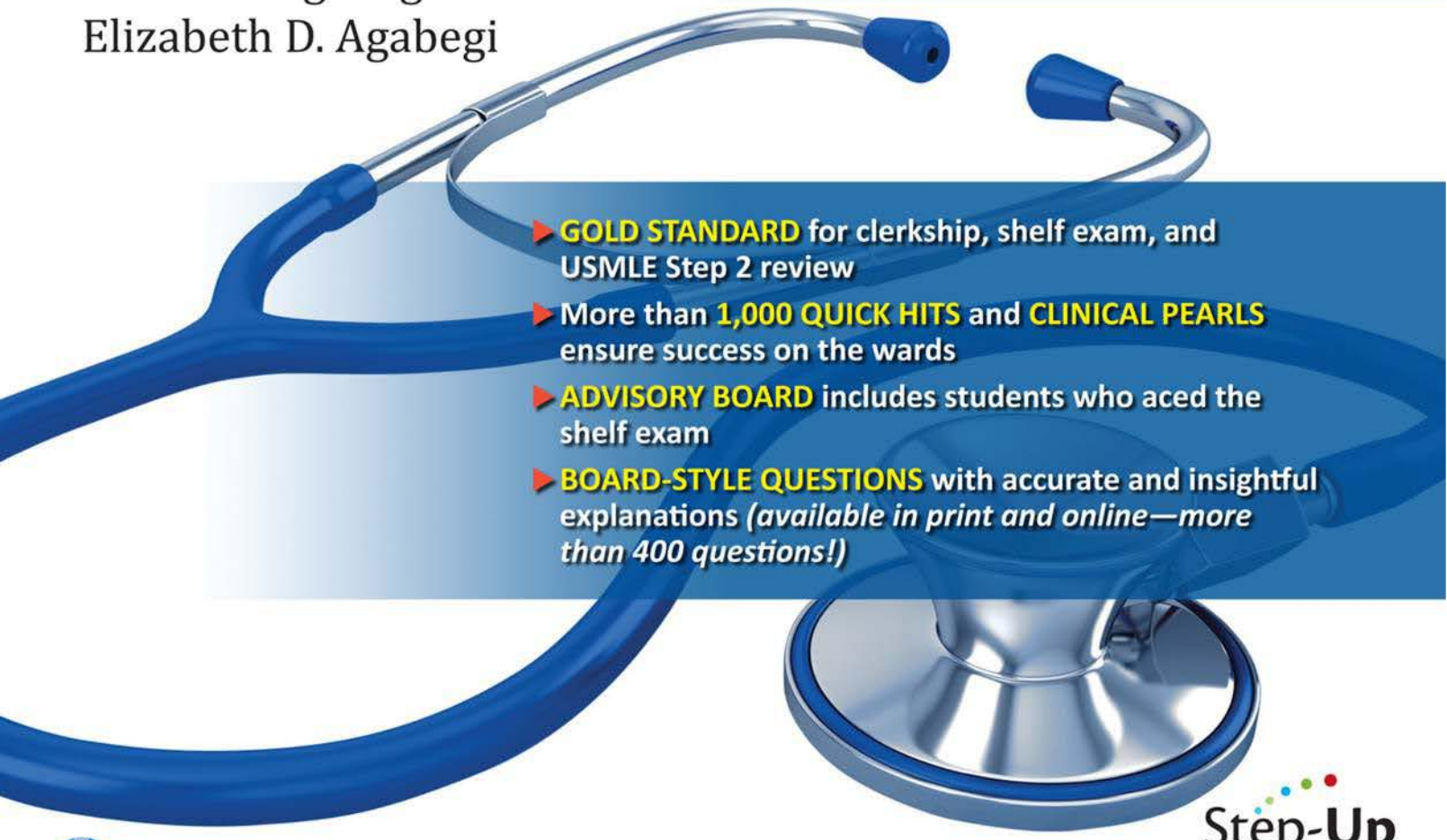
# STEP-UP to MEDICINE

FOURTH EDITION

Steven S. Agabegi
Elizabeth D. Agabegi



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# STEP-UP to MEDICINE

FOURTH EDITION

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**Elizabeth D. Agabegi, MD**

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# PREFACE

We wrote the first edition of *Step-Up to Medicine* during our third year of medical school because we could not find a review book that was concise, yet covered the breadth of pathology encountered during the internal medicine clerkship and the corresponding NBME shelf examinations. Our goal was to create a single "study tool" to spare medical students the hassle and expense of trying to extract pertinent information from multiple sources.

Now in its fourth edition, *Step-Up to Medicine* has been completely revised based on extensive feedback by both faculty and students. In addition, we welcomed an Advisory Board of students and residents to the team that worked collaboratively to enrich the content and ensure that the most tested topics were covered. And, since we know that medical students and interns have no time to waste, we retained and enhanced the high-yield outline format, Quick Hits, and Clinical Pearls. Finally, to pull it all together, we added a new 100-question, clinically-oriented practice exam at the end of the book for self-assessment. Before looking at the answers, take time to answer these questions because these are the questions you will be faced with in clinical practice.

We hope that the new edition of *Step-Up to Medicine* continues to be a valuable tool for students during the clinical years of medical school. However, we recognize the changing nature of science and medicine and encourage you to send comments or suggestions to www.lww.com.

We would like to thank the Advisory Board, and all the reviewers for their efforts in improving the content for this edition. In particular, we would like to give special thanks to Stacey Sebring, with whom we worked for the last eight years, for her tireless efforts and dedication in bringing this and previous editions of Step Up to Medicine to fruition.

***Steve and Liz Agabegi***

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# DISEASES OF THE CARDIOVASCULAR SYSTEM

# 1



## Ischemic Heart Disease

### Stable Angina Pectoris

#### A. General characteristics

1. Stable angina pectoris is due to fixed atherosclerotic lesions that narrow the major coronary arteries. Coronary ischemia is due to an imbalance between blood supply and oxygen demand, leading to inadequate perfusion. Stable angina occurs when oxygen demand exceeds available blood supply.
2. Major risk factors
   a. Diabetes mellitus (DM)—worst risk factor
   b. Hyperlipidemia—elevated low-density lipoprotein (LDL)
   c. Hypertension (HTN)—most common risk factor
   d. Cigarette smoking
   e. Age (men >45 years; women >55 years)
   f. Family history of premature coronary artery disease (CAD) or myocardial infarction (MI) in first-degree relative: Men <55 years; women <65 years
   g. Low levels of high-density lipoprotein (HDL)
3. Minor risk factors (less clear significance) include obesity, sedentary lifestyle (lack of physical activity), stress, excess alcohol use.
4. Prognostic indicators of CAD
   a. Left ventricular function (ejection fraction [EF])
      • Normal >50%
      • If <50%, associated with increased mortality
   b. Vessel(s) involved (severity/extent of ischemia)
      • Left main coronary artery—poor prognosis because it covers approximately two-thirds of the heart
      • Two- or three-vessel CAD—worse prognosis

#### B. Clinical features

1. Chest pain or substernal pressure sensation
   a. Lasts less than 10 to 15 minutes (usually 1 to 5 minutes)
   b. Frightening chest discomfort, usually described as heaviness, pressure, squeezing, tightness; rarely described as sharp or stabbing pain
   c. Pain is often gradual in onset
2. Brought on by factors that increase myocardial oxygen demand, such as exertion or emotion
3. Relieved with rest or nitroglycerin
4. Note that ischemic pain does NOT change with breathing nor with body position. Also, patients with ischemic pain do not have chest wall tenderness. If any of these are present, the pain is not likely to be due to ischemia

**Quick HIT**

CAD can have the following clinical presentations:
- Asymptomatic
- Stable angina pectoris
- USA pectoris
- MI—either NSTEMI or STEMI
- Sudden cardiac death

**Quick HIT**

In a patient with CAD, goal of LDL is less than 100 mg/dL.

**Quick HIT**

**Typical Anginal Chest Pain**
- Substernal
- Worse with exertion
- Better with rest or nitroglycerin

**CLINICAL PEARL 1-1**

### There Are Two Conditions Termed Syndrome X

1. **Metabolic Syndrome X**
   - Any combination of hypercholesterolemia, hypertriglyceridemia, impaired glucose tolerance, diabetes, hyperuricemia, HTN.
   - Key underlying factor is insulin resistance (due to obesity).
2. **Syndrome X**
   - Exertional angina with normal coronary arteriogram: Patients present with chest pain after exertion but have no coronary stenoses at cardiac catheterization.
   - Exercise testing and nuclear imaging show evidence of myocardial ischemia.
   - Prognosis is excellent.

## C. Diagnosis (of CAD)

1. Note that physical examination in most patients with CAD is normal (see Clinical Pearl 1-1)
2. Resting ECG
   a. Usually normal in patients with stable angina
   b. Q waves are consistent with a prior MI
   c. If ST segment or T-wave abnormalities are present during an episode of chest pain, then treat as unstable angina (USA)
3. Stress test—useful for patients with an intermediate pretest probability of CAD based upon age, gender, and symptoms.
   a. Stress ECG
      - Highest sensitivity if patients have normal resting ECG, such that changes can be noted.
      - Test involves recording ECG before, during, and after exercise on a treadmill.
      - 75% sensitive if patients are able to exercise sufficiently to increase heart rate to 85% of maximum predicted value for age. A person's maximum heart rate is calculated by subtracting age from 220 (220—age).
      - Exercise-induced ischemia results in subendocardial ischemia, producing ST segment depression. So the detection of ischemia on an ECG stress test is based on presence of ST segment depression.
      - Other positive findings include onset of heart failure or ventricular arrhythmia during exercise or hypotension.
      - *Patients with a positive stress test result should undergo cardiac catheterization.*
   b. Stress echocardiography
      - Performed before and immediately after exercise. Exercise-induced ischemia is evidenced by wall motion abnormalities (e.g., akinesis or dyskinesis) not present at rest.
      - Favored by many cardiologists over stress ECG. It is more sensitive in detecting ischemia, can assess LV size and function, can diagnose valvular disease, and can be used to identify CAD in the presence of pre-existing ECG abnormalities (see Clinical Pearl 1-2).
      - *Again, patients with a positive test result should undergo cardiac catheterization.*

**Quick HIT**

Best initial test for all forms of chest pain is ECG.

**Quick HIT**

Stress testing is used in the following situations:
- To confirm diagnosis of angina
- To evaluate response of therapy in patients with documented CAD
- To identify patients with CAD who may have a high risk of acute coronary events

**Quick HIT**

Exercise stress ECG is ideal initial test if able to exercise and normal resting ECG (readily available and relatively inexpensive).

**Quick HIT**

A stress test is generally considered positive if the patient develops any of the following during exercise: ST segment depression, chest pain, hypotension, or significant arrhythmias.

**CLINICAL PEARL 1-2**

### Types of Stress Tests

| Test | Method of Detecting Ischemia |
|---|---|
| Exercise ECG | ST segment depression |
| Exercise or dobutamine echocardiogram | Wall motion abnormalities |
| Exercise or dipyridamole perfusion study (thallium/technetium) | Decreased uptake of the nuclear isotope during exercise |

c. Information gained from a stress test can be enhanced by stress myocardial perfusion imaging after IV administration of a radioisotope such as thallium 201 during exercise.
   - Viable myocardial cells extract the radioisotope from the blood. No radioisotope uptake means no blood flow to an area of the myocardium.
   - *It is important to determine whether the ischemia is reversible,* that is, whether areas of hypoperfusion are perfused over time as blood flow eventually equalizes. Areas of *reversible* ischemia may be rescued with percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG). Irreversible ischemia, however, indicates infarcted tissue that cannot be salvaged.
   - Perfusion imaging increases the sensitivity and specificity of exercise stress tests, but is also more expensive, subjects the patient to radiation, and is often not helpful in the presence of a left bundle branch block.

4. If the patient cannot exercise, perform a *pharmacologic stress test.*
   a. IV adenosine, dipyridamole, or dobutamine can be used. The cardiac stress induced by these agents takes the place of exercise. This can be combined with an ECG, an echocardiogram, or nuclear perfusion imaging.
   b. IV adenosine and dipyridamole cause generalized coronary vasodilation. Since diseased coronary arteries are already maximally dilated at rest to increase blood flow, they receive relatively less blood flow when the entire coronary system is pharmacologically vasodilated.
   c. Dobutamine increases myocardial oxygen demand by increasing heart rate, blood pressure, and cardiac contractility.
5. Holter monitoring (ambulatory ECG) can be useful in detecting silent ischemia (i.e., ECG changes not accompanied by symptoms). The Holter monitor is also used for evaluating arrhythmias, heart rate variability, and to assess pacemaker and implantable cardioverter-defibrillator (ICD) function.
   a. Continuously examines patient's cardiac rhythm over 24 to 72 hours during normal activity
   b. Useful for evaluating unexplained syncope and dizziness as well
6. Cardiac catheterization with coronary angiography (see Clinical Pearl 1-3, Figure 1-1)
   a. Coronary angiography—definitive test for CAD. Often performed with concurrent PCI or for patients being considered for revascularization with CABG.

## CLINICAL PEARL 1-3

**Cardiac Catheterization**

1. Most accurate method of determining a specific cardiac diagnosis.
2. Provides information on hemodynamics, intracardiac pressure measurements, cardiac output, oxygen saturation, etc.
3. Coronary angiography (see below) is almost always performed as well for visualization of coronary arteries.
4. There are many indications for cardiac catheterization (generally performed when revascularization or other surgical intervention is being considered):
   - After a positive stress test.
   - Acute MI with intent of performing angiogram and PCI.
   - In a patient with angina in any of the following situations: When noninvasive tests are nondiagnostic, angina that occurs despite medical therapy, angina that occurs soon after MI, and any angina that is a diagnostic dilemma.
   - If patient is severely symptomatic and urgent diagnosis and management are necessary.
   - For evaluation of valvular disease, and to determine the need for surgical intervention.

**Coronary Arteriography (Angiography)**

1. Most accurate method of identifying the presence and severity of CAD; the standard test for delineating coronary anatomy.
2. Main purpose is to identify patients with severe coronary disease to determine whether revascularization is needed. Revascularization with PCI involving a balloon and/or a stent can be performed at the same time as the diagnostic procedure.
3. Coronary stenosis >70% may be significant (i.e., it can produce angina).

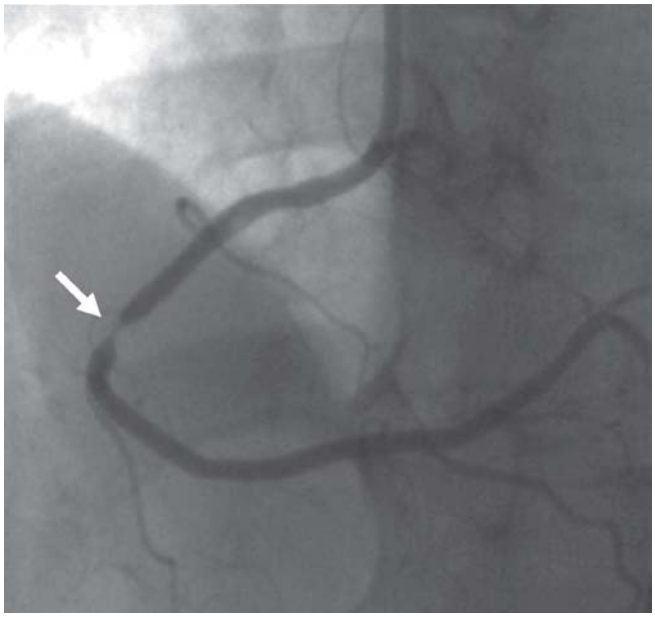

**FIGURE 1-1** **Coronary angiogram. Injection of the right coronary artery shows a stenosis in the midportion of the vessel, indicated by the *arrow*.**
(From Lilly LS. *Pathophysiology of Heart Disease*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2011:152, Figure 6.8; Courtesy of Dr. William Daley.)

b. Contrast is injected into coronary vessels to visualize any stenotic lesions. This defines the location and extent of coronary disease.
c. Angiography is the most accurate test for detecting CAD.
d. If CAD is severe (e.g., left main or three-vessel disease), refer patient for surgical revascularization (CABG).

## D. Treatment

1. Risk factor modification
   a. Smoking cessation cuts coronary heart disease (CHD) risk in half by 1 year after quitting.
   b. HTN—vigorous BP control reduces the risk of CHD, especially in diabetic patients.
   c. Hyperlipidemia—reduction in serum cholesterol with lifestyle modifications and HMG-CoA reductase inhibitors (statins) reduce CHD risk.
   d. DM—type II diabetes is considered to be a cardiovascular heart disease equivalent, and strict glycemic control should be strongly emphasized.
   e. Obesity—weight loss modifies other risk factors (diabetes, HTN, and hyperlipidemia) and provides other health benefits.
   f. Exercise is critical; it minimizes emotional stress, promotes weight loss, and helps reduce other risk factors.
   g. Diet: Reduce intake of saturated fat (<7% total calories) and cholesterol (<200 mg/day).
2. Medical therapy
   a. Aspirin
      • Indicated in all patients with CAD
      • **Decreases morbidity—reduces risk of MI**
   b. β-Blockers—block sympathetic stimulation of heart. First-line choices include atenolol and metoprolol.
      • Reduce HR, BP, and contractility, thereby decreasing cardiac work (i.e., β-blockers lower myocardial oxygen consumption)
      • **Have been shown to reduce the frequency of coronary events**
   c. Nitrates—cause generalized vasodilation
      • Relieve angina; reduce preload myocardial oxygen demand
      • May prevent angina when taken before exertion

**Quick HIT**

Standard of care for stable angina is aspirin and a β-blocker (only ones that lower mortality), and nitrates for chest pain.

**Quick HIT**

Side effects of nitrates:
- Headache
- Orthostatic hypotension
- Tolerance
- Syncope

- Effect on prognosis is unknown; main benefit is symptomatic relief
- Can be administered orally, sublingually, transdermally, intravenously, or in paste form. For chronic angina, oral or transdermal patches are used. For acute coronary syndromes (see below), either sublingual, paste, or IV forms are used

d. Calcium channel blockers
- Cause coronary vasodilation and afterload reduction, in addition to reducing contractility.
- Now considered a **secondary treatment** when β-blockers and/or nitrates are not fully effective. None of the calcium channel blockers have been shown to lower mortality in CAD. In fact, they may increase mortality because they raise heart rates. Do not routinely use these drugs in CAD.

e. If congestive heart failure (CHF) is also present, treatment with ACE inhibitors and/or diuretics may be indicated as well.

3. Revascularization
   a. May be preferred for high-risk patients, although there is some controversy whether revascularization is superior to medical management for a patient with stable angina and stenosis >70%
   b. Two methods—PCI and CABG—see Clinical Pearl 1-4
   c. Revascularization does **not** reduce incidence of MI, but does result in significant improvement in symptoms
4. Management decisions (general guidelines)—risk factor modification and aspirin are indicated in all patients. Manage patients according to overall risk
   a. Mild disease (normal EF, mild angina, single-vessel disease)
      - Nitrates (for symptoms and as prophylaxis) and a β-blocker are appropriate
      - Consider calcium channel blockers if symptoms continue despite nitrates and β-blockers
   b. Moderate disease (normal EF, moderate angina, two-vessel disease)
      - If the above regimen does not control symptoms, consider coronary angiography to assess suitability for revascularization (either PCI or CABG)
   c. Severe disease (decreased EF, severe angina, and three-vessel/left main or left anterior descending disease)
      - Coronary angiography and consider for CABG

**Quick HIT**

The COURAGE trial showed essentially no difference in all cause mortality and nonfatal MIs between patients with stable angina treated with maximal medical therapy alone versus medical therapy with PCI and bare metal stenting.

**Quick HIT**

PCI is referred to as angioplasty.



## CLINICAL PEARL 1-4

**Percutaneous Coronary Intervention**

- Consists of both coronary angioplasty with a balloon and stenting.
- Should be considered in patients with one-, two-, or three-vessel disease. Even with three-vessel disease, mortality and freedom from MI have been shown to be equivalent between PTCA with stenting and CABG. The only drawback is the higher frequency of revascularization procedures in patients who received a stent.
- Best if used for proximal lesions.
- Restenosis is a significant problem (up to 40% within first 6 months); however, if there is no evidence of restenosis at 6 months, it usually does not occur. New techniques and technologic improvements such as drug-eluting stents are attempting to reduce this problem.

**Coronary Artery Bypass Grafting**

- While CABG remains the standard of care at some institutions for patients with high-risk disease, the PRECOMBAT and SYNTAX trails have shown that PTCA with stenting may be as good as CABG even in patients with left main CAD. CABG is still used as the primary method of revascularization in a small number of patients with STEMI. In addition, it may be indicated in patients with cardiogenic shock post-MI, after complications with PCI, in the setting of ventricular arrhythmias, and with mechanical complications after acute MI.
- Main indications for CABG: Three-vessel disease with >70% stenosis in each vessel. Left main coronary disease with >50% stenosis, left ventricular dysfunction.