TEACHERS' TOPICS

Management of Stable Angina and Acute Coronary Syndromes

Judy W.M. Cheng, PharmD[a,b]

[a]College of Pharmacy, Long Island University
[b]Department of Pharmacy, Mount Sinai Medical Center

This article describes the presentation and the experience of a pharmacotherapeutics lecture on the management of ischemic heart disease (IHD). The lecture is designed for first-professional degree doctor of pharmacy (PharmD) students and includes 4 hours of case-based approach lecture and 2 hours of recitation (combined with pharmacology/medicinal chemistry). The lecture begins with a brief review of the pathophysiology, diagnosis, and non-pharmacologic management of IHD. Students are then presented with patient cases. Definition of patient problems, development of pharmacotherapeutic goals, treatment regimens, treatment endpoints, monitoring parameters, and patient education are discussed using the cases. During recitation, students are expected to develop care plans for patients with different types of IHD. Multiple-choice examinations that focus on the behavioral objectives of the lecture are used to assess the students' core knowledge. Objectives-focused, case-based lectures with recitation appears to be an effective approach in teaching IHD.

Keywords: acute coronary syndromes, pharmacotherapy, ischemic heart disease, case-based approach

INTRODUCTION

Pharmacotherapeutics courses are a crucial component of a first-professional degree doctor of pharmacy curriculum. In the PharmD program at Arnold and Marie Schwartz College of Pharmacy and Health Sciences, pharmacotherapeutics is team taught through 5 courses (*Pharmacotherapeutics I* to *V*) in 5 consecutive semesters. Each course is 3 to 5 credits and composed of 4 lecture hours and 1 recitation hour weekly (or 2 recitation hours every other week). Recitations are small group (<25 students per group) case study workshops designed to further develop the students' ability to assess patient cases, select appropriate therapies, determine reasonable treatment alternatives, and justify their choices using knowledge acquired from the lectures and other courses. With most recitations, students are provided several patient cases at least 1 week prior to the session. Students are expected to develop pharmaceutical care plans for the patients prior to coming to recitations. The format of the pharmaceutical care plan is well defined for our students and is used consistently throughout the 5 pharmacotherapeutics courses as well as for clinical clerkships. This is done to reinforce students' development of a systematic problem-solving process. The format follows a critical thinking process,

Corresponding Author: Judy W.M. Cheng, PharmD.
Address: Mount Sinai Medical Center, Department of Pharmacy, Box 1211, One Gustave L. Levy Place, New York, NY 10029. Tel: 212-241-7718. Fax: 212-987-0198. E-mail: judy.cheng@liu.edu

from identifying abnormalities using physical examination findings and laboratory data, to formulating a pharmacotherapy/drug-related problem list. With the problem list, pharmacotherapeutic goals are defined and therapies are selected and justified. With the selected therapies, specific endpoints and monitoring parameters are derived and finally, patient education information is provided.

Pharmacology and medicinal chemistry are taught in our college in 3 combined courses (combined *Pharmacology/Medicinal Chemistry*) delivered concurrently with *Pharmacotherapeutics I* to *III*. Topics taught are synchronized between *Pharmacology/Medicinal Chemistry* and *Pharmacotherapeutics* so that the discussion of the pharmacology and medicinal chemistry of a class of drugs that is used to treat certain disease states always immediately precedes the discussion of the treatment of the disease states in pharmacotherapeutics. In addition, for *Pharmacotherapeutics II* and *Pharmacology/Medicinal Chemistry II*, a combined recitation is shared between the 2 courses. The combined recitation allows students to relate the basic science and clinical information together. Cardiovascular pharmacotherapy is taught in *Pharmacotherapeutics II*.

Cardiovascular disease is the number one killer of Americans.[1] Practicing pharmacists will encounter patients with cardiovascular diseases; therefore, cardiovascular pharmacotherapeutics constitute a major portion of *Pharmacotherapeutics II*. Cardiology is often considered one of the most evidence-based areas of clinical

practice. The clinical trial information driving development of standards of practice is enormous and continuously expanding. Management guidelines are constantly being updated. Pharmacy students often find the amount of information intimidating and overwhelming. In *Pharmacotherapeutics II*, cardiovascular disease-related topics and their lecture hour allocation are as follow. (Those for which I am usually responsible are indicated by an asterisk).

Cardiovascular Diseases Risk Factors Management
- smoking cessation (1 hour)
- obesity (1 hour)
- hypertension including hypertensive crisis (4 hours)*
- hyperlipidemia (3 hours)*

Cardiovascular Diseases Management
- ischemic heart diseases, eg, stable angina and acute coronary syndromes (4 hours)*
- heart failure and cardiogenic shock (5 hours)*
- arrhythmias (4 hours)*
- peripheral vascular diseases (1 hour)*

To help students manage the high volume of information and to ensure that they learn and apply the materials, the division of pharmacy practice encourages a philosophy of teaching pharmacotherapeutics using a case-based approach whenever possible. This approach is utilized in the cardiovascular pharmacotherapeutics lectures. In addition, it is essential for faculty members to critically evaluate what information a first-professional degree PharmD student really needs to know. It is crucial for a faculty member to understand that there is never going to be enough time to cover all aspects of a topic. It is more beneficial for the students to understand a small amount of information really well and be able to apply it than to try to memorize a large amount of material.

This article outlines the lecture objectives, instructional methods, content (at a first-professional degree PharmD students' level), and assessment of the specific topic, "Management of Stable Angina and Acute Coronary Syndromes (ACS)." Experiences learned in teaching this topic and methods to enhance the students' interest in the management of cardiovascular diseases are also discussed.

Lecture Objectives

The specific objectives for the lecture, "Management of Stable Angina and Acute Coronary Syndromes (ACS)," are listed below. The importance of developing specific objectives cannot be overemphasized. It not only helps students study but also forces the instructor to think about what is important for the students to know at this level, thus preventing the instructor's subconscious desire to "over" teach. To ease students' anxiety, it is important to reassure them

that the lectures and the examinations will focus only on accomplishing the objectives for the course, to which we will often refer.

The objectives for the course are:
1. List the risk factors and common etiology for the development of stable angina and ACS.
2. Given a patient case history and laboratory and electrocardiographic (ECG) findings, differentiate between chronic stable angina and ACS, including unstable angina, non-ST segment elevation myocardial infarction (NSTEMI), and STEMI.
3. List the medical complications of STEMI.
4. Describe the role of different classes of pharmacological agents in the management of stable angina and ACS, as well as their major side effects, significant drug interactions, and contraindications.
5. Describe the role of non-pharmacological management of stable angina and ACS.
6. When given a patient case, design a pharmaceutical care plan for managing patient's stable angina or ACS.

INSTRUCTIONAL METHODS

"Management of Stable Angina and Acute Coronary Syndromes (ACS)" is covered by 4 lecture hours and 2 recitation hours. Before beginning the lecture, the behavioral objectives are reviewed with students. The students are also provided with lecture handouts containing detailed information to be discussed in class. Web sites of suggested readings (the major treatment guidelines for stable angina and ACS developed by the American Heart Association and the American College of Cardiology) are also provided to them.[2-4]

Throughout the course, I emphasize to students what information is and is not important to retain at their level. I also emphasize that examination questions focus on material discussed in class. Whether learning should be an examination-driven process is a controversial topic. Doing so may reduce the students' motivation for learning other materials not likely to appear on the examination. However, based on my experience, there are many different factors determining the motivation of student learning. Students who take an interest in a subject will learn the extra material whether or not it is going to be on the examination. For students who are struggling, it is hoped they will learn the most essential materials for future practice. For the purpose of this lecture, only the dosages of 1 or 2 selected drug(s) in each class need to be remembered. I have adopted this strategy through several years of not requiring students to memorize numerous drug dosages (except 1 or 2 commonly prescribed ones) as I

find students often do not retain such information unless they repeatedly encounter the same drug names. This has eased some pressure off students so they can focus on the optimal regimen for patient management and therapeutic monitoring. The students are also reminded that during the pharmacotherapeutics lecture, a minimal amount of time is spent on reviewing the mechanism of action and pharmacologic profile of drugs. They are responsible for reviewing the pharmacology and medicinal chemistry of different classes of drugs prior to coming to class.

Student background. At the point this particular lecture is delivered, students will have already been exposed to the pathophysiology of IHD (including pertinent ECG findings), the pharmacology and medicinal chemistry of all medications utilized to manage this disease, clinical biochemistry of laboratory tests for diagnosing MI (creatine kinase, CK-MB and troponin), and the pharmacotherapeutic management of some risk factors for developing IHD (smoking, obesity, hypertension, and hyperlipidemia). It is important to determine student background in order to tailor the amount of time spent on each subtopic. Knowing what other diseases students have already learned will also allow us to incorporate the previously learned materials into our patient cases. This not only reinforces information learned before, it also allows students opportunities to begin to relate diseases together and practice managing patients with multiple problems. For example, smoking, hyperlipidemia, and hypertension should definitely be incorporated into some of the cases that I discuss in this lecture. But incorporating diabetes into the patient's past medical history would not be fair since students have not learned about that disease yet, despite that diabetes is one of the most important risk factors for developing IHD.

Lecture content. To begin the lecture, the epidemiology of cardiovascular diseases is discussed in brief. The students are asked to raise their hand if they know anyone with risk factors for developing cardiovascular diseases or who have developed cardiovascular disease. This helps to illustrate the high prevalence of the disease. A brief review of the pathophysiology of IHD and the definition of the different types of IHD then follows.

IHD can be divided into chronic stable angina and ACS. ACS can be further categorized into unstable angina, NSTEMI, and STEMI. IHD is usually caused by atherosclerosis of the coronary arteries. However, Prinzmetal angina refers specifically to the type of IHD that is caused by coronary vasospasm, which obstructs blood flow. Patients who have Prinzmetal angina can be stable or unstable, and if symptoms persist, the patient can also develop NSTEMI or STEMI. Symptoms of chronic stable angina usually occur due to physical exertion, while symptoms that occur at rest, or change in intensity, frequency, or duration are suggestive of ACS. Students are presented Table 1 to compare and contrast the predisposing risk factors, signs and symptoms, and important laboratory and ECG findings of different types of IHD.

A brief discussion of different types of diagnostic tests, such as an ECG or exercise stress test, and interventional management of IHD, such as percutaneous coronary intervention and bypass surgery, then follow. Students are told they will not be held responsible for this information on the examination. However, as interventional management of IHD has become increasingly important, it is crucial for students to know this information.

The rest of the discussion regarding pharmacotherapy for treatment of the disease is presented in a case-based approach. Major sections of the case-based approach discussion include case presentation, assembling patient medical/drug-related problem lists, defining pharmacotherapeutic goals, selecting pharmacotherapy, defining specific endpoints for each therapy, and selecting monitoring parameters and monitoring frequency, as well as providing important patient education information. The case-based approach resembles the way students develop their pharmaceutical care plan in recitations. This is to reinforce a systematic way for evaluating patient cases. The only difference is that pharmaceutical care plans developed in recitation focus on drug-related problems, while during lecture, the pharmaceutical care plans focus on medical problems. However, students are at times asked to categorize the medical problems to one or more of the categories of drug-related problems. Our college encourages the use of the PRIME (Pharmaceutical, Risks to patients, Interactions, Mismatch Between medications and Indications and Efficacy Issues) approach for screening and categorizing drug-related problems.[5] The PRIME approach is derived from regrouping the drug-related problems described by Strand et al and the Omnibus Budget Reconciliation Act.[6,7]

Developing a Pharmaceutical Care Plan for Patients With Stable Angina

Patient case. A 55-year-old white male without significant past medical history reported to the emergency department complaining of squeezing substernal chest pain an hour ago. Onset of pain occurred while mowing the lawn. At the time of the interview in the emergency department, the patient's chest pain is gone but he does recall similar chest discomfort over the past 3 weeks while mowing the lawn, which was relieved by resting.

Significant Physical Examination Findings. Vital signs: blood pressure, 150/95 mm Hg; heart rate, 98 beats

Table 1. Definitions of Stable Angina and Acute Coronary Syndromes

	Prinzmetal Angina	Stable Angina	Acute Coronary Syndromes		
			Unstable Angina	Non-ST-segment Elevation MI	ST-segment Elevation MI
Symptoms	Similar symptoms as others. Precipitating factors: occur at rest, often in the morning hours	Substernal chest pain (heaviness, tightness, pressure), nausea, diaphoresis, shortness of breath. On physical examination, usually tachycardia with elevated blood pressure	Same as stable angina but may be more intense	Same as stable angina but may be more intense	Same as stable angina but may be more intense
Risk factors	Conditions that trigger vasospasm: - adrenaline surge - drug induced: cocaine	Risk factors that cannot be changed: heredity, gender (male > female), race, age (men > 45 y, women > 55 y) Risk factors that can be modified: smoking, hypertension, hyperlipidemia, diabetes, low HDL Other contributing factors: obesity, lack of exercise, excessive stress	Same as stable angina	Same as stable angina	Same as stable angina
Pathophysiology	Vasospasm	Atherosclerosis	Atherosclerosis or plaque rupture	Atherosclerosis or plaque rupture	Atherosclerosis or plaque rupture
ECG changes	ST ↑, ST↓, T-wave inversion	ST ↑, ST↓, T-wave inversion	ST ↑, ST↓, T-wave inversion	ST ↑, ST↓, T-wave inversion	ST ↑
Cardiac enzymes CK, CK-MB, Troponin	No change	No change	No change	↑	↑

per minute; respiratory rate, 20 per minute; temperature, 99°F; cholesterol panel: total cholesterol, 250 mg/dL; triglyceride, 180 mg/dL; high-density lipoprotein, 36 mg/dL; low-density lipoprotein, 178 mg/dL. Others laboratory values, including cardiac enzymes, are within normal limits.

Medical/Drug-related Problem List. Students are asked to create the problem list and provide supporting evidence (clinical signs and symptoms and laboratory data) to justify their assessment.

1. Stable angina (drug-related problem: mistmatch between medications and indications [condition untreated])
2. Hyperlipidemia (drug-related problem: mistmatch between medications and indications [condition untreated])
3. Hypertension (drug-related problem: mistmatch between medications and indications [condition untreated])

Pharmacotherapeutic Goals. Students will be asked to create a list of possible goals such as:

(1) relieve symptoms; (2) increase future exercise tolerance; (3) prevent progression to ACS; (4) prevent future cardiovascular events; and (5) modify primary risk factors such as hypertension and hyperlipidemia.

Pharmacotherapy

This patient has risk factors of IHD. His signs and symptoms are also consistent with stable angina. Since the patient is no longer having pain, ECG may not yield significant findings at this point. Cardiac enzymes are likely normal considering the short duration of chest discomfort. To make a diagnosis, the patient will probably undergo an exercise stress test (or a pharmacological stress test if patient is unable to walk on a treadmill). The results of the test will determine whether the patient requires further angiography or percutaneous coronary

intervention. Regardless of whether he undergoes percutaneous coronary intervention he will be put on medical therapy to modify his risk factors, control his symptoms, and prevent future cardiovascular events.

Goal 1 & 2: Relieving symptoms and increasing exercise tolerance. For symptom relief, medical therapy aims to restore a balance between myocardial oxygen supply and demand. At this point, students are again encouraged to review the pharmacology and medicinal chemistry of these agents. To decrease myocardial oxygen demand, options include β-blockers, calcium channel blockers, and nitrates. If the patient has angina due to coronary vasospasm (Prinzmetal angina), then β-blockers are relatively contraindicated as blocking the beta-2 receptors on the endothelium of the coronary arteries leads to unopposed alpha-1-receptor stimulation by adrenaline, which may cause more vasoconstriction and worsen vasospasm. In patients with Prinzmetal angina, calcium channel blockers or nitrates, which relax the smooth muscles of the coronary vessel wall, would be the appropriate choices. This applies for any further discussion of utilizing β-blockers in other forms of IHD. To increase oxygen supply, options include nitrates, calcium channel blockers, antiplatelet agents, and anticoagulants. Once again, it is emphasized to the students that in patients with Prinzmetal angina who truly have "clean," non-atherosclerotic coronary arteries, antiplatelets and anticoagulants are not necessary. This applies to any further discussion of utilizing antiplatelets and anticoagulants in other forms of IHD.

Goal 3 & 4: Control progression to acute coronary syndrome. Clinical studies have demonstrated that antiplatelets, β-blockers, angiotensin-converting enzyme inhibitors (ACE inhibitors), and statins reduce long-term cardiovascular mortality and morbidity in patients with IHD. Although the specific clinical trials are not discussed in depth at this level, students who are interested are asked to consult the instructor for the specific references to the studies. (The concept of evidence-based practice is emphasized throughout different lectures pertaining to management of cardiovascular diseases. Students who pursue a cardiology elective rotation later in year 6 of the program will be given a list of the most significant clinical studies in cardiology to review).

Goal 5: Proper management of risk factors. Students are asked to review their hypertension, hyperlipidemia, and smoking cessation pharmacotherapeutic lectures. According to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VII) guidelines,[8] the antihypertensive of choice in a patient with IHD or its risk factors are β-blockers and ACE inhibitors. Aldosterone antagonists are recommended in patients with a history of MI, as well as those who have left ventricular dysfunction but good renal function after optimization of ACE inhibitor therapy. Also, according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines,[9] this patient should receive statin therapy to bring his LDL level to <70 mg/dL.

At this point, important therapeutic considerations of using each class of agents for treatment of IHD are discussed with students. Students are asked to recall the mechanism of action of each class of drug as the discussion proceeds. Students are asked to name examples of several specific agents under each class (both brand and generic names and dosing).

Nitrates. Nitrates do not improve long-term morbidity and mortality and therefore are mainly used only for symptom control. An important point to remember about using nitrate therapy is the development of nitrate tolerance. The onset of tolerance can be as early as 24 hours in some patients. To prevent nitrate tolerance, maintaining a nitrate-free interval of 6-12 hours daily is crucial. During the nitrate-free period, patient may develop angina (as there are no nitrates in the body to protect them). Therefore, nitrates should never be used alone as the only anti-anginal therapy for patients. They should always be used with one or more of the other anti-anginal therapies, such as β-blockers or calcium channel blockers.

Beta-blockers. In patients with IHD or history of myocardial infarction, β-blockers reduce recurrent cardiovascular events. In using β-blockers in patients with IHD, no β-blockers with intrinsic sympathomimetic activities should be used because their partial agonistic effect may increase instead of decrease myocardial workload. Between β-blockers and calcium channel blockers, β-blockers are generally considered the anti-ischemic agent of choice except in the case of Prinzmetal angina where β-blockers are relatively contraindicated because of possible coronary vasospastic effects. Dosing β-blockers in IHD is different from dosing in hypertension where achieving a target blood pressure is the goal. Our therapeutic target is a resting heart rate of 50 to 60 beats per minute (provided the patients' blood pressure remains stable).

Calcium antagonists. For the management of IHD, calcium channel blockers (verapamil, diltiazem, nifedipine, amlodipine) are generally considered in patients who have contraindications to β-blockers (ie, Prinzmetal angina and other contraindications discussed previously). This is because in some post-MI clinical trials, calcium channel blockers increased mortality in patients with left ventricular dysfunction.

ACE inhibitors. In patients who have chronic stable angina and left ventricular dysfunction, ACE inhibitors should be used to reduce the progression of left ventricular dysfunction and prevent future cardiovascular events (more discussion to follow in heart failure lecture). Recent clinical trials have demonstrated that the use of certain ACE inhibitors (ie, Ramipril) in patients with hypertension, diabetes, or IHD, even with normal left ventricular dysfunction, can reduce future cardiovascular events. The issue of tissue versus non-tissue ACE inhibitors are discussed here, but I emphasize to students that the issue is controversial. Therefore, as long as patient blood pressure can tolerate, ACE inhibitors should be added. If patients cannot tolerate ACE inhibitors due to cough, an angiotensin receptor blocker (ARB) can be used instead.

Antiplatelet agents. Examples of antiplatelet agents are aspirin, clopidogrel, and glycoprotein IIb/IIIa receptor antagonists. Aspirin and clopidogrel can be used across the spectrum of IHD. Glycoprotein IIb/IIIa receptor antagonists are used in patients with ACS only, as part of their in-hospital regimen.

Aspirin. There is strong evidence that the use of aspirin in IHD can reduce future cardiovascular events. Therefore, unless absolutely contraindicated, patients across the spectrum of IHD should receive aspirin, 81-325 mg orally, once a day, indefinitely.

Clopidogrel. Clopidogrel has been demonstrated to reduce cardiovascular events in IHD, and may be slightly more effective than aspirin (based on one study). Clopidogrel is to be used in patients who cannot tolerate aspirin for primary and secondary prevention of MI. In patients who have coronary stent placement, clopidogrel should to be used in combination with aspirin for 12 months after stent placement to prevent stent thrombosis. There are also clinical data demonstrating that the early initiation of aspirin and clopidogrel combined therapy in patients with unstable angina or NSTEMI is better than aspirin alone in reducing recurrent cardiovascular events. Data on combination use of aspirin and clopidogrel beyond 12 months is not available.

Glycoprotein IIB/IIIA receptor antagonists. Glycoprotein IIB/IIIA receptor antagonists are currently only available in intravenous forms and therefore only used for managing ACS in hospitals. They are used during precutaneous coronary intervention to prevent acute platelet aggregation and thrombosis. The 2 small molecules glycoprotein IIb/IIIa inhibitors (tirofiban and eptifibatide) can also be used for medical stabilization of patients. As students have not received much information on the pharmacology of this particular class of drugs, more details are provided to them.

Specific treatment endpoints. Specific endpoints are to ensure blood pressure <140/90 mm Hg (according to JNC VII guidelines, blood pressure goal is <140/90 mm Hg and in patients with diabetes or chronic kidney disease, it is <130/80 mm Hg), a resting heart rate of 50 or 60 beats per minutes, and to improve exercise tolerance.

Monitoring parameters and monitoring frequency. Monitoring parameters include blood pressure, heart rate, and episodes of symptoms and side effects of individual pharmacologic agents. Since this is a stable angina case, the patient can be encouraged to obtain a home blood pressure monitoring device to check his own blood pressure and heart rate several times a week and during symptoms. The patient should have regular follow-up visits with his physicians. The patient should report any increase in symptoms or intolerable side effects to drugs immediately.

Patient counseling. In general, patients with any form of IHD should receive education regarding symptoms of ACS and seeking prompt medical assistance as appropriate. Also, patients should be educated to modify their lifestyles and properly manage their risk factors. To learn and practice effective counseling techniques, students are randomly selected in class to perform patient counseling for each drug.

At this point, the guidelines for treatment of chronic stable angina are summarized:

- Every patient should receive aspirin, 81-325 mg daily, indefinitely (if allergic to aspirin, may use clopidogrel, 75 mg daily).
- Patients who have coronary stents should receive aspirin and clopidogrel together for 12 months, then back to aspirin alone (dose of aspirin is 325 mg for the first month, then 81 mg thereafter).
- All patients should have sublingual nitroglycerin for relief of chest pain as needed.
- Add β-blockers, then titrate until resting heart rate reaches approximately 50 to 60 beat per minute.
- If use of β-blockers are contraindicated or if patient has Prinzmetal angina, use calcium channel blockers.
- Add long-acting nitrates if angina is frequent (make sure a 6- to 12-hour nitrate-free interval is incorporated into the regimen).
- Never use nitrates alone without β-blockers or calcium channel blockers as an antianginal.
- A combination of β-blockers, and calcium channel blockers (and nitrates) may be used for severe disease (titrate to the most optimal dose based on heart rate, blood pressure, and symptoms).

- Add ACE inhibitors when patient's blood pressure can tolerate them (make sure systolic blood pressure >90 mm Hg).
- Add statins to keep LDL cholesterol level <70 mg/dL.
- Manage other risk factors.

This summary is essential for students putting the whole picture together and allows the instructor to re-emphasize the most important points discussed.

Developing a Pharmaceutical Care Plan for Patients With Unstable Angina and NSTEMI

Patient case. CD is a 68-year-old white man with a medical history of stable angina and hypertension. Tonight, 2 hours after an argument with his wife, he experienced some chest heaviness and shortness of breath, which were not relieved after taking 6 sublingual nitroglycerin tablets (it will be emphasized here that patient should have called for help sooner). He called 911 and was brought to the hospital.

Significant Physical Examination Findings. Vital signs: blood pressure, 180/95 mm Hg; heart rate = 110 beats per minute; respiratory rate, 30 per minute; temperature, 99°F; ECG: 2 mm ST segment depression in leads V1-V4, T wave inversion V2-V4; CK, 180 mcg/L (normal < 200 mcg/L); CK-MB, 4% (normal < 5%); Troponin, 5 ng/ml (normal = 0 ng/ml). His medications included aspirin, 325 mg daily; metoprolol, 50 mg twice daily; and sublingual nitroglycerin.

Medical/Drug-Related Problem List:

1. Unstable angina (patient with ACS are to be admitted to the hospital). If the cardiac enzymes are positive, this is a NSTEMI case (drug-related problem: mistmatch between medications and indications [condition untreated]).
2. Hypertension (drug-related problem: mistmatch between medications and indications [condition untreated]).

Pharmacotherapeutic Goals. (1) Relieve symptoms; (2) prevent future symptoms; (3) prevent progression to NSTEMI or STEMI.

Pharmacotherapy

Goal 1: Relieve symptoms. Upon arrival to the emergency department, the patient should be given intravenous nitroglycerin for pain relief and an aspirin, 325 mg, to chew and swallow. Intravenous morphine may be used if pain is severe or does not subside after aspirin and intravenous nitroglycerin. Patient is hypertensive and tachycardic; therefore, intravenous β-blockers should also be given to reduce myocardial workload.

Goals 2 & 3: Prevent future symptoms and prevent progression to NSTEMI or STEMI. Upon admission to the emergency department, the patient should be given an aspirin (325 mg) to chew as mentioned before. There are also data suggesting that early initiation of clopidogrel (300 mg loading dose, then 75 mg daily) in combination with aspirin, given to patients with unstable angina or NSTEMI can better reduce future recurrent cardiovascular events as compared to aspirin alone (clopidogrel has a slow onset of action, so a loading dose is required). Blocking 2 pathways of platelet aggregation is more effective in preventing thrombosis than just blocking 1 pathway. However, this practice has not been widely adopted, as most patients admitted for ACS will undergo cardiac angiography to determine whether percutaneous coronary intervention or bypass surgery is necessary. If it is determined that bypass surgery is necessary, clopidogrel therapy needs to be delayed for at least 5 days to prevent excessive bleeding during the operation. Therefore, if clopidogrel therapy is needed it should be delayed until diagnostic angiography is performed and it is determined whether the patient will need bypass surgery. In addition to antiplatelet therapy, an anticoagulant (IV unfractionated heparin or subcutaneous low molecular weight heparin [LMWH]) should also be given. Antiplatelets and anticoagulants prevent the size of the thrombus from continuing to grow and when any clot lyses occurs spontaneously by the patient's endogenous tissue plasminogen activator, these agents will prevent further platelet aggregation and thrombin formation at the site of lyses. If the patient's symptoms do not subside at this point, intravenous glycoprotein IIb/IIIa receptor blockers can be added. Addition of statin therapy in an acute setting has also been demonstrated to help prevent future events. Once BP is stabilized, ACE inhibitors may be added. Similar to treatment of patients with chronic stable angina, modification of risk factors is important. In ACS patients, the early use of aggressive lipid-lowering therapy to attain a low-density lipoprotein level of <70 mg/dL may further reduce future cardiovascular events.[10]

At this point, important therapeutic considerations for using each class of agents for treatment of ACS are discussed with students. Students are asked to recall the mechanism of action of each class of drug as the discussion proceeds. Antiplatelets, β-blockers, and ACE inhibitors have already been discussed with chronic stable angina. Anticoagulants are discussed at this point.

Anticoagulants

Heparin. Several clinical trials indicated that early administration of unfractionated heparin is associated with a reduction in the incidence of STEMI and ischemia

in patients with unstable angina and NSTEMI. Heparin is also used during precutaneous coronary intervention to prevent acute thrombosis. When using heparin, patient should be monitored for signs of bleeding and thrombocytopenia (students have a lecture before on heparin monitoring and heparin-induced thrombocytopenia), as well as activated partial thromboplastin time (aPTT) for therapeutic efficacy.

Low molecular weight heparin. Low molecular weight heparins (LMWHs) that have been studied for treatment of ACS include enoxaparin and dalteparin. It is clarified for the students that either heparin or LMWH is to be used (not both). The advantages and disadvantages of heparin and LMWH are compared.

Direct thrombin inhibitors (agatroban, bivalirudin). Clinical data suggest that direct thrombin inhibitors have a potential role in management of ACS in place of heparin. However, more studies are needed to confirm this finding. Since this class of drug is more expensive then heparin and LMWH, they are presently indicated only for patients with a history of heparin-induced thrombocytopenia. Bivalirudin has also been studied for use during precutaneous coronary intervention to reduce the occurrence of rethrombosis.

Warfarin. Warfarin is not routinely used to treat ACS except in certain subgroups of patients: (1) post STEMI for 3 months; (2) complicated PTCA with dissection of coronary arteries; (3) clot detected during angiography. If warfarin is to be used, the international normalized ratio (INR) should be maintained between 2 and 3.

Specific endpoints. Specific endpoints for unstable angina or NSTEMI include resolution of ECG changes and normalization of cardiac enzymes (refer to CK and CK-MB only). Troponin has a long half-life and can stay elevated for up to 7-10 days), blood pressure <140/90 mm Hg; heart rate, 50 or 60 beats per minute; and if receiving heparin, aPTT that is 1.5 to 2 times baseline.

Monitoring parameters and frequency. Parameters that should be monitored in patients with unstable angina or NSTEMI include ECG changes (daily and when symptoms recur); cardiac enzymes (every 8 hours until enzymes start trending down, then daily until discharge); blood pressure (continuously); heart rate (continuously); hemoglobin, hematocrit, and platelet (daily); APTT and INR (if receiving warfarin); (aPTT every 6 hours while on heparin therapy until therapeutic goal is achieved, then daily, INR daily); and side effects of medications.

Patient counseling. For guidelines on counseling patients regarding treatment with nitroglycerin, β-blockers, ACE inhibitors, aspirin, and clopidogrel, students are to refer to the chronic stable angina discussion. As patients are unlikely to go home on intravenous heparin, counseling is not necessary. Patients are unlikely to be discharged while taking LMWH unless it is used as bridging therapy until their warfarin INR becomes therapeutic. In this case, patients should be counseled on the proper administration technique of LMWH and important information on taking warfarin. Students receive a separate lecture in a different course later in the same semester on how to properly administer a subcutaneous injection.

At this point, the guidelines for treatment of patients with unstable angina or NSTEMI are summarized:

- Administer aspirin, heparin (or LMWH), intravenous nitroglycerin, and intravenous/oral β-blockers.
- If patient is not going to have bypass surgery for the next several days, administer clopidogrel (300 mg orally load, then 75 mg orally daily). Clopidogrel must be discontinued at least 5 days prior to cardiac surgery.
- Add glycoprotein IIB/IIIA inhibitor in patients who do not respond to the above or if patients is to undergo precutaneous coronary intervention.
- Consider administration of calcium channel blockers in a subset of patients who have refractory ischemia on β-blockers and in those with variant or Prinzmetal angina.
- Discontinue heparin/LMWH therapy after the patient is pain free for 48 hours or after precutaneous coronary intervention, whichever is earlier.
- Add ACE inhibitors if patient is not hypotensive.
- Add statins to keep LDL cholesterol level <70 mg/dL.

Developing a Pharmaceutical Care Plan for Patients with STEMI

Patient case. A 77-year-old active white female with a history of hypertension (treated effectively with a diuretic), hyperlipidemia, thrombotic stroke (without residual symptoms) 5 years ago, was brought to the emergency department by ambulance with a chief compliant of shortness of breath with chest heaviness 6 hours ago and nausea. The patient received 2 sublingual nitroglycerin tablets in the ambulance, which did not relieve her chest discomfort. In the emergency department, the patient received 2 additional sublingual nitroglycerin tablets and 4 mg morphine sulfate, but her chest discomfort was still not relieved.

Significant Physical Examination Findings. Blood pressure, 190/94 mm Hg; heart rate, 94 beats per minute; respiratory rate, 22 per minute; afebrile. A 12-lead ECG was performed and revealed: new 3 mm ST segment

elevation in leads II, III and aVF (inferior leads), CK, CK-MB and Toponin are all elevated. On physical examination, the patient appears anxious and short of breath, but has no rales or jugular venous distention and normal heart sounds. Medications administered at the time of admission include aspirin, 325 mg daily; pravastatin, 40 mg daily; and hydrochlorothiazide, 25 mg daily.

Medical/Drug Related Problem List:

1. Acute ST-segment elevation myocardial infarction (drug-related problem: Mistmatch between medications and indications [condition untreated])
2. Hypertension (drug-related problem: Efficacy issues [diuretics no longer providing optimal control])
3. Hyperlipidemia (drug-related problem: Efficacy issues [pravastatin no longer providing optimal control])
4. Previous thrombotic stroke (drug-related problem: risk to patient. Due to this patient's history, when adding new therapy for other active problems, agents that could cause possible adverse drug reactions should be avoided or used cautiously. For example: possible hemorrhagic stroke caused by fibrinolytic therapy)

Pharmacotherapeutic Goals: (1) relieve symptoms; (2) reverse the damage; (3) prevent/manage complications; and (4) reduce mortality and prevent recurrent cardiovascular events.

Pharmacotherapy

Goal 1: Relieve symptoms. Similar to stable angina, unstable angina and NSTEMI, intravenous nitroglycerin can be given for chest pain relief. If necessary, morphine may also be given. Beta-blockers will also help relieve symptoms by reducing the myocardial workload.

Goal 2: Reversal of the injury process. Removing the coronary thrombus and restoring blood flow as soon as possible is essential to preserve myocardial tissue. Two major ways of restoring coronary blood flow include administration of fibrinolytics or primary angioplasty. Similar to treatment of unstable angina and NSTEMI, aspirin, 325 mg, should also be administered upon presentation to prevent further platelet aggregation at the injury site. Heparin or LMWH should also be administered to prevent rebound thrombosis after thrombolysis.

Goal 3: To prevent/manage complications. Unlike patients with other types of ACS, patients with STEMI are subject to complications post infarction. Part of the pharmaceutherapeutic management of STEMI patients is to prevent these complications and manage them properly if they occur. Common post STEMI medical complications include recurrent angina, heart failure/cardiogenic shock, and arrhythmias. Post STEMI angina is managed similar to unstable angina or NSTEMI. At the time of this lecture, students have not learned the management of heart failure/cardiogenic shock, or arrhythmia. Therefore, the "nuts and bolts" are summarized for them and they are told that more discussion will follow.

Goal 4: To reduce mortality and prevent recurrent cardiovascular events. Aspirin, thrombolytics, β-blockers, and ACE inhibitors given acutely post-STEMI reduce mortality, re-infarction, heart failure, and arrhythmias. Aspirin, β-blockers, and ACE inhibitors, as well as statin (regardless of whether they have a history of hyperlipidemia), when used long term, also reduce long-term risk of mortality and prevent recurrent cardiovascular events. In patients with left ventricular dysfunction, the addition of an aldosterone antagonist to the regimen have been shown to lower mortality and morbidity. In addition, in patients who develop left ventricular thrombi due to a massive anterior wall MI or other risk factors (such as severe heart failure, atrial fibrillation, or known apical akinesia or dyskinesia), warfarin therapy may be necessary to prevent thromboembolic events. Should warfarin be used, it should be dosed to achieve an INR of 2-3 and therapy should be continued for 3 months. Modification of other risk factors for developing cardiovascular diseases continues to be important. At this point, important therapeutic considerations of using each class of agents for treatment of STEMI are discussed with students. Students will be asked to recall the mechanism of action of each class of drug as the discussion proceeds.

Thrombolytic (Fibrinolytic) therapy. Fibrinolytic therapy is indicated for STEMI patients with symptom onset within the prior 12 hours and ST elevation in at least 2 contiguous precordial leads, or in at least 2 adjacent limb leads, or a new left bundle branch block, provided no contraindications exist. Students are asked to recall the absolute and relative contraindications of fibrinolytic therapy. STEMI patients with substantial risk of intracranial hemorrhage or any other contraindications to fibrinolytic therapy should be treated with primary precutaneous coronary intervention instead. Four fibrinolytic agents are approved by the Food and Drug Administration for use in management of MI: streptokinase, alteplase, reteplase, and tenecteplase. In terms of efficacy, out all drug names (alteplase (r-tPA), reteplas (RPA), and tenectplase (TNKase) are equivalent and they are all superior to SK. However, they also have a slightly higher risk of intracranial hemorrhage than SK and are approximately 5-10 times more expensive.

If immediately available, primary precutaneous coronary intervention is the preferred reperfusion strategy

over fibrinolytic therapy. However, cardiologists need to weigh the risks of bleeding versus the delay for reperfusion when making a decision between fibrinolytic therapy and primary percutaneous coronary intervention.

Aldosterone antagonists. Aldosterone antagonists provide additional inhibition of the renin-angiotensin-aldosterone system and have been studied in patients in the post-STEMI setting. Eplerenone has been studied in patients post-MI with heart failure and spirinolactone has been studied in patients with Class III/IV heart failure. These therapies should be recommended in post-MI patients with left ventricular dysfunction, provided the patients have good renal function (serum creatinine <2.5 mg/dL in men and < to 2.0 mg/dL in women) and normal serum potassium levels. When using aldosterone antagonists in patients with STEMI, potassium levels must be monitored closely. Most of these patients are also receiving ACE inhibitors or ARB concurrently, so the risk of developing hyperkalemia is increased. For other medications used in STEMI patients, students are referred to the previous discussion.

Specific endpoints. Specific endpoints for STEMI patients include resolving ECG changes (decrease ST segment elevation within 90 minutes after reperfusion therapy is administered), normalization of cardiac enzymes, BP <140/90 mm Hg; heart rate around 50 or 60 beats per minute, relief of symptoms, and if patient is receiving heparin, an aPTT 1.5-2 times baseline.

Monitoring parameters and frequency. Monitoring parameters are similar to unstable angina and NSTEMI. In addition, patients should be monitored for occurrence of complications such as arrhythmia or heart failure.

Patient counseling. For counseling on the use of nitroglycerin, β-blockers, ACE inhibitors, aspirin, clopidogrel, warfarin, and statins, students are to refer to the previous discussion. It is not necessary to counsel patients on treatment with fibrinolytic agents. Patients who will continue on aldosterone antagonist therapy at home should be told to follow up with their physicians for potassium and renal-function monitoring. Counseling on risk factor modification is also important.

Once again, at the end of the lecture an overview of the therapeutic management of STEMI is presented:

- Administration of aspirin, 325 mg, chewed immediately, and then administered on a daily basis indefinitely.
- Evaluate patient's eligibility to receive a fibrinolytic agent. (If contraindicated, patients will be refer for emergent angioplasty. If emergent angioplasty is available and can be performed within a short period of time, then it is preferred over fibrinolytic agents).

- Administration of intravenous nitroglycerin, and intravenous morphine if necessary for further pain relief.
- Administration of intravenous Heparin or LMWH.
- Administration of intravenous β-blockers for the first hour, then orally administered indefinitely.
- If blood pressure can tolerate, start ACE inhibitors.
- If patient is going for primary percutaneous coronary intervention, glycoprotein IIb/IIIa inhibitors should be administered prior to the procedure.
- After the patients is stabilized and all drug dosages are optimized, aldosterone antagonists should be administered to patients who have left ventricular dysfunction if potassium and renal functions are normal.
- Management of other potential complications, such as heart failure and arrhythmia.

Recitation Section

The lecture is structured to reflect the thought process that students need to go through when presented with a patient case at their recitation section or clinical clerkships. As mentioned before, the *Pharmacotherapeutics II* has a combined recitation with *Pharmacology/Medicinal Chemistry II*. Students are given the case a week prior to their recitation section. Students are expected to come to recitation with their own care plan (first draft). During the recitation, students are to discuss their care plan with their group members. Each group finalizes one care plan, hands it in to the recitation facilitator, and presents the plan to the other recitation groups. To tie in pharmacology and medicinal chemistry concepts, when choosing a therapeutic agent for the patient, the students also need to define the class of agent, its mechanism of action, absolute contraindications, and major side effects of the medications. In addition, for each drug chosen, if there are multiple drugs in that particular class, students are also required to justify why the specific drug and dosage form were selected. For example, students may recommend administration of intravenous metoprolol for a patient. Students would then have to justify their choice, which was based on the fact that metoprolol can be given either intravenously or orally. Using the intravenous form initially ensures faster onset of action. Metoprolol is also a beta-1 selective blocker. It is chosen so we can focus the pharmacologic effect on the heart and minimize peripheral side effects. Facilitators grade the care plans according to the answer key provided by the instructor (the author). Facilitators do not provide any answers or hints to the

students during the recitation section, but do guide students toward arriving at their own answer.

DISCUSSION

Overall, the whole *Pharmacotherapeutics II* course has 3 multiple-choice examinations (2 midterm and 1 final examination). Examinations of cardiovascular disease topics are in the second and third examination. All examination questions are created based on the learning objectives. Although multiple-choice examinations may not be the best way to assess critical thinking skills, due to the large class size (200 students per class), this testing format is the best means of determining whether students have learned the most essential materials. On the examination, whenever a drug is named, both the brand and generic names are provided. This is to familiarize students with both generic and common brand names of medications, as the NAPLEX may only provide them with one or the other. They are both provided for the students' benefit. Most of our students have work experience in community pharmacy where brand names are more often used. During the semester, sample examinations are available in the library on reserve so students can become familiar with the format of my examination questions. This is essential, especially for the team-taught courses. This helps students in adapting to the different teaching and assessment styles of instructors.

SUMMARY

Over the years I have been using this approach in delivering my lecture on IHD, feedback from students has been positive. The students have expressed that the case-based approach helps them develop pharmaceutical care plans both during recitation and during clerkships. Case-based approach lecturing can be done even with our class size of more than 200 students. The lecture objectives have helped them focus when studying for examinations. The sample examination questions placed on reserve in the library have been particularly helpful in familiarizing students with the format of my examination questions and is particularly essential in a course taught by multiple faculty members with different styles. The 4 lecture hours assigned may be tight for such a big topic. Therefore, it is important for the faculty member/instructor to carefully consider what is truly important for students at this level to learn and retain and what the majority of students are going to encounter in future courses/lectures. It is better that the students learn less information well than a lot of information that they really do not understand. Trying to help the students focus with learning objectives as well as repeatedly emphasizing what is and is not important throughout the lecture is also crucial for the lecture to be effective. It is also extremely important to reemphasize to students that they need to review the pharmacology/medicinal chemistry of medications used for this disease before coming to the lecture in order to be productive.

REFERENCES

1. Heart Diseases and Stroke Statistics: 2004 Updates. American Heart Association. Available at: http://www.americanheart.org/presenter.jhtml?identifier=3000090. Accessed August 19, 2004.
2. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction) http://www.americanheart.org/presenter.jhtml?identifier=3001260. Accessed March 1, 2005.
3. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patient with ST-Segment Elevation Myocardial Infarction) http://www.americanheart.org/presenter.jhtml?identifier=3023107. Accessed March 1, 2005.
4. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Chronic Stable Angina) http://www.americanheart.org/presenter.jhtml?identifier=1930. Accessed March 1, 2005.
5. Canaday BR, Yarborough PC. Documenting pharmaceutical care: creating a standard. *Ann Pharmacother.* 1994;28:1294-6.
6. Strand LM, Morley PC, Cipolle RJ, Ramsey R, Lamsam GD. Drug-related problems: their structure and function. *Drug Intell Clin Pharm.* 1990;24:1093-7.
7. Omibus Budget Reconciliation Act of 1990. Pub. L. No. 101-508. § 4401, 104 Stat. 1388. Washington, DC: US Government Printing Office; 1990.
8. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VII). Available at: http://www.nhlbi.nih.gov/cgi-bin/redir.pl?url=http://hyper.ahajournals.org/cgi/content/full/42/6/1206. Accessed 19 August, 2004.
9. Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Full Report. Available at: http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm. Accessed August 19, 2004.
10. Pravastatin or Atorvastatin Evaluation and Infection Therapy – Thrombolysis in Myocardial Infarction 22 Investigators. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med.* 2004;350:1495-504.

Appendix 1. Sample Recitation Pharmaceutical Care Plan

Drug-Related Problems	Pharmacotherapeutic Goal	Recommendation(s) for Therapy	Specific Desired Endpoint	Monitoring Parameter(s)	Monitoring Frequency
Mismatch between medications and indications (Untreated condition)					
1. NSTEMI (Substernal chest pain at rest, shortness of breath ECG changes ST segments elevation, depression and T wave inversion, positive CK, CK-MB, troponin) Efficacy Issues: (Subtherapeutic Doses/Improper Drug Selection)	1. Chest pain relief. Reversal of ECG changes. Prevention of progression to STEMI (i.e. Permanent ischemic damage).	1. Aspirin 325 mg po, first dose chewed, then once daily indefinitely. IV nitroglycerin 5 mcg/min, increased dose by 5 mcg/min every 5 minutes until pain is relieved or SBP = or <90 mm Hg, continue therapy for no more then 72 hours to prevent tachyphylaxis. Metoprolol, 5 mg intravenous, push every 5 minutes for three doses, then 25 mg q6h for the first day, then 50 mg bid afterwards, titrate per blood pressure and heart rate. Therapy continued indefinitely. Heparin therapy 70 U/kg bolus, then 15 u/kg/hour intravenous for an average of 48 hours after pain is relieved. Glycoprotein IIb/IIIa therapy since this is a high-risk patient (one of the following): Abciximab 0.25 mg/kg intravenous bolus, then 0.125 intravenous mcg/kg/min, OR Tirofiban 0.4 mcg/kg/min intravenous for 30 minutes, the 0.1 mg/kg/min intravenous thereafter, OR Eptifibatide 180 mcg/kg intravenous bolus, then 2 mcg/kg/min intravenous thereafter Therapy continued until 12 hours after coronary interventional procedure is completed.	1.Pain relief BP <140/90 mm Hg HR between 50-60 beats per minute APTT 1.5-2 times baseline Resolve of ECG changes	1. Pain relief, BP, HR, cardiac enzymes, ECG Aspirin: CBC, symptoms of GI distress Nitrates: BP, HR, headache Metoprolol: BP, HR Glycoprotein IIb/IIIa inhibitors: CBC (especially platelets), bleeding IV heparin: CBC (especially platelets), bleeding, APTT	1. BP, HR, pain: q6h for the first several days, then daily CBC, GI distress, bleeding: daily APTT: 6 hours after initiation of heparin therapy, then every 6 hours if doses are adjusted. Once achieved therapeutics APTT, then check once daily.

2. Hypertension BP 170/99 mm Hg Efficacy Issues: (Subtherapeutic Doses)	2. Controlling of BP and heart rate.	Try to add ACE inhibitor if patient's BP can tolerate. ACE inhibitor has been demonstrated to reduce future cardiovascular events. 2. B-blockers, ACE inhibitor should be able to control patient's BP adequately. If not adequate, can add hydrochlorothiazide. (Base on JNC 7 hypertension management guideline)	2. BP < 140/90 mm Hg (but keep systolic BP > 90 mm Hg)	2. BP	2. BP q6h for the first several days, then daily ACEI: potassium, serum creatinine daily, cough daily
3. Hyperlipidemia Total cholesterol 240 mg/dL, triglyceride 120 mg/dL, HDL 40 mg/dL Calculated LDL: 240-40-(120/5) = 176 mg/dL	3. Maintain good cholesterol profile to prevent further ishemic events.	3. Start a statin. Anyone is fine. Although I would recommend Atorvastatin. Since patient needs to have LDL reduced from 176 to <70. I doubt other agents will be strong enough. Therapy to be continued indefinitely Low cholesterol, low fat diet Exercise	3. Total cholesterol <200; triglyceride <150, HDL >40, LDL <70	3. Cholesterol profile, LFT, CPK	3. Cholesterol profile 6-8 weeks after initiation of statins therapy. LFT at baseline, then at 3 month, 6 month and once a year. Muscle pain, check CPK at baseline, patient should be told to report to physician if experience pain. Fasting blood sugar daily, HgbA1C every 3-4 months.
4. Effficacy Issues (Patient non-compliance)	4. Improve patient compliance and prevent further events.	4. Once stabilized, try to change drugs to formulation that can be taken once daily to improve compliance. Also provide patient education to improve his understanding of taking his medications and optimal outcomes	4. >80% compliance		