD, Saver JL, Albers GW, et al. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. *Stroke* 2009;40; 2276–2293.
- Fauci AS, Kasper DL, Longo DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill Medical; 2008.
  - Antman EM, Braunwald E. ST-segment elevation myocardial infarction. 1532–1544.
  - Antman EM, Selwyn AP, Braunwald E, Loscalzo J. Ischemic heart disease. 1514–1527.
  - Braunwald E. Hypoxia and cyanosis. 229-231.
  - Braunwald E. Pericardial disease. 1488-1495.
  - Darwin JP, Czany-Ratajcak. Heritable disorders of connective tissue disease. 2461–2469.
  - Karchmer AW. Infective endocarditis. 789-798.
  - Kotchen TA. Hypertensive vascular disease. 1549-1562.
  - Low PA, Engstrom. Disorders of the autonomic nervous system. 2576–2582.
  - Mann D. Heart failure and cor pulmonale. 1443–1455. Marchlinski F. The tachyarrhythmias. 1425–1442.
  - O'Gara P, Braunwald E. Valvular heart disease. 1465–1480.
  - O'Rourke RA, Braunwald E. Physical examination of the cardiovascular system. 1382–1388.

- Prockop DJ, Czarny-Ratajczak M. Heritable disorders of connective tissue. 2461–2469.
- Rader DJ, Hobbs HH. Disorders of lipoprotein metabolism. 2416–2429.
- Wynne J, Brauwald E. Cardiomyopathy and myocarditis. 1481–1488.
- Forest Laboratories, Inc. *Important correction of drug information about Bystolic (nebivolol) tablets*. Publication #44-1014486. St. Louis: Forest Laboratories; 2008.
- Fraker TD Jr, Fihn SD (writing on behalf of the American Heart Association 2002 Chronic Stable Angina Writing Committee). 2007 Chronic angina focused update of the ACC/AHA 2002 guidelines for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association Task Force on Writing Group to Develop the Focused Update of the 2002 Guidelines for the Management of Patients with Chronic Stable Angina. *Circulation*. 2007; 116:2762–2772.
- Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients with Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation.* 2006;114:e257–e354.
- Gonzales R, Kutner J. Current Practice Guidelines in Primary Care 2009. New York: McGraw-Hill Medical; 2009. Gonzales R, Kutner J. Disease management: Cholesterol and lipid management in children. 135.
  - Gonzales R, Kutner J. Disease management: Hypertension. 148–151.
  - Gonzales R, Kutner J. Disease screening: cholesterol and lipid disorders. 40–41.
  - Gonzales R, Kutner J. Disease screening: diabetes mellitus, type 2. 49–51.
  - Gonzales R, Kutner J. Disease screening: hypertension, children and adolescents. 65.
  - Gonzales R, Kutner J. Disease screening: obesity. 72-75.
  - Gonzales R, Kutner J. Appendix IV: 95th percentile of blood pressure for boys and girls. 198.
  - Gonzales R, Kutner J. Appendix VII: Estimate of 10-year stroke risk for men. 203–204.
- Grundy SM, Cleeman JI, Bairey Merz CN, et al., for the Coordinating Committee of the NCEP. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation*. 2004;110(2):227–239.
- Hirsh H, Fuster V, Ansell J, Halperin JL. American Heart Association/American College of Cardiology foundation guide to warfarin therapy. *Circulation*. 2003;107:1692–1711.
- Johnson JL. Manifestations of hemoptysis. *Postgrad Med.* 2002;112(4):101–113.
- Judge DP, Dietz HC. Marfan's syndrome. *Lancet.* 2005;366 (9501):1965–1976.
- Kavey RE, Daniels SR, Lauer RL, Atkins DL, Hayman LL, TaubertK; American Heart Association. American Heart Associationguidelines for primary prevention of atherosclerotic

cardiovascular disease beginning in childhood. *Circulation*. 2003;107:1562–1566.

- Maron BJ. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism. *Circulation*. 2007;115:1643–1655.
- McCrindle BM, Urbina EM, Dennison BA, et al. Drug therapy of high-risk lipid abnormalities in children and adolescents: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee, Council of Cardiovascular Disease in the Young, with the Council on Cardiovascular Nursing. *Circulation*. 2007;115:1948–1967.
- National Cholesterol Education Program. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285:2486–2502.
- Onion DK, series ed. *The Little Black Book of Primary Care*.
  5th ed. Sudbury, MA: Jones & Bartlett Publishers; 2006.
  Onion DK. Cardiology. 2.1 Medications. 49–68.
  Onion DK. Cardiology. 2.2 ASHD. 68–93.
  Onion DK. Cardiology. 2.3 Arrhythmias. 93–109.
  - Onion DK. Cardiology. 2.5 Endo/Peri/Myocarditis. 119– 128.
  - Onion DK. Cardiology. 2.9 Miscellaneous. 15.
  - Onion DK. Endocrine/Metabolism. 5.4 Hyperlipidemias. 1104–1117.
  - Onion DK. Prevention and health maintenance. 14.4 Preventive maneuvers for children. 929–936.
  - Onion DK. Rheumatology/Orthopedics. 18.7 Inherited and Other Rheumatologic Diseases. 1104–1117.
- Pagana KD, Pagana TJ. Mosby's Diagnostic and Laboratory Test Reference. 8th ed. St. Louis: Mosby Elsevier; 2007 (multiple pages utilized to provide normal reference values for laboratory tests).
- Poston WC II, Stevens J, Hong Y, Fortmann SP, Franklin BA, et al. (American Heart Association Council on Epidemiology and Prevention, Interdisciplinary Committee for Prevention). Population-based prevention of obesity: the need for comprehensive promotion of healthful eating, physical activity, and energy balance: a scientific statement

from American Heart Association Council on Epidemiology and Prevention, Interdisciplinary Committee for Prevention (formerly the Expert Panel on Population and Prevention Science). *Circulation*. 2008;118:428–464.

- Sutherland JA [Onion DK, series ed. *The Little Black Book of Cardiology*. 2nd ed. Sudbury, MA: Jones & Bartlett Publishers; 2007]
  - Sutherland JA. Arrhythmias. 139-164.
  - Sutherland JA. Atherosclerotic coronary artery disease. 83–138.

Sutherland JA. Cardiomyopathies. 189-201.

- Sutherland JA. Hypertension. 217-242.
- Sutherland JA. Myocarditis, pericardial disease, and cardiac tumors. 203–215.

Sutherland JA. The EKG. 33-43.

- Sutherland JA. Valvular heart disease. 165-188.
- U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institutes. *Estimation of 10-Year Cardiac Risk for Men Based on the Framingham Study*. NIH Publication #01-3305. Washington, DC: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institutes; 2001.
- Wilson W, Taubert K, Gewitz M, et al. Prevention of Infective Endocarditis: Guidelines from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality Care and Outcomes Research Interdisciplinary Working Group. *Circulation.* 2007;116:1736–1754.
- Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: a report of the American College of Cardiology/ American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation*. 2006;114:e385–e484.