Clinical pharmacology is the study of drugs in humans. Therefore, a clinical pharmacologist could be defined as an individual who studies the action of drugs in humans. Implied in the definition is the study of the therapeutic aspects of drug usage as well as the basic mechanisms of drug action. The clinical pharmacologist, therefore, must be well trained in pharmacology as well as in clinical medicine. The clinical training can be in any area of medicine. However, this definition does not adequately define the activities or goals of a clinical pharmacologist in a modern hospital. In my view, the purpose and all consuming desire of a clinical pharmacologist is to improve drug usage by physicians. He attains this goal in part by participating in the research needed to obtain the facts upon which to base rational therapy; in part by translating this information to his medical colleagues; and in part by participating in the activity of the various committees of the hospital such as the Pharmacy and Therapeutics and Human Subjects Committees. At present, clinical pharmacologists are found only in medical schools and large hospitals.

Perhaps I can best illustrate the role of a clinical pharmacologist in a large medical center by outlining the activities of the Division of Clinical Pharmacology at the University of Kansas Medical Center where I was Director for 5 years. I must emphasize that although critical mass of personnel and equipment is necessary, each hospital need not have a group as large as ours to function adequately. Indeed, ours is one of the larger ones in the United States and is used only as an example.

The Clinical Pharmacology-Toxicology Center has thirteen staff positions including five clinical pharmacologists with training in internal medicine and two with training in pediatrics. The remaining individuals have specialized training in toxicology, biochemical pharmacology, pharmacokinetics, organic chemistry and mass spectrometry and basic pharmacology. The laboratories are equipped to analyze drugs and metabolites by spectrophotometry, gas chromatography, high pressure liquid chromatography, gas chromatography/mass spectrometry, fluorescence, and immunoassay. Adequate facilities are available for animal studies as well as a special clinical research center for it is essential that the clinical phar-
macologist be able to move his investigations from man to animals and back as he pursues answers to rational use of drugs in man. It is important that he also have the in-patient and out-patient facilities necessary to study patients carefully.

What role does the clinical pharmacologist fulfill in a college of health sciences? Our group constitutes the attending physicians on a 20-bed general internal medicine service. Participation in patient care in some form serves several purposes. It allows the clinical pharmacologist to maintain his clinical skills since it is absolutely necessary for him to be prepared to treat any untoward effects which might occur during a study of a patient or healthy volunteer with a drug. It keeps the clinical pharmacologist on the “fighting line” so he is aware of the practical problems physicians face in their day to day use of drugs and the care of their patients. It affords him the opportunity to teach about and demonstrate the rational use of drugs at the bedside. The latter is quite important since physicians are more likely to heed the clinical pharmacologist’s words if he sees that the clinical pharmacologist can adequately treat humans, not just regurgitate results of studies about dogs, mice or monkeys or even man. This effort is very time consuming and can only be undertaken by units with sufficient personnel.

What about teaching? The clinical pharmacologist has a significant role in teaching the principles of rational drug therapy. His efforts start in the medical student pharmacology course. However, at every opportunity he must be willing and prepared to discuss the use of drugs in patients. The opportunities arise informally on ward rounds and more formally during conferences of various types. Particularly today, with the emphasis on postgraduate medical education, the clinical pharmacologist must undertake his share of all types of teaching.

Although well versed in the principles of drug usage and evaluation, the clinical pharmacologist is not and should not be expected to be an expert on every class of drugs. However, he should always know where to obtain the necessary information about a drug when requested. Thus, the clinical pharmacologist, perhaps in concert with a drug information specialist, should be the primary source of drug information for the hospital.

Consultations concerning drug related problems should be a significant activity of the clinical pharmacologist. The consultations should include a variety of types, such as: therapeutic problems, adverse drug reactions, both accidental and suicidal poisonings, and clinical pharmacokinetic problems. These services should be provided on a 24-hour basis. Pharmacokinetic problems may provide the majority of consultation requests. Included in the consultation is the result of a plasma drug level determination. With these activities the clinical pharmacologist provides a needed service for the hospital. Except on an out-patient basis, plasma levels are not done without a consultation request. The reason, as you well know, is that the “therapeutic values” cannot be stated in statistical terms as can a serum potassium or SGOT, but rather must be evaluated in relation to when the last dose of the drug was administered, the clinical response of the patient, the bioavailability of the dosage form, etc.

The Clinical Pharmacology Division at the University of Kansas has noted a marked increase in the number of pharmacokinetic-related consultations in the past few years. I pre-
sume, or at least I hope, that the number of requests has increased because the physicians at our hospital observed the usefulness of the consultation in treating their patients. We also provide plasma level analyses for other local hospitals.

The consultation requests also provide the data for useful and interesting research projects and the data should not be wasted. For example, several years ago we reviewed the charts of 43 patients who were receiving digoxin, and while unaware of the serum concentrations of the glycoside, classified each patient into one of four groups. Based on clinical and electrocardiographic findings, individuals in Group I (subtherapeutic) were still in congestive heart failure, those in Group II (therapeutic) were satisfactorily treated, those in Group III were considered potentially toxic and those in Group IV were definitely toxic. The results of the serum digoxin concentrations and other pertinent laboratory data for these patients are shown in the next slide. There was a statistically different level of serum digoxin in each group although the variance was large. The patients in Group I were the heaviest and received the smallest doses whereas those in the toxic group received the largest doses. A multiple regression analysis was done and we found that 50% of the variance could be absorbed by level alone and only another 5% could be absorbed by adding the all other factors. With a critical discrimination analysis, 76 of 84 patients were classified correctly into therapeutic or toxic. Five were incorrectly classified as toxic and three incorrectly as therapeutic. Abnormal responses in individual patients also lend themselves to further potentially useful data and research endeavors.

The major effort of the clinical pharmacologist should be in acquiring new knowledge; therefore, research should occupy a significant amount of the clinical pharmacologists' time. Sophisticated, basic studies in humans certainly can and should be done. For example, we recently studied the dosage requirements of phenytoin and clofibrate in patients with nephrosis. However, there is also an excellent opportunity for the clinical pharmacologist to perform very practical and useful therapeutic trials of various types. He should be knowledgeable in the design of drug trials and be available as a consultant for all the protocols of drug studies within the hospital even though he does not participate in these studies personally. However, either by himself or in conjunction with various specialists, he should participate in carrying out a few clinical trials. Our group is particularly interested in hypolipidemic drugs.

The clinical pharmacologist has been at the forefront in developing reviews of the ethical aspects of the study of drugs in humans. As such he has a significant part in the activities of the Human Subjects or Ethics Committee. I am well aware that many hospitals do not have a committee of this type and equally well aware that mores and ethics may vary from country to country. I certainly would not presume to tell colleagues in other countries they should do things in the manner that we do them. Instead, let me explain the function of this committee and what the clinical pharmacologist does as a member. The Human Subjects Committee decides whether the benefits of studies to be done in humans outweigh the risks. The committee must decide if the proposed study is scientifically sound and will provide valid results. Otherwise, any risk is too great. The committee must also decide if informed consent will be obtained.
from the volunteers and in an adequate manner. I must stress that all individuals, whether ill or healthy, who participate in drug studies, must be volunteers and these individuals should have their rights as human beings protected.

The clinical pharmacologist frequently serves as chairman of the Pharmacy and Therapeutics Committee. The Pharmacy and Therapeutics Committee selects those drugs and dosage forms to be available for use in the hospital. These decisions are not capricious, but based on data obtained from the scientific literature. We can see no good reason why the hospital pharmacy should stock more than two or three dosage forms containing the same active drug or a favorite remedy of a physician if there is no scientific or even clinical evidence that the drug is effective and safe. This committee also sets standards for drug administration. For example, how long can a narcotic be given before a renewal order is required; how long can antibiotics be given without a renewal order; should nurses or pharmacists be allowed to add medications to intravenous infusion? These questions may seem trivial to some of you, but be assured they can be of the utmost importance in reducing medication errors and in rational health care delivery. The committee is not autonomous and reports to the executive committee of the hospital staff. Whenever a major decision is made, the proposed changes are reported in a monthly hospital publication of the committee (which is circulated to all members of the hospital staff) for comment before a final decision is reached. The monthly bulletin is also an excellent way to disseminate information about drugs to the clinical staff.

Difficulties may develop between the clinical pharmacologist and the clinicians on one hand and the basic pharmacologists on the other. These have frequently been due to petty jealousies over prerogatives. They should not and cannot exist since the major concern of all physicians must be the welfare of the patient. The clinical pharmacologist as a member of the group has something to offer. Physicians have become reasonably good diagnosticians. However, once they have made the correct diagnosis, they have only a few therapeutic choices. They can cut out the difficulty with a scalpel blade and in some instances this is correct. They can try psychotherapy and in fewer instances this is helpful. They can do nothing and this is helpful in the proper circumstances. However, in the majority of instances, they administer a series of chemicals which no longer are the essentially nonactive natural products of past years, but rather, very potent drugs with the potential for causing great harm as well as good. Rational therapy has been suggested as the administration of the proper drug at the proper time in the proper dose for the proper diagnosis. It must be remembered that adverse effects arise not only from the toxic effects of the drug, but equally important by progression of the patient’s illness from inadequate or improper therapy. Unfortunately, I regret to say, many physicians are not satisfactorily trained in the use of these agents. The clinical pharmacologist is the individual who by training and experience can help improve rational drug usage. The aim of therapy should be to maximize the rational use of drugs, not rationalize the maximal use of drugs.