CLINICAL PHARMACOLOGY

Subcommittee:

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The Subcommittee on Clinical Pharmacology sought to identify three general subtopics for the teaching of Clinical Pharmacology to medical students. The Subcommittee recommends a core of factual and conceptual information, i.e., clinical pharmacology "facts" that are distinct from the information taught in basic pharmacology courses. The Subcommittee also recommends clinical pharmacologic skills that students should master in order that they can effectively evaluate and prescribe drugs. Lastly, the Subcommittee recommends the clinical pharmacology attitudes and behaviors which students should develop as they mature to become prescribing physicians.

These facts, skills and attitudes/behaviors should be taught throughout the four years of medical school. Many of the facts and introductory material are initially taught in the 2nd year Medical pharmacology course but the attitude and skills should be taught by example throughout medical school. Because the student's attitudes may dictate the development of appropriate skills and even facts throughout their medical education, attention to preferred attitudes on therapeutics should begin very early in medical school.

Ideally, many of the clinically-related facts should be taught in the fourth year after the students have learned enough clinical medicine so they can integrate the facts and principles of rational therapeutics into habits for

patient management. However, there are many different and effective ways to teach the material, and different schools have developed their own balance of lectures, seminars, patient-based problem solving, rounds, etc.

1. **Clinical Pharmacologic Facts**

   a. Principles of clinical pharmacokinetics
   b. Principles of therapeutic drug monitoring
   c. Principles of prevention and management of adverse drug reactions, including drug allergy.
   d. Principles and management of drug-drug interactions.
   e. Principles and prevention of drug-food and drug- botanical interactions.
   f. Pharmacogenetic causes of variable response to drugs.
   g. Sex and gender as causes of variable response to drugs.
   h. Special problems of prescribing to elderly patients.
   i. Special problems of prescribing to pediatric patients.
   j. Special problems of prescribing to pregnant or nursing women.
   k. Special problems of prescribing to patients with underlying diseases such as renal or hepatic disease.
   l. Principles of evaluation and treatment of the poisoned patient.
   m. Rules and regulations affecting drug prescriptions.
   n. The process of new drug development and approval.
   o. Principles of error prevention in prescribing.
   p. Principles of integrating prescribing with the full healthcare team (pharmacists, nurses, patients and their families).
   q. Principles of utilizing modern infomatics and databases in safe and effective prescribing.

2. **Clinical Pharmacologic Skills**

   a. Pharmacokinetics: Students should be able to quickly and accurately solve the common pharmacokinetics problems presented by patients. They should be adept at computing loading doses and maintenance doses using their knowledge of volume and distribution and clearance when prescribing drugs. They should be able to anticipate interindividual differences or changes in pharmacokinetics parameters due to genetics, sex and cardiac, renal or hepatic function.

   b. Therapeutic drug monitoring: Students become skilled at appropriately ordering the measurement of plasma drug concentrations (including "free" rather than total drug concentrations) when indicated. Ability to interpret drug concentration measurements in the context of the therapeutic window, along with derivation of dosage adjustments to maintain

therapeutic concentrations, should be mastered. They should become skilled at avoiding the overuse and over reliance on this technique, and learn to avoid generating misleading data by ordering drug levels at incorrect times or under inappropriate clinical conditions.

c. Adverse drug reactions: Students should develop reasonable skill at analyzing complicated cases in which patients have several diseases, several symptoms, and are receiving several drugs. Students should practice and sharpen their skills at separating symptoms and signs caused by disease from those caused by the drugs per se. Students should understand how to access the MedWatch voluntary ABR reporting system maintained by the FDA.

d. Drug interactions: Students should become skilled in recognizing and anticipating common drug interactions for the drugs taken by their patients, especially metabolically based interactions due to genetic differences (using knowledge of polymorphisms of cytochrome P450 isozymes, etc). The skill should include a multi-faceted approach to incorporate other healthcare providers and information resources. They should be skilled in using up to date reference sources and electronic databases to screen for potential drug interactions for the drugs they will be prescribing.

e. Special factors in each patient: Students should be able to recognize patient factors (such as age, sex, underlying disease, pregnancy, nursing, etc.) which would require alternate therapeutic plans. In addition, students should have the skills to find available data in these areas in standard reference and electronic data sources.

f. Obtaining and interpreting drug information: Students should be skilled at retrieving and understanding scientific data available from experts, internet sources, books, and other databases. Students should be able to evaluate a new drug's efficacy and toxicity by reviewing primary, peer-reviewed papers. Students should develop a reasonable level of competency in accessing web-based or CD-ROM based information programs that give the latest information about individual drugs, drug classes, drug interactions, drug information for patients, drugs listed by indicators or contraindication, etc.

g. Prevention and management of drug overdoses: Students should be skilled in recognizing presentations of common drug overdose, and in initiating therapy when appropriate. In addition, they

should develop an approach to such problems that can be used in any such patient even before the casual agent has been confirmed. Finally, students also should be skilled in the use of common reference sources for rapidly obtaining accurate information enabling the diagnosis and treatment of toxic emergencies.

h. Substance abuse: Students should become skilled in recognizing the presentations of intoxication, withdrawal, and medical complications of the common drugs of abuse. They should also develop facility with taking a substance abuse history, and should learn techniques for uncovering unsuspected substance abuse problems.

i. Prescribing: Students should master the paradigm for rational therapeutic decision making, that assures selection of appropriate drug therapy only when drug therapy is warranted, at effective individualized and safe dosages, and commit to monitoring therapy with appropriate dosage adjustments and changes or termination of drug therapy. Students should also master the requirements for complete drug prescription. They should be skilled in prescribing complete, accurate, safe and legible written or electronic prescriptions for drugs used in both in-patients and out-patients, including drugs with special restrictions such as those requiring a DEA license. Students should understand the special requirements for prescribing 1) drugs that are investigational, 2) those which are being used for a non-approved indication, and 3) those which are available only from physicians granted an IND.

j. Communications skills: Students should become skilled in talking with their patients to assess and stimulate drug compliance, and to ascertain history (including prescription and nonprescription drugs, topical preparations, dietary supplements, botanicals, etc.). Students should know how to use the various written materials that are available as patient inserts (medication guides).

k. Integrating basic and clinical science: Students should develop the essential skills to enable them to incorporate principles of basic pharmacology into their clinical decision-making patterns, as well as incorporate clinical factors into their approach to evaluating the pharmacology of medications.

l. Recognition of pressures to prescribe irrationally: Students should develop the ability to recognize in themselves tendencies to irrational prescribing, and recognize the forces encouraging

such habits. They should understand the potential for being misled by biased information when they learn about medications from advertisements, detail personnel, colleagues (word of mouth), special sponsored symposia, etc. Although some useful information can be imparted in these ways, students must place the information in context. They should neither blindly accept information from potentially biased sources nor should they refuse to consider the merit of the information. They should also recognize that anecdotal experiences, even their own, can be misleading.

3. <u>Clinical Pharmacologic Attitudes</u>:

a. Balanced approach to drug prescribing: Students should avoid the extremes of therapeutic nihilism and gross over-prescribing. Students should be impressed by the power of drugs to help cure and treat disease, but this should be balanced by respect for the power of drugs to cause serious and even fatal adverse reactions. They should embrace their ethical commitment to monitor the outcome of each prescription in each patient until the intended effect is achieved or a change in therapy is warranted.

b. Conscious attempt to optimize benefit and minimize risk: Students should recognize that each patient is a special case for drug therapy until proven otherwise. They should also be aware that the best drug for a particular patient may change as the dynamic process of the patient's disease unfolds.

Students should recognize that treatment of any disease or syndrome can often involve several or many combinations of drug choices and treatment regimens. The best choice for a given patient must be sought in a specific effort to maximize the chance of a therapeutic outcome, and minimize the chances of drug-induced toxicity or failure. Those factors which make each patient unique should be consciously sought and considered. This attitude is essentially the opposite of the "cookbook" approach to drug therapy.

c. Balanced approach to the introduction of new drugs: Students should not refuse to prescribe a new drug product just because it is new, nor should they enthusiastically embrace all new drugs as being the latest and the best. Rather, students should understand that the place of a new drug in the current pharmacopoeia may not initially be clear, and that subsequent data may radically change the manner in which the drug is prescribed. Students should be willing to take responsibility for developing their own

approach to learning about new drugs as they are approved by the FDA and marketed.

d. Importance of the therapeutic contract: Students should understand that at the heart of drug prescribing is a contract between the physician and the patient. Communication is essential so that the physician can learn enough information to prescribe optimally, and then again to ensure optimal compliance. In addition, the physician must understand that the contract requires him or her to follow the patient over time to see whether the therapeutic trial results in beneficial or unwanted effects.

e. Acceptance of the need to prescribe as a team leader with responsibility to the patient to utilize all resources available to maximize the benefits of therapy. This requires the student to accept the fact that they cannot memorize all of the facts required for optimal prescribing and must rely on computerized databases, nurses, pharmacists, the patient and the patient's family as members of the therapeutic team.

Recommendations:

Some schools have chosen to provide the bulk of this teaching in a fourth year course; others have incorporated the teaching of clinical pharmacology in the second year Medical Pharmacology course (Peck, CC and Halkin, H, J. Med. Ed. 56:1024-6, 1981). Much of the material of clinical pharmacology cannot be taught effectively during the second year because the students have usually not had an adequate clinical experience to fully integrate and appreciate the material or principles involved. Therefore, a formal course, problem solving instruction and/or small group discussions are often incorporated in the third and fourth years to reinforce the principles and expand upon the database of clinical pharmacology (Cantilena and Woosley, Clin. Pharm. Ther. 60:1-7, 1996).

Most courses in the fourth year require 20-25 hours focusing on general principles and core topics with commonly used drugs. Some schools have devoted over 70 hours to courses that include, not only core material, but also detailed discussion of a variety of therapeutic topics. An innovative fourth year course at Georgetown University was recently described (Knollman, B. et al, Naunyn-Schmeideberg's Archives of Pharmacology, March, 2002).