Case Presentation: A 65-year-old male presents for evaluation of chest pain. He describes substernal chest pressure that comes on when he plays doubles tennis or walks up a hill on the golf course. His discomfort is associated with dyspnea and is relieved within a few minutes by rest. On one occasion, a golfing partner gave him one of his sublingual nitroglycerin tablets. This brought prompt relief of the discomfort. He denies any chest pain at rest or at night. He has a history of hypertension, for which he is taking a diuretic. On a routine physical examination last year, his cholesterol was 240, with low-density lipoprotein (LDL) cholesterol of 150. He is trying to follow a low-fat diet and lose weight to reduce this. He has smoked 1 pack of cigarettes a day most of his adult life, although he did quit for a year or 2 on 2 separate occasions in the past. He has no history of diabetes. Both his mother and father lived into their late eighties and died of cancer. He is an only child.

On physical examination, his blood pressure is 145/95 mm Hg. His heart rate is 72 beats per minute and regular. His cardiac examination is normal. His resting ECG is normal.

The patient undergoes a treadmill exercise test. He completes 6 minutes of exercise according to a Bruce protocol. He stops because of fatigue but does note some mild chest pressure at peak exercise. Peak exercise heart rate is 135 beats per minute, and the peak exercise blood pressure is 190/100 mm Hg. Exercise electrocardiography shows 0.5 mm of up-sloping ST depression measured 80 seconds after the J point at peak exercise.

To better define the patient’s diagnosis and prognosis, he then undergoes exercise myocardial perfusion imaging with sestamibi. He again exercises for 6 minutes according to a Bruce protocol and achieves a peak heart rate of 132 beats per minute and a peak blood pressure of 185/98 mm Hg. He again stops because of fatigue, but still describes some chest pressure at peak exercise. Electrocardiographic findings are similar to his previous exercise test. The perfusion images show a small area of inferior ischemia. The ejection fraction shown by gated single photon emission computed tomography is 61% with normal regional wall motion.

After discussion of these findings with the patient, his physician decides to manage the patient medically. What is appropriate therapy for this patient, as outlined in the American College of Cardiology/American Heart Association/American College of Physicians-American Society of Internal Medicine (ACC/AHA/ACP-ASIM) Guidelines for Management of Stable Angina?*

The flow diagram for appropriate therapy is shown in Figure 1. The left portion of this flow diagram focuses on antianginal drug treatment. The specific recommendations in the guideline for pharmacotherapy to prevent myocardial infarction and death and reduce symptoms are reproduced in Table 1. This patient clearly requires therapy with aspirin, β-blockers, and sublingual nitroglycerin. The right portion of the flow diagram focuses on risk factor modification. The specific guideline recommendations for treatment of risk factors are detailed in Table 2. This patient clearly merits a smoking cessation program, a recheck of his lipids with initiation of drug therapy to bring his LDL cholesterol to less than 100 (if his LDL cholesterol remains >130 on recheck), recheck of his hypertension on β-blockers to make certain that it is better controlled, initiation of an exercise program, review of his diet, and education.

This illustrative case example is intended to demonstrate the application of ACC/AHA practice guidelines. The purpose of this review is to provide an overview of the guidelines process and its fundamental principles.

Rationale for Guidelines

Why do the ACC and AHA invest considerable time and effort in the development of guidelines like these? The history of the process offers some insight into the rationale. In the early 1980s, it became apparent to federal authorities that the appropriate indications for permanent pacemaker implantation were not clear, and that the justification for implants provided in some medical records was incorrect. They approached both the ACC and AHA and sought their help in developing appropriate practice guidelines regarding this issue. This led to the formulation of the first writing committee for an ACC/AHA clinical practice guideline, which was chaired by Dr Robert Frye from the Mayo Clinic.* Several
years later, data were published showing that definite justification for permanent pacemaker implantation was present in medical records <50% of the time, and justification was totally inadequate about 20% of the time. Although the actual magnitude of the problem may be overstated because of inadequate record keeping, these data demonstrated the need for the development of guidelines that would detail appropriate indications.

The perceived need for clinical practice guidelines has increased in recent years with the publication of data regarding the overall quality of cardiovascular care. The Worcester Heart Study (Figure 2) demonstrated that the prevalence of aspirin use in patients presenting to the hospital with acute myocardial infarction who had a history of previous infarction gradually increased over the late 1980s and early 1990s, but that this percentage remained less than 50% (in patients...
without contraindications to aspirin) as recently as 1995 (Figure 2). Surveys of the use of angiotensin-converting enzyme (ACE) inhibitors in patients with heart failure have shown that less than 50% of eligible patients are taking ACE inhibitors and that the dosages are optimal in less than 50% of them.

Regional practice variations have provided another source of concern. The rate of utilization of percutaneous intervention, β-blockers after myocardial infarction, and ACE inhibitors after myocardial infarction vary enormously in different regions of the country, even after adjustment for basic demographic variables (Figure 3). In response to data like these, both the ACC and AHA have committed considerable resources to their joint effort for the development of clinical practice guidelines, consistent with their stated mission to improve the quality of care in the country.

### Selection of Topics and Writing Committees

How are the topics and writing committees for guidelines chosen? The ACC/AHA guideline effort is directed by a joint 10-member committee called the Task Force on Practice Guidelines. The members of this group are senior, very well-respected individuals who commit considerable time to this effort despite their many other commitments. The current presidents of the ACC and AHA are ad hoc members. The Task Force establishes overall policy, chooses the individual topics for guidelines, and monitors existing guidelines to determine when revisions and updates are required. Once a topic is identified, a writing committee is organized to develop that practice guideline. The Task Force is intimately involved in the first step of this process — the selection of the chairperson of the writing committee. The recommendations from the Task Force for these chair positions must be approved by both the ACC and AHA presidents before an individual is invited to serve in this capacity. The individual members of the writing committees are carefully selected on the basis of input from the Task Force, the writing committee chair, the appropriate ACC and AHA committees, the ACC Board of Governors, and other collaborating organizations. The members of each writing committee attempt to balance the number of content experts and senior practicing clinicians, and incorporate representation from a variety of different regions in both academic and non-academic settings. The writing committees are demanding assignments, which require tremendous volunteer effort from already busy individuals. They typically require 4 or 5 meetings over the

### TABLE 1. Recommendations for Pharmacotherapy to Prevent Myocardial Infarction and Death and to Reduce Symptoms

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class I</strong></td>
<td></td>
</tr>
<tr>
<td>Aspirin in the absence of contraindications</td>
<td>A</td>
</tr>
<tr>
<td>β-Blockers as initial therapy in the absence of contraindications in patients with prior MI</td>
<td>A</td>
</tr>
<tr>
<td>β-Blockers as initial therapy in the absence of contraindications in patients without prior MI</td>
<td>B</td>
</tr>
<tr>
<td>ACE inhibitor in all patients with CAD* who also have diabetes and/or LV systolic dysfunction</td>
<td>A</td>
</tr>
<tr>
<td>ACE inhibitor in all patients with CAD* without prior MI</td>
<td>B</td>
</tr>
<tr>
<td>LDL-lowering therapy in patients with documented or suspected CAD and LDL cholesterol &gt;130 mg/dL, with a target LDL of &lt;100 mg/dL</td>
<td>A</td>
</tr>
<tr>
<td>Sublingual nitroglycerin or nitroglycerin spray for the immediate relief of angina</td>
<td>B</td>
</tr>
<tr>
<td>Calcium antagonists† or long acting nitrates as initial therapy for reduction of symptoms when β-blockers are contraindicated</td>
<td>B</td>
</tr>
<tr>
<td>Calcium antagonists† or long-acting nitrates in combination with β-blockers when initial treatment with β-blockers is not successful</td>
<td>B</td>
</tr>
<tr>
<td>Calcium antagonists† and long acting nitrates as a substitute for β-blockers if initial treatment with β-blockers leads to unacceptable side effects</td>
<td>C</td>
</tr>
<tr>
<td><strong>Class IIa</strong></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel when aspirin is absolutely contraindicated</td>
<td>B</td>
</tr>
<tr>
<td>Long-acting nondihydropyridine calcium antagonists† instead of β-blockers as initial therapy</td>
<td>B</td>
</tr>
<tr>
<td>In patients with documented or suspected CAD and LDL cholesterol 100 to 129 mg/dL, several therapeutic options are available:</td>
<td>B</td>
</tr>
<tr>
<td>Lifestyle and/or drug therapies to lower LDL to &lt;100 mg/dL</td>
<td>B</td>
</tr>
<tr>
<td>Weight reduction and increased physical activity in persons with the metabolic syndrome</td>
<td>B</td>
</tr>
<tr>
<td>Institution of treatment of other lipid or nonlipid risk factors; consider use of nicotinic acid or fibrac acid for elevated triglycerides or low HDL cholesterol</td>
<td>B</td>
</tr>
<tr>
<td>ACE inhibitor in patients with CAD* or other vascular disease</td>
<td>B</td>
</tr>
<tr>
<td><strong>Class IIb</strong></td>
<td></td>
</tr>
<tr>
<td>Low-intensity anticoagulation with warfarin in addition to aspirin</td>
<td>B</td>
</tr>
<tr>
<td><strong>Class III</strong></td>
<td></td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>B</td>
</tr>
<tr>
<td>Chelation therapy</td>
<td>B</td>
</tr>
</tbody>
</table>

MI indicates myocardial infarction; ACE, angiotensin-converting enzyme; CAD, coronary artery disease; LV, left ventricular; LDL, low-density lipoprotein; and HDL, high-density lipoprotein.

*Significant CAD shown by angiography or previous myocardial infarction.
†Short-acting, dihydropyridine calcium antagonists should be avoided.
course of 12 to 18 months, with extensive writing and review requirements in between.

Principles of Guideline Development
What principles are followed in developing ACC/AHA Practice Guidelines? The paramount principle is that these guidelines should be evidence-based. Appropriate literature searches are performed with the help of the ACC scientific staff and, when available, evidence-based practice centers supported by the Agency for Health Care Quality. The writing committee for stable angina had the support of the University of California San Francisco-Stanford Evidence-Based Practice Center, which developed summaries of the literature comparing β-blockers versus calcium antagonists

### Table 2. Recommendations for Treatment of Risk Factors

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of hypertension according to Joint National Conference VI guidelines</td>
<td>A</td>
</tr>
<tr>
<td>Smoking cessation therapy</td>
<td>B</td>
</tr>
<tr>
<td>Management of diabetes</td>
<td>C</td>
</tr>
<tr>
<td>Comprehensive cardiac rehabilitation program (including exercise)</td>
<td>B</td>
</tr>
<tr>
<td>LDL-lowering therapy in patients with documented or suspected CAD and LDL cholesterol ≥130 mg/dL, with a target LDL of &lt;100 mg/dL</td>
<td>A</td>
</tr>
<tr>
<td>Weight reduction in obese patients in the presence of hypertension, hyperlipidemia, or diabetes mellitus</td>
<td>C</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class IIa</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients with documented or suspected CAD and LDL cholesterol 100 to 129 mg/dL, several therapeutic options are available</td>
<td>B</td>
</tr>
<tr>
<td>Weight reduction and increased physical activity in persons with the metabolic syndrome</td>
<td>B</td>
</tr>
<tr>
<td>Institution of treatment of other lipid or nonlipid risk factors; consider use of nicotinic acid or fibric acid for elevated triglycerides or low HDL cholesterol</td>
<td>B</td>
</tr>
<tr>
<td>Therapy to lower non-HDL cholesterol in patients with documented or suspected CAD and triglycerides of &gt;200, with a target non-HDL cholesterol of &lt;130 mg/dL</td>
<td>B</td>
</tr>
<tr>
<td>Weight reduction in obese patients in the absence of hypertension, hyperlipidemia, or diabetes mellitus</td>
<td>C</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class IIb</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folate therapy in patients with elevated homocysteine levels</td>
<td>C</td>
</tr>
<tr>
<td>Identification and appropriate treatment of clinical depression to improve CAD outcomes</td>
<td>C</td>
</tr>
<tr>
<td>Intervention directed at psychosocial stress reduction</td>
<td>C</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class III</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiation of hormone replacement therapy in postmenopausal women for the purpose of reducing cardiovascular risk</td>
<td>A</td>
</tr>
<tr>
<td>Vitamin C and E supplementation</td>
<td>A</td>
</tr>
<tr>
<td>Chelation therapy</td>
<td>C</td>
</tr>
<tr>
<td>Garlic</td>
<td>C</td>
</tr>
<tr>
<td>Acupuncture</td>
<td>C</td>
</tr>
<tr>
<td>Coenzyme Q</td>
<td>C</td>
</tr>
</tbody>
</table>

### Figure 2. Prevalence of aspirin use on admission in patients presenting with acute myocardial infarction who have a history of previous myocardial infarction and no contraindications to aspirin. Reprinted with permission from reference 4.

### Figure 3. Rate of utilization of percutaneous coronary interventions, by Medicare referral region, adjusted for age and gender. Reprinted with permission from reference 5.
(Figure 4) and of the literature on garlic therapy (Table 3) that were considered by the committee. The committee concluded that calcium antagonists are generally as effective as β-blockers in relieving angina, and that garlic therapy is not effective. A second important principle is consistency with other guidelines, including national guidelines on hypertension and cholesterol management, other ACC/AHA practice guidelines, ACC expert consensus documents, and AHA scientific statements. A third important principle is that the process focuses on information that is already published in the peer-reviewed literature. There is a very restricted use of scientific abstracts and of presentations (often late-breaking trials) at national meetings. A writer’s manual for the process is published on the ACC and AHA web sites and available for review by interested readers. Writing committees are now using an electronic, web-based system to facilitate committee interaction and the development of each draft of the proposed guideline.

Conflict of Interest
Are these guidelines “tainted” by various conflicts of interest of the writing committee members? Concern about conflict of interest has increasingly been raised in both the scientific and lay press. Recognizing the importance of this issue, both the ACC and AHA have strict organizational policies regarding disclosure. The Task Force developed a policy for the guideline process that incorporates several unique elements. Each writing committee member is required to make full oral disclosure at the initial writing committee meeting of any potential conflicts of interest. At each subsequent meeting, a written summary of these disclosures is provided to the entire committee, and each member is asked to update his or her information regarding any new potential conflicts of interest. Full disclosure is felt to be paramount to the credibility of the process, and this issue is carefully monitored by the Task Force. Choudhry et al7 published a set of criteria regarding conflicts of interest. The only criterion not met by the ACC/AHA guidelines was actual publication with the guideline of these potential conflicts of interest; the task force has now adopted this as a new policy.

Classes of Recommendations
What do the classes of recommendations I, II, and III mean? These are standardized classifications that were adopted by the ACC/AHA Task Force several years ago to ensure consistency across guidelines (Figure 5). Class I refers to

| TABLE 3. Randomized Trials and Meta-Analyses of Garlic Therapy for Risk Treatment of Risk Factors |
|---------------------------------|-------|--------|-----------------|-----------------|
| **Hypercholesterolemia**        |       |        |                 |                 |
| Berthold et al⁹                 | 1998  | RCT    | 25+             | 10 mg steam distilled oil | No difference in multiple measures |
| Isaacs et al ⁱ⁰                 | 1998  | RCT    | 40              | 900 mg powder     | No difference in multiple measures |
| Jain et al¹¹                    | 1993  | RCT    | 42              | 900 mg powder     | Reduction in LDL of 11% vs 3% for placebo |
| Warshafsky et al²²             | 1993  | Meta-analysis | 5 trials | 1/2 to 1 clove per day | Reduction in total cholesterol of 95 mg/dL |
| **Hypertension**                |       |        |                 |                 |
| Silagy and Neil ¹³              | 1994  | Meta-analysis | 8 trials | 600 to 900 mg powder | Small reduction in systolic and diastolic BP |

⁹Cross-over study.
conditions for which there is evidence or general agreement that a given procedure or treatment is useful and effective. In contrast, class III refers to conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful. Class II recommendations fall in between, and indicate conditions for which there is conflicting evidence or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. Class IIa indicates that the weight of evidence/opinion is in favor of usefulness/efficacy. Class IIb indicates that the usefulness/efficacy is less well established by evidence/opinion. In simple terms, class I recommendations are the “dos,” class III recommendations are the “don’ts,” and class II recommendations are the “maybes.”

Levels of Evidence
What do the levels of evidence describe? These are again standardized definitions that try to summarize the available published evidence in support of the given recommendations. They reflect the precision of the estimate of the treatment effect (Figure 6). The strongest weight of evidence (A) is assigned if there are multiple randomized trials with large numbers of patients. An intermediate weight (B) is assigned if there are a limited number of randomized trials with small numbers of patients, careful analyses of non-randomized studies, or observational registries. The lowest rank of evidence (C) is assigned when expert consensus is the primary basis for the recommendation. The level of evidence is sometimes confused with the class of recommendation. The assignment of a C level of evidence to a class I recommendation should not be interpreted to mean that this is a “weak” recommendation. This may simply reflect the ethical or logistical difficulty of ever performing a randomized trial to test the treatment or procedure in question. For example, there is a class I recommendation in the Stable Angina Guideline for echocardiography in patients with a systolic murmur suggestive of aortic stenosis or hypertrophic cardiomyopathy, for which the level of evidence is a C. It is highly unlikely that any institutional review board would ever approve a randomized trial in which patients with suspected aortic stenosis were denied echocardiography.

Review Process
Should these guidelines carry any more weight with the reader than a review article in a peer-reviewed scientific publication? Definitely. As official policy statements from both organizations, the guidelines undergo much more scrutiny before publication than any typical publication (Figure 7). As already stated, these evidence-based documents represent the thoughtful deliberations of the 12 to 15 carefully selected committee members, as well as appropriate literature searches, compared with the limited number of authors of the usual review. The final draft from the writing committee is reviewed by 3 official reviewers from each of the 2 organizations, 1 to 3 official reviewers from each other participating organization (because ACP-ASIM was a full partner in the stable angina guideline, they also had 3 official reviewers), a reviewer for pharmacy details, additional content reviewers selected by the writing committee, and the Task Force.
official reviewers from each organization take this task very seriously and typically provide many pages of suggested edits. The largest such review ever submitted exceeded 40 single-spaced pages! The total number of review comments usually number in the hundreds, and sometimes in the thousands. The writing committee must consider and respond to all comments. Given the large number of comments, a coding system is often used for this purpose:

Y = Yes
N = No, followed by a reason
S = Style issue
D = Discussed by committee
C = Consistency with other guidelines
U = Unpublished material
I = Insufficient evidence

Some of the reviewers may identify pertinent new evidence that has been published since the writing committee submitted its draft for review. For example, the text of the stable angina guideline regarding vitamin E was modified to reflect the publication of the Heart Protection Study (Figure 8), which provided further support for the Class III recommendation from the committee.8 This process is overseen by a designated “lead reviewer” from the Task Force, who consults with the task-force chair regarding controversial or unresolved issues. When appropriate, the chair may choose to ballot the Task Force regarding these issues, or commission additional reviewers (which was done for stable angina). When this extensive review process is complete, the fully revised document is submitted to the ACC Board of Trustees and the AHA Science Advisory and Coordinating Committee (as well as to other organizations who are partners or who wish to consider the guideline for endorsement) for a formal endorsement vote. This process usually leads to additional suggestions for minor edits.

### Publication Issues

The output of this process is a full-length document that typically numbers 50 to 100 text pages, with appropriate tables and figures and many hundreds of references. The Guidelines for the Management of Stable Angina are 1 of 7 sets of guidelines regarding patient conditions (Table 4); there are also 9 sets of guidelines regarding procedures (Table 5). In the past, these full text documents were published in Circulation and the Journal of the American College of Cardiology on an alternating basis. In the past few years, they have been published on the ACC and AHA web pages, but not in print. A shorter executive summary that incorporates all of the specific recommendations and much more limited text is published in both journals. In an effort to provide abbreviated, user-friendly versions that can bring the guidelines to the bedside, pocket versions were begun in 1995.

### Table 4: Disease-Specific ACC/AHA Guidelines

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Original Publication</th>
<th>Update</th>
<th>Pocket Version</th>
<th>PDA Version</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>2001</td>
<td>In progress</td>
<td>2002</td>
<td>No</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1996</td>
<td>1999</td>
<td>2000</td>
<td>Yes</td>
</tr>
<tr>
<td>Perioperative evaluation</td>
<td>1996</td>
<td>2002</td>
<td>1997</td>
<td>No</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>1998</td>
<td>In progress</td>
<td>2000</td>
<td>Yes</td>
</tr>
<tr>
<td>Stable angina (joint with ACP-ASIM)</td>
<td>1999</td>
<td>2002</td>
<td>2000</td>
<td>Yes</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>2000</td>
<td>2002</td>
<td>2001</td>
<td>In progress</td>
</tr>
<tr>
<td>Atrial fibrillation (joint with ESC)</td>
<td>2001</td>
<td>In progress</td>
<td>2002</td>
<td>No</td>
</tr>
</tbody>
</table>

PDA indicates personal digital assistant; ESC, European Society of Cardiology.
Commitment to Quality Improvement

This extensive effort requires committed personnel and resources from both organizations, as well as considerable volunteer effort from the Task Force, the writing committees, particularly the chair, and individuals involved in the extensive review process. Despite increasing time demands on both academic and non-academic physicians, the ACC and AHA have been pleased at the level of commitment that their members have shown to this effort. The individuals involved provide this effort primarily out of a sense of professional responsibility. The 1 or 2 entries on their curriculum vitae that result do not in any way reflect the magnitude of the effort performed for each pocket guideline.

PTCA indicates percutaneous transluminal coronary angiography; PCI, percutaneous coronary intervention; ASNC, American Society of Nuclear Cardiology; ASE, American Society of Echocardiography; AICD, automatic implantable cardioverter-defibrillator; NASPE, North American Society of Pacing and Electrophysiology; and CABG, coronary artery bypass grafting.

All guidelines are available at http://www.acc.org/clinical/topic.htm#guidelines.

*Pocket and personal digital assistant version available.
†Pocket version available.

Aspirin and antianginals

Beta-blocker and blood pressure

Cholesterol and cigarettes

Diet and diabetes

Education and exercise

References


American College of Cardiology/American Heart Association Clinical Practice Guidelines: Part I: Where Do They Come From?
Raymond J. Gibbons, Sidney Smith and Elliott Antman

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