DRUGS AND SOCIETY

bernard barber

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In DRUGS AND SOCIETY a leading social scientist explores man's uses and abuses, now and in the past, of all the varied substances that have been called "drugs". Throughout history, Bernard Barber shows, drugs have been used for every social purpose, e.g., aesthetic reasons, as implements of war, for relief of pain, for social and psychological escape, and for the control of thought and behavior. In considerable measure, his functional approach makes very clear, it is social naming that establishes a substance as a drug or not a drug. And the important consequence of this approach is that no aspect of drug definition, discovery, distribution, use, experimentation, therapy, or control can be successfully studied without equally taking into account the biological, psychological, and social facets of drug behavior, and especially the interrelations of these three.

Guided by this view of drugs, Professor Barber organizes and criticizes what has been learned about drug behavior by such varied specialists as biologists, medical researchers, pharmacologists, sociologists, practicing physicians, pharmacists, historians of science, economists, health administrators, and government officials. He brings out the implications of what is now known, the perils of continued ignorance in many areas, and the need for a great deal of specific new research.

The author raises fascinating questions about a great many drug problems in contemporary society. For example, he examines the ethical considerations relating to experimentation with drugs on human subjects. He indicates that our social policy

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Drugs and Society

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Drugs and Society

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For Leslie,

Chris, Flip, and

John

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Preface

SOME SEVEN OR EIGHT YEARS ago, while we were collaborating on some work in the sociology of science in which we used the drug industry as one research site, Dr. Renée C. Fox and I made up a rough outline for a book on the sociology of drugs. Unfortunately, because of other work commitments, we never got beyond the outline. Then, a couple of years ago, in the course of one of those pleasant, informal, discursive, and stimulating conversations which I have had with him over the last several years, Dr. Orville G. Brim, Jr., President of Russell Sage Foundation, made the remark that drugs were already a terribly important matter in our society and were bound to become even more so in the future. When I told him about the outline for a book on this subject that was in my file, he suggested that I take the enterprise up again and offered to make available the funds for research time and research assistance. Fortunately, not long after, I was able to act upon his suggestion, and this book is the result. I should like to thank Dr. Brim for his original stimulus and for his continuing intellectual and moral support down to the present.

Since I have discussed the perspectives and purposes of this book

in the introduction, there is no need to say very much more here on those matters. I should like only to underline two important points. One is that the study of drugs provides an excellent site for theory and research on a wide variety of fundamental sociological topics. I hope my book provides ample illustration on this score for my colleagues in the social sciences. The second point is that the study of drugs reveals an area undergoing basic processes of social change and therefore offering opportunities for constructive programs of social action and improvement. So far as some desirable and multi-sided reforms are concerned, I have tried to cast my discussion in the spirit of what the historians call "the revolution of the moderates" rather than of what they call "the revolution of the radicals," though I am fully aware that history shows many failures for the moderates. Yet I think that even at this time, despite the limited knowledge available to us, we could engage in a variety of judicious, cooperative programs for constructive reform in several of the areas where drugs play their different functions in society.

Given the comprehensive perspective of this book, I have had to treat many different subjects which are specialized areas for research in their own right. I have been fortunate in obtaining the help of experts in a number of these specialized areas. Their intensive critiques of a first draft of this book have, I think, made it possible for me to write a much better final version. It is a pleasure to acknowledge the help of the following: Professor John A. Clausen, Director, Institute of Human Development, University of California, Berkeley; Professor Eliot Freidson, Department of Sociology, New York University; Dr. Gilbert Honigfeld, Assistant Chief, Central Neuro-Psychiatric Research Laboratory, Veterans Administration; Professor Alex Inkeles, Department of Social Relations, Harvard University; Allen S. Kushen, Esq., Attorney, Schering Corporation; Professor Ovid C. Lewis, School of Law, Western Reserve University; Professor A. R. Lindesmith, Department of Sociology, Indiana University; Professor Walter Modell, Department of Pharmacology, Cornell University Medical College; Dr. Wilbert E. Moore, Sociologist, Russell Sage Foundation; Professor Charlotte Muller, School of Public Health and Administrative Medicine, Columbia University; Dr. John W. Riley, Jr., Vice President and Director of Social Research, The Equitable Life Assurance Society; Professor Edwin M. Schur, Department of Sociology, Tufts University; and Pro-

fessor Cedric W. M. Wilson, Department of Pharmacology, University of Dublin.

I am grateful to Professor Marvin B. Sussman for providing the opportunity to give a University Lecture on Drugs and Society at Western Reserve University and to Dr. George G. Reader of Cornell University Medical College for inviting me to talk on the same subject to his seminar on social aspects of medicine. Both occasions helped me to clarify my views. Professor David C. Glass, of Russell Sage Foundation and The Rockefeller University, has been a helpful monitor and friend. I would like to thank Mrs. Linda K. Bock for excellent research assistance. As always, Elinor G. Barber has been of invaluable help.

BERNARD BARBER

Dobbs Ferry, N.Y.
September, 1966

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Introduction

AS THE TITLE of this book suggests, and as the chapter headings further indicate, the scope and purposes of the book are quite broad. The study of drugs frequently suffers from the researcher's taking too specialized a point of view, and also from taking the excessively negative view that results from limited perspectives. We do need a great deal of the specialists' knowledge about each of the many different things called "drugs." For example, we need good specialized knowledge about therapeutic drugs and "religious" drugs and "addictive" drugs. But we also need the comprehensive perspective that enables us to see that there are all these different sides to the study of drugs. The specialist is usually talking only about his own concerns when he thinks of "drugs," and he does not realize how easy it is to overgeneralize from those concerns to quite different ones.

We also need to avoid the excessively favorable and excessively negative views of drugs that frequently are expressed when people have only one kind of drug in mind. If we think only of therapeutic drugs, we are inclined to be too favorable, and if we think only of "addictive" drugs, too negative. Actually, therapeutic drugs have their

negative side, as we have all learned from the occurrence of catastrophic side effects in such drugs as thalidomide. And conversely, "addictive" drugs have their somewhat favorable side. They have been used from the beginning of time to relieve pain and to give joy. And they are sometimes possibly less harmful than various alternatives for which they seem to be substitutes. Hostility and violence and depression may, under some circumstances, be worse than drug dependence. None of these, of course, is desirable in an ideal world. In sum, "drugs" are much too complex a set of matters to be treated only from a single or limited point of view.

Another way of putting this is to recognize that almost anything can be called a "drug." There is nothing intrinsic to any physical or biological substance that makes it a drug or does not. The same substance can be called a "drug" in one social context and called something else in another. For example, the ink that is used in fountain pens is not a drug when used in that way, but it may legally be defined as a drug if it is used as a diagnostic agent in connection with anti-fungal materials which are also defined as drugs. Some people think of alcohol as a drug; others obviously do not. When we look at drugs in a generalized and comprehensive way, what we see is that it is not so much the substance of a material that makes it a drug, but rather some particular social definition. And this social definition always takes into account not just the physiological functions of various substances, but their psychological and social functions. The meaning of something that is called a "drug," or not so called, always has to be studied in all three of these inter-related aspects: the physiological, the psychological, and the social.

Not only can nearly anything be called a "drug," but things so called turn out to have an enormous variety of psychological and social functions—not only religious and therapeutic and "addictive," but political and aesthetic and ideological and aphrodisiac and so on. Indeed, this has been the case since the beginning of human society. It seems that always and everywhere drugs have been involved in just about every psychological and social function there is, just as they are involved in every physiological function.[1]

[1] The topics of this and the preceding paragraphs, namely, how a drug is to be defined and what its several functions are, have been treated intensively and systematically in the last chapter of this book. Here we are just calling attention to some important points of view about drugs.

Historical and comparative evidence is particularly valuable in helping us to take a comprehensive view of the several meanings and functions of drugs. Such evidence shows that some things remain constant. For example, opium in some form has been used in many different parts of the world, and apparently for as far back as we can read history. Or again, therapeutic drugs from plants have been concocted by our pre-historic ancestors, by tribes of our "primitive" contemporaries, and are still concocted by our most advanced drug companies. This "green medicine," as it has been called, has been around for a long time and is with us still. But comparative and historical evidence also shows how some things vary by time and place. The epidemiology of opiate addiction in nineteenth-century United States was different from what it is today. Many more middle-class people and women were addicted then. And today, addiction is different in Great Britain as compared with the United States. There are many fewer addicts there, and they do not come so disproportionately from the poorer urban minority groups, as they do here. There are interesting comparative differences even within countries; whereas the poor in the United States are nowadays more likely to use heroin or marijuana, the better-off have taken the barbiturates and LSD as their "drugs of choice."

In the long-term historical perspective, of course, a fundamental fact about drugs is the pervasive and rapid rate of change that very recently has affected nearly every aspect of their development and use. There has been, to mention only a few examples, rapid change in the number of scientific discoveries, the number of professional researchers, the amount of drug testing, the scope of therapeutic effectiveness, the scale and profitability of the drug industry, the seriousness of problems of government control and supervision, and public awareness of the several troubles that drugs can help to cause, such as "addiction," harmful side effects, high costs of therapy, and illegitimate control of behavior and personality. It would seem, sometimes, that the rate of change throughout the area of drugs is of the exponential kind. Price has suggested that the whole of modern science apparently grows in an exponential way.[2] One of the basic determinants of the rapid rate of growth in drug discovery is, of course, the intensive pace of discovery in its essential underlying fields of science. Consider the case of one of these

[2] Derek J. de Solla Price, *Science Since Babylon,* New Haven: Yale University Press, 1961; and Derek J. de Solla Price, *Little Science, Big Science,* New York: Columbia University Press, 1963.

fields, chemistry. Here the drug industry has had a lot to work with, as a recent report on basic research in chemistry has made clear. "On the average," says a National Academy of Sciences committee, "a new chemical compound is synthesized every five minutes."[3] And the committee continues, "Somewhere between 30 and 50 per cent of the chemical products now on the market were unknown, uneconomic, or unavailable 25 years ago."[4] As to drugs specifically, three of what are now the eight major classes of therapeutic drugs were unknown about thirty years ago. These three are the antibiotics, the antihistamines, and the psychoactive drugs. Two other major classes of present therapeutic drugs were introduced between World War I and World War II. These are the sulfa drugs and vitamins. Two other of the eight major classes of drugs are older, but still products of the present century. These are the barbiturates and hormones. Of these eight classes, only narcotic drugs were known to antiquity, and today's representatives of even this class, with the exception of morphine and codeine, are largely modern drugs. No wonder that the physiologist-sociologist L. J. Henderson is said to have remarked that 1912 was the first year in human history in which the random patient with a random disease consulting a random physician had a better than 50–50 chance of benefiting by the encounter. If the odds have gone up sharply in our times, it is because of the therapeutic effectiveness of new drugs.

In sum, it is evident that both the scope and rapidity of change in the last sixty years throughout the field of drugs has been enormous, with perhaps especially great changes during the last twenty-five years. A number of problems have resulted from the lags in adjustment to this rapid change and from our failure to make all the necessary social innovations to cope with these changes and their consequences. Among these problems are the alleged windfall profits of the drug companies, inadequate government controls over the testing of drugs, the shortage of competent drug researchers, inadequate education of doctors for the newer drug therapeutics, and the persistence of police approaches to the addiction problem when a socio-medical approach is needed. The various social systems concerned with drugs have been somewhat deranged just by the rapidity of the change occurring in them. Some-

[3] National Academy of Sciences—National Research Council, *Chemistry: Opportunities and Needs,* Washington, D.C.: National Academy of Sciences, 1965.

[4] *Ibid.,* p. 7.

thing has already been done to make these systems operate more effectively, much more is even now being accomplished, but there is still a great need for social inventiveness in this area.

In the case of ethical controls on experimentation with human beings, for example, a kind of experimentation which has increased greatly because of all the new drug discoveries and the consequent need for testing, we need to invent new standards for ethical behavior and new mechanisms for applying and refining these standards. Every institution in which human subjects are subjected to drug testing probably ought to have a review and approval committee to advise about and oversee all such testing. And such committees ought to be made up not only of active, experienced, and prudent researchers from the institution itself, but of similar "outsiders," to give greater impersonality and objectivity to the committee's proceedings. In addition, probably, a social scientist and a lawyer who are experienced in problems of the formulation and application of social norms ought to be members of the committee, for such committees will be dealing with what are not just medical and physiological phenomena, but social phenomena as well, with what are social rules and processes.[5]

Finally, it should be noted that the study of drugs is illuminated by, and in turn provides a useful focus for, several areas of scholarly specialization in sociology and the social sciences generally. Chief among these are the sociology of scientific discovery, the study of education and communication processes, the sociology of the professions, the study of "social problems," many aspects of medical sociology, and the theory of functional analysis of social systems.

Hopefully, we shall one day soon have a sociology of drugs. As with all good scientific disciplines, this one will have both applied and theoretical branches.

[5] On problems and policy for the ethics of experimentation on human subjects, see infra, Ch. 4, and Bernard Barber, "Experimenting With Humans," *The Public Interest,* Winter, 1967, pp. 91–102.

2

Discovery and Testing Processes

THE BIOLOGICAL and chemical research now going on around drugs is an important and perhaps increasingly large part of all scientific research. It is, therefore, an important site for research on all the problems that come up in the sociology of scientific discovery.[1] But drug research, like much scientific research, has its special character. Drug research is more empirical than some other areas; it is nearer, in many respects, to folk knowledge than is, say, physics. Therefore, somewhat different problems of research and testing arise here than in the more theoretically and methodologically mature sciences. The similarities and differences are equally worth attention in the study of discovery and testing processes.

Discovery Processes, Folk and Scientific

There is no human society without a considerable amount of rational empirical knowledge of the physical, the biological, and the social aspects of the world. This knowledge has often been discovered by

[1] Bernard Barber, *Science and the Social Order,* New York: Collier Books, 1962 (originally published, 1952). Bernard Barber and Walter Hirsch, editors, *The Sociology of Science,* New York: The Free Press of Glencoe, 1962.

trial and error rather than by the use of systematic theory and observation, but it is nonetheless useful in providing some control over the reality man faces. So it has been with drugs. Our earliest historical records, and even some archaeological evidence, indicate that man always had some useful folk knowledge of drugs to heal, to soothe spirits, to relieve pain. For example, in the Ebers Papyrus, which dates from approximately the sixteenth century B.C., there are described more than seven hundred herbal remedies which were known and used by Egyptians, including many which are still familiar today.[2] Even so modern a remedy as aspirin has its ancient folk forebears. In a monograph on the salicylates, the active agent in aspirin, Gross and Greenberg point out, "The naturally occurring salicylates (salicin and methyl salicylate) found in the bark, leaves, and fruit of many plants and trees are ancient remedies. . . . Hippocrates, some 2,400 years ago, recommended juice of the poplar tree (containing natural salicylates) for eye diseases, and leaves of the willow tree (the same) in childbirth."[3] If we run down the list of drugs that were more or less anciently known, we find quinine, hashish, digitalis, penicillin, ergot, opium, cocaine, belladonna, datura, hemlock, veratrine, strychnine, caffeine, colchicine, ephedrine, chaulmoogra oil, and curare.[4] Peyote has an ancient record in written sources, and goes back still farther, probably, into a historical antiquity in middle America.[5] In sum, as Dubos has put it, "All primitive people (and all earlier civilized ones) have discovered by empirical means a large variety of powerful and useful drugs, many of which are still in use today, and they have applied these widely to the relief of human suffering. . . . Thus an immense amount of useful knowledge of therapeutics had been accumulated from purely empirical observations long before the scientific era."[6]

[2] Trevor Williams, *Drugs from Plants,* London: A. L. Atkinson, Ltd., 1947, p. 9.

[3] Martin Gross and Leon A. Greenberg, *The Salicylates: A Critical Bibliographic Review,* New Haven: Hillhouse Press, 1948.

[4] Williams, *op. cit.*

[5] T. N. Campbell, "Origin of the Mescal Bean Cult," *American Anthropologist,* 60(1958), pp. 156–160.

[6] René Dubos, "On the Present Limitations of Drug Research," in Paul Talalay, editor, *Drugs in Our Society,* Baltimore: The Johns Hopkins Press, 1964. See also Chauncey D. Leake, "The History of Self-Medication," in *Annals of the New York Academy of Sciences, Home Medication and the Public Welfare,* Vol. 120(1965), Article 2, pp. 815–822. Leake discusses the relationship between early self-medication and treatment by "professionals."

But, until very recently, indeed until the nineteenth century, all this useful knowledge remained highly empirical. Folk knowledge does not include understanding the effective activity of drugs on chemical or biological grounds. Typically, drugs in folk preparations are in the form of what were long known as galenicals. That is, the raw or crude plants and minerals were steeped, dissolved, or suspended in fluids, the active agents in them along with all the inactive materials. This was because the active ingredient was not known. If the concoctions worked, that was enough.

In the early nineteenth century, however, knowledge of drugs was put on a more theoretical and systematically scientific basis. Through chemical analysis, the active agents in plants and raw minerals are isolated, then often synthesized in a purer form than that in which they were found in their natural sources, and finally administered in a more controlled and effective way because the active agent could be observed and tested. The case of opium is probably typical. It has been known since antiquity that something in the poppy was soothing and pain killing. Laudanum and paregoric, tinctures or solutions of the opium poppy, were used in Europe and America as household remedies well into the nineteenth century. In 1830, however, a German pharmacist isolated the active alkaloid of opium, morphine; and a few years later another natural alkaloid, codeine, was also isolated from the poppy. By testing, the former was found to be the more analgesic. As a result of these discoveries, and also as a result of the invention of the hypodermic syringe for the administration of the drug, opium came into more widespread and more effective use. Finally, a superior analgesic, heroin, was synthesized in the 1890's by heating morphine and acetic acid. Unfortunately, also, heroin has proved to be even more addictive than morphine and codeine. In sum, the nineteenth century produced a revolutionary scientific advance, in which therapeutics was able to move from indeterminate drugs and drug action to much more specific drugs and drug action, though this action is still far from being wholly specific.

If the development of opium was typical, there was a great deal of similar development from galenicals to specifics in the nineteenth century. "Well over 30 alkaloids" from roots, barks, and leaves, "were discovered during the early part of the century. The list embraces morphine . . . atropine . . . and hyoscyamine. . . . the last two were from the plant Atropa belladonna, quinine from cinchona bark, emetine from

ipecacuanha root, brucine and strychnine from *Nux vomica* . . . caffeine from tea . . . and santonin from wormseed."[7] Temkin has pointed out that in the fifty years from the 1820's to the 1870's, "a number of potent substances had been isolated, such as morphine, codeine, emetine, iodine, bromine, strychnine, quinine, physostigmine, and, above all, ether and chloroform."[8] The chief centers for this research were in Germany and France.[9]

What started in the early nineteenth century continued to develop all during that century and has developed still more rapidly during the twentieth century. Even expert witnesses, when they are describing twentieth-century drug developments, use such terms as "revolution," "spectacular," "explosion," "unexpected," "breathless rapidity," and the like. Yet, despite the great improvements which have occurred as a result of the transformation of drug research from folk practice to scientific specialty, a great deal of empiricism remains. For example, although aspirin "is one of the most remarkable as well as the most widely used of all drugs," a pharmacologist points out that "the exact mechanism of its action remains a mystery."[10]

"To a very large extent," says Dubos, "the discovery of new drugs is still essentially an empirical enterprise. True enough, the scientific techniques of bioassay greatly facilitate and render more sophisticated the testing of new substances. Furthermore, organic chemistry makes it possible to produce many useful modifications of substances already known to have biological activity. But there does not exist any sound theoretical basis on which to build a rational approach to the search for really new types of drugs."[11] Or, for a particular field, Himwich says, "thus far, in the field of psychopharmacology, practice has outstripped theory. Though we recognize that tranquillizers correct certain schizophrenic symptoms, there is little agreement on the

[7] Leslie G. Matthews, *History of Pharmacy in Britain*, Edinburgh and London: E. & S. Livingstone, 1962, p. 323.

[8] Owsei Temkin, "Historical Aspects of Drug Therapy," in Talalay, *op. cit.*, p. 11.

[9] Richard Harrison Shryock, *The Development of Modern Medicine*, New York: Alfred A. Knopf, 1947 (a revised version of 1936 edition), pp. 139, 161, 162.

[10] Arthur Grollman, "The Efficacy and Therapeutic Utility of Home Remedies," in *Annals of the New York Academy of Sciences, Home Medication and the Public Welfare*, Vol. 120(1965), Art. 2, pp. 911–930.

[11] Dubos, *op. cit.*, p. 37.

mechanism by which the improvements are achieved. Whether or not they effect cures is a problem for the future. But the practical value of the advance should not be underestimated. It may be compared with the advent of insulin, which counteracts symptoms of diabetes without removing their cause."[12] Theory, on the one hand, and empiricism, on the other, are never absolutes; they are relative to one another, states of relative advance toward determinate scientific explanation and control. Although drug research has gone far beyond the empiricism of folk knowledge, in relation to other scientific knowledge it remains in a relatively empirical condition. A National Academy of Sciences report on basic knowledge and research in chemistry asks that, "Hopefully, future progress will increasingly be guided by rational principles rather than by the semi-empirical procedures of the past."[13]

The relatively empirical condition of drug research is indicated by four typical patterns of research and development: the continued use of folk knowledge and raw plants as a basis for drug discovery; the resort to trial-and-error mass "screening" approaches to drug discovery and formulation; the frequent occurrence of the pattern of serendipity, or happy accidental discovery; and the mixture of university and industrial research laboratories.

The Continued Use of Folk Knowledge

Because of the lack of a rational theory of drugs, folk knowledge of medicinal plants remains an important source of drug discovery. For example, in Russia, "The clinical use of new pharmaceuticals is approved by the Pharmacological Committee of the Health Ministry of the USSR. The Ministry is also responsible for the publication of the pharmacopoeia. The eighth edition was issued in 1952 and listed 728 items. A substantial proportion (about 40 per cent) of the preparations are of herbal origins. The use (and the rediscovery) of drugs of herbal origins is frequently and approvingly mentioned in the Soviet medical

[12] Harold E. Himwich, "Biochemical and Neurophysiological Action of Psychoactive Drugs," in Leonard Uhr and James G. Miller, editors, *Drugs and Behavior*, New York: John Wiley and Sons, 1960, pp. 41–85.

[13] National Academy of Sciences—National Research Council, *Chemistry: Opportunities and Needs, Washington*, D.C.: National Academy of Sciences, 1965.

press as a logical answer (and a cheaper one, too) to the pharmaceutical needs of the Soviet Union."[14] It would be extremely interesting to have comparative figures from the pharmacopoeias of the several Western countries as to the relative proportion of drugs coming directly from laboratory synthesis and those coming indirectly from herbal sources.

In England, to take another example, plants from the old herbals have been tested for active drug agents. "The systematic chemical investigation of plants," says Williams, "has revealed the existence of a number of new drugs which, because of the small traces in which they normally occur, would have passed unnoticed if the crude material alone had been used. An excellent example of the value of such research is provided by the work recently carried out at Oxford and later, independently, in the United States. The old herbalists had many salves for the treatment of green wounds, i.e., infected wounds. In view of the claims made for these salves it was thought possible that some of the plants might contain antibacterial substances. Accordingly, extracts of some 3,000 different plants were prepared by methods similar to those of the old herbalists and were tested against cultures of simple infective bacteria such as Staphylococcus aurus and B. coli. Results were very encouraging. The extracts of some 30 different families of plants were found to contain substances which inhibited the growth of bacteria."[15] It should also be noted that some of these effective plants, when used at concentrations high enough to kill bacteria, were toxic and irritating and so could not be used medicinally. The results from searching through old herbals are occasionally rewarding.

In the United States, also, drugs based on natural and plant materials remain of great importance. "Of the 300 million *new* prescriptions written last year (1963), over 47 per cent contained a drug of natural origin as the sole active ingredient or as one of two or more main ingredients," according to an analysis by the prescription auditing firm, R. A. Gosselin & Co. Put another way, the average doctor in the United States writes at least eight prescriptions for natural drugs every day. According to industry figures, sales of drugs from botanical sources

[14] Mark G. Field, "Pharmaceuticals, Pharmacies, and Pharmacists in Soviet Russia," *American Professional Pharmacist*, 25(1959), pp. 24–29, 106–110, 174–178.

[15] Williams, *op. cit.*

alone increased at least five-fold from 1950 to 1960 and the trend is sharply upward. The market for medicinal plants is rapidly approaching the $300,000,000 mark."[16] Competition among pharmaceutical manufacturers for new plants as sources of drugs is intense; the companies sponsor botanical expeditions in all parts of the world. There are about 350,000 botanical species presently known to science, with about 2,000 new ones identified each year. It is estimated that only about 40 per cent of all known species have been analyzed so far. One company alone, Smith, Kline & French, has assayed about 15,000 species of plants for the presence of alkaloids; they are screening about one-third of those which are alkaloid positive. Thus, given the empirical condition of drug research, there is obviously a big field for future research here.

Because the search for plant sources of drugs is now so large and vigorous, a group of specialists from among botanists, chemists, pharmacologists, and related specialists have founded the American Society of Pharmacognosy, whose special interest is the discovery, identification, analysis, and testing of natural plants. They find scope for their activity everywhere (it is not clear that plants from tropical areas are more productive of drugs than those from temperate climes) and with every type of plant. "Current research is turning up medicinal properties in everything from lettuce, used by the ancients as a sedative, to apples and onions. A quick sampling to indicate the scope of these investigations shows that: compounds from daffodils may prove effective in treating myasthenia gravis and multiple sclerosis; a neuroactive factor in the perennial sweet pea is now being tested on animals; an extract from the lady slipper has been found to exert an effect on high blood pressure; derivatives from the common snowdrop relieve some glaucoma patients not responding to other medication; buttercup juice stops the growth of strep, staph, pneumococci, anthrax, and tuberculosis germs, and that of quavering anemone has similar bactericidal qualities . . . antibiotic properties exist in so many plants that it would take many pages just to list their names. New drugs may come not only from rare jungle vegetation but also from the commonest field and garden flowers and everyday foods."[17] The most recent intensive search for

[16] Margaret B. Kreig, *Green Medicine: The Search For Plants That Heal,* Chicago: Rand McNally, 1964, p. 8.

[17] *Ibid.,* p. 162.

active agents in the plant field has been in connection with cancer. The Sloan-Kettering Institute for Cancer Research alone has tested about 56,000 materials of natural origin.[18] Plant materials from the sea are now being tested for drug activity.

Trial-and-Error Screening

Empiricism in drug research is also manifested in large-scale screening projects in which, by trial and error, thousands and even tens of thousands of possibly active substances are tested for actual activity. One of the early and best known of these screening enterprises was that undertaken by Paul Ehrlich when he was trying to find that particular one of the large number of organic arsenic compounds that would be effective in killing trypanosomes in sick mice. It was the six-hundred-and-sixth compound which worked; and Ehrlich's remedy for syphilis, because it would also kill the treponema pallidum, came to be known popularly as "606" even though he himself called it salvarsan.[19]

Screening programs are now widely used for many different kinds of drugs, the most large-scale search probably being that recently made for anti-cancer agents. As Dubos has put it, "In practice, the discovery of most new drugs has come from the primitive but nevertheless very useful faith that for each biological threat there exists in nature or there can be synthesized some substance capable of counteracting the action of this threat. All screening programs are based on this faith. The search for microbial antagonists (so-called antibiotics) in soil, sewage, etc., corresponds to a somewhat more sophisticated yet still grossly empirical expression of this primitive faith."[20] "Another older approach to chemotherapy is the empirical method . . . a 'screening' process. It is still essential for the empirical approach to be used and supported in the research laboratories of the drug industry, because the time has not yet arrived when successes from theory alone will yield an adequate level of profit. . . . I suspect that the empirical approach and the approach by 'molecule-improvement' are the mainstay methods in the laboratories of most firms today and yield the major portion of

[18] *Ibid.*, pp. 298, 303.

[19] Shryock, *op. cit.*, pp. 301–302.

[20] Dubos, *op. cit.*, p. 37.

success. . . . As the years pass, I believe that more and more of the therapeutic successes will result from theoretical approaches."[21]

The Serendipity Pattern

Happy accidental discovery, or the coming by chance upon good things in science not explicitly being looked for, known as the serendipity pattern, occurs in all the branches of science.[22] But it would seem that it might occur more frequently in the more empirical areas of science, where the researcher is proceeding more by trial and error, by hunch, rather than by rational theory. If so, it would occur quite frequently in drug discovery. And so it has. The best known case is Fleming's discovery of penicillin, when an antibiotic mold alighted by chance on a bacterial culture. It was Pasteur, as much a biologist as a chemist, who said that "Chance favors the prepared mind." And Lasagna has said, "The history of therapeutic discoveries is in large measure a tribute to chance, the prepared mind, and serendipity. It is not necessary to go back to quinine or digitalis to illustrate the role of luck . . . in the search for new drugs. Penicillin can be traced back to contaminated culture plates and a keen mind, and the most interesting recent group of anti-cancer drugs, the Vinca alkaloids, developed from the fortuitous finding of marrow suppression by an extract of the periwinkle mistakenly considered a useful folk remedy for diabetes."[23] Among the psychoactive drugs, chlorpromazine was first suggested as an antihistaminic and sedative. "Its effects on the regulation of body temperature and blood pressure later led to its use in surgical procedures. Incidental observations of its effects on behavior finally resulted in its present use as one of the tranquillizing drugs."[24] Also among the psychoactives, iproniazid was originally tried as an antituberculosis drug. When it was seen that it had an euphoric effect on tuberculosis patients, it was tried on depressed mental patients and has come to be relatively

[21] Karl Folkers, "Drug Research in Industry," in Talalay, *op. cit.*, p. 138.

[22] Bernard Barber and Renée C. Fox, "The Case of the Floppy-Eared Rabbits: An Instance of Serendipity Gained and Serendipity Lost," *American Journal of Sociology*, 64(1958)), pp. 128–136.

[23] Louis Lasagna, "On Evaluating Drug Therapy: The Nature of the Evidence," in Talalay, *op. cit.*, pp. 91–105.

[24] Roger W. Russell, "Drugs as Tools in Behavioral Research," Uhr and Miller, *op. cit.*, p. 21.

effective for this use.[25] Finally, the mental effects of LSD-25 were discovered by chance. "On April 16, 1943, after working with a few milligrams of this compound and its isomer, the chemist A. Hofman felt restless, dizzy, and on lying down with his eyes closed, he experienced fantastic visual images of extraordinary plasticity, with a kaleidoscopic play of colors, lasting about two hours. To verify his inference about the cause of these experiences, Hofman ingested 250 mg of LSD-25-tartrate in aqueous solution on April 22, 1943."[26] The inference was indeed verified by the "heroic" dose taken in this test. It is now known that LSD is effective in very much smaller amounts than this.

University and Industrial Research Laboratories

Because of its empirical origins, and also because of its highly practical and profitable significance, drug research has been carried on, from the very beginning of the drug revolution of the early nineteenth century, in industrial laboratories as well as in academic institutes and departments. In both Germany and England, the drug research organizations established in industrial companies have long been given considerable autonomy and wide scope for fundamental research. This arrangement has been longer in coming into being in the United States. In Russia, even during Czarist times, fundamental pharmaceutical research has been carried out in government research institutes.[27]

Inevitably, the relative contributions of the non-profit and academic laboratories, on the one hand, and the private, industrial laboratories, on the other, have come into question. In a recent very extensive review of the matter, the Nobel Laureate, Professor Ernst Chain, Professor of Biochemistry at the Imperial College of Science and Technology, London, himself an important discoverer in the field of penicil-

[25] Louis Lasagna, *The Doctors' Dilemmas,* New York: Harper & Bros., 1962, pp. 227ff.

[26] Abraham Wikler, *The Relation of Psychiatry to Pharmacology,* Baltimore: Williams and Wilkins, 1957, p. 67.

[27] "The Soviet and American Pharmaceutical Systems: Some Paradoxical Contrasts," Arthur D. Little, Inc., (unpublished report), 1962. [An abridged version of this appears as an article in *Harvard Business Review,* 1962.] Raymond A. Bauer and Mark G. Field, "Ironic Contrast: U.S. and U.S.S.R. Drug Industries," *Harvard Business Review,* 40(1962), pp. 89–97. Field, *op. cit.*

lin, has argued for the joint and important contributions of both the industrial and the academic laboratories.[28] Chain has reviewed the discovery of some 66 drug compounds, from aspirin to the very latest broad spectrum antibiotic. "His analysis shows that nine of these compounds came solely from universities and research institutes. Twice as many were the products of joint university-industry collaboration, and twice as many again, or thirty-eight of the sixty-six, were born in an industry laboratory. . . ."[29] This summary of Chain's analysis is accurate, but it leaves out one important point. That is that the distinguished record for basic drug discoveries by private industrial laboratories is a record earned by the European laboratories so far, not by the American. For example, in the industrial laboratory operated by Sir Henry Dale for the Burroughs-Wellcome Company in Britain, several fundamental discoveries have been made. Similarly in Germany, Switzerland, and France. So far, the record for the American companies is far better on their collaborations with university discoverers, or in further developing the discoveries made in Europe, than it is in making basic discoveries on their own. The American laboratories, however, are constantly improving. Indeed, some evidence of improvement is already in hand. According to Paul de Haen, authoritative chronicler for the American drug industry, only 16 new chemical entities were introduced in new drugs in this country in the year 1963. Of these, 4 originated in Europe, the rest in the United States.[30] Of the 23 new chemical entities introduced in 1965, 14 were from American industrial laboratories.[31]

In defense of the capacity of American commercial drug manufacturers to make basic discoveries, Dr. Austin Smith, President of the Pharmaceutical Manufacturers Association, the trade association of the drug manufacturing industry, appearing before a Congressional committee, claimed that "over 90 per cent of the 365 basic new drugs intro-

[28] Ernst B. Chain, "Academic and Industrial Contributions to Drug Research," *Nature,* 200(1963), pp. 441–451.

[29] John T. Connor, "The Functions of the Pharmaceutical Industry in Our Society," in Talalay, *op. cit.,* pp. 117–130.

[30] *Drug Trade News,* February 17, 1964.

[31] Paul de Haen, "New Products Parade, 1965," New York: Paul de Haen, Inc. 1966, mimeo. This report contains other evidence for the improving performance of American laboratories as well as evidence for the increasing multi-national character of drug research.

duced in the United States since 1941 originated in this country's pharmaceutical industry."[32] It would be good to have both a definition of what this claim means by "basic" and some of the supporting evidence.

Since they recognize their still considerable dependence on university scientists for making the basic discoveries which they then transform into producible and tested pharmaceuticals, the drug companies oppose any changes which might interfere with what they consider a mutually beneficial relationship between themselves and the university scientists. For example, when the United States Government recently ordered that the patents on all products and drugs that were produced by university scientists using Government research funds belong to the Government, and neither to the scientist nor to any company to which he might assign his patent rights, the drug companies were alarmed at the harmful consequences of this new regulation for their collaboration with university scientists. To avert the potential difficulties, the possible disruption of the relationship between the university scientists and the commercial drug companies, Mr. Walter A. Munns, President of Smith, Kline & French Laboratories, one of the ten largest ethical drug manufacturers in the United States, suggested the following patent arrangements when he testified before the Subcommittee on Patents, Trademarks, and Copyright of the Committee on the Judiciary, United States Senate, August 19, 1965:

> 1. Where a scientist working in a nonprofit institution and supported by Government funds discovers a new compound that may have medicinal use, the patent rights should belong to his institution, subject to certain Government-retained controls.
>
> 2. The nonprofit institution should have the right to negotiate with industry to carry out screening, testing and development work, and may further negotiate a royalty-bearing license with industry upon such terms as they may agree upon—subject again to Government-retained controls. The license agreement may also define the respective rights of the nonprofit institution and the industrial concern as to new uses and related development and improvements which may result from collaborative work between them.
>
> 3. In view of the substantial expenses which must be borne by the industrial concern to develop and test the compound—and considering

[32] *Drug Trade News,* June 22, 1964.

further that the royalties will accrue to the institution and be available for further research (with such reward to the individual inventor as the institution deems appropriate)—the license to the concern must be attractive enough to invite its participation in this research and development.

It would be highly desirable to have a series of intensive studies of the laboratories of the American pharmaceutical firms to see what advantages and disadvantages they have for making basic discoveries. Similar and comparative studies of the European laboratories would also be highly illuminating. It seems that one advantage the European industrial laboratories have is that they are organized much like their academic counterparts, around one "strong man" who is pushing some basic idea very hard.[33] This arrangement often pays off in basic discoveries, though it has special disadvantages of its own, such as rigidity over the long run. In all countries, the amount of money being spent on drug research is increasing, and quite rapidly. In 1960, for example, in England, some seven-and-a-half million pounds (about $20. million) was spent on drug research, a four-fold increase since 1955; in the United States, for the same year, about $250. million was spent; Switzerland spent just about as much as Britain.[34] Of the 58,000 people employed in the British pharmaceutical industry, some 4,000 or 7 per cent are engaged in research. This means that the pharmaceutical industry employs the highest proportion of high-skill people of all British industries.[35] Comparative figures for other countries would be interesting.

Testing Processes

Two factors in combination lead to a great new need for the controlled scientific testing of drugs. The first is the great increase in the number of discoveries, or rather, we should say potential discoveries, since a new finding should probably not be labeled a discovery until it is tested and proved. The second is the relatively empirical character of the knowledge about drugs. In the absence of rational scientific theory to *predict*

[33] R. P. Grant, C. P. Huttrer, and C. G. Metzner, "Biomedical Science in Europe," *Science,* 146(1964), pp. 493–501.

[34] Matthews, *op. cit.*

[35] *Ibid.*

what drug action will be, only controlled testing can tell, *post hoc,* what the effective activity of a drug actually is.[36]

The newness of controlled testing is as important a fact about drugs as is the great increase in the amount of discovery. The last twenty-five years have seen great changes in attitudes toward testing and in practice. Speaking from the United States, Lasagna says, "In therapeutics, however, the widespread use of control groups has been a development of the past twenty-five years." For Great Britain, J. H. Gaddum, formerly Professor of Pharmacology at Edinburgh, says: "When the first edition of my textbook *Pharmacology* appeared in 1940, properly controlled clinical trials were almost unknown, and the section dealing with them was theoretical. This was the first general discussion of the subject, and it has been gratifying to find that it was justified by later events and that some of the general principles which I put forward at that time have been adopted by those responsible for clinical trials during the last twenty years."[37]

Because of this newness of testing, adequate controlled studies are sometimes not made even for widely used drugs. For example, the first published report in English on the therapeutic effectiveness of chlorpromazine appeared in 1952. When Bennett, in 1957, reviewed some 962 studies on chlorpromazine published since 1952, he found only ten that described controlled studies.[38] Or again, when about 90 published studies on the efficacy of meprobamate, which was introduced in 1955, were reviewed in 1958, the reviewers concluded that "only a handful" met their minimum standards for controlled studies in random allocation of subjects to different treatment groups, in control of the placebo group, and in the double-blind technique.[39] These reviewers report a "barrage of other enthusiastic, uncontrolled clinical reports. A

[36] For some strong statements on how little is known about the effectiveness of some drugs, see Wikler, *op. cit.*, Introduction and David Krech, "Horizons of Psychopharmacology," in Seymour M. Farber and Roger H. L. Wilson, editors, *Control of the Mind,* New York: McGraw Hill Book Co., 1961.

[37] J. H. Gaddum, "A Perspective on Pharmacology," in Talalay, *op. cit.*, pp. 17–26.

[38] Julian L. Lasky, "Veterans Administration Cooperative Chemotherapy Projects and Related Studies," in Uhr and Miller, *op. cit.*, p. 540.

[39] Victor G. Laties and Bernard Weiss, "A Critical Review of the Efficacy of Meprobamate (Miltown, Equanil) in the Treatment of Anxiety," *Journal of Chronic Diseases,* 7(1958), pp. 500–519.

fair proportion of these are so poorly executed or reported that they warrant no discussion."[40] Thus, there is clearly no lack of some kinds of reports on some kinds of testing. But good reports on good testing are very much in the minority still, although the proportion of good reports has probably been increasing steadily. There are six different problems of good drug testing which we can profitably consider.[41]

The Shortage of Trained Personnel

Those who are knowledgeable about the condition of drug testing in the United States all agree that there is a shortage of trained personnel to do the testing which is necessary. There is, says Lasagna, "but a handful of investigators in the country (who) are trained to evaluate drugs in man, and the number of industrial products requiring accurate and careful study is extremely large."[42] In his summary of the discussion at a recent conference on drugs and society attended by many different distinguished specialists, Talalay says that it was evident from the discussion that "there is a desperate shortage of physicians with training adequate to the task of evaluating the large number of new drugs being constantly introduced."[43]

To help overcome this shortage, Brodie and his colleagues have recently recommended that "several centers of research in pharmacology and toxicology should be created to serve as focal points of basic research and training in the broad area of interactions of chemicals with biological systems. Each center should be an integral part of a university and should be of sufficient magnitude and scope to contribute substantially to important public health problems. A particularly important duty of the centers would be the training of pre- and postdoctoral students who would participate in the activities of the center

[40] *Ibid.*

[41] For an excellent general and inclusive discussion of drug testing, see Walter Modell, "Principles of Choice of Drugs and the Application of Clinical Pharmacology," in Walter Modell, editor, *Drugs of Choice, 1964–1965*, St. Louis: C. V. Mosby, 1964.

[42] Louis Lasagna, "On Evaluating Drug Therapy: The Nature of Evidence," in Talalay, *op. cit.*, pp. 91–106.

[43] Paul Talalay, "A Summary of Comments by the Editor," in Talalay, *op. cit.*, p. 272.

in connection with their research interests and career objectives."[44] Fortunately, the kind of center of research recommended by Brodie and his colleagues will shortly have its first exemplar at the University of Michigan where, according to a recent announcement, the nation's first research and training center devoted to clinical pharmacology will be started with a $1 million gift from the Upjohn Company, a Michigan drug manufacturer, and hoped-for funds from the Federal Government. The center will be a part of the medical complex of the University. It will study the safety and effectiveness of drugs in man, train physicians in advanced research abilities, and provide a locus for patient care related to pharmacological research and training.[45]

As might be expected in a situation of such acute shortage, competent clinical testers can choose from among a variety of drugs offered them by the pharmaceutical companies. They choose those which look intellectually exciting, says Lasagna, and the result is that the shortage of trained personnel is even greater for the average drug than for the extremely promising one.[46] Because the 1962 Amendments to the Food, Drug and Cosmetic Act require proof of "efficacy" as well as "safety," many drugs which have been on the market for some time may now have to be re-tested, to prove their efficacy. Such re-tests are very likely to seem intellectually unexciting in many instances, and so the shortage of competent testers will be most strongly felt here.

The inevitable result of the great need for testing in a situation of shortage of trained personnel has been that the poorly-equipped medical scientist and the untrained practicing physician were sometimes used. Under United States Government regulations, a drug manufacturer can send new drugs for testing to any doctor at all. As a result of the thalidomide disaster, it was discovered that the manufacturing firm had sent the drug to 1,200 doctors for testing. The physician who received a shipment of this "investigational" drug was required to do nothing beyond sending the company a signed statement that he was qualified to do testing. Many of the doctors did not even send in these statements and a great many kept incomplete records on the persons

[44] Bernard B. Brodie, George J. Cosmides, and David P. Rall, "Toxicology and the Biomedical Sciences," *Science*, 148(1965), p. 1553.

[45] *The New York Times*, February 1, 1966.

[46] Louis Lasagna, "Problems of Drug Development," *Science*, 145(164), pp. 362–367.

to whom they had given the drug and on what its effects had been.[47] Nor did the company take effective measures to have the statements signed and returned.

These inadequate procedures were apparently not uncommon among drug manufacturers. Since 1962 and the passage of the Kefauver Bill Amendments, although the manufacturer is still legally permitted to use any doctor at all as a tester, the situation has been improved. The Food and Drug Administration now exercises better control over the choice of testers through its powers of approval of new drug applications. Drug manufacturers themselves are now more careful to select only competent and responsible people. It is probably now true that incompetents have been entirely weeded out of the drug-testing process, though there is still a shortage of competent researchers and even these are not all of the highest quality.

As a result there still seems to be considerable competition among the drug companies for these testers who are in short supply. This competition has a further consequence, unintended but somewhat harmful. In their competition for testers, and as a result of their desire for results obtained with a reasonable degree of dispatch (since they themselves are competing with one another), the drug companies put the same drug out for testing with several different scientists and physicians. Such multiple testing is also required by law and helps to insure good results. Like all scientists, these multiple competitive testers strive for the prestige that comes from priority of discovery.[48] Talalay has described this unintended consequence as it appeared to the members of the Johns Hopkins conference: "One factor believed to contribute to this lack of depth and scientific value of many clinical studies on new drugs is the competitive atmosphere in which such studies are frequently conducted. When a new drug is distributed by the industry for clinical testing, it may come almost simultaneously into the hands of perhaps a dozen groups of clinical investigators. These groups are then under the pressure of mutual competition to publish their results quickly. . . . Consequently, there is little time to undertake a substantive and detailed study which would represent a lasting contribution to pharmacology

[47] *The New Yorker,* March 28, 1964.

[48] Robert K. Merton, "Priorities in Scientific Discovery: A Chapter in The Sociology of Science," *American Sociological Review*, 22(1957) pp. 635–659.

and to medical progress."[49] Thus, the shortage of trained personnel may be magnified by an unplanned system in which something less than the most effective use is made of the scarce resources that are available.[50]

The competition for scarce testers is carried on by the pharmaceutical companies with a variety of reward mechanisms. In some cases, the company offering a clinical tester a drug is offering him just what he wants: funds to do research on an interesting and practically important problem, with an opportunity for eventually sharing in the prestige given to those who have made a first-rate discovery. In this situation, the business-for-profit and the scientific systems are meshing harmoniously, with mutual advantage. But where this harmonious meshing cannot occur, because of the shortage of trained testers, then a number of abuses come into being.[51] For example, a certain amount of petty corruption occurs; physicians make themselves available as clinical testers because they are given small gifts or unusually expensive entertainment and hospitality. Or again, a few doctors may send form letters provided by the drug company to the F.D.A. testifying to the adequacy of a tested drug. In one documented case of this kind, F.D.A. received nine letters in identical wording and not even on the doctor's own letterhead in some instances.[52] Another practice leading to possible abuse is the writing and placing in journals by drug company employees of articles supposedly entirely written by a physician or medical scientist author and supposedly reporting research carried out by him entirely independently. In one case, letters from the subpoenaed files of a New York drug company showed that articles published in the *Journal of the American Medical Association,* in *Radiology,* and in the *Southern Medical Journal*—all very respectable journals—were

[49] Talalay, *op. cit.*

[50] It should be noted, of course, that neither the participants in the Hopkins Conference, nor anyone else, could offer any solid research evidence on the amount of dysfunctional competition that actually occurs. Such research evidence should replace individual impressions and could be a valuable influence on policy in this field.

[51] On outright "rigged research," which is apparently rare, though sometimes important in its consequences, and on why "fraudulent reports (are) hard to spot when done by scientists," see *The Wall Street Journal,* June 30, 1965.

[52] See signed article by Stuart H. Loory, *New York Herald Tribune,* June 19, 1964, reporting documented cases before Representative L. H. Fountain's Intergovernmental Relations Subcommittee of the Committee on Government Operations.

actually written for their doctor-authors by a drug company employee or its hired advertising or public relations agency.[53] Very probably, such abuses are now quite limited in extent, but their sources are important because they show the pressures on both testers and drug companies when there is a scarcity of competent clinical testing personnel. When "the hunt for competent investigators willing to do testing under these conditions becomes feverish and open to abuse, with the jobs often going to the not-so competent," then articles about the testing of drugs may become mere advertising "testimonials," instead of reports on reliable scientific research.[54]

The Problem of Volunteer Subjects

In addition to the ill patients who are seen in clinical or private practice, drug testers often have to use healthy or well volunteer subjects, as presumably normal controls in an experimental situation. In either case, it is often assumed that the volunteers, sick or well, are a randomly selected group of the population. But a few studies have suggested that this is not so, that volunteers may be self-selected in special ways and have special characteristics which affect the way in which they respond to active drugs and to placebo controls. This self-selectivity may be especially marked in experiments with drugs that have psychological effects, and if so, it would particularly bias the results of such experiments. However, the non-randomness of volunteers could influence the outcome of any drug experiment. It would be highly desirable to have more research on the social and psychological characteristics of volunteers and on the ways such characteristics have influenced study results.

Research of this kind has a few prototypes to follow and improve. One of the first was carried out by Lasagna and von Felsinger in the early 1950's.[55] In the course of pharmacological studies using male volunteer subjects, all college students in their twenties, these researchers noted what they thought was a high incidence of homosexuality. This suggested to them that many of their volunteer subjects might

[53] *Ibid.*

[54] Lawrence Lessing, "Laws Alone Can't Make Drugs Safe," *Fortune,* March, 1963.

[55] Louis Lasagna and J. M. von Felsinger, "The Volunteer Subject in Research," *Science,* 120(1954), pp. 359–361. Louis Lasagna, *The Doctors' Dilemmas,* New York: Harper & Bros., 1962, pp. 200ff.

be psychologically disturbed, in a variety of ways. Accordingly, they obtained Rorschach tests and intensive psychological interviews with fifty-six subjects. Twenty-five were diagnosed as suffering from one of the following psychological maladjustments: psychosis, psychoneurosis, psychopathic personality, alcoholism, overt homosexuality, severe peptic ulcer, and severe stutter. Lasagna and von Felsinger felt that important conclusions followed from their findings: "(i) Volunteers may differ quite markedly from nonvolunteers in a number of important aspects. (ii) . . . the personality of such subjects or their reasons for volunteering, or both, may be important determinants of their responses in an experimental situation. . . . (iv) Placebo controls, although important, are not adequate safeguards. . . . (v) Generalizations from data based on 'volunteers' should be cautiously made."[56]

A study on eighty-three volunteers at the National Institute of Mental Health also carried out psychological evaluations of the volunteers and found a seemingly disproportionate number of the psychologically disturbed.[57] And finally, the same conclusion was reached after psychological evaluations of fifty-six volunteers for hallucinogen studies at the New York State Psychiatric Institute.[58]

If it is possible, and it certainly seems so on the basis of these studies, that volunteers are not a random group of the population, particular groups of non-volunteer subjects may also be similarly nonrandom. Research on ill and well volunteers, and there should be much more of it, should be supplemented by research on the social and psychological characteristics of all subjects of drug tests. The need for this research has been emphasized by Pollard and Bakker, "We have yet to learn of a study where the attitudes of patients to drug taking has even been considered, let alone evaluated."[59] Such attitudes, and many others,

[56] *Ibid.*

[57] Seymour Perlin, William Pollin, and Robert N. Butler, "The Experimental Subject: The Psychiatric Evaluation and Selection of a Volunteer Population," *A.M.A. Archives of Neurology and Psychiatry*, 80(1958), pp. 65–70. Reprinted in Irving Ladimer and Roger W. Newman, editors, *Clinical Investigation in Medicine: Legal, Ethical, and Moral Aspects: An Anthology and Bibliography*, Boston: Boston University, Law-Medicine Research Institute, 1963.

[58] Harold Esecover, Sidney Malitz, and Bernard Wilkens, "Clinical Profiles of Paid Normal Subjects Volunteering for Hallucinogen Drug Studies," *American Journal of Psychiatry*, 117(1961), pp. 910–915.

[59] John C. Pollard and Cornelis Bakker, "What Does the Clinician Want to Know about Psychoactive Drugs?" in Uhr and Miller *op. cit.*, p. 203.

have important influences on drug activity; they should, therefore, be an important part of research seeking to determine what that activity is for particular drugs.

The Problem of Achieving Double-Blinds

Medical scientists and practicing physicians who carry out drug testing on their patients and other subjects interact with these patients and subjects in a variety of ways which may affect the outcome of the tests. "The physician's knowledge of the medication he is prescribing," says Modell, "is exceedingly important in the clinical experiment, for, regardless of how much he tries, if he knows what he is prescribing, in one way or another he will communicate his feelings about the medication to the patient. If he has deep concern over the adverse possibilities of the new and poorly understood medication he is using, he will communicate his concern to the patient. If he is bursting with enthusiasm, he will communicate this attitude."[60] Not only the doctor's but the patient's knowledge and attitudes about the drugs may similarly influence the experiment. Even the knowledge that he is participating in an experiment of any kind may have an effect upon the patient and his response to treatment.

Drug testing, then, is a *situation of human interaction* in which all parties to the interaction are affected by their knowledge and their attitudes about what is going on. To control these interactional influences, to isolate the specific physiological influence of a drug substance which is being tested, drug-testing scientists have invented the double-blind technique, a procedure in which neither the administrator of the test drug nor the subject know which is the active substance and which the inert placebo. But it is often hard to achieve a good double-blind experiment. The administering doctor may be tempted to peek or cheat a bit, the patient may sense that he is in an experiment, and attending nurses and other technical personnel may give away what should be a complete secret. As a result of these difficulties and others, Sheps has proposed what she calls the "all-blind" technique. This provides that "the knowledge of the treatment a patient receives shall not be available

[60] Modell, *op. cit.*, pp. 30ff.

(a) to those who decide whether he should enter the trial; (b) to those responsible for his care while he is under treatment; (c) to those responsible for laboratory and other examinations; and (d) to those who are making the final assessment."[61]

Thus, although the systematic application of the "double-blind" technique is relatively new, some of its weaknesses have already become apparent and improvements have been made. However, since the continuing weakness of the "double-blind" technique derives from the fact that it is difficult to make any kind of human interaction completely "blind," that is, very highly controlled, progress in this direction of improving control will come in greatest measure from systematic sociological and psychological study of the drug testing situation. Ideally, such study will be the product of collaboration between the medical and other scientists who do drug testing, on the one hand, and the social and psychological scientists who are expert at studying human interaction, on the other.

The double-blind procedure is not equally necessary in all drug investigations. Indeed, at an extreme, it may not be necessary at all. In some cases, where the efficacy tests are quite clear and where the attitudes of the investigator and the subjects can be shown to have a minimum effect as against that of the active agent being tested, the double-blind is less necessary, and perhaps not necessary at all. As one experienced person expressed this note of caution: "Blind attachment to double-blinds can sometimes lead up blind alleys."

The problem of placebo reactivity. "The term 'placebo effect'," says Honigfeld in his outstanding two-part summary of the subject, "refers to any effect of medical intervention which cannot be attributed to the specific action of the drug or treatment given."[62] The placebo effect is probably as old as the practice of curing itself, and awareness of it among practitioners is also probably very old. Doing something, anything, especially if it was done with conviction and enthusiasm, was

[61] Mindel C. Sheps, "Problems in Clinical Evaluation of Drug Therapy," *Perspectives in Biology and Medicine,* 5(1962), pp. 308–323. Reprinted in Ladimer and Newman, *op. cit.* George F. Archambault, "A Drug Moves into Human Trials," *Journal of the American Pharmaceutical Association,* NS3 (1963), pp. 124–127, 136–137, for a recommendation of "remote coding" in any "blind" study.

[62] Gilbert Honigfeld, "Non-Specific Factors in Treatment: I. Review of Placebo Reactors; II. Review of Social-Psychological Factors," *Diseases of the Nervous System,* 25(1964), pp. 145–156, 225–239.

early seen by doctors and their prototypes to have [placebo] effects which they did not understand. Enthusiasm was usually more likely when something new and possibly effective became available, that is, when the doctors themselves could believe that the new treatment might do some good. A famous dictum of nineteenth-century medical men was, "Use the new drugs quickly, while they still have the power to heal." It is estimated that even today some twenty to forty per cent of all prescriptions written are intended by the prescribing physician to have a placebo effect rather than some specific physiological one.[63] Experienced doctors speak with respect of "the powerful placebo." And one skeptical doctor has referred to the effects of all the psychoactive drugs as "the triumph of the impure placebo."[64]

But the placebo effect has come to have a much greater importance recently, and a somewhat different one. In his own review on placebos, Honigfeld lists twenty extensive reviews of the placebo problem and three bibliographies. He says: "A. K. Shapiro's review of the literature through 1957 revealed beginnings of a trend that is even more marked today. Between 1900 and 1950 only a scattering of articles pertaining to the placebo and its effects appeared. By 1957, Shapiro noted a definite trend toward a greater interest in this area. Since that time the number of relevant references has been accelerating each year."[65] Honigfeld himself makes references in his review to 345 different items. There seems to have been an exponential growth rate in interest in the placebo effect in the last ten to fifteen years.

The chief reason for this accelerated growth rate is fairly clear. The term "placebo" has come to be used to describe the inert substance that a drug tester gives to his experimental control group, preferably in a "double-blind" fashion. A great deal of the recent discussion of placebos, then, is connected with the discussion of drug testing and the newer and improved techniques for carrying it out. The growth of drug testing and the increase in the discussion of placebos has gone hand in hand, both at a rapid rate. There is at least one other reason for the greater

[63] *Ibid.*

[64] A witty, extreme, but tongue-in-cheek statement of this point of view can also be found in Edgar F. Borgatta, "The New Principle of Psychotherapy," *Journal of Clinical Psychology,* 15(1959), pp. 330–334.

[65] Honigfeld, *op. cit.*

interest in placebos, especially in their older meaning. The newer social and psychological cast of medicine has made practicing physicians and experimenters more aware of the inevitability of placebo effects as a consequence of the interaction between doctor and patient or between experimenter and subject. Placebo treatment is less and less thought of as something to be used covertly and shamefacedly, more and more as something manifestly necessary in good medical practice.

The fact of placebo reactivity in all drug testing is now taken for granted by all good experimenters as a problem to be dealt with explicitly. Cole says: "The administration of every pill or capsule, no matter how pharmacologically active the drug may be, carries with it the possibility of 'placebo' response, either positive or negative. Most of the recent work has focused on the positive . . . properties of placebos, but future research . . . will certainly have to take into account negative, adverse 'placebo' responses both to placebos and to potent drugs."[66] Thus, placebo reactivity is so common and so strong that it occurs not only apart from, but on top of specific pharmacological reactivity. As for some of the psychoactive drugs, in their discussion of the hallucinogens, Barron and his colleagues say, "The point is that in all the hallucinogen-produced experiences it is never the drug alone that is at work. As in the case of alcohol, the effects vary widely depending on when the drug is taken, where, in the presence of whom, in what dosage, and—perhaps most important—by whom."[67] These researchers also say that it may even occur that someone who has not taken the drug himself but is present when someone else is taking an hallucinogenic drug will behave as though he were under the influence of an hallucinogen. Finally, on the basis of a review of fifteen studies carried out in the period from 1933 to 1964 on drug treatments for the relief of pathological pain, Beecher says that "the average effectiveness of placebos in relieving pathological pain is 35 per cent."[68]

What kinds of placebo reactions occur? "The clinical folklore," says Honigfeld, "has it that psychosomatic symptoms and subjective

[66] Jonathan O. Cole, "Behavioral Toxicity," in Uhr and Miller, *op. cit.*, p. 177.

[67] Frank Barron, Murray E. Jarvik, and Sterling Bunnell, Jr., "The Hallucinogenic Drugs," *Scientific American,* 210 (1964), No. 4, pp. 29–37.

[68] Henry K. Beecher, "Quantitative Effects of Drugs on the Mind," in Talalay, *op. cit.*, p. 84.

effects are most responsive to placebo treatment. . . . Careful observation, however, has shown that objectively measured changes do occur, and these are sometimes more dramatic than the subjective effects. Using a group of medical student subjects, Modell and Garrett examined the effects of placebo and sodium pentobarbital on high-amplitude finger tremor after competitive mental work (Stroop test). They reported a significant increase in tremor rate with placebo from 60 to 198 per min.; after sodium pentobarbital the tremor rate rose only 162 per min.; without drug or placebo, the rate rose only to 152 per min."[69] Placebo effects of many different kinds must be kept in mind in all drug testing.

Marked physiological effects of placebos seem also to be evidenced in "their ability to heal certain kinds of tissue damage," as in the placebo treatment of warts.[70] In such treatment, warts are painted with a brightly colored but inert dye and the patient is told that his warts will "be gone when the color wears off." Frank asserts that this form of treatment "is as effective as any other form of treatment, including surgical excision." Further, when patients "fear drugs and distrust doctors . . . , a placebo may produce severe untoward physiological reactions including nausea, diarrhea, and skin eruptions."[71]

The near-universality of placebo reactivity is, then, clear. What are its sources? What causes these "non-specific reactions," as they are often called? One good review of the literature on placebo reactivity concludes, "Little is known about the 'why' of placebo reactivity. The evidence so far tells us only that it is the resultant of many variables."[72] Perhaps we can begin to sort out what some of these variables may be.

In such a sorting out, one of the first variables on which we can find evidence is the psychological one. In a seminal study reported in 1954, Lasagna, Mosteller, von Felsinger, and Beecher found that subjects with certain psychological characteristics were more likely than

[69] *Op. cit.*

[70] Jerome D. Frank, *Persuasion and Healing: A Comparative Study of Psychotherapy*, New York: Schocken Books, 1963 (originally published 1961), pp. 67–68.

[71] *Ibid.*

[72] Albert A. Kurland, "Placebo Effect," in Uhr and Miller, *op. cit.*, p. 156.

those without them to be what they called "placebo reactors."[73] They found that their placebo reactors were more productive of responses, more anxious, more self-centered and preoccupied with internal bodily processes, more emotionally labile, less mature, and so forth. These findings were produced by a combination of methods: interviews, questionnaires, Rorschachs, and Thematic Apperception Tests. However, a later study reports that placebo reactivity occurs not in a definite but in a random fashion and calls the study of Lasagna and his colleagues into question.[74] Commenting on these few studies, Honigfeld says, "More recently, the idea of consistent placebo reactors, identifiable by a fixed set of personality characteristics, has fallen from popularity in favor of a more sophisticated view which takes cognizance of the marked variations in experimental and clinical conditions."[75]

In sum, research in the area of placebo reactivity ought to be genuinely social-psychological, that is, to consider both the social and psychological factors to be important by themselves and in specifiable combinations. On these grounds, if one can hold either the social or the psychological factor constant, one can determine weights for the other. But also, research may want in some instances to determine the combined weight of some set of social and psychological characteristics.

In fact, a variety of social determinants have already been seen to be probably important in placebo response along with psychological influences. Honigfeld suggests that the clinical and the experimental situations of placebo administration may have different effects; that many dimensions of variation in hospital environment may have different effects; that many characteristics of the therapist may have different effects; and, finally, of course, that many social characteristics of subjects—age, sex, marital status, education, and occupation—may have different effects on placebo reactivity.[76] Indeed, just the knowledge on the part of the subjects that they are participating in an experiment

[73] L. Lasagna, et al., "A Study of the Placebo Response," *American Journal of Medicine*, 16(1954), pp. 770–779.

[74] Stewart Wolf, et al., "Chance Distribution and the Placebo 'Reactor'," *Journal of Laboratory Clinical Medicine*, 49(1957), pp. 837–841.

[75] Honigfeld, *op. cit.*

[76] *Ibid.*

seems enough to induce a placebo response in some of them. This reaction to the social situation of the experiment itself is what has come to be known, in social science, as "the Hawthorne effect," owing to the fact that it was first explicitly noted in experiments being conducted at the Hawthorne plant of the Western Electric Company.[77]

More and better research on all social aspects of the drug testing situation could be carried out, either keeping the psychological factors constant, or studying both types of factors in combination. Such research, as we shall suggest below, would be useful to basic social science as well as to the practical problems of the research methodology of drug testing.

The problem of "effectiveness." With so many shortcomings in test-research methodology already noted, it is no surprise to find that there is also a problem in determining the "effectiveness" of a drug by what Sheps calls reliable "criteria of effect."[78] "The complexity and qualitative nature of many medical problems frequently make it difficult to frame a meaningful and answerable question in a trial. How can the dozens of tranquillizers for treatment of psychoses of 'anxiety' be assessed without objective criteria for establishing the presence of anxiety, or even of schizophrenia, and acceptable criteria for successful treatment. Similar difficulties attend investigation of many other important conditions, such as hypertensive disease, coronary artery disease, cerebral vascular disease, or chronic arthritis."[79] In their review of the many early tests of meprobamate, Laties and Weiss make the same point, "We have tried not to evaluate the reliability or validity of the techniques used to gauge response to the drug. But we would like to note that, for the most part, these techniques seem to be singularly inadequate, and reflect a lack of appreciation that reliable index of effect is needed in order to make a reliable judgment of efficacy."[80] In a recent

[77] F. J. Roethlisberger and William J. Dickson, *Management and the Worker*, Cambridge: Harvard University Press, 1939.

[78] Sheps, *op. cit.*

[79] *Ibid.*

[80] Victor G. Laties and Bernard Weiss, *op. cit.* A basic discussion of effectiveness of psychoactive drugs can be found in Lawrence S. Kubie, "A Psychoanalytic Approach to the Pharmacology of Psychological Processes," in Uhr and Miller, *op. cit.*, pp. 209–224.

conference on drugs, the distinguished pharmacologist Louis Goodman remarked, "My learned colleagues only confused me. After posing the question, I just let them talk. The result confirmed my own suspicion that the term 'effective drug' means different things to different people."[81] In cancer chemotherapy generally, and in the use of cytotoxic drugs for epithelial tumors specifically, says Moore, who has carried out clinical investigations in this area, there is very little to rely on as criteria of effect because of "the self-limited nature of the disease" and the lack of "discriminating chemical indices."[82] All that one can use in such circumstances is crude clinical observation extending over indefinite periods of time. Long study, says Modell, is required before reliable judgments of effectiveness of drugs can be made. "Under our present system, it usually takes two or three years of clinical use before the full potential for harm as well as the limits of utility are realized."[83] Time is all the more important because, as Wintrobe has pointed out, "The mechanisms of the majority of adverse reactions are not understood at all. Not only may adverse effects of drugs not be appreciated in very extensive animal tests, but they may even escape discovery in the preliminary clinical trials. Their incidence sometimes may be so low that hundreds, maybe even thousands, of patients may be given the drug before an adverse effect is discovered."[84] The case of the drug thalidomide is a good instance in point of the problem of "effectiveness" of drugs, effectiveness for both good and ill, effectiveness in the short run and the long run.

As we have already indicated, one of the chief innovations of the Kefauver-Harris Amendments of 1962 to the United States Food, Drug, and Cosmetic Act is that drug manufacturers are now required to demonstrate the efficacy of their products, as well as their safety. This requirement certainly applies to all drugs introduced after the passage of the Amendments. The question of whether it applies to drugs manu-

[81] Louis S. Goodman, "The Problem of Drug Efficacy: An Exercise in Dissection," in Talalay, *op. cit.*, p. 50.

[82] Francis D. Moore, "New Problems for Surgery," *Science*, 144(1964), pp. 388–392.

[83] Modell, *op. cit.*, pp. 23–24, 30ff.

[84] Maxwell M. Wintrobe, "The Therapeutic Millennium and Its Price: Adverse Reactions to Drugs," in Talalay, *op. cit.*, p. 110.

factured and approved before 1962 has been made a matter of litigation in the Federal Courts between the pharmaceutical manufacturers and the Food and Drug Administration.[85] Judging by the recent action of the Food and Drug Administrator in banning the sale of antibiotic throat lozenges on the grounds that their efficacy had not been demonstrated, the Food and Drug Administration intends to push the view that the efficacy requirement holds for all drugs currently being sold, no matter when they were approved and introduced.

The problem of organization for better testing. As the amount of testing of drugs has increased, and as the serious shortcomings in present practices have been pointed out and criticized, it has become apparent that some of these shortcomings might be reduced by a better organization of testing facilities. The organization of cooperative studies might, for example, make more efficient use of trained personnel and might also set common problems and common standards which would result in earlier and more reliable knowledge of drug effectiveness. In the United States, some of this organization for better testing has been under the auspices of governmental agencies. In the field of psychoactive drugs, for instance, the Veterans Administration has promoted a cooperative research program among a number of hospitals and mental hygiene clinics, a program which began in 1956. The Executive Committee set up by the Veterans Administration "selects problem areas for study, recommends major features to be incorporated into new projects, reviews and revises reports prior to publication, and formulates general policy."[86] The Committee is assisted by special sub-committees which cope with each of the several component problems of drug testing. Also in 1956, the National Institute of Mental Health set up its Psychopharmacology Service Center "to establish huge multi-hospital cooperative studies to investigate certain of the more potent tranquillizers."[87] More recently, the Psychopharmacology Service Center has supported smaller projects in preference to

[85] Joseph Sadusk, Jr., "Regulatory and Medical Aspects of Public Policy on Home Remedies," in *Annals of The New York Academy of Sciences, Home Medication and the Public Welfare,* Vol. 120(1965), Art. 2, pp. 868–871.

[86] Lasky, *op. cit.,* pp. 540–541.

[87] Louis Lasagna, *The Doctors' Dilemmas,* New York; Harper and Bros., 1962, p. 241.

large-scale ones. In addition to these government-sponsored organizational arrangements, there have been multi-hospital drug testing arrangements set up by committees of the participants themselves, sometimes with government subsidies.[88] These large-scale organizational arrangements have not been without their own disadvantages. For example, in some studies there has been a lack of flexibility, a premature closure on research goals and methods, which has hampered some of the participating research groups as their work has progressed. Some of this may be the inevitable cost or it may come from the lack of knowledge and experience of these new and necessary organizational arrangements. Careful and systematic study of a set of these new testing organizations would be highly valuable.

The Usefulness for Social Science of Placebo Reactivity and "Non-specific" Reactions

We have already seen that there is a considerable amount of placebo reactivity in nearly all drug testing and that the medical scientist, given his purposes, defines this reactivity as "non-specific," that is, as not specifically due to physiological system processes. We have also seen that some medical scientists have entertained the possibility that these "non-specific" reactions may be due to specific psychological and social system processes.[89] A small amount of research based on this point of view has been carried out by medical scientists, sometimes with the assistance of social scientists.

From the social science point of view, the postulate that drug testing and drug taking involves social and psychological system processes as well as physiological ones needs to be stated explicitly and emphati-

[88] Moore, *op. cit.;* Sheps, *op. cit.*

[89] In addition to what has already been cited, see the article by the anthropologist Anthony Wallace suggesting the importance of "cultural" variations in the drug situation as determinants of responses to drugs. Note especially his succinct statement about drug testing: "Drug and Cultural Controls Should Ideally Be Combined in One Design." Anthony F. C. Wallace, Cultural Determinants of Response to Hallucinatory Experience," *A.M.A. Archives of General Psychiatry,* 1(1959), pp. 58–69.

cally. On this postulate, the testing and taking of drugs provides an excellent opportunity for social science theory and research. Systematic social science theory can be used to frame specific hypotheses about the social and psychological conditions of drug testing and drug taking, but they are likely also to have general significance, that is to say, to shed light on behavior in general.

Theory is not enough, of course. The opportunities provided by drug testing and drug taking require systematic and rigorous research designs and methods if they are to be used for the achievement of new social science knowledge. Specialized and intensive programs of theory-guided research by social scientists should replace the occasional and *ad hoc* studies that have been pioneered by medical scientists thus far.

Some excellent beginnings in this direction have already been made. Examples of what is desirable can be found in the work of at least two social scientists, the psychologist Stanley Schachter and the sociologist Henry Lennard. We can find in their work the beginnings of the psychopharmacology and sociopharmacology that is invaluable not only for the social sciences but for "regular" or physiological pharmacology as well.

Schachter's work is concerned with the basic and general psychological problem of how emotions are determined and of how states of physiological arousal, psychological factors, and social factors interact to produce a specific emotion.[90] His theorizing starts with the fact that the best evidence now available indicates that a state of physiological arousal alone is not sufficient to induce an emotion. His view is that, given a state of physiological arousal, induced by drugs or otherwise, "one labels, interprets and identifies this stirred up state in terms of the characteristics of the precipitating situation and one's apperceptive mass." To put it another way, cognition, which is influenced by both the social and psychological situations in which it occurs, "exerts a steering function" in the production of specific emotions. Since the "same state of physiological arousal could be labeled 'joy' or 'fury' or any of a great diversity of emotional labels depending on the cognitive

[90] The present summary of his work follows Schachter, "The Interaction of Cognitive and Physiological Determinants of Emotional State," in L. Berkowitz, editor, *Advances in Experimental Social Psychology*, New York: Academic Press, 1964. References are there given to Schachter's other work and to related theory and research by other psychologists.

aspects of the situation," then given a state of physiological arousal for which the individual has no immediate explanation, "he will 'label' this state and describe his feelings in terms of the cognitions available to him."

This is the hypothesis about the determinants of emotion that Schachter has sought to test with the help of drugs. In his experiment, a set of subjects were told that they were going to get a vitamin injection to test its effects on vision. Then they were given injections of either epinephrine or placebo by an M.D. Epinephrine (or adrenalin) is a sympathomimetic drug that causes discharge of the sympathetic nervous system. Of those subjects who received the drug, some were told what the actual physiological effects would be; some were told nothing; and some were misinformed by being told about different possible effects. Those given the placebo were told nothing. When the drug had had a chance to work, the subjects were put in the company of a stooge, either one trained to act euphorically or one trained to express the emotion of anger.

Finally, the actual induced emotional state of the subjects was observed and they were also asked to report their emotions. The experimental results confirmed Schachter's hypothesis. Those subjects who had received epinephrine but were not informed about its effects "proved readily manipulable into the disparate feeling states of euphoria or anger." Those who had been injected and also informed about actual effects were immune to the attempted manipulation of cognitions by the stooges. The subjects who were given placebo and who did not experience any physiological arousal also did not react to the stooges. It is of interest to note that some of the placebo subjects did get physiologically aroused, apparently in response to the needle-injection alone. Here are Schachter's own conclusions from his experiment: "I would guess that the labels and hedonic valuation attached to an amazing variety of bodily conditions are cognitively determined. Obviously there are limits . . . I suspect though that the limits are astonishingly wide." It would seem that through similar rigorous experiments and similar use of drugs Schachter and other researchers could find out just how wide the limits are, just how much the social and psychological determinants of cognition act through cognition to determine emotions.

Lennard's attempts to define a field of sociopharmacology and his beginnings of research in that field complement and are congruent

with Schachter's work.[91] His basic hypothesis is that social system processes and social expectation settings affect the outcomes of drug agents in important and determinate ways. In collaboration with Murray Jarvik, a pharmacologist interested in the physiological effects of LSD, Lennard made a study of how interaction among a group of subjects injected with LSD was affected by a social situation in which the subjects in effect constituted a problem-solving group. The discussion produced during the interaction of the group was tape-recorded and then analyzed in terms of Bales' theory of interaction in problem-solving small groups. In contrast to the depersonalization, hostile behavior, paranoid ideation, and generally psychotomimetic responses usually reported for subjects injected with LSD, Lennard found an interaction pattern "different from what I had been led to expect." There was "less hostility, less disagreement, less antagonism . . . there was an increase in supportive acts, more orientation, more questions and cue search." How to account for these different and unexpected results? Lennard's tentative conclusion is, "There appears to be an interaction between the drug and the situation. Under the drug subjects nonetheless responded to the demands of the problem-solving task." Although there was some impairment of individual functioning under LSD, some "reparative social system mechanisms were set into motion" to produce problem-solving rather than chaotic or hostile behavior. It is now Lennard's view that subjects who report "transcendental" or religious experiences as an effect of LSD do so because they take the drug in social and psychological situations which structure and encourage those responses. Such a view should be put to the kind of rigorous experimental test that Schachter has used in his work. Lennard's interesting beginning in the field of sociopharmacology needs to be extended into a whole program of theory-guided research.

[91] In the present summary I am following Henry L. Lennard, "A Proposed Program of Research in Socio-Pharmacology," unpublished paper prepared for the Symposium on Psychobiological Approaches to Social Behavior, Harvard Medical School, April 18–20, 1963, and Henry L. Lennard, "Socio-Pharmacology," a lecture to a joint meeting of the General Seminar and the Mental Health Seminar of the Bureau of Applied Social Research, Columbia University, January 24, 1964.

3

Education and Communication Processes

THE PROCESSES AND structures of education and communication are important determinants of how drugs get used and what their consequences are. On these matters, it is soon evident, we have all too little systematic and reliable knowledge. However, there is some, and what there is points the way to needed new research. We shall review first what we know about educational and communication processes on drugs among the professional therapists; then we shall turn to the lay users of drugs, who sometimes act on the advice of professionals where drugs are concerned, sometimes independently. We seem to know much more about the professionals than we do about lay users of drugs.

Education and Communications Among Professional Therapists

In a social situation where there is very little knowledge of drugs and where new knowledge is developed slowly, the training of professional or proto-professional therapists takes place almost entirely through personal apprenticeship, and communication occurs almost entirely through

informal networks of friendly relationships. This was the situation in which therapists using drugs found themselves until early in the nineteenth century. Now, informal structures of education and communication retain their importance, but to them has been added a large set of formally-organized arrangements. Even with these arrangements, it is difficult, because of the rapid rate of introduction of new drugs, for a therapist to remain competent in their use. After describing various formal agencies for giving information to doctors about new drugs, including such medical journals as the one he edits, *The New England Journal of Medicine,* Dr. Joseph Garland says, "It is all very well to expect the practicing physician to make independent judgments on the uses and toxic side effects of one new product after another, but a trained clinical pharmacologist can scarcely keep up with the field, and the average physician needs help beyond the smattering of pharmacology that he acquired in medical school."[1] "Every year," says Lasagna, "300 to 400 'new' formulations hit the market, each with an average life span of well under five years. Many of these are merely combinations of old remedies—there are 300 antibiotic preparations on the market, but only a dozen or so useful single antibiotics—but in any case the doctor is faced with the overwhelming task of evaluating these new remedies, their claimed effects and side effects, and integrating them into his practice."[2] The "lifetime learning for physicians" which Dryer has recommended for all kinds of medical knowledge is certainly required with respect to drugs.[3]

There are at least two general problems facing the contemporary therapist who wants to keep up with drug knowledge. One is the problem of the inadequacy of much of the training and communication he receives about drugs. Often his training and information are shallow, erroneous, or distorted. Second is the problem of the confusion caused by the many and often conflicting sources of information he has. It may

[1] Joseph Garland, "Dissemination of Information on Drugs to the Physician," in Paul Talalay, editor, *Drugs in Our Society,* Baltimore: The Johns Hopkins Press, 1964, p. 211.

[2] Louis Lasagna, *The Doctors' Dilemmas,* New York: Harper & Bros., 1962, p. 140.

[3] Bernard V. Dryer, "Lifetime Learning for Physicians," *Journal of Medical Education,* 37(1962) part 2, (mimeo).

be that the professional therapist now is offered simply too much information about drugs, too much in sheer quantity, all apart from its sometimes inferior quality. On the basis of their exhaustive study of the research data on this subject, Bauer and Wortzel say, "Any serious consideration of the practicing physician's job situation, and of the amount of information about drugs which is available to him, quickly leads to the conclusion that communication channels leading to the physician are overloaded."[4] We should keep each of these two problems in view as we consider the several different formal and informal processes and structures of education and communication that now determine the behavior and attitudes of the therapist in regard to drugs.

TRAINING IN MEDICAL SCHOOL

There seems to be a consensus that present arrangements in medical schools for giving students knowledge about drugs are inadequate. "The physician leaving medical school," says Lasagna, "is lucky if he is well versed in the use of the increasingly large number of 'standard' drugs used most often in practice."[5] A course in pharmacology is taught in every school, but these courses are often mediocre and not up-to-date. Medical students do learn something about pharmacology and the art of medication in all the clinical courses they take. However, newer concepts and techniques of clinical pharmacology do not have a "favorable atmosphere in the majority of medical centers."[6] Lasagna recommends that "each medical school should have a clinical pharmacology group by 1970. Without a more formal concern for research on, and teaching of, therapeutic and toxic effects of drugs, medical education will suffer."[7]

In Great Britain, complaints have been made not only about the substantive defects of training in drugs in medical schools, but also

[4] Raymond A. Bauer and Lawrence H. Wortzel, "Doctor's Choice: The Physician and His Sources of Information About Drugs," *Journal of Marketing Research*, Vol. 3(1966), pp. 40–47.

[5] Lasagna, *op. cit.*, p. 140.

[6] Louis Lasagna, "Problems of Drug Development," *Science*, 145(1964), pp. 362–367.

[7] *Ibid.*

about the failure of the schools to train students in the problems of the costs of prescribing.[8] The problem of the costs of drug prescriptions has been especially apparent in the nationalized health system in Great Britain, where the Government pays a large part or all of these costs, and where drug costs amount to a considerable part of the total national health bill. But even in the United States, with its system of private or privately-insured payment of medical costs, expenses for drugs are no less considerable than elsewhere. They may even be a little larger, if it is the case, as some have suggested, that American doctors are quicker to give, and American patients quicker to want, some kind of drug therapy.[9] Doctors should have accurate information on what drugs cost the user.

Despite the present dissatisfaction with medical school training in drug therapy, little is apparently being done to reform the situation. This is probably due to the overcrowded medical school curriculum and also to the pressure for other kinds of new knowledge to be admitted to the curriculum. One innovation in teaching pharmacology to medical students is quite interesting. This was an experimental program, carried out during a period of three years at the Albany Medical College under the direction of Dr. Solomon Garb, to teach students how to evaluate the flood of drug advertising which would inundate them as practicing physicians.[10]

As it developed, the teaching program was changed somewhat in details, but this is how it proceeded in its third year. Fourteen groups of students in a second-year pharmacology course, with four or five stu-

[8] Great Britain Ministry of Health, *Final Report of the Committee on the "Cost of Prescribing,"* London: Her Majesty's Stationery Office, 1959.

[9] For some research in metropolitan hospitals on patterns of prescribing by physicians and of purchasing by hospital pharmacists, see Charlotte Muller, "Medical Review of Prescribing," *Journal of Chronic Diseases,* 18(1965), pp. 689–696; Charlotte Muller, "Institutional Drug Purchasing: Factors Influencing Drug Choices by Pharmacists and Physicians," *Hospitals,* 39(1965), pp. 94–100. Charlotte Muller and Ruth Westheimer, "Formularies and Drug Standards in Metropolitan Hospitals," *Hospitals,* 40(1966), pp. 97–102.

[10] Solomon Garb, "The Reaction of Medical Students to Drug Advertising," *New England Journal of Medicine,* (Special Article), Vol. 259, No. 3, July 17, 1958, pp. 121–123. Also see editorial on this article "The Student Looks at Drug Advertising," pp. 143–144. Solomon Garb, "Teaching Medical Students to Evaluate Drug Advertising," *The Journal of Medical Education,* 35(1960), pp. 729–739.

dents in each group, randomly drew the name of one large and one small drug manufacturing company. For each of these companies there was a folder containing all the advertisements it had mailed to a faculty member during the previous four-month period. From each folder were taken from two to five advertisements which the group of students was supposed to evaluate as part of its overall evaluation of the company. In addition to the advertisements, the student groups were given fact sheets and general references discussing the problems of drug advertising in general, the importance of drug toxicity, the desirability of rational drug choice, and the seriousness of excessive and misleading advertising. These fact sheets presented the views of the spokesmen of the pharmaceutical industry, as well as of its critics. The student groups were asked to send letters to their companies requesting further information on the toxicity and side effects of the drugs being evaluated. They were also supposed to read the journal references given in the advertisements and to look at related advertisements in the medical journals. Finally, the student groups met with detail men, and sometimes also with higher officials, from the company. The students and detail men were asked to treat each other as if they were in the situation of the practicing physician. After specific discussions of their advertised drugs, students, drug company representatives, and faculty members joined in a general discussion of the problems of drug advertising. On the basis of all this activity, which consumed only eleven class hours, but much outside time as well, the students were asked to evaluate each of their two companies as reliable or unreliable. "If the company, through any means, has given the student a fair picture of the drug's unfavorable aspects, the company was ordinarily rated reliable." Thus, the evaluations were not based on the worth of the drug but on the truthfulness and helpfulness of the company's advertisements and of its representatives' letters and discussions.

Of the twenty-six companies rated, only eleven were considered reliable; however, these eleven produce a substantial proportion of all drugs sold. In many practices it might be possible to fill most prescriptions with the products of these firms. The faculty participants were surprised to find that the students considered the company's detail men to be an important determinant of their overall judgment about the firm's reliability. In addition to being able to make an overall rating, the students learned several important things about drugs and drug

advertising in this program. They learned that only a small proportion of advertised drugs could be considered basically new. They learned that many drug manufacturers tried to exaggerate the positive value of their drugs and to minimize the undesirable effects. The students were impressed by the reluctance of some manufacturers to reply to a request for further information about toxicity. And, finally, they became quite critical about the "Madison Avenue" slickness and "hard sell" in the drug advertisements in the medical journals. Judging by this program of the Albany Medical College, which has been adopted or is under consideration by a number of other medical schools, it seems that a relatively small expenditure of effort in classroom teaching can give medical students valuable knowledge in what will be an important part of their skill as practicing physicians, the evaluation of drug advertising in all its forms.

INFORMAL COLLEAGUE RELATIONSHIPS

Despite the great increase in the number and quantity of formal arrangements for socialization and communication about drugs, informal colleague relationships seem to have retained their importance.[11] Fortunately, we have a series of studies from the Bureau of Applied Social Research, Columbia University, which provides systematic data on the patterning and effects of these informal colleague relationships on the adoption and use of new therapeutic drugs.[12] The series began in a pilot study in a small New England community and continued in a group of four small Midwest cities. In all of the communities, at least 80 per cent of the practicing physicians were included in the study. Each of the

[11] See Sanford M. Unger, "Mescaline, LSD, Psilocybin, and Personality Change: A Review," *Psychiatry*, 26(1963), pp. 111–125 for reference to this matter in connection with the use of LSD.

[12] This summary is based on: James Coleman, Elihu Katz, and Herbert Menzel, "The Diffusion of an Innovation Among Physicians," *Sociometry*, 20(1957), pp. 253–270; Herbert Menzel, "Public and Private Conformity Under Different Conditions of Acceptance in the Group," *Journal of Abnormal and Social Psychology*, 55(1957), pp. 398–402; Herbert Menzel, "New Concepts of Research on the Physician's Acceptance of Pharmaceuticals," Bureau of Applied Social Research, Columbia University, mimeo, 1959; Herbert Menzel, James Coleman, and Elihu Katz, "Dimensions of Being 'Modern' in Medical Practice," *Journal of Chronic Diseases*, 9(1959), pp. 20–40; Herbert Menzel and Elihu Katz, "Social Relations and Innovation in the Medical Profession: The Epidemiology of a New Drug," *Public Opinion Quarterly*, 19(1955–1956), pp. 337–352.

doctors was asked a set of sociometric questions (Whom do you ask for advice? Whom do you meet most frequently on social occasions? Whom do you talk with most often about drug therapy?) in order to determine the actual network of informal social relationships within the medical group. Each doctor was also asked how he had learned about specific new drugs. Finally, the prescription files of the local pharmacies were searched to discover when each doctor had in fact first prescribed the drugs in question.

The findings indicate the importance of informal colleague relationships. Those doctors who were at the center of the informal networks (the "stars"), as determined by the sociometric questions, were the ones most often consulted by the doctors at the periphery of these cliques and by each other on matters of drug therapy. These "stars" participated in what has been called "the two-step flow of information." They were likely to learn about new drugs by reading the medical journals and then to transmit their information to their friends who consulted them in informal situations. The marginal doctors, or sociometric "isolates," depended on the "stars," but they also made larger use of commercial channels of information, especially direct-mail advertising and the drug-house detail men. Doctors consult informally with their "star" colleagues more often on cases that are medically ambiguous and uncertain than on those in which treatment and a "drug of choice" are fairly clear. All the doctors were asked about two different types of drugs: one which is applicable to certain acute conditions which call for immediate action and where there are few alternative methods of treatment; another which is applicable to certain chronic conditions where dozens of treatments compete and where the effectiveness of the therapy is difficult to judge. Informal consulting relations were substantially more numerous under the latter conditions (22 per cent in the latter as compared with only 7 per cent on the former). Information provided in informal colleague relationships is apparently more reassuring than that available through formal channels. Finally, it was found that "integrated" doctors, who were named by three or more colleagues as "friends," were quicker to adopt new drugs than doctors who were not thus involved in these informal consulting and friendship cliques. It would seem that informal relationships provide a necessary kind of support and information for early adoption of drug innovations.

Some caution about these studies is necessary. The researchers themselves have said, "We don't know just how far we can generalize without further research." The informal information processes described are important, but what their distribution is among the total population of physicians in the United States, these studies cannot tell. For example, the education and information processes may be different in rural areas, and different also in a metropolis with one or more highly scientific medical centers. It is also the case that these studies were done in the early- and mid-nineteen fifties, when the newness, unexpectedness, and rapidity of introduction of basic new drugs was somewhat greater than it is now. Doctors may have braced themselves somewhat differently for the winds of drug change which still blow about them so heavily. Further research of the kind undertaken in these model studies would be highly desirable.

PUBLISHED MATERIALS: THE U.S. PHARMACOPEIA

A variety of published materials is available to the doctor or scientist who wants to know more about therapeutic drugs. One of the oldest forms of these aids is the pharmacopoeia, a compendium of drug materials, including their standards of purity and specifications as to their use. Until the nineteenth century, pharmacopoeias were published by hospitals, medical groups, or private individuals; there was little uniformity or standardization among them. In the nineteenth century, however, attempts to unify and standardize were finally successful. In the United States, for example, the *United States Pharmacopeia* has been published decennially since 1820; beginning in 1940, because of the greater rapidity of drug development, a revision has been published every five years. There are also interim revisions in the form of supplements. The *United States Pharmacopeia* is revised and published by a private, non-profit organization, The United States Pharmacopeia Convention, Incorporated. This organization has a very small permanent staff; but its membership includes all the organizations that have an interest in its product—the accredited colleges of medicine (about eighty of them), a similar number of colleges of pharmacy, seven agencies of the United States Government, the state medical and pharmaceutical organizations, and twelve national professional associations in the fields of medicine and pharmacy. These members have set up a working Committee of Revision, which is made up of sixty experts,

forty from pharmacy and twenty from medicine. The Committee has divided itself into various specialist sub-committees to cope with the present-day complexity of drug materials, and these sub-committees may be aided by various *ad hoc* panels of specialist consultants.

Unfortunately, no one knows just what informational purposes the *United States Pharmacopeia* actually serves. In thirty-seven states, pharmacists are required by law to purchase the latest edition. Thus a large sale is guaranteed; recently, each edition has sold about 60,000 copies. It is known that the medical committees that supervise hospital pharmacies may use the volume as a basis for setting up their own formularies, and this in turn will influence doctors' practices with regard to drugs. But just how out-of-hospital pharmacists or doctors use it is not known. Indeed, with the great increase in pre-packaged drugs, which require no compounding, it is entirely possible the *Pharmacopeia* has lost many of its original functions. There is, therefore, an important need for research on how the *Pharmacopeia* is now actually used. Such research could be a guide to necessary revision in either the less important or even the more fundamental of its characteristics.[13]

PUBLISHED MATERIALS: MEDICAL JOURNALS

A massive amount of information on therapeutic drugs is available to medical doctors in a very large number of medical journals. It has been variously estimated that something like five hundred such journals are published in the United States alone.[14] It has been suggested, though without evidence, that, "A larger number of professional publications . . . are available to the American physician than are available to any other professional person."[15] These medical journals are of three broad types—national journals of general medical interest, such as the apparently widely read *Journal of the American Medical Association;* local

[13] The above discussion has been based on the Foreword to the Pharmacopoeia; on a mimeographed "Statement Prepared for Presentation Before Senate Sub-Committee on Anti-Trust and Monopoly (1960)"; and on an interview with Dr. Lloyd C. Miller, Director of Revision of the *United States Pharmacopeia.*

[14] Richard A. Deno, Thomas D. Rowe, and Donald C. Brodie, *The Profession of Pharmacy: An Introductory Textbook,* Philadelphia: J. B. Lippincott Co., 1959, p. 166. Harry F. Dowling, "How Do Practicing Physicians Use New Drugs?" *Journal of the American Medical Association,* 185(1963), p. 233.

[15] Deno, Rowe, and Brodie, *op. cit.*, p. 166.

city, county, state, or regional journals; and journals dealing with special branches of medical practice, such as the *American Journal of Surgery*. In all of these, information about drugs is purveyed to the physician in articles and advertisements.

Even this large number of medical journals is frequently considered inadequate to the task of informing doctors fully and correctly about therapeutic drugs. Some new journals have been established recently to deal specifically with new drugs. One of these specialized journals was founded in England in 1961.[16] This is *The Prescribers' Journal,* published bimonthly by a committee made up of experts from the medical schools, some general practitioners, some pharmacists, and officials of the Ministry of Health. "It is issued to provide the doctor with early and reliable information about new pharmaceutical products . . . [and it] reviews existing drugs. . . . Reports are compiled about the value of these drugs in practice and give information about possible toxic effects; notes are also given on the relative costs of various treatment schedules."

An American journal founded a little earlier, in 1959, and very critical of some of the other sources of information about drugs, especially commercial drug advertising, is *The Medical Letter,* established as a non-profit, independent source of "unbiased critical evaluations" of all drugs, but especially the newer ones. It contains no advertising. It is published every other week in a four-page letter format so as to be as up-to-date as possible. Each issue intensively reviews and appraises a few drugs "in terms of their effectiveness, toxicity, side effects, and possible alternative medications." From among a large panel of consultants, the Advisory and Editorial Board use experts to help them appraise new drugs soon after they appear; they are especially anxious to point out misleading promotional material put out by the producing drug firms. Before an article is published, however, it is sent to the firm that produces the drug under review for comments as to accuracy and completeness. The manufacturing firm is not always satisfied with this review procedure. The representative of at least one major firm has complained that errors in the original article, which were pointed out to the editors of *The Medical Letter,* had not been corrected in the final,

[16] C. W. M. Wilson, R. E. A. Mapes, J. A. Banks, and S. M. T. Korte, "Therapeutic Sources for Prescribing in Great Britain," *Journal of New Drugs,* 3(1963), pp. 276–286.

printed version. Because of its critical character, *The Medical Letter* has aroused strong support in some quarters and equally strong opposition in others. The circulation of *The Medical Letter* has grown rapidly. By 1964, it had about 27,000 subscribers, most of whom were in the United States and Canada, but there were at least a few subscribers in each of fifty-six other countries. The Health Insurance Plan of Greater New York distributes *The Medical Letter* free to one thousand of its participating physicians. The General Health Services Board in Northern Ireland reproduces the *Letter* in somewhat smaller format and distributes it to about the same number of practicing physicians. Apart from these two clusters, and although *The Medical Letter* has made some efforts to find out, it is not clear just who its subscribers are and just how they use the information in this journal. One of the members of the Advisory Board of the *Letter,* Dr. Louis Lasagna, has said, "There is little doubt in my own mind that these subscribers are highly atypical" members of the medical profession.[17] If this is so, it would be helpful to know the reasons for this unrepresentative pattern of interest and distribution and what could be done to change it. Perhaps this lack of representativeness in the readership is determined by the somewhat rationalistic, perfectionist bias which is revealed in *The Medical Letter* and which seems to be characteristic of other "consumer protection" journals.[18]

In general, there is little precise or reliable knowledge about the part that medical journals of any kind, whether specializing in drug information or not, play in the information processes that practicing physicians use. The studies of The Bureau of Applied Social Research indicate that a minority of doctors who are at the centers of informal social networks do use the journals to keep informed about new knowledge, and that they then pass it on to their socially and informationally dependent colleagues. But whether the others do not read the journals at all, or whether they look at the advertisements without reading the articles, we do not know, despite frequent allegations to this effect by those who are critical of what they consider to be the "slickness" and "misleading" character of the advertisements. It would be good to have

[17] Louis Lasagna, "Problems of Drug Development," pp. 362–367.

[18] The above description of *The Medical Letter* is based on a complete reading of its issues, on a "Report to Subscribers" it issued in 1961 or 1962, and on George Baehr, "Drug Costs and the Consumer," in Talalay, *op. cit.*, p. 182.

studies of how doctors actually get information about drugs from medical journals, studies of the kind that the American Psychological Association has recently made of how its members use psychology journals for keeping up with relevant research.[19]

PUBLISHED MATERIALS: THE HANDBOOK OF THERAPEUTIC DRUGS

Another type of published informational aid for the practicing physician which has recently become more important is the handbook of therapeutic drugs, which offers itself as "a practical guide to selection of the best drug for a particular therapeutic problem."[20] An excellent example of this source of information is the handbook, *Drugs of Choice,* edited by Walter Modell, Professor of Clinical Pharmacology at Cornell Medical College, a man who has been a continuing and effective leader among those in the medical profession who have been concerned with defining and solving the new problems of drug research and drug therapeutics. In the Preface to the first, the 1958–1959, edition of this book, Modell gave a number of reasons why he felt such a book was necessary. First, he said, "Due to the extremely fertile mating of the synthetic chemist and the pharmaceutical manufacturer, drugs appear on the market almost too quickly to learn the names, to say nothing of distinguishing which are the same drugs with different proprietary names. It is a Herculean job to learn enough about them to evaluate their relative therapeutic merits." Second, Modell said, "there is almost nowhere for the physician to turn for the kind of help he needs; certainly no place where unbiased, authoritative, and definitive information bearing on this problem is brought together and made easily available." Moreover, third, "Each day the drug manufacturer bombards his target through the mails with a barrage of attractive and eminently readable but far from disinterested literature which he regularly follows up with the attack direct by his detail man. Here, the physician has his troubles, for although he may know that the drug house is perhaps the least likely source of disinterested opinion on the choice of drugs, it is understand-

[19] American Psychological Association, *Reports of the American Psychological Association's Project on Scientific Information Exchange in Psychology,* Vol. 1, Washington, D.C., 1963, especially Report #9.

[20] Statement in Preface to the first (1958–1959) edition of Walter Modell, editor, *Drugs of Choice, 1964–1965,* St. Louis: C. V. Mosby, 1964.

ably difficult for him to stand firm against this well-organized campaign." And finally, "The physician who reads the literature [including the journal articles, usually, though not of course more critical ones like *The Medical Letter* which became available only about the same time as Modell's handbook] will find that the early reports on new drugs tend to be sanguine, the possibilities for utility emphasized, and the limitations minimized. . . . Too often, the first hopes are not borne out by later experience and, at best, require considerable revision and modification. Most drugs need time and experience for final evaluation."

It is to deal with all these difficulties, and perhaps especially, now that *The Medical Letter* is available for the short-run span, to deal with the need for "time and experience" that *Drugs of Choice* has been created. Modell has sought to gain this "time and experience" without becoming out-of-date. Because of the rapid rate of introduction of new drugs and the increasing accumulation of clinical and test results, this is a problem for useful and reliable handbooks. "Trial has shown," says Modell in the Preface to the latest edition, "that the two-year interval between revisions is a satisfactory one. A shorter period would be too brief for substantial experience with the drugs introduced in the interval . . . whereas a longer period would allow the current edition to become badly dated." In addition to Modell's own Preface and article, *Drugs of Choice* has articles by forty-eight contributors, all with distinguished clinical, research, and teaching connections. Yet even Modell has emphasized that the handbook "is a volume of expert *opinion*" and has sought to "provide fresh insights and a forum for different points of view" on "controversial issues" by changing the authorship of a few chapters in each edition. In the latest edition there is also an entirely new chapter, on adverse drug reactions, to cope with the problems involved in those phenomena. Even handbooks of drug therapeutics, though taking a somewhat longer and more experienced point of view, have to emphasize the theme of caution in the use of new drugs.

A commercially-sponsored handbook of therapeutic drugs is *Physicians' Desk Reference,* which contains descriptions of the major therapeutic drug products of 234 manufacturers, the descriptions being those furnished by the manufacturers themselves. This handbook is sent free to all registered medical doctors in the United States. It is apparently widely used by them and also used in hospitals by nurses as well as doctors. There is some evidence that users are unaware of, or

even are favorably disposed to, its commercial sponsorship.[21] Such a handbook cannot, of course serve common purposes nearly as well as does *Drugs of Choice.*

PHARMACISTS

Pharmacists are sometimes highly professional and readily available sources of drug information for medical practitioners. It would be good to have reliable and precise knowledge of what their functions actually are in this respect and, better still, what they might more usefully become. Unfortunately, we have only one study that has sought to get this knowledge, and it is a study with a number of shortcomings.[22] The chief shortcoming is that only the pharmacists were asked about their relations with doctors; no group or sample of doctors was asked about its informational relations with pharmacists. It would also seem that those pharmacists who answered the study's questionnaire may not be a representative sample because of the low rate of response from those receiving the questionnaire. What we have, then, is only the beginnings of what we need.

The study was conducted by the research editor of *The American Professional Pharmacist* with the commercial purpose of showing that the professional pharmacists who read this journal do influence the prescribing habits of doctors and that therefore drug advertising in the journal is worthwhile. *The Pharmacist* mailed 3,400 questionnaires to a nation-wide random sampling of retail and hospital pharmacists. The retail pharmacists were subdivided into three groups: those filling fewer than twenty-five prescriptions a day; those filling between twenty-five and seventy-five; and those filling more than seventy-five. The rate of return of questionnaires was low: 6 per cent for the least active retail

[21] On *Physicians' Desk Reference,* see Paul J. Folsom, Foreword, *Physicians' Desk Reference To Pharmaceutical Specialties and Biologicals,* 18th ed., 1964; *American Journal of Nursing:* Advertising Research Department, *The Nurse and Drugs in Hospitals,* New York, 1965; Bernard B. Brodie, George J. Cosmides, and David P. Rall, "Toxicology and the Biomedical Sciences," *Science,* 148(1965), pp. 1544–1547; Morton Mintz, *The Therapeutic Nightmare,* Boston: Houghton Mifflin Company, 1965, p. 86. In general, doctors seem to be favorably disposed to the commercial sources of their drug information. For a summary of the evidence, see Bauer and Wortzel, *op cit.*

[22] Lawrence E. Newman, "Do Pharmacists Really Influence Physicians' Prescribing Habits?", *American Professional Pharmacist,* 27(1961), p. 19.

pharmacists; 21 per cent for the other two groups of retail men; and 32 per cent for the hospital pharmacists. The representativeness of these returns is not known. According to their responses, pharmacists think they provide drug information to doctors in any one or more of the following ways—describe new drug products in news bulletins sent to doctors; describe such products in mailed postcards; personally advise doctors about drug products; set up drug exhibits in hospitals; maintain a file of drug literature to answer doctors' questions and lend this literature to the doctors; and participate in inter-professional meetings. The hospital pharmacists receive more requests than any of the retail pharmacists, and among these, the more active men receive more requests than those who fill fewer prescriptions per day. The hospital pharmacists seem also to engage in more consequential activity with the doctor: they give him more advice, plan more drug exhibits in hospitals for him, and meet with him more often in inter-professional meetings. The retail pharmacists are consulted chiefly by phone, and then on less important aspects of drugs such as names, dosages, and strengths of various products. The hospital pharmacist is joined in a stronger professional colleagueship with the doctor, it appears—one that is more useful to the doctor for getting drug information. Why are professional relations between doctors and retail pharmacists weaker in this respect? Do they need to be strengthened? How could they be? Further studies are needed to answer these questions, studies which would examine the needs, attitudes, and practices of doctors as well as of the pharmacists.

DRUG INFORMATION FROM GOVERNMENT AGENCIES: THE ENGLISH CASE

In countries like England, where the cost of medical care has been taken over by a system of nationalized health insurance, the problem of providing information about drugs by the relevant government agencies is raised not only by matters of the effectiveness of these drugs but also by the matter of their cost. However, it turns out that in most cases the two are related; excessively costful prescribing seems to be uninformed prescribing. At least this is what the National Health Service of the Ministry of Health in England thinks it has discovered and has now adopted as its basic assumption about "extravagant" prescribing by a minority of doctors. The Ministry of Health has two ways of coping with the problem. For one, it issues a publication called *Prescribers' Notes* which tries to inform the doctors about the high costs of

many new drugs, and their relative ineffectiveness in some cases. For another, through a system of Regional Medical Officers, doctors employed by the Government to visit local doctors in practice, the Ministry seeks to persuade and advise these local doctors to use a more effective and less expensive pattern of drug prescribing. In his account of national controls on medical practice in England, Martin sums up the informational and cost problem, and its attempted solution, as follows: ". . . one can discern the growth of the view, never explicitly stated though surely implied by Ministerial policy, that much *prima facie* 'extravagant' prescribing is merely *uninformed* prescribing. The economy drive at heart, therefore, is more truly seen as an educational one. From 'control' conceived largely in administrative terms there seems to have been a shift in emphasis towards an interpretation based more on professional considerations. Within the limits set by Ministerial policy, maximum stress seems to be placed on the informative and advisory work of the Regional Medical Officer, whose role is becoming, in some ways, similar to that of the post-graduate teacher, with its emphasis on collaboration rather than instruction."[23]

ADVERTISING BY DRUG COMPANIES

One of the largest, perhaps among the most important, and certainly the most controversial, source of drug information for medical practitioners is the drug advertising by commercial pharmaceutical manufacturers. This advertising takes a number of forms—advertisements in medical journals, direct mail advertising, paramedical publications, films, closed-circuit television programs, canned radio programs, exhibits at medical conventions, samples, premiums, small gifts, and visits from detail men.

Although we do not have any thoroughly reliable and precise data on the volume of this advertising, it seems to be very large. "The fact remains," says Pierre Garai, himself an advertising man, "that, in absolute terms, approximately three-quarters of a billion dollars is spent every year by some sixty drug companies in order to reach, persuade, cajole, pamper, outwit, and *sell* one of America's smallest markets—the 180,000 physicians. . . . And it is not too much to say

[23] J. P. Martin, *Social Aspects of Prescribing*. London: William Heinemann, 1957, p. 55. See also the Foreword by Professor R. M. Titmuss.

that perhaps no other group in the country is so insistently sought after, chased, wooed, pressured, and downright importuned as this small group of doctors who are the *de facto* wholesalers of the ethical, i.e., prescription, drug business."[24] In a recent summary statement on drug advertising, the trade publication, *Advertising Age,* gave a slightly lower estimate of costs than Garai. "It has been estimated," this publication said, "that producers of ethical drugs spend more than $225,000,000 a year on advertising, primarily in medical publications and direct mail campaigns. Since there are some 200,000 physicians in the country, this works out to an expenditure of more than $1,000 per year per doctor."[25] It has been alleged that some drug houses spend up to 20 per cent of their total costs on promotion and that at least one company spent almost $2,000,000 on promotion of a single drug. According to a study by an ethical drug advertising agency described in *Advertising Age,* "the average doctor today is exposed to more than four times the number of medical journal advertisements he was exposed to 10 years ago."[26] In the same publication it is reported that "In 1952, Charles Pfizer produced a 12-page magazine, 'Spectrum,' and placed it as an advertising insert in the *J.A.M.A.* It ran this way for four years, representing the largest single contract in medical advertising history." *Advertising Age* also reports, "In the case of the A.M.A., more than half of its total revenue is derived from the pharmaceutical advertising placed in its various publications. The *Journal of the American Medical Association* now carries nearly 6,000 advertising pages a year, a volume exceeded by only one other weekly periodical in the country, *Oil and Gas Journal.*" It has also been estimated that 10 per cent of the value of the drugs sold in Great Britain is spent on advertising.[27]

The volume of direct mail advertising of drugs to doctors is as imposing as the journal advertising. Direct mail pieces may consist of a simple card or blotter bearing the name of a prescription drug with a brief message, but they are often more elaborate folders, booklets,

[24] Pierre Garai, "Advertising and Promotion of Drugs," in Talalay, *op. cit.,* p. 191.

[25] *Advertising Age,* "Medical Advertising—Sales Tool, Postgraduate Course for M.D.," January 15, 1963, pp. 216–219.

[26] *Ibid.*

[27] C. H. Blenkiron, "Advertising by the Pharmaceutical Industry," *Pharmaceutical Journal,* 190(1963), pp. 112–113.

and even costly brochures. According to a statement by Richard Deno and his colleagues in 1959, "An eastern medical journal recently completed a survey which indicated that the practicing physician receives annually by direct mail more than 4,000 pieces of pharmaceutical literature."[28] Like journal advertising, direct mail has been increasing over the last ten to fifteen years. In the 1963 study reported in *Advertising Age,* already referred to, it was reported that the average doctor "receives more than twice as many direct mail pieces as in 1950."[29] Again we see how everything connected with drugs has been changing and getting larger during the very recent past.

Just what the effect of all this drug advertising is, how beneficial and how harmful it is (for this is certainly a situation of mixed effects), has not yet been carefully studied. Certainly, given the place of advertising in our socio-economic system as a whole, there is nothing intrinsically bad about drug advertising, nor are there any necessarily bad consequences from a "large" volume of advertising. Many medical scientists and doctors are, however, disturbed by the advertising and have voiced strong, but empirically unsupported, complaints. What is the gist of these complaints? First, there is the charge that the sheer volume of drug advertising "bombards" and overwhelms the doctor, capturing his prescribing practices by mass and weight alone. Then there is a complaint on the matter of style, that drug advertising is too "slick," too much the product of a "Madison Avenue approach," which would be more suitable for less vital products than health-giving drugs. There is, third, the complaint that drug advertising is not disinterested, but that it has assumed a function which belongs to more objective, scientific, disinterested social agencies. And, finally, there is the complaint that the search for profits makes the drug houses too sanguine in their advertising; they greatly exaggerate the benefits of their new products and minimize their known defects or the fact that little is still known about them.[30]

Some do not blame only the pharmaceutical companies for the alleged evils of drug advertising. The advertising man Pierre Garai

[28] Deno, Rowe, and Brodie, *op. cit.,* p. 166.

[29] *Loc. cit.*

[30] For a typical and comprehensive bill of complaints against drug advertising, see Charles D. May, "Selling Drugs By 'Educating' Physicians," *Journal of Medical Education,* 6(1961), pp. 1–23.

blames medical practitioners as well as drug companies. He wonders why only 25,000 out of 180,000 doctors have subscribed to such an effective antidote to drug advertising as *The Medical Letter*. And he says, "No conceivable form of government regulation can do half so much to raise the standards of pharmaceutical industry and of ethical advertising as the growth of intelligent, disciplined medical skepticism. . . . Let the doctors withhold their approval of new drugs until conclusive evidence has been presented in support of claims, and it will cease being economically feasible to market new drugs without this evidence."[31] The editor of the volume reporting the proceedings of the conference at which Garai spoke, said: "The discussion at the conference emphasized the point made in many of the formal papers that there is much room for improvement in the quality of ethical drug advertising. Doctors should be better educated and more discerning about drug advertisements. If they disapprove of certain advertising techniques, they should take the time to say so. Medical institutions and professional organizations might well consider whether they have not by default allowed the instruction and guidance of the physician in drug therapy to be taken over to a large extent by the pharmaceutical industry."[32] Dr. Garb's educational program on drug advertising at the Albany Medical College has shown that it is possible to train medical students in the skepticism and discernment recommended by Garai and Talalay.[33]

A qualified defense of American commercial drug advertising in the large, from a broad comparative perspective, has been entered by two students of medical practice and drug therapeutics in the Soviet Union. They point out that a few of the more extreme critics of the high costs of drug promotion in the United States, who "argue for re-

[31] The standard of "conclusive evidence" seems to be on the utopian side, but Garai would probably be satisfied if doctors were somewhat more critical and cautious than they now are.

[32] Paul Talalay, "A Summary of Comments by the Editor," in Talalay, *op. cit.*

[33] For some criticisms and defenses of drug advertising in England, see Alan G. Nicholls, "Pharmaceutical Mailing Lists," *British Medical Journal*, Nov. 17, 1962, p. 1326, Correspondence; H. W. S. Rankin, "Pharmaceutical Mailing Lists," *British Medical Journal*, Dec. 1, 1962, p. 1472, Correspondence; Cyril Hart, "Pharmaceutical Mailing Lists," *British Medical Journal*, Dec. 1, 1962, p. 1472, Correspondence. See also some material in Seymour E. Harris, *The Economics of American Medicine*, New York: The Macmillan Co., 1964.

ducing promotional activity to some minimum system of announcement of new drugs, with the major job of communicating the drug's characteristics and usefulness to be performed by the medical profession, or the government, or both," do not appear to realize that the

> assumptions behind these criticisms are more complex than are generally recognized, and seem to be based on the following beliefs: 1. A satisfactory noncommercial source of information about drugs can be established without too much difficulty; 2. If information is reasonably available, physicians will take the initiative to see that they keep up to date; 3. The well-informed physician will not be concerned with the reputation of the firm producing the drug, but only with the drug's properties as described in an official pharmacopoeia.[34]

Bauer and Field question these assumptions, and of course there is some evidence from the United States to support their questioning. They feel that their questioning of these assumptions has strong support in the Russian situation, where drugs are apparently as much "underpromoted" as they may be "overpromoted" in the United States. "While there may be difficulties associated with an 'overpromoted' drug system," Bauer and Field say, "the Soviet experience indicates that 'underpromotion' produces its own characteristic problems." The implication of the perspective provided by this comparative analysis is clearly not that the American system may not need reform. It is, rather that the system as a whole should not be scrapped; that it is performing essential functions; and that reforms or functional alternatives should be constructed to continue these essential educational and informational functions, not to abandon them.[35]

PHARMACEUTICAL COMPANY "DETAIL MEN"

Apparently the most effective, and certainly the most expensive component of the system of commercial drug advertising to medical practitioners is the "detail man." The detail man is a kind of salesman, or

[34] Raymond A. Bauer and Mark G. Field, "The Soviet and American Pharmaceutical Systems: Some Paradoxical Contrasts," Arthur D. Little, Inc., (unpublished report), 1962. Raymond A. Bauer and Mark G. Field, "Ironic Contrast: U.S. and U.S.S.R. Drug Industries," *Harvard Business Review*, 40(1962), pp. 89–97.

[35] An extension of this analysis of the positive functions of the American system of commercial drug advertising, based on an exhaustive study of the available research data, can be found in Bauer and Wortzel, *op. cit.*

"medical service representative," as the companies prefer to call him, who visits practicing and teaching physicians to inform them in depth about his company's new and, in lesser measure, old products. The detail man usually does not sell directly, that is, he does not usually take orders from the doctors, but is supposed to be of help to them in their prescribing practices by providing them with new and valuable information. The pharmaceutical companies prefer to hire knowledgeable people for this work, particularly people like graduate pharmacists, but it is likely, given the crude estimate that there may be "somewhere between 20,000 and 50,000" detail men in all, that many of them have had no graduate medical, pharmaceutical, or equivalent training.[36] Instead they are trained "on the job," by the companies. Doctors in the medical departments of the pharmaceutical houses give intensive courses to detail men on the diseases or syndromes that specific drugs are supposed to be helpful for and on the particular uses, advantages, and (ideally) the defects of those drugs. During the last four years, several pharmaceutical companies have used the new "programmed instruction" courses to provide this intensive training for detail men. These "programmed instruction" courses cover both substantive medical fields, such as "Microbiology and Antibiotics," and techniques of salesmanship, such as "Effective Listening." In some cases, the courses in substantive medical fields have been made available also to medical doctors and medical students. When the Charles Pfizer company recently offered doctors a seven-hour "programmed instruction" course on "Allergy and Hypersensitivity," it received some 24,000 requests from doctors. The great majority of doctors and medical students who wrote in about their experience with the course expressed satisfaction with it. This course is now used in some of the country's medical schools.[37] In addition to "in-house" instruction, detail men also learn "on the job" from some of the doctors they inform; what they learn from one doctor they communicate to other doctors and probably also to each other.

The expensiveness of this arrangement of employing well-paid, trained or even professional men for personal visits to physicians is obvious. According to Richard Deno and his colleagues, "A monthly

[36] Norman Hawkins, "The Detail Man and Preference Behavior," *Southwestern Social Science Quarterly*, 40(1959), pp. 213–224.

[37] *Drug Trade News*, October 11, 1965, pp. 62, 66.

periodical, *Modern Medicine,* recently reported to manufacturers that the average cost per detail visit was $7.69. In contrast, the average cost per reader of literature sent by mail was about seventeen cents, and the cost per reader of a journal advertisement was about one cent. The precision of these figures may be open to question, but the relative cost of the several types of promotion is approximately as indicated. The manufacturers are convinced of the effectiveness of the detail visit; otherwise, they would not be willing to continue to bear the high cost of this type of promotion."[38]

Like the rest of the system of commercial drug promotion, the detail man has come in for severe criticism, and on much the same grounds, of "hard-sell" techniques and at least subtle misrepresentation.[39] However, at best, detail men could be useful socializers of doctors; they could, in the midst of all the other pressures of practice, help to direct doctors' attention to drug innovations; and they could save time for the busy doctor. This is what the pharmaceutical industry believes firmly enough to justify the large investment it makes in detailing. But we do not know much about the detail man nor about his actual social relations with doctors. Who are the detail men: what are their professional and other backgrounds? how well are they trained by their companies? what are their earnings and incentives? are they career men? how do they actually help or hurt by the advice they give doctors?

What little research evidence we have seems to point to a usefulness of the detail man system for the doctor.[40] In the Albany Medical College program, Dr. Garb and his colleagues were surprised to find that although the students had reservations about the role of the detail man, on the whole their slight experience had given them a generally favorable opinion of his potential value to the physician.[41] The students felt that not only were the men representing the reliable companies generally reliable but that even the men from the companies rated unreliable "almost uniformly adhered to high ethical standards." The

[38] Deno, Rowe, and Brodie, *op. cit.,* pp. 166ff.

[39] Karl Evang, *Health Service, Society, Medicine,* London: Oxford University Press, 1960, pp. 119, 128.

[40] For an analysis of some of the useful functions of detail men and for a summary of the few studies that have touched upon the nature and extent of their influences, see Hawkins, *op. cit.*

[41] Garb, *op. cit.*

students felt, further, that the inadequacies of the detail man resulted from his unsatisfactory knowledge of the drugs, and from his being uninformed by the company, rather than from any deliberate attempt to mislead. When the detail man knew about the danger of his drugs, he gave out the information willingly. "In general, it appeared" to these students "that the detail men regarded themselves as being more than mere salesmen, and considered themselves to be professional assistants or associates of the physician."

This generally favorable opinion of the detail man was shared by the "isolates," the doctors who, the Bureau of Applied Social Research found, were not much involved in networks of personal relationships with their colleagues.[42] As a result of their lesser contact with other doctors, they learned about drugs more often from the detail man than did their less-isolated colleagues. Moreover, the detail man performed other functions for these "isolates." Menzel and Katz report, "Two of the four doctors who received no friendship choices volunteered the information that they often talked with the detail man on subjects other than drugs: 'We'll get off the track sometimes on economics, politics, family affairs,' said one. Another relatively isolated doctor commented on the detail men as follows: 'They are helpful—they know all the doctors in the communities around here and give you all the dirt and incidental news about what is going on amongst the doctors in this community.' " Thus, in addition to purveying useful knowledge about drugs, say Menzel and Katz, "This pharmaceutical salesman evidently serves as a near-professional companion for men who are relatively cut off from informal contacts with other physicians."[43] In this respect, detail men seem to resemble the publishing houses' traveling "book men," who not only spread information about the new books their companies are publishing but also various other kinds of useful professional information, and this especially to those academic men who are not otherwise in the communications networks which would bring them this information. Evidently, pharmaceutical detail men have a variety of functions, all of which should be studied intensively: to carry information from manufacturers to doctors; to report information from doctors back to their companies; to

[42] Menzel and Katz, *op. cit.*, pp. 337–352.

[43] *Ibid.*

diffuse knowledge and experience from doctor to doctor, perhaps especially from those at the centers of communication and activity to those at the margins; to provide companionship and support for some doctors; and, finally, to spread non-drug but professionally important information within the community of doctors.[44]

In any research on detail men, it would be valuable to have a comparative perspective. If it is true that there is much less use of detail men in Europe, and of traveling salesmen generally, why is this so and what are its consequences?[45] Are there functional alternatives to the detail man? In England, we have seen, the Regional Medical Officer may function, in part, as a kind of alternative to the privately-employed detail man.[46] In Russia, according to Bauer and Field, where various efforts are being made to correct the "under-promotion" of new drugs, a functional alternative to the detail man consists in the representatives of the government pharmaceutical manufacturing enterprises who are being sent to the clinics to inform physicians about what new drugs are available.[47] "These representatives," they say, "are, doubtless, the functional equivalents of the U.S. drug industry's detail men . . . Soviet

[44] Some of these functions are performed also for the auxiliary medical groups. A mail questionnaire study of a sample of 800 American hospitals found that "supervisors and directors of nursing in hospitals of all sizes welcome consultation" with detail men. This welcome is especially strong in the smaller, more isolated hospitals. See American Journal of Nursing: Advertising Research Department, *The Nurse and Drugs in Hospitals,* New York, 1965, pp. 41ff.

[45] The lesser use of detail men is what has been reported on an impressionistic basis, in private communication, by William Glaser of the Bureau of Applied Social Research, Columbia University, whose various researches on European medicine have made him very knowledgeable in these matters.

[46] For a report on the occupational background and training of a small sample of privately-employed detail men working in the Liverpool area in the winter of 1962–1963, see J. A. Banks, S. M. T. Korte, R. E. A. Mapes, and C. W. M. Wilson, "The Drug House Representative," *Sociological Review,* 12(1964), pp. 155–168. This study touches upon the degree of "professionalism" of these English detail men. The matter of professionalism is discussed and recommended at much greater length in C. W. M. Wilson, "Pharmaceutical Representatives: Commercial or Professional?," *British Medical Journal,* iv(1965). The more knowledgeable the detail man, the more concerned to serve the doctor and his patients, the more independent of his commercial employer—in short, the more professional he was, the better he would be able to function positively in the process of informing and socializing the doctors he visits. They would be changed from his "customers" to his "colleagues" or "clients."

[47] Bauer and Field, *op. cit.*

criticism is leveled at those pharmacies that do not use detail men, or do not engage intensively in promotional activity, while praise is heaped on those that do." However, Bauer and Field offer a qualification, "One might well wonder, however, whether such mass presentations adequately can meet the need which is served by the person-to-physician presentations provided by the U.S. detail men." Perhaps both group and individual information presentation techniques are necessary in both countries. The aim of research on the detail man and his functional equivalents or alternatives is to provide the knowledge on which the most effective policy for providing drug information to doctors could be established.

EMERGENCY DRUG INFORMATION FOR DOCTORS: THE CASE OF MEDIPHONE, INC.

In addition to their routine and continuing needs for information about drugs, doctors occasionally have more urgent, emergency needs, especially in the event of unexpected and dangerous toxic reactions. To meet such emergency needs, there was established in 1961 in Washington, D.C., a private organization named Mediphone, Inc. It was ostensibly designed as a round-the-clock clearinghouse of information on drugs for physicians, with special emphasis on toxicity, contraindications, antidotes, and special applications. Having paid a one year's membership fee of $20, and being liable to a service charge of $3 for each call, a physician anywhere in the United States could call Mediphone at any time about any drug. The service was available to hospitals, medical groups, and industrial health facilities at a membership fee of $50 a year. Mediphone was soon forced to close, "for financial reasons."[48] Mediphone seems also to have suffered because word got about that it had been organized by a large drug advertising company as a "cover" device by which the company could get information on the kinds of questions doctors ask about drugs. It may be that there is not a great enough need for this emergency service or that it is already adequately taken care of by other agencies, such as hospitals or medical schools. The medical departments of some of the larger pharmaceutical manufacturing firms also provide seven-day-a-week, twenty-four-hour-a-day, on-call service for doctors seeking emergency information or

[48] The above description is based on U.S. Senate, 87th Congress, Interagency Coordinating Committee Hearings.

advice about the use of the products these firms manufacture. However, there ought to be some research into the extent and character of the need and some consideration of whether the need could be met by a government agency or by a subsidized non-profit establishment located in a large metropolitan clinical, teaching, and research medical center.

COMPREHENSIVE AND SYSTEMATIC RESEARCH ON DRUG ADVERTISING: THE CASE OF THE RESEARCH PROJECT ON PRESCRIBING

Such research as now exists on sources of information about drugs and on patterns of prescribing has usually had other primary purposes and been concerned with drugs only secondarily and indirectly. Recently, however, there has come into existence in Great Britain an interdisciplinary group of scientists whose purpose is the comprehensive, systematic, primary, and direct study of the professional therapists' sources of information about drugs. This team is called the Research Project on Prescribing and has been located in the Departments of Pharmacology, Psychology, and Social Science at the University of Liverpool. Its members include the leader, who is both a medical doctor and a Ph.D., a sociologist, a psychologist, and a statistician. Because their studies have been limited to Liverpool, it is not yet known whether their results can be generalized to all of Great Britain, let alone to the United States or other countries. However the initial procedures and findings of the Research Project demonstrate the feasibility of this kind of research and its potential value on a larger scale. As a pioneer in what is needed in this area, the Research Project deserves close attention.[49]

The establishment of the Research Project was stimulated by the discussion of the costs of prescribing under Great Britain's National

[49] The present summary of their work is based on four papers published as of 1964: C. W. M. Wilson, R. E. A. Mapes, J. A. Banks, and S. M. T. Korte, "Therapeutic Sources for Prescribing in Great Britain," *Journal of New Drugs*, 3(1963), pp. 276–286; "Influence of Different Sources of Therapeutic Information on Prescribing by General Practitioners," *British Medical Journal*, ii(1963), pp. 599–604; "The Assessment of Prescribing: A Study in Operational Research," in G. McLachlan, editor, *Problems and Progress in Medical Care*, London: Oxford University Press, 1964; D. B. Bromley, S. M. T. Korte, R. E. A. Mapes, and C. W. M. Wilson, "The Associative Value of Drug Names," *The Practitioner*, 192 (1964), pp. 388–394.

Health Service. That discussion, which is of course part of the more general discussion of the costs of medical care, resulted during the late 1950's in an investigation and report on the subject by the Hinchcliffe Committee, appointed by the Government.[50] The Hinchcliffe Committee Report pointed out that costs of prescribing were obviously influenced by the doctors' patterns of prescribing and made some remarks about these patterns, but indicated that no research had been done on what these patterns actually were. The Liverpool research is in response to this deficiency of knowledge about an important matter.

The Research Project made a random selection of thirty-nine general practitioners in Liverpool and studied them twice, once in February, 1962, and then again in October of the same year. The findings were stable for the two different periods. Each doctor was asked to record the incidence of disease in his practice and the sources of therapeutic information. The diseases were to be classified into twenty-eight categories and the doctors were to decide from which of a set of possible sources of information they derived the therapeutic knowledge for every item they prescribed for every disease they diagnosed. The following were the sources of socialization and information the doctors could check:

a. medical training for general practitioners, including courses, hospital work, and being an assistant to a principal practitioner
b. advice of specialist consultants
c. textbooks and periodical medical journals
d. the British National Formulary (B.N.F.) which is compiled by a committee composed of members of the medical and pharmaceutical professions. It is a comprehensive list of preparations under their pharmacological classification, with a short account of actions and uses
e. the *Prescribers' Journal,* which, as we have already seen, has been issued since 1961 by the Ministry of Health. Its editorial board consists of representatives of the Ministry, men from the medical schools, pharmacists, and some general practitioners. It is supposed to provide early and reliable information about new drugs, with notes on relative costs of different treatment schedules

[50] Ministry of Health, *Final Report of the Hinchcliffe Committee on the Cost of Prescribing,* London, H.M.S.O., 1959.

f. the *Monthly Index of Medical Specialties*, an up-to-date list of proprietary preparations according to therapeutic classes, sent out monthly by the pharmaceutical industry to all general practitioners
g. the pharmaceutical companies, including both direct mail material and visits from detail men. The Research Project discovered that general practitioners in Liverpool receive an average of 160 direct mail items per month and an average of 9.2 visits from detail men in the same period
h. discussion with general practitioner colleagues: at medical society meetings, with their partners in group practice, and with doctors with whom they exchange weekend, vacation, and other fill-in services.

The data collected in this way produced a number of findings. The basic ones are that "the sources from which the doctors admitted they drew most of their knowledge when writing prescriptions" were medical training, the pharmaceutical industry, and the British National Formulary, in that order. Knowledge "derived from textbooks, periodical medical journals, the *Prescribers' Journal, M.I.M.S.,* and discussion with medical colleagues provided only a small proportion of the practitioners' sources of knowledge for treating disease." Only a relatively small percentage of these doctors read medical journals thoroughly. "Although 95 per cent of the doctors in the sample belonged to the British Medical Association and received the *British Medical Journal,* only 14 per cent of them read it." There was a slight increase in use of the new journal, *Prescribers' Journal,* between the February and October studies, indicating the possibility of some further increase as this journal became better known. Older doctors relied on the pharmaceutical industry more than their younger colleagues. Finally, so far as knowledge of new drugs is concerned, "the majority of the doctors' knowledge about advances in drug therapy came from the pharmaceutical industry. A small proportion comes from the British National Formulary and a little comes from consultant advice." Apparently the specialist consultant gets his knowledge from the medical journals and then passes it on to the general practitioner, another instance of the two-step flow of information found in the Bureau of Applied Social Research studies. In explanation of the dependence of these doctors on the pharmaceutical industry for knowledge of new drugs, the Research Project says, "The doctors, insofar as they consider it necessary to

who will use the drugs. An official name is as useless as a proprietary name if they are both derived from chemical terminology which the user does not understand and with which he is unfamiliar." On the other hand, the report continues, "Although the proprietary names of drugs may be relatively meaningless in themselves, one or two of their syllables have high associative values which help to recall their therapeutic actions to the prescriber." Bromley and his colleagues conclude, "Doctors today are not greatly concerned about the intricate nature of the drugs which they employ. . . . The use of new and unfamiliar condensed chemical nomenclature for the construction of the official names may be partly responsible for the reluctance on the part of doctors to prescribe official preparations in the National Health Service."

Thus, commercial drug companies have a number of advantages in getting doctors to use their drugs: first, they take the initiative and bring knowledge to the doctor through the mails and the visits of detail men; second, they use trade names for new drugs which suggest the therapeutic value of those drugs; and, third, they build up general reputations for reliability, on the basis of which doctors are willing to take their new drugs on trust. Anyone who would radically alter or mildly reform the present practices by which doctors get their information about drugs needs to consider these several functions which drug companies now have.

Education and Communication Among Lay Users

The lay users of drugs get their education and information about the use of drugs in part from professional therapists, in part elsewhere. Since how the final user actually takes drugs—in the proper dosage, on the right schedule, even with the right attitude—is important for their effectiveness, the agencies that educate and inform him may be as significant in the therapeutic result as those that influence the professional prescriber. These agencies are even more significant, of course, where the lay user has not consulted a professional therapist at all, and many drugs are used without benefit of such consultation. For example, it has been estimated that some $2 billion was spent on patent medicines

in the United States in 1963, and undoubtedly much of this was without medical advice.[52]

We know all too little about what influences the professional in drug choice, but we know still less about how the lay user is trained and informed in these matters that are of vital importance to him. There exists here a large area for useful research.

THE FAMILY

The family gets the individual first for education in nearly everything, and in nearly everything its influence in determining basic attitudes and knowledge is considerable. Surely it must be so for drugs, and yet among all the studies in family sociology and medical sociology, we have almost nothing on this subject. Sometimes we can see family influence indirectly, by inference, as when we see that there are social class differences in patterns of use of drugs and we infer that here, as elsewhere, class differences are at least partly the result of family training. Thus, in a study of a small up-state New York rural community, Koos found class differences in the possession and use of home drug remedies.[53] The highest of three classes was much more likely to have analgesics than the lowest class; and the lowest class was more likely to have "kidney pills," "liver pills," "stomach medicine," and "tonics." Kinship connections, we also know, are one of the important sources of education in the use of the hallucinogenic drug, LSD-25, among middle-class users. The lines of influence seem to run from husband to wife, though not vice versa, and occasionally from children to par-

[52] For this estimate, and other useful statistics on various home remedies, see George H. Mandel, "Therapeutic Range and Extent of Use of Home Remedies," in, *Annals of the New York Academy of Sciences, Home Medication and the Public Welfare*, Vol. 120(1965), Art. 2, pp. 902–910. Mandel reports only on the United States. For material on the United Kingdom and other countries of Western Europe, see in the same volume of the *Annals*, pp. 855–863, the article on these countries by W. G. Hollis, "Home Remedies in the United Kingdom and Western Europe". Despite the lack of direct medical advice, apparently, the large amount of money spent for home medication is, on the whole, spent safely and effectively. (This is the chief conclusion of the conference on home medication reported in the volume of the *Annals* just cited.)

[53] Earl Lomon Koos, *The Health of Regionville*, New York: Columbia University Press, 1954.

ents.[54] The influence of the family on drug use of all kinds deserves some direct and systematic study.

THE "LAY-REFERRAL" SYSTEM

Family influence overlaps with what Freidson has analyzed and described as the "lay-referral" system, a system of interactions and communications in which laymen advise one another about professional therapists, medical procedures, and drug treatments.[55] In this informal system, laymen often consult members of their immediate families first, then friends, neighbors, more distant relatives, and fellow workers, in that order. There has been a little study of this "lay-referral" system among "folk" groups who are in, but not assimilated to, modern societies, for example, the uneducated Spanish-Americans in the Southwest.[56] But there has been no study of this type of education and information system within the urban, assimilated, educated, and uneducated groups, among whom it seems also to exist. In this "lay-referral" system in the "folk" groups, it is reported—what is probably the case also for other types of groups—that there are certain sociometric "stars," like the key doctors in the communities studied by the Bureau of Applied Social Research in their investigations of the diffusion of new-drug information. These "stars" are the persons who, "because of age, experience, or special interest, may have a more extensive knowledge than their neighbors and friends and thus acquire a somewhat specialized status."[57]

The informal "lay-referral" system of family, friends, and acquaintances is perhaps even more important in the induction into the

[54] For research evidence on this point, see Richard Blum and Associates, *Utopiates: The Use and Users of LSD-25*, New York: Atherton Press, 1964, especially at p. 95.

[55] Eliot Freidson, "Client Control and Medical Practice," *American Journal of Sociology*, 65(1960), pp. 374–382. See also the excellent study of the lay-referral system and the use of folk medicine in three Greek peasant villages, in Richard Blum and Eva Blum, *Health and Healing in Rural Greece*, Stanford, Calif.: Stanford University Press, 1965, especially pp. 88–89, 107–108, 144–148, and 166–171.

[56] Lyle Saunders, *Cultural Difference and Medical Care*, New York: Russell Sage Foundation, 1954, pp. 141–142; Arthur J. Rubel, "Concepts of Disease in Mexican-American Culture," *American Anthropologist*, 62(1960), pp. 795–814.

[57] Saunders, *op. cit.*, pp. 160–161; Blum and Blum, *op. cit.*, pp. 193–196.

use of illegal drugs than of therapeutic drugs. In his studies of the users of marihuana, for example, Becker speaks of the necessity for the potential or novice user to be inducted into "this otherwise vague and ambiguous experience" by friends and informal acquaintances who are experienced users.[58] The same pattern of diffusion and instruction among friends is an important one in the use of LSD-25, though there are also, as we have seen, patterns of education by kin. There seems also to be some education of laymen by professionals using the drug on them therapeutically or experimentally.[59] Some of the attention that has been given to induction into the use of marihuana and LSD and heroin might be duplicated for the therapeutic drugs.

Informal, friendly, indeed, quasi-family patterns are also important in the processes of intensive re-socialization by which the recently-established Synanon houses attempt to cure drug addicts.[60] In condensed form, here is what seems to be important in this family-like re-education process: addicts and non-addicts living together in the same house, on a long-term basis, and engaging in interaction at least as intensive as that in a family; a complete break with former, forbidden behavior; expressed willingness to change bad attitudes; a continuous process of assimilation to new behavior and alienation from old attitudes and behavior; strong identification with new norms and equally strong rejection of the old ones; severe sanctions for relapsing, e.g., total exclusion from the group, though second chances are given; endless informal self- and other-criticism sessions, called "synanons," a term which is apparently a corruption of "symposium" and "seminar";

[58] H. S. Becker, "Marihuana Use and Social Control," *Social Problems,* 3(1953), pp. 235–242.

[59] Richard Blum and Associates, *op. cit.,* pp. 23, 29, 31, 34, 39, *et passim;* R. E. L. Masters and Jean Houston, *The Varieties of Psychedelic Experience,* New York: Holt, Rinehart, Winston, 1966.

[60] The present description is based on Rita Volkman and Donald R. Cressey, "Differential Association and the Rehabilitation of Drug Addicts," *American Journal of Sociology,* 69(1963), pp. 129–142, and Lewis Yablonsky, *The Tunnel Back: Synanon,* New York: Macmillan, 1965. For an account of not dissimilar re-education processes in Alcoholics Anonymous, see Robert F. Bales, "Social Therapy for a Social Disorder—Compulsive Drinking," *Journal of Social Issues,* 1(1945), pp. 14–22. See also John Lofland and Rodney Stark, "Becoming a World-Saver: A Theory of Conversion to a Deviant Perspective," *American Sociological Review,* 30(1965), pp. 862–875.

mutual help in the work and activity of the group, as in a family; rewards for achievement in the form of increased prestige for the length of time off drugs; and, finally, permanent belonging to the group, again as in the family, for one must keep up ties with Synanon even if "off" drugs for a long time.

THE SCHOOL

The school supplements the educational influence of the family in many areas and also inculcates new knowledge and attitudes. So far as the use of drugs is concerned, little is known about what the school does to train its students, or what it could do. It would be useful to have a study of the school nurse and college doctor. With what attitudes do they dispense drugs? What do they teach their students about them? It would also be useful to know what students learn about drugs in the "hygiene" courses which are widely given in high schools and colleges. An examination of three recent hygiene textbooks, one the leading high school text, the other two college books, reveals a serious imbalance in the discussion of "drugs."[61] All of these books discuss only the psychoactive (in lesser measure) and the addictive (with heavy emphasis) drugs, in one instance somewhat realistically, otherwise not. None of these books has any discussion of therapeutic drugs generally, either as home remedies or in the form of doctors' prescriptions.

Since the school fails to provide adequate training in the use of drugs, it has been recommended that a "broad consumer education program, sponsored by government, industry, and the medical profession," be established instead.[62] "Educational material should be developed not only for the mass media but also for cooperating community agencies such as public health departments, schools, safety councils, and Red Cross."[63]

[61] See Harold S. Diehl, *Textbook of Healthful Living,* New York: McGraw-Hill, 1960, 6th edition, pp. 129, 131; C. E. Turner, *Personal and Community Health,* St. Louis: C. V. Mosby Company, 12th edition, 1963, pp. 116–168; and Warren R. Johnson, Doris E. Terry, M. Josephine Gaines, and James H. Humphrey, *Health Concepts for College Students,* New York: Ronald Press, 1962, p. 95ff.

[62] Irving Sunshine, "Use and Misuse of Self-Medication," in, *Annals of the New York Academy of Sciences, Home Medication and Public Welfare,* Vol. 120 (1965), Art. 2, pp. 931–941.

[63] *Ibid.*

THE MASS MEDIA

One of the most visible sources of information on drugs for the lay user are the various mass media. Not only do media carry much general medical science and drug news, but they are attended to, and on the whole approvingly, by a large audience, according to a national sample survey of the American population.[64] Somewhat more mixed attitudes toward the medical and drug news carried in the mass media are expressed by the medical profession than by laymen.[65] Some doctors feel that there is much factual, informative, and judicious reporting of drug news. They themselves feel it useful to read such reporting in *The New York Times, The Wall Street Journal,* and *Time,* to mention a few especially competent and reliable sources. But some of them feel that "these examples of excellent medical reporting are not to be taken as representative of newspaper coverage."[66] Doctors deplore inaccuracies, lack of qualifications, over-selling of results, and general sensationalism in mass media reports on new and old drugs. They also deplore what they call "premature publicity," which may mean over-selling of results or may mean release of news to the general public before it has been communicated to the medical community at large. It is far from satisfactory, says Talalay in summing up the attitudes of some medical doctors as expressed at a recent conference on drugs, to have a patient read about a new "miracle" or "breakthrough" even before his family physician, and long before the discovery has been thoroughly tested.[67] The prematurity and sensationalism may be due to a number of causes. For one, the mass media and their staffs may strive for a good "human interest" story, with lesser regard for accurate qualifications and necessary cautions about results. With this in mind, one doctor has recommended: "The medical profession needs to take a positive approach to this problem; it must provide correct, sensible

[64] Survey Research Center, University of Michigan, *The Public Impact of Science in the Mass Media: A Report on a Nation-wide Survey for the National Association of Science Writers,* 1958.

[65] This ambivalence is clearly expressed in Lasagna, *op. cit.*, p. 209.

[66] *Ibid.*

[67] Paul Talalay, "A Summary of Comments by the Editor," in Talalay, *op. cit.*, pp. 297–298.

information and must use modern communications media for this purpose.[68] Agreeing with this recommendation, some doctors do now write regular "Dear Doctor" columns of information in the newspapers and also feature articles in the magazines. These contain valuable information and attitudes about drugs.[69] Another source of difficulty, the prematurity of some stories, comes from the reporter's need for a scoop or from the medical scientist's need to claim priority for his discovery.[70] And, finally, stories are sometimes released too early because of the desire of a drug manufacturing firm to get publicity for its product. One of the largest of the pharmaceutical public relations firms, Medical and Pharmaceutical Information Bureau of New York, for example, has sent a newspaper column prepared in mat form ready for printing to 2,000 of the small daily and weekly newspapers across the country. These mats were sent as news, not labeled as advertising, and they contained the trade names of drugs manufactured by the agency's clients.[71] Such practices do not guarantee reliable information about drugs to the public. What information on drugs people actually get from the mass media, what they want and why, and what they could genuinely profit from; these are subjects on which a great deal of research is needed.

THE PROFESSIONAL THERAPIST

Finally, there is the obvious point, that there is always a considerable amount of education and information about the use of drugs given to the lay user by his professional therapist. But little is known about this directly, and perhaps less is known about how information and education from therapists interacts with other kinds of information and training. How, for example, does the doctor respond when his patient

[68] Maxwell M. Wintrobe, "The Therapeutic Millennium and Its Price: Adverse Reactions to Drugs," in Talalay, *op. cit.*, p. 113.

[69] Walter C. Alvarez, "The Extent of Lay Medical Knowledge and Its Relationship to Sound Medication," in *Annals of the New York Academy of Sciences, Home Medication and the Public Welfare,* Vol. 120(1965), Art. 2, pp. 955–958.

[70] On priority claims by scientists, see Robert K. Merton, "Priorities in Scientific Discovery: A Chapter in the Sociology of Science," *American Sociological Review,* 22(1957), pp. 635–659, and N. Reif, "The Competitive World of the Pure Scientist," *Science,* 134(1961), 1957–1962.

[71] *The New Yorker,* March 21, 1964, report on Kefauver Committee hearings.

tells him about some new drug he has had recommended to him by a friend or has read about in a magazine? Or again, where no other sources of information but the professional therapist are involved, it is well known that many drugs are taken incorrectly by the patient, or not at all. How often does this occur? Why? Is the professional therapist responsible for these mistakes and evasions, or is the patient otherwise improperly trained or informed? Again, the need for research is clear.

4

Professional Specialists: Their Functions and Problems

THE DISCOVERY, TESTING, prescribing, and dispensing of drugs reveals both the functions that a variety of specialized professionals perform and some problems connected with the carrying out of those functions. These functions and problems are not, of course, peculiarly restricted to their connection with drugs, but they do manifest themselves as clearly in that context as in any of the others in which our professionals operate. Since there has been considerable specialization of function among medical doctors, we shall look separately at each of four specialized medical types: doctors in clinical practice; clinical investigators, as some medical researchers have come to be called; doctors who are employed in the medical departments of drug firms; and, doctors who are full-time research scientists in drug firms. We shall also look at the problems of pharmacists.

Medical Doctors

The four types of specialized doctors we shall treat separately are not entirely distinct from one another, either analytically or concretely.

Analytically, for example, we shall see that some of the same problems occur for doctors in clinical practice and those in clinical investigation, though in different measure and intensity. One of these problems, or sets of problems, consists of the ethical dilemmas of using human beings as test subjects for new drugs. And, concretely, these different specialized roles are connected because some medical doctors participate in more than one of them at a time. Some doctors, for instance, give part of their time to clinical practice and part to clinical investigation. The roles are also connected because occasionally some doctors give up their full-time commitment to one and move to another, again on a full-time basis. As we consider each type of role, we should remember these connections and overlappings.

CLINICAL PRACTICE

Doctors in clinical practice face at least three problems in which the use of drugs plays a role. One is the problem of the conflict between therapy and testing. Another is the problem of the uncertainty and lack of control in the treatment of illness with drugs. And a third is the problem of risk and legal responsibility resulting from the use of drugs.

The conflict between therapy and testing. The training of the modern medical doctor strongly stresses the ancient and continuing medical ideal of the doctor's primary commitment to therapy, to the care and cure of the patient's illness. Also strongly stressed in this training are the knowledge, use, and even development of medical science. The relative emphasis on these two important modern medical ideals varies from medical school to medical school, and within different subjects even in the same medical school. As a result of their training and of other determining influences, most doctors make a strong and wholehearted commitment to one or the other of these two ideals. For them, there is no experienced conflict between them. But for other physicians, even while they have in fact committed themselves primarily to therapy or to medical science, there remains some ambivalence, some wish to fulfill both the ideal of therapy and the ideal of contributing to medical knowledge.

To doctors in clinical practice who feel this ambivalence, the increasing and widely-offered opportunities by drug companies to participate in the clinical testing of new drugs provide a way of resolving their conflict. With a little bit of effort, such doctors are told and

come to feel, they can remain therapists and still be medical scientists, perhaps even get the satisfaction and prestige that comes from having a small paper published in a local medical journal. In some measure this mode of resolving the conflict between the therapeutic and scientific ideals is effective. Some useful clinical testing of drugs is carried out by doctors who are primarily engaged in clinical practice. But apparently much of this testing is futile, or even worse insofar as it gives a false or inadequate warranty of drug effectiveness. Most doctors in clinical practice, despite their scientific ideals, do not have the knowledge or facilities to carry out the testing of drugs under what are minimum standards of sampling, double-blindness, and the determination of effects. It is hard enough to meet necessary standards of testing even where there are large and specialized personnel resources. Untrained doctors in clinical practice, or those without the facilities to meet the necessary standards of scientific testing, should not be encouraged by the drug companies to participate in clinical testing. It is only harmful to play in this way upon the conflict such doctors feel about therapy and medical science.

Fortunately, the Food and Drug Administration has increasingly been making it harder for doctors in individual clinical practice, who do not have the required competence or facilities to do testing, through its insistence on higher standards of scientific ability and adequate testing facilities. More and more, testing is being limited to the larger clinical and research organizations which can meet these higher standards.

The problem of uncertainty and lack of control. In the use of drugs, as in so much else of medical practice, the doctor is constantly faced in the therapeutic situation with the problem of uncertainty and lack of control in both diagnosis and treatment. "Unfortunately," says Modell, in his summary statement about the use of drugs, "statistical expressions of toxicity and safety with drugs do not necessarily apply to the individual. He may deviate markedly from the average patient. For him only careful observation will supply the necessary safeguards against serious reaction."[1]

In a systematic discussion of the patterned limitations on toxicity

[1] Walter Modell, "Principles of Choice of Drugs and the Applications of Clinical Pharmacology," in Walter Modell, editor, *Drugs of Choice, 1964–1965*. St. Louis: C. V. Mosby, 1964, p. 26.

tests for drugs, Brodie and his colleagues have classified eight major patterns of such limitations, and several sub-patterns.[2] The eight major patterns concern such matters as the following: predictability of data from animals to man, excessive action on physiological control systems, processes affecting intensity and duration of drug response, individual variations in drug metabolism in man, enzyme stimulation and inhibition, drugs in combination, structural or biochemical changes, and effects of enzyme induction. In recognition of these patterns, they express the following typical cautions:

> Our modern system of drug development, therefore, depends on the assumption of a high degree of correlation between effects in animals and man. That such predictions are often unreliable raises serious questions regarding these tests. . . .
>
> . . . variation in drug metabolism within and between species is now known to be the rule rather than the exception. . . .
>
> . . . profound differences are found in pathways and rates of drug inactivation among various species and individuals, including man.
>
> A common cause of toxic reactions arises from "overdosage" because of person-to-person variability in rates of drug metabolism; the same daily dose of a drug may cure, may cause severe toxicity, or have no effect whatsoever.
>
> The increasing use of two drugs together can produce undesirable effects which are sometimes predictable, but often are not. . . .[3]

The uncertainty and lack of control present in clinical practice have been interestingly revealed in a little study which one practitioner made of his prescribing patterns. We do not know how representative Dr. Eimerl's data are, but his investigation could easily be replicated with representative samples of the physician and patient populations. Dr. Eimerl kept a record of his prescriptions for a period of four weeks. For each prescription he made an estimation of his therapeutic intent. And in our terms, "intent" varied clearly on the two dimensions of certainty and degree of control. His five categories of prescribing intent (with examples) are as follows: specific (insulin in diabetes), probable (antibiotics in infections), possible (corticosteroids in bronchial asthma), hopeful (mixed corticosteroids and tranquillizers), and

[2] Bernard B. Brodie, George J. Cosmides, and David P. Rall, "Toxicology and the Biomedical Sciences," *Science,* 148(1965), pp. 1544–1547.

[3] *Ibid.*

placebo (any preparation given with the intention of relieving mental stress and which the prescriber believes possesses minimal pharmacological activity).[4] The results are shown in the accompanying table:

Intention	*Number*	*Percentage*
Specific	44	7.55
Probable	87	15.03
Possible	149	25.69
Hopeful	124	21.38
Placebo	176	30.35
Total	580	100.00

If we take the middle categories to express uncertainty in diagnosis and treatment, and the placebo category to indicate minimal control, then it is clear that the physician is constantly facing these two conditions in his use of therapeutic drugs.

As a specific example of a whole class of drugs which present the clinical practitioner with the problem of uncertainty and lack of control, we may take the psychoactive drugs, where both the number and variety of new developments have been very large during the last ten to fifteen years. Two different authoritative statements concur in the confusing and unreliable character of these drugs in medical practice. "Problems about the modes of action and possible usage of psychoactive drugs," say John Pollard and Cornelis Bakker, "are extremely complicated. The study of these problems has met with difficulties that go far beyond those for any other types of pharmaceuticals. This is apparent from the thousands of papers that have been published on the action of only a limited number of such compounds with relatively little substantial increase in our understanding of their action upon which the clinician can depend when prescribing them. He still has to rely on rather vague hunches, and most of the time he is in the process of learning by trial and error."[5] And Dr. Jonathan Cole, who is Chief of the Psychopharmacology Service Center, National Institute of Mental Health, says, "Physicians now have an extensive experience in using

[4] T. S. Eimerl, "The Pattern of Prescribing," *College of General Practitioners Journal,* 5(1962), pp. 468–479.

[5] John C. Pollard and Cornelis Bakker, "What Does the Clinician Want to Know about Psychoactive Drugs?" in Leonard Uhr and James G. Miller, editors, *Drugs and Behavior,* New York: John Wiley and Sons, 1960, p. 199.

these drugs to control behavior, and I think most physicians would agree that the reliability with which existing drugs control specific behaviors leaves much to be desired."[6] Cole points out that psychoactive drugs "produce startling improvements" in a minority of patients, leave a much larger proportion of treated patients only either moderately or slightly improved, and do not improve at all, or make worse, something like 20 or 30 per cent of treated patients. What is additionally important for the uncertainty and lack of control this means for the clinical practitioner, he says, is that, "To date, clinicians have been notably unsuccessful in predicting which patients will respond in which ways."[7]

There are two patterned ways in which the doctor in clinical practice seems to respond to the problem of uncertainty and lack of control. Since he is under pressure to do something, under pressure from his own wish to be helpful and from the patient's appeal for help, he can either use a drug which he knows to be useful in some cases and hopes will be helpful in this one, or he can prescribe a placebo, that is, a drug which at the most has such minimal activity that it cannot do any harm, and may help by its psychological effect on the patient. The first pattern results in the overuse or abuse of some drug or class of drugs. The most recent example of this pattern, probably, was the overuse and abuse of the antibiotics during the 1950's, an overuse which has been diminished more recently by the widespread awareness of its harmful consequences. For a while, in the 1950's, many doctors were prescribing antibiotics for every cold and fever, and without concern for the immediate and long-run harmful effects.[8] As overuse reduced the indi-

[6] Jonathan O. Cole, "Drugs and Control of the Mind," in Seymour M. Farber and Roger H. L. Wilson, editors, *Control of the Mind,* New York: McGraw-Hill Book Co., 1961.

[7] Techniques and experiments for making such predictions somewhat more successful are described in James C. Klett and Edward C. Mosely, "The Right Drug for the Right Patient," *Journal of Consulting Psychology,* 1965.

[8] See Osler L. Peterson, Leon P. Andrews, Robert S. Spain, and Bernard Greenberg, "An Analytical Study of North Carolina General Practice, 1953–1954," *Journal of Medical Education,* 31(1956); H. Welch, C. N. Lewis, H. I. Weinstein, and B. B. Boeckman, "Severe Reactions to Antibiotics: A Nationwide Survey," *Antibiotic Medicine,* 4(1957), pp. 800–813; E. A. Reimann, "Infectious Diseases: Annual Review of Significant Publications," *Archives of Internal Medicine,* 102 (1958), pp. 217–253; John Lear, "Taking the Miracle Out of Miracle Drugs," *The Saturday Review,* January 3, 1959, pp. 135–141.

vidual's resistance to certain kinds of infections, and as it resulted in epidemics of infections in hospitals, doctors abandoned this way of "doing something" in situations of uncertainty and lack of control.

A less harmful pattern in response to these situations is the use of placebo drugs, a pattern which relies on the ancient medical maxim, "do no harm," and on the hope of spontaneous recovery, or *vis medicatrix naturae*. So widely used is placebo treatment with drugs that Modell, in a comprehensive and authoritative statement, calls it "the ubiquitous medicament."[9] "Many patients," he says, "will have negative reactions to their visit to the physician if they do not come away with a prescription for medication. Such patients require and benefit from placebo." Of course, "placebo should never be a substitute for rational medication and well-considered therapy." But, because of the uses it has in situations of uncertainty and lack of control, Modell concludes, "when the physician uses the placebo expertly, he will also be an accomplished and perceptive therapeutist, for he will be exploiting the only *universal medicament.*" Placebo drugs are, as Modell calls them, with emphasis, the "universal medicament" only because uncertainty and lack of control are universal in medical practice.[10]

The problem of risk and legal responsibility. Uncertainty and lack of control in medical practice help to engender another problem for the doctor; whenever he takes action, he accepts the risk of doing harm as well as good. Therapeutic action with drugs is very much a case in point. It is "a paradox," says Lasagna, that "the drug industry generates certain anxieties in physicians in direct proportion to the rate at which it introduces new drugs on the market. Such anxieties do not require that these drugs be worthless or 'me-too' products; indeed I would suspect that the greatest unrest would derive from the marketing of large numbers of unique and excellent drugs!"[11]

[9] Modell, *op. cit.*, pp. 36ff. Note the excellent bibliography on placebo that Modell appends to his remarks.

[10] For a statement of the arguments against the use of placebo drugs, see R. P. C. Handfield-Jones, "Bottle of Medicine from the Doctor," *Lancet*, 1953, pp. 824–825. For an empirical study of how an organized group of clinical physicians modify their evaluations of one another's competence because of their recognition of the omnipresence and persistence of uncertainty and lack of control in treatment, see Eliot Freidson and Buford Rhea, "Knowledge and Judgments in Professional Evaluations," *Administrative Science Quarterly*, 10(1965), pp. 107–124.

[11] Louis Lasagna, "Problems of Drug Development," *Science*, 145(1964), pp. 362–367.

Even good drugs cause anxiety because no one of them eliminates risk, and the large and increasing number of them seems to multiply occasions for risk. After describing the various modes of testing drugs before clinical use, Gaddum says, "In all these ways it is possible to reduce the risk that new drugs will produce unexpected effects when they are first put on the market, but it is probably impossible to eliminate it completely."[12] Hill points out that "No one of the enormously beneficial treatments that have revolutionized therapeutics over the last 20 years is free of undesired side-effects or without any hazard to the patient."[13] In their article in Modell's *Drugs of Choice,* Norman and Cluff say, "Untoward reactions to drugs are increasing in frequency and importance as indicated by the number of recent articles, reviews, and books on the subject. The increased frequency of adverse drug reactions undoubtedly is attributable in large part to the voluminous number of drugs administered by physicians. . . . The information required to assess accurately the magnitude of the problem is unavailable."[14] Of course, some of the increase in adverse drug reactions may be due to greater awareness of their likelihood and to improved techniques of diagnosis rather than to an actual net change in their number. Finally, summing up the discussion at an authoritative conference on drugs, Talalay says, "The participants emphasized that the medical profession and the general public are only now becoming fully aware of the magnitude of the hazards accompanying the use of the many new and powerful drugs which are basic to modern therapy. Undesired and often unexpected effects caused by the use of drugs . . . have been termed 'diseases of medical progress' and make up an increasing proportion of the problems encountered by hospitalized patients."[15] Talalay reports that a study by Schimmel at the University Medical Service at Yale in 1960 and 1961 "showed that the hospital stay of every fifth patient . . . was complicated by such 'diseases of medical progress' and that more than half of these resulted from adverse reactions to

[12] J. H. Gaddum, "A Perspective on Pharmacology," in Paul Talalay, editor, *Drugs in Our Society,* Baltimore: The Johns Hopkins Press, 1964, pp. 17–26.

[13] Austin Bradford Hill, "Medical Ethics and Controlled Trials," *British Medical Journal,* 1(1963), pp. 1043–1049.

[14] Philip S. Norman and Leighton E. Cluff, "Adverse Drug Reactions and Alternative Drugs of Choice," in Modell, *op. cit.,* pp. 50–65.

[15] Paul Talalay, "A Summary of Comments by the Editor," in Talalay, *op. cit.,* p. 280.

drugs." In part, Schimmel suggested, these adverse drug reactions are the result of the cumulative risk that is caused by the administration of several drugs to the same patient. When several drugs, each with an incidence of unfavorable side effects on only .1 per cent, are taken together, they can combine to cause a 20 per cent chance that a patient will have adverse complications. And a recent study at the Johns Hopkins Hospital, according to Schimmel, demonstrates how common the practice of multiple drug treatment has become. A study of all hospitalized patients receiving methicillin during one two-month period revealed that they had all received at least seven other drugs and that one patient had received thirty-five different drugs during the hospital stay.

Even patients have now become more aware of the risk that they and their doctors face when they take drugs. According to the Executive Director of the American Pharmaceutical Association, pharmacists report that a "drug-safety uncertainty" syndrome has developed among their customers.[16] "Patients are asking pharmacists," he says, "to assure them that the drugs which have been prescribed for them are 100 per cent 'safe.' This represents a marked change from a few decades ago when the public sought assurance from the pharmacist that a drug was 100 per cent 'effective.' "[17] Fortunately, as the public has become more concerned with safety, the Food and Drug Administration, which formerly monitored safety alone, has recently become almost equally concerned for the effectiveness of drugs, under the new duties and powers in this regard prescribed for it by the 1962 Amendments to the Food, Drug, and Cosmetic Act. With its action against antibiotic throat lozenges in 1966 for their lack of proof of effectiveness, the FDA opened up what will be a broad and long campaign against unsupported claims to effectiveness in drugs.

In the face of the risk that they and their patients run with drug treatment, medical doctors have sought some safeguards, some way of

[16] William S. Apple, American Pharmaceutical Association statement before the House Subcommittee on Intergovernmental Relations, March 25, 1964, *Journal of the American Pharmaceutical Association,* NS4 (1964), pp. 212–216.

[17] The same point has been made by Harry E. Tebrock, "The Role of Home Medication in the Practice of Occupational Medicine," in *Annals of The New York Academy of Sciences, Home Medication and the Public Welfare, V*ol. 120 (1965), Art. 2, pp. 807–1024.

diminishing their risks. One of these is a book entitled *Diseases of Medical Progress,* which offers itself as "a ready reference for the physician who intends to use a drug for the first time."[18] The editor of this collection of warnings by various specialists says, "One would like to think that (it) will find its way to the desk of every physician, and that each will study the pertinent section before initiating, in any one of his patients, a therapeutic measure of whose dangerous potentialities he may not be fully aware." Some fourteen different classes of diseases of medical progress are covered in this collection.

Another safeguard consists of various mechanisms for collecting information about the incidence of drug-induced adverse reactions and of reporting this information to doctors in clinical practice. Individual drug manufacturers perform this service to some extent, and there is now available to doctors in practice a standard report form from the Adverse Reactions Section of the American Medical Association's Council on Drugs.[19] But since much of medical practice now centers on the hospital, it seems desirable to some doctors that the hospital should be the essential collecting and reporting agency. "The time has come," says Wintrobe, "when hospitals should be expected and required to record all adverse drug reactions."[20] Some time ago, he says, "it became an acceptable conclusion that hospitals in the United States in order to become accredited by the Joint Commission on Accreditation of Hospitals, would be expected to keep records of postoperative infections and other complications, to subject to scrutiny tissues removed surgically, and to carry out autopsies in a substantial proportion of hospital deaths." Adverse Reaction Committees in all hospitals would be the functional counterpart of these earlier safeguards, the Tissue Committee and the autopsy. Hospital Committees could report to some central collecting and reporting agency, either in the A.M.A. or in the government.

Progress is being made in the establishment of such Adverse

[18] Robert H. Moser, editor, *Diseases of Medical Progress,* Springfield, Ill.: Charles C. Thomas, 1964.

[19] *Journal of the American Medical Association,* 188(1964), pp. 603–604, for a description of this new monitoring program.

[20] Maxwell M. Wintrobe, "The Therapeutic Millennium and Its Price: Adverse Reactions to Drugs," in Talalay, *op. cit.,* pp. 111ff.

Reaction Committees in hospitals. Such progress is often stimulated by the inadequacy of the first efforts made. At the Johns Hopkins Medical Institutions, for example, "a preliminary survey indicated that methods used in earlier years for the epidemiological surveillance of hospital-acquired infections proved inadequate for collecting information on drug reactions. A sample review of patient records revealed that less than one of every five adverse reactions was reported and that adverse drug reactions of varying severity were occurring with considerable frequency."[21] As a result, a new system has been set up, under the direction of Dr. L. E. Cluff, with the cooperation of the Hospital Committee on Pharmacy and Therapeutics. This new system depends for its comprehensiveness and accuracy on the use of a computer that began to be used in 1963 for auditing charges for drugs administered to patients. The computer makes it possible to analyze drug usage by services and wards; to detect "drug fads and indiscriminate drug usage"; to get systematic data on "attack rates" of adverse reactions; and to describe the particular populations of patients susceptible to different kinds of drug reactions. Where long-delayed reactions are involved, the computer provides retrospective identification of all patients who have received the dangerous drug. The computer is now programmed to furnish epidemiological information on the use of sixty drugs which either are in widespread use or result in a high incidence of adverse reactions. Each month, in a drug letter, the new Johns Hopkins system reports the findings of the computer data on "significant and interesting reactions." Not all hospitals will have available or could use a system of this kind based on a computer. But it is obvious that the systematic collection and analysis of adverse drug reactions, with whatever means are suitable, are necessary to increase the clinical practitioner's knowledge in this area and cut down the risk he encounters in using therapeutic drugs.

In recent years there has been a considerable increase in malpractice suits, that is, suits holding doctors responsible for adverse effects alleged to be the result of their negligence. Many of these suits have been brought in connection with drug treatments. Individual clinical practitioners have much more often been the defendants in these suits than clinical laboratories, which have few direct patient contacts, or

[21] Talalay, *op. cit.*, pp. 281ff.

clinical investigation groups.[22] As a result, to cover themselves against this risk, individual medical practitioners now carry large malpractice insurance. According to Justice Schaefer, Supreme Court of Illinois, in an authoritative discussion of the legal responsibilities of physicians, until 1950 prescribers of drugs were subject to various provisions of tort and contract liability in the common law tradition, but the extent of this liability was not very great.[23] Since 1950, however, "courts across the country" have begun to evolve "a doctrine of strict liability." Under this stricter doctrine, "with regard to drugs that may be dispensed only upon prescription, recent cases indicate that the duty to warn of potential danger runs primarily to the doctor," assuming, of course, that he has been adequately informed of the danger by the manufacturing firm. If not, then the liability is theirs. Unfortunately for the practicing physician, the courts have not made it clear just what such warnings of potential danger should consist of. Nor have they made it clear just what they mean by "informed consent" when they hold that a doctor must have the "informed consent" of the patient who has been told that there is some potential danger in the drug treatment he is about to receive.[24] It is clear that legal decision and legal doctrine about the responsibility of the doctor for adverse drug and other reactions are in process of change. The doctor in clinical practice can diminish his financial risk with malpractice insurance, but the professional and moral risk remains. Better knowledge about the causes of adverse drug reactions would clarify the whole problem of responsibility and diminish this aspect of the doctor's professional and financial risk.[25]

[22] Don Harper Mills, "Malpractice and the Clinical Laboratory," *Science,* 144 (1944), pp. 638–642.

[23] Walter V. Schaefer, "Drugs and the Common Law," in Talalay, *op. cit.,* pp. 234ff.

[24] On "informed consent," see Patricia Hatry, "The Physician's Legal Responsibility in Clinical Testing of New Drugs," *Clinical Pharmacology and Therapeutics,* 4(1963), pp. 4–9, and Ovid C. Lewis, "Restrictions On The Use of Drugs, Animals, And Persons in Research," unpublished paper given at the Conference on Science and the Social Role of Law, The Rockefeller University, April, 1965.

[25] See Kenneth B. Haas, "The Veterinarian and the Law," *Veterinary Medicine,* 57(1962), series of four articles, pp. 63–64; 165–167; 254–256; 349–350, for a discussion of the risk and responsibility that veterinarians encounter as a result of their use of drug therapy with animals.

CLINICAL INVESTIGATORS

Clinical investigators are the medical doctors who do research, part- or full-time, either on sick people, that is, patients in clinics or hospitals, or on well people who volunteer as research subjects. At least two problems arise in connection with clinical investigation. One is the problem of the relations between the clinical investigator and the commercial drug firms which provide some part of his research support. The second is the problem of the ethical and legal responsibility of the clinical investigator for his experimentation on human beings.

Relations with commercial drug firms. Clinical investigators and commercial drug firms have a considerable degree of dependence on one another. The clinical investigator needs the "interesting" or potentially useful drugs developed by the research departments of the commercial drug firms and he needs the funds and fees the firms are willing to provide him for the facilities and services used in testing these drugs. The firms, in turn, need the medical research skills of the clinical investigator and his legitimate access to human subjects on whom the drugs can be appropriately tested. Their own research departments have access only to animals for testing purposes. This interdependence has resulted in relationships which are of great mutual benefit, and of benefit as well, often, to the larger society; but there are also strains in the relationship. The drug houses, says Lasagna, not only want their drugs to be proved effective but want them proved so in the speediest possible clinical trials. "The scene is therefore set," he says, "for pressure—conscious or unconscious, direct or indirect, subtle or flagrant—on the investigator of new drugs to come up with the 'right answer' in a hurry. . . . Pressure can also arise in regard to recording results for publication. . . . For example, one well-known research group experienced two remarkably frontal attacks on published data and material presented before scientific meetings. In both cases, attempts were made to change the tone or content of the papers to be published so as to present a picture of the drug in question which would be more favorable, even if untrue. In both instances, the pressure had no effect, but one wonders how often investigators have their papers 'rewritten' by drug-house personnel, particularly when the investigator is under obligation to the firm for past or future financial support."[26]

[26] Louis Lasagna, *The Doctors' Dilemmas*, New York: Harper & Bros., 1962, pp. 144ff. See also Morton Mintz, *The Therapeutic Nightmare*, Boston: Houghton Mifflin Company, 1965, Ch. 14.

In addition to these possible pressures for distortion of results and for dangerous speed, the clinical investigator resents the pressure from the commercial drug firm that keeps him working on particular and limited projects, testing particular and sometimes unrelated drugs. The clinical investigator wishes to establish a research team which works on fundamental problems rather than particular projects. "To do this efficiently," says Lasagna, "he prefers smaller amounts of steady support to larger grants appearing erratically. He also wants to be able to pursue an exciting lead, even one without obvious commercial implications, if it arises in the course of clinical research; and he is naturally disappointed if a drug house withdraws support at this stage of an investigation. But most firms continue doggedly to prefer a *quid pro quo* type of operation." Some of the drug firms do in fact provide some relatively "free" and general funds for fundamental research to certain investigators, but the firms, of course, have no way around the necessity for having their specific drugs tested. They cannot avoid requiring a certain amount of project research. They are in business, ultimately, to make profits, not to provide unlimited support for "free" research, however fundamental.[27] That is the business of the universities, of non-profit foundations, and of the government. The clinical investigator who does not appreciate the constraints put upon the commercial drug firm by its own ultimate interest in profits is likely to create conflict out of the strain that exists between this interest and his own, conflict instead of a mutually beneficial resolution of the strain through the giving and receiving of a mixture of general and project funds.

In sum, the relations between clinical investigators and commercial drug firms are relatively new, still unsettled, of obvious mutual benefit, but not without their structured strains. It would be useful to go beyond anecdote and speculation in our knowledge of these important relations. Social science research in this area could yield the kind of knowledge necessary for increasing the effectiveness of these relations to both partners and to the larger society which benefits so much, indirectly.

Ethical and legal responsibility for experimentation on human

[27] Bernard Barber, "Is American Business Becoming Professionalized? Analysis of a Social Ideology," in E. A. Tiryakian, editor, *Sociocultural Theory, Values, and Sociocultural Change: Essays in Honor of Pitirim A. Sorokin,* New York: The Free Press of Glencoe, 1963, pp. 121–145.

beings. From the earliest times, medical therapy has always in some measure verged on experimentation, that is, the deliberate trial of unproved and risky procedures and substances. And probably there has always been some concern among both practitioners and laymen about the ethics of such experimentation, about its justification both in general and in any particular case. Recently, however, such concern has increased greatly. First of all, this concern has been increased because of the flagrant violations of the ethics of human experimentation committed by the Nazi doctors. And second, the increase, and perhaps accelerating increase, in the amount of experimentation on human beings has enlarged the concern about the moral risks involved. Unfortunately, although there seems to be a consensus about the increase in the amount of human experimentation, there are no useful statistics on the matter.[28] Finally, concern has been increased because it is now seen that a great deal of experimentation on human beings is inevitable for scientific and medical progress. As Dr. Henry Beecher, who has made this subject one of his primary concerns, says, "Although prior experimentation in animals is absolutely necessary when possible, the crucial study of new techniques and agents must be carried out in man. . . . Man as the final test site has come into prominence only in recent decades. The current development of human biochemistry, human physiology, and human pharmacology has made it plain that man is the 'animal of necessity' here."[29]

Evidence for the increased concern with the ethics of human experimentation can be found in the recent appearance of a whole anthology of writings on the subject, an anthology which also includes a very extensive and comprehensive bibliography.[30] Judging by the anthology, this is still a field where practically no social science research

[28] Renée C. Fox, "Some Social and Cultural Factors in American Society Conducive to Medical Research on Human Subjects," *Clinical Pharmacology and Therapeutics,* 1(1960), pp. 423–443.

[29] Henry K. Beecher, "Experimentation in Man," *Journal of the American Medical Association,* 169(1959), pp. 461–478.

[30] Irving Ladimer and Roger W. Newman, editors, *Clinical Investigation in Medicine: Legal, Ethical, and Moral Aspects: An Anthology and Bibliography,* Boston: Boston University, Law-Medicine Research Institute, 1963. See also Lewis, *op. cit.* And on behavioral research, see Oscar M. Ruebhausen and Orville G. Brim, Jr., "Privacy and Behavioral Research," *Columbia Law Review,* 65 (1965), pp. 1184–1211.

has been carried out. There is much wisdom in this collection of articles, the wisdom that comes from long and reflected-upon experience with research on human beings and with the problems such research involves. The articles by lawyers are in the solid tradition of legal scholarship, seeking out precedents, making analogies, and the like, but again, there is practically no research reported. Research is very much needed here.

For a very long time in medical history, the Hippocratic Oath was the primary code for the ethics of experimentation on humans, as it was for all other ethical problems in medicine. In the nineteenth century, with the beginnings of scientific medicine, many new codes and statements referring to this subject were produced. The first general codification of medical ethics in the United States was written by the American Medical Association in 1848; this was patterned on an English code, Sir Thomas Percival's *Medical Ethics* of 1803. One of the classic statements on human experimentation, still very frequently referred to, is in Claude Bernard's *Introduction to the Study of Experimental Medicine,* 1865, thus making this great work a very important moral as well as scientific and methodological treatise.

As a result of the Nazi medical atrocities on involuntary human subjects, a whole set of codes specifically on the ethics of experimentation on humans has been written since World War II. The most important of these is the Nuremberg Code, on which many of the other codes are based. In addition, codes have been formulated by the United Nations; the World Medical Association, in two versions; the United States Public Health Service, for its Clinical Centers for Medical Research at the National Institutes of Health; the French National Academy of Medicine; the American Medical Association; and various British medical groups.[31]

In contrast to the willingness of these large social and medical organizations to formulate codes is the reluctance of individual medical schools to do so. One doctor, "being unable either to define a code or to accept one that was already available," decided to consult with other American clinical investigators.[32] He wrote to every university medical

[31] Beecher, *op. cit.*

[32] Louis G. Welt, "Reflections on the Problems of Human Experimentation," *Connecticut Medicine,* 25(1961), pp. 75–78. Reprinted in Ladimer and Newman, *op. cit.*

school in the country, asking if they had "a procedural document dealing with problems of human experimentation," as well as other questions relating to this problem. Responses were received from sixty-six schools, and of these only eight said they had such a documentary code. The reasons for this reluctance to have a detailed documentary code will perhaps become clear when we discuss some of the difficult problems of applying the very general statements which the existing codes include.

Here are the ten principles of the Nuremberg Code for medical research involving human subjects:

1. The voluntary consent of the human subject is absolutely essential.
2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
3. The experiment should be designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problems under study so that the anticipated results will justify the performance of the experiment.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an *a priori* reason to believe that death or disabling injury may occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
8. The experiment should be conducted only by scientifically qualified persons.
9. During the course of the experiment, the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him impossible.
10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has

> probable cause to believe, in the exercise of the good faith, superior skill, and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.[33]

These ten principles of the Nuremberg Code, which are representative of the essential prescriptions contained in other codes formulated in the last twenty years, are of undoubted assistance to the clinical investigator looking for guidance on the ethics of experimentation using human beings. Yet there remain some difficult problems in the application of these principles to the actual, work-a-day experience of the investigator; he gets some help, but he feels he needs more. What are some of these problems of application of ethical codes?

The basic, and most comprehensive problem, the one cutting across all others, perhaps, is the difficulty which seems to exist for codes of ethics in all branches of human behavior, applying very general norms to very particular cases. Commenting on Claude Bernard's very noble but very general maxim of 1865, "Christian morals forbid only one thing, doing ill to one's neighbor," Dr. Henry Beecher remarks, "Unfortunately, decision is usually not so simple as this sounds; choice often lies among various shades of gray, not between black and white."[34] And speaking more directly to more recent codes, Beecher says, "In most cases the problems of human experimentation do not lend themselves to a series of rigid rules. Although one purpose of the present study is to set down views, concepts, and even 'rules' that have been accepted by one group or another, this is done so that the investigator, troubled by a given problem, can find . . . a framework against which he can measure his problems in terms of the experiences and conclusions of others in similar situations."

Beecher's views are widely shared among clinical investigators. Summing up the views of those attending a conference on drug use and drug testing, Talalay says, "Although codes of ethics for therapeutic trial in man are relatively easy to state, their translation to prac-

[33] George F. Archambault, "A Drug Moves into Human Trials," *Journal of the American Pharmaceutical Association*, NS3 (1963), pp. 124–127, 136–137.

[34] *Op. cit.*

tice was regarded as frequently much more difficult."[35] And the reluctance of the clinical investigators in America's medical schools to formulate general procedural documents for governing experimentation with humans, as reported in Welt's study, seems to have been due to their feeling that only the individual could be ultimately responsible for the application of general norms to particular cases.[36] "Documents and codes," says Welt, "cannot substitute for the integrity of the individual investigator. Ultimately the answer to these problems lies in the possession by those in responsible positions of the qualities of integrity, understanding, a respect for the dignity of one's fellow man, accompanied by an intelligent curiosity and the ability to design safe and critical experiments." Lasagna reports that when the members of the French Academy of Political and Moral Sciences discussed a code of ethics for human experimentation they felt that "the responsible, experienced, prudent scientist—who is the only type of experimentalist to be tolerated—will draw his own limit."[37] And this view, says Lasagna, "is one that is certainly close to the heart of many scientists."

Yet this view of how to apply general norms to particular cases gives too much discretion and responsibility to the lone scientist. In practice, even where the individual is "ultimately" responsible, he apparently consults informally with his peers, or may even be required by the institution in which he works to consult with them formally, by getting the advice and approval of a review committee for all experiments on human beings. Although only eight of the sixty-six medical schools that replied to Welt's questions said they had a general procedural document governing such matters, twenty-four of them said they either had or favored having a committee to review problems in human experimentation.[38] While no committee, they felt, can take final responsibility from the individual investigator, "careful and responsible review by a committee of peers" can provide "more certain assurances of safety." Beecher goes beyond Welt's respondents on the functions of a committee. "Whenever even remote hazard is a possibility," he

[35] *Op. cit.*, p. 278.

[36] *Op. cit.*, pp. 75–78.

[37] Louis Lasagna, *The Doctors' Dilemmas*, p. 199.

[38] *Op. cit.*

says, "group decision supported by a proper consultative body should be employed."[39] Speaking from his experience and scholarship in the field of law, though not to the point of how much responsibility a review group ought to take, Cahn emphasizes the essential importance of the group of peers in participating in the decision-process, "Since the moral problems attached to experiment on human beings arise in highly specific and variable circumstances, the investigator will rarely find an easy formulary answer. Experience has shown the wisdom of consulting a group or panel of colleagues, who may not only assist in structuring the experiment but also influence its developing course. None of us can claim impartiality in his own enterprises; we all do well to seek detached, objective, and disinterested judgment. Merely as a matter of self-protection, the investigator ought regularly to seek outside counsel."[40]

Somehow, then, by individual and by group processes, the problem of how general values about the ethics of human experimentation should be specified in particular norms for particular cases is being constantly resolved. For several reasons this area should be attractive for research. First, we might learn more about the general processes by which systems of norms are constructed for human behavior. Second, we might understand better the overlapping relationships of quasi-private, quasi-public normative codes. And, third, in a society where claims to professional autonomy are increasing, we might learn more about the formation of those professional codes which are of such great consequence to the publics whom the professions aspire to serve.

A second problem in the application of the principles of ethical codes about experimentation on humans to actual experience arises in connection with the principle of voluntary consent, which is considered so important a principle that it is usually placed first in the list of ethical imperatives.[41] The problem here is to define satisfactorily what constitutes "voluntary consent," or, as it is sometimes even more restrictively

[39] *Op. cit.*

[40] Edmond Cahn, "Drug Experiments and the Public Conscience," in Talalay, *op. cit.*, p. 265.

[41] See Hatry, *op. cit.*, pp. 4–9; Lewis, *op. cit.;* and Ruebhausen and Brim, Jr., *op. cit.*

described, "voluntary and informed consent." The social and psychological distinction between "voluntary" and "coerced" behavior may be hard to make. For example, one doctor asserts that charity patients who are asked to give permission for the use of experimental drugs before they are admitted to the hospital are, in effect, coerced because they think they will not otherwise get the care to which they are entitled.[42] Are the laboratory assistants and students whom the clinical investigator often uses in his experiments true volunteers or a "captive population"? Members of religious groups (Quakers, Mennonites, Assembly of God believers, Church of the Brethren members) who make a religious principle of letting themselves be used for medical research seem to be true volunteers, but what about federal prisoners who are trading risk for remission of time?[43] How voluntary is the consent given by those who are partially incompetent because of age or illness?

And what about consent which is voluntary but not "informed" as to the risks involved? "Lay subjects," says Beecher, "sick or well, are not likely to understand the full implications of complicated procedures even after careful explanation."[44] In a recent speech at a symposium on clinical research sponsored by the Upjohn Company, Beecher gave new and more urgent expression to his fears about the prevalence of unethical behavior among those who engage in clinical experimentation. He cited twenty examples of clinical experiments from the immediate past that he thought were ethically questionable. Not all of these involved drugs.[45] Most patients, Beecher feels, and many doctors agree with him, "will consent to any proposal that is made." And finally, when is it ethical to proceed without the consent of the patient because giving him information will cause him unnecessary anxiety or will spoil the design of the experiment?

In a recent legal decision, the Appellate Division of the New York State Supreme Court held that doctors who injected live cancer cells into patients were not required to get the consent of the patients because

[42] Theodore Greiner, "The Ethics of Drug Research on Human Subjects," *Journal of New Drugs*, 2(1962), pp. 7–22.

[43] Fox, *op. cit.*

[44] Beecher, *op. cit.*

[45] For a report on his speech, see *The New York Times*, March 23, 1965. The speech has recently been published in *The New England Journal of Medicine*, 274 (1966), pp. 1354–1360.

this injection "was not a cause of increased risk to the patient" and knowledge of the procedure would only have caused him unnecessary anxiety.[46] But just the opposite view of the matter in this case was asserted by a special committee on discipline of the New York State Board of Regents, which has jurisdiction over the behavior of all the licensed professions in New York State, excluding the legal profession. After a lengthy and careful investigation of the facts in the case, the Regents adopted the recommendation of its sub-committee and held the two doctors involved in the experimentation guilty of "unprofessional conduct" and of "fraud and deceit in the practice of medicine." Their licenses were suspended for one year, but execution of this sentence was stayed; the doctors were put on probation for one year and allowed to practice during that time. The Regents found that the patients involved in this case were not clearly informed either that the experimental procedure was a research project unrelated to the medical treatment of their own conditions, nor that the substance to be injected was live cancer cells. Two important principles were stated by the Regents. "A patient," they said, first, "has the right to know he is being asked to volunteer and to refuse to participate in an experiment for any reason, intelligent or otherwise, well-informed or prejudiced. A physician has no right to withhold from a prospective volunteer any fact which he knows may influence the decision." In short, the patient's right to be "emotional" or "irrational" about live cancer cells or any other substance cannot be taken away from him by the experimenting physician. And, second, the Regents stated that the physician, when he is acting as experimenter, has no claim on those rights of the doctor-patient relationship which do permit him, in a therapeutic situation, to withhold information when he judges it to be in the best interest of the patient.

The Regents made it explicit that they knew the penalties imposed on the doctor-experimenters in this case were severe. But, they said, "We trust that this measure of discipline will serve as a stern warning that zeal for research must not be carried to the point where it violates the basic rights and immunities of a person." How these two principles so clearly stated by the Regents will affect legal decisions in New York State and legal and administrative decisions in other jurisdictions is yet to be seen. Very likely, however, the Regents' findings and

[46] *The New York Times,* July 8, 1964.

the penalty imposed will not only be taken into account in legal and administrative circles but will lead everywhere to much greater self-scrutiny and self-control among researchers using human subjects.[47]

Clearly there is a need for a great deal of research on the actual social and psychological meanings of "voluntary and informed consent" to clinical investigators and their human subjects. In the absence of the knowledge such research would produce, clinical investigators are perhaps unnecessarily fearful of the restrictions which might be placed on their work by more explicit procedures for dealing with this problem. One of the innovations of the Kefauver-Harris Bill of 1962 was to make explicit the requirement that clinical investigators in their tests of drugs get the consent of the patient. The Drug Amendments of 1962 require "that experts using such drugs for investigational purposes certify . . . that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings."[48]

Despite the fact that the qualification stated at the end of this rule apparently gave the clinical investigator more freedom with regard to "voluntary and informed consent" than he had had under previous common law principles of tort liability, many clinical investigators have expressed alarm that the Food and Drug Administration, which enforces this rule, will place great restrictions on their research. "Several participants" in a recent drug conference, says Talalay, "expressed concern that the attention which the new regulation focuses on consent will increase the legal jeopardy of the investigator."[49] Such fears on the part of clinical investigators, and different fears among the patients who are potential or actual subjects for experimentation, will continue to flourish until our knowledge about the nature of "voluntary and informed consent" is solidly grounded in research findings.

[47] For an excellent account and analysis of this whole case and the Regents' decision, see the report by Elinor Langer, *Science*, 151(1966), pp. 663–666.

[48] Quoted in Talalay, *op. cit.*, p. 278.

[49] Talalay, Comments, in *ibid.*

A third problem, briefly, in the application of ethical codes about experimentation on human beings to actual experience is the difficulty in determining the relationship between public welfare and private good. Clinical investigations vary a great deal in the degree to which they are likely to be of personal benefit to the research subject. Schreiner, for instance, has constructed a complex five-fold classification of investigations in terms of the degree of likelihood that the subject will directly gain from participating in them.[50] Although "human experimentation is essential for the welfare of the race," says Beecher, "the scientist or physician has no right 'to choose martyrs for society,' as Kety has put it."[51] Even the "hopelessly incurable," Beecher feels, are coerced martyrs for the public good if the experimentation which is carried out on them is not related in the most direct way to the possibility of their own private therapeutic good.

The emergence of clinical research on human beings on a large scale and with significant consequences is so recent a development that the clinical investigators themselves, we have been seeing, are still in the midst of working out satisfactory working codes of ethics. As one might expect, there is an even greater lag in legal cognizance and control of these activities. Ladimer, who has specialized in the study of the legal aspects of medical research, says that "reported cases have not yet considered modern controlled medical research as such . . . [they] have tended to confuse or have failed to recognize the distinction between research and practice."[52] Ladimer feels that the "increasing extent and expansion" of clinical investigation "today warrants recognition as a separate endeavor affected with a public interest as significant as medical practice itself." This view is shared by Beecher.[53] Yet clinical investigators are ambivalent about legal cognizance and control of their activities. On the one hand, they would like the legitimation that legal cognizance would give them; wise statutes and decisions would be welcomed for the protection and guidance they would provide.

[50] George E. Schreiner, "Liability in Use of Investigational Drugs," *Journal of the American Medical Association*, 185(1963), p. 259.

[51] *Op. cit.*

[52] Irving Ladimer, "Ethical and Legal Aspects of Medical Research on Human Beings," *Journal of Public Law*, 3(1955), pp. 467–511. Reprinted in Ladimer and Newman, *op. cit.*

[53] *Op. cit.*

On the other hand, clinical investigators are fearful of the intrusion of uninformed and unsympathetic outsiders into their activties, where they know that much moral ambiguity prevails. Greater legal cognizance and control will almost certainly be introduced in the near future; indeed, the Kefauver-Harris Bill may have been the beginning of the process, though it is not clear whether even its provisions distinguish between therapeutical medical practice and medical research on human beings. What seems to be needed in this area is a system of administrative and judge-made law in the making of which the opinion and customs of clinical investigators play a considerable part.[54] Ultimate appeal, of course, for both clinical investigators and their subjects, would be to the highest lay courts, which have in their keeping the final decision about moral and legal responsibility.

DOCTORS EMPLOYED IN THE MEDICAL DEPARTMENTS OF DRUG FIRMS

As a result of the great expansion of research and production of drugs by commercial firms and of the subsequent clinical testing of these drugs by medical doctors, there has emerged a new and essential intermediary role, the medical doctor employed by the commercial drug firm to serve as a liaison with the clinical investigator and for various other functions.[55] The primary task of the medical doctor who fills this new kind of role is the selection of competent clinical investigators to test the company's drugs on their patients or on volunteer subjects. This task requires him to balance a number of considerations, professional and commercial. The medical employee of the drug firm is interested, both for professional reasons and in the ultimate best interests of his employer, to select the most competent clinical investigators, men who will put scientific concerns and the welfare of their patients first. But commercial considerations also affect his selection; he wants clinical investigators who will give him reasonably prompt and definite results, and sometimes the most competent men are too busy to do so,

[54] Benjamin N. Cardozo, *The Nature of the Judicial Process,* New Haven: Yale University Press, 1921, p. 62.

[55] This account follows the exploratory study by Renée C. Fox, *op. cit.* Fox's study is based on interviews with seven doctors in a small medical department in one firm. There is obviously a need for further research on other firms, especially perhaps some larger ones where there is probably more specialization, more "career" problems for doctors, and so on. See also Lasagna, "Problems of Drug Development," *op. cit.*

or do not care to bother with the particular drug he offers for testing. For commercial reasons he also wants clinical investigators whose names carry weight on the national and various regional medical scenes, for their research will be used in advertising to recommend successful drugs in national and regional medical journals. There are regional as well as national prestige systems in medical research.

Another function of the medical doctor employed by the commercial drug firm is to advise management on the desirability of manufacturing certain tested drugs. Again, he has to balance professional and commercial considerations. Professional standards require him to evaluate very carefully what the clinical investigators' reports say about effectiveness and safety. His duty to his employers is to describe the commercial possibilities of the tested drugs.

Another function is to provide medical guidance to the sales department in the promotion of the tested drugs once it has been decided to produce them. The medical employee writes the printed "statement of directions to the physician" that goes with every package of the drugs and advises the sales and advertising departments what style and "line" they should use in selling the drugs to the physician through direct-mail and journal advertising. He also gives courses of instruction, intensive or otherwise as needed, to the detail men who will purvey the drugs directly to doctors in personal office calls.

Finally, the medical doctor employee of the commercial drug firm consults with those practitioners who have actually used the firm's drugs and who apply, by mail and phone, for further information about schedules of treatment, possible side effects, and actual emergency adverse reactions. Again, in his responses, the doctor has to balance off his professional obligations to a fellow doctor and his concern for the commercial interests of his employer.

In all his functions, thus, functions which are more and more being divided up among doctors specializing in each of them, the medical employee of the commercial drug firm has to be responsive to both professional and commercial considerations. Obviously, there is a possibility of strain here, a possibility of general or particular conflict between the two types of consideration. But the possibility of conflict does not mean that in fact it occurs all the time, or even in any considerable measure. How much actual conflict there is we do not know; this might well be ascertained by research on a representative sample of

companies. Certainly any such research should keep in mind the existence of accommodative mechanisms for forestalling conflict or resolving it satisfactorily once it occurs. Doctors employed by commercial drug firms are not in a unique sociological situation; other kinds of professionals, for example, research scientists, are also employed by commercial companies. Accommodative mechanisms of various kinds have been constructed to reduce the possibilities of conflict between the professional and commercial obligations of the research scientist.[56] It is very likely that these and other accommodative mechanisms exist in the medical departments of commercial drug firms, or would be constructed by management if they could not otherwise hire medical employees.

RESEARCH SCIENTISTS IN DRUG FIRMS

The amount of scientific research being carried on by drug manufacturing firms has been growing constantly in recent years, and perhaps at an increasing rate. "The pharmaceutical industry," says Talalay, "has rapidly become an important center of biological and medical research."[57] This means that an increasing number of research scientists are being employed by, and make their careers in, drug firms. Among these scientists, a not inconsiderable minority are holders of the medical doctor degree: in 1961, of the 2,874 members of the scientific staffs with doctoral degrees in 86 of the pharmaceutical companies, 466 or 16.2 per cent were M.D.'s; the rest were Ph.D.'s, Sc.D.'s, D.D.S.'s, or D.V.M.'s.[58] Thus, M.D's who commit themselves to full-time scientific research are moving into industry as well as into university and government organizations.

At the end of 1963, the pharmaceutical manufacturers included slightly more than 14,000 of their employees in the category of "manpower engaged in research."[59] Of this total, 7,801 were scientists, the

[56] Bernard Barber, "Some Problems in the Sociology of the Professions," *Daedalus*, Fall, 1963, pp. 669–688.

[57] *Op. cit.*, p. 289.

[58] Pharmaceutical Manufacturers Association, "Results of PMA Survey of Personnel in Drug or Medical Research and Development, 1961"; "Sales—Research and Development Activity, 1962. Prescription Pharmaceutical Industry"; "Pharmaceutical Industry. Research and Development Activity, 1963–1964" (mimeographed sheets).

[59] Data in this summary from *ibid.*

rest technicians and supporting personnel. Among the scientists, 2,750 had some kind of doctoral degree; about 100 of the technicians and supporting personnel had doctoral degrees. Scientific research in drug firms is clearly a large enterprise in terms of personnel. It is also an enterprise with definite tendencies to concentration in larger units. In 1961, for example, the twenty-three largest firms (those with annual sales of over $30 million) employed 85 per cent of all the research staff; the ten largest companies (annual sales over $100 million) employed more than 50 per cent of all research staff in the industry. The larger companies had higher proportions of their scientists in the biological and physical sciences; the smaller companies leaned toward men in pharmacy and clinical medical sciences. This difference seems to suggest that the larger companies do somewhat more fundamental research than the smaller ones. Among other activities, the scientific staff of the pharmaceutical firms were involved, in 1962, in the pharmacological testing of more than 168,000 chemicals and substances. Of this large number, some 1,300 agents were eventually tested in humans. A considerable number of different scientific specialties contribute to pharmaceutical company research. In the research laboratories of one of the larger companies, for example, "some thirty-five separate scientific disciplines are represented."[60] This company is Merck, where, according to its then-President, John T. Connor, expenditures for research had risen by "2052 per cent" in the period from 1940 to 1964.

The number of research scientists employed by the pharmaceutical industry and the importance of their activities suggest the need for social science research on who these people are, what they do, and what their typical problems are. So far, no such research has been done. In many ways, of course, research scientists in the pharmaceutical industry may be no different from research scientists in other types of industry, or even those working for the government, on both of whom some research has been done.[61] But it would be useful to explore the possibility of two kinds of difference. One, scientific research in private drug

[60] John T. Connor, "The Functions of the Pharmaceutical Industry in Our Society," in Talalay, *op. cit.*, p. 126.

[61] William Kornhauser, *Scientists In Industry: Conflict and Accommodation*, Berkeley: University of California Press, 1962. Simon Marcson, *The Scientist In American Industry*, Princeton, Princeton University, Industrial Relations Section, 1960. Barney G. Glaser, *Organizational Scientists: Their Professional Careers*, Indianapolis: Bobbs-Merrill, 1964.

firms may be different in subtle but important ways from research in other social settings. And two, within the private drug firm, the research scientist trained as a medical doctor may have different roles and problems from his colleagues who have other kinds of doctoral training.

One general problem for industrial research scientists which may affect the scientist in the pharmaceutical industry in some special ways is the problem of secrecy and communication with other scientists. A certain amount of secrecy is necessary here, as elsewhere, because of the commercial advantage to be derived from the early marketing of new drug products. How much does this cut the pharmaceutical industry scientist off from his colleagues in the university? At a recent conference on drugs, says Talalay, "Several university professors emphasized that in their experience the inability of scientists from industry to talk and write freely about their work is in fact very real and frequently encountered." They felt "it seriously impedes exchange of ideas."[62] However, spokesmen for the drug industry "cautioned against generalization. While many firms still follow the European practices of close secrecy, others have found it to their advantage . . . to adopt a liberal policy on publication of the results of work being done in their laboratories. These members of the conference felt it is not impossible to balance a demand for secrecy with the need for free communication and that some measure of success has already been achieved." Neither view, unfortunately, can take its support from any careful and precise study of the problem; some research would be of considerable help in making possible a more accurate account of the desirable balances between secrecy and open communication that can be drawn by the drug firm looking to its own interests and those of science and society.

Government patent policy on discoveries made in the course of health research which it subsidizes has recently erected another barrier to free communication between scientists in the pharmaceutical industry and those outside, the majority of whom are now either working for the government or receiving government research grants. In 1963, by Presidential order, it was decided that all rights to discoveries in the health field would fall to the government, in other fields to the private contractor. "Industry, which has in the past maintained close relations with such scientists (those working with government funds),

[62] *Op. cit.*, p. 289.

is now reluctant to consult, collaborate with, or assist these scientists, knowing that under the current patent situation it is not likely to derive the commercial benefits necessary to its existence." The effect has been "to isolate industry from other centers of research in medicine and biology."[63] Such barriers between the different segments of science may be of great consequence for the development of new knowledge and for the satisfaction of scientists working in these different segments.

Pharmacists

Next to doctors, the largest professional group dealing with drugs consists of licensed pharmacists, of whom there were 122,788 in the United States in 1962, or about two-thirds as many as there are doctors.[64] Among these, 56 per cent had four or more years of college, 14 per cent had three years, 16 per cent had two years, and 14 per cent had one year or less. On the basis of a sample survey of some 5,000 of these pharmacists, it appears that 91 per cent of them are in general or retail pharmacy, 8 per cent in hospital pharmacy, and the other 1 per cent in various other types of pharmaceutical activities. The retail pharmacists practice in more than 52,000 retail stores.[65] About half of the retail pharmacists are owners, partners, or stockholders of their retail enterprises; the other half are employees. In 1961, the median annual earning for pharmacists was $8,060. In part because the American pharmacist is so often a businessman as well as a professional, women pharmacists are few in number; in 1962, only about 5 per cent of all pharmacists were women. This is in contrast to the situation in Great Britain, where in 1962 there were some 5,400 women pharmacists, almost 20 per cent of all pharmacists listed in the British Register.[66] The proportion of women to men students in Britain is now even higher than 20 per cent. In contrast to the American situation

[63] *Ibid.*, pp. 287–288. See also remarks by John T. Connor, *ibid.*, pp. 127–128.

[64] This and other figures in this section are from Madeline Oxford Holland, "Pharmacy in the United States," *Pharmaceutical Journal*, 190 (1963), pp. 374–375, which is a useful summary of the material in U.S. Dept. of Health Service, *Health Manpower Source Book*, Sec. 15, "Pharmacists."

[65] Richard A. Deno, Thomas D. Rowe, and Donald C. Brodie, *The Profession of Pharmacy: An Introductory Textbook*, Philadelphia: A. B. Lippincott, 1959, p. 4.

[66] Leslie G. Matthews, *History of Pharmacy in Britain*, Edinburgh and London: E. & S. Livingstone, 1962, p. 170.

further, women make up 90 per cent of Soviet pharmacists and 70 per cent of Yugoslav pharmacists.[67]

In addition to the pharmacists who practice in retail stores and in hospital pharmacies (there are more than 3,000 members of the American Society of Hospital Pharmacists), pharmacists teach in the 76 colleges of pharmacy in the United States, work for the federal or state governments, act as detail men for drug manufacturers, and are employed in various research and other capacities in the laboratories of drug companies. The small amount of social research that has been done on pharmacists has been entirely on the retail pharmacist. It would be good to know about the pharmacist in his other specialties, even though these constitute a minority of jobs, especially since some of these specialties are attracting the better-educated and more highly professional members of the pharmaceutical group. More research on the retail pharmacist is also needed. This research should make distinctions among the types of situations in which retail pharmacists find themselves: owner vs. employee; the drug-only pharmacy vs. the store that sells drugs and nearly everything else: the store in a lower-class, uneducated neighborhood vs. the store in a higher-class, educated one; and so forth.

A central problem for the pharmacist, one around which several others cluster, is the problem of his professional status. This problem has two major aspects: one is the potential conflict between the businessman role, in which many pharmacists also function, and his professional role; the other is the question of the degree to which he can call himself "really" professional, especially in comparison with such other groups as the medical profession.

On its very first page, an excellent introductory textbook for student pharmacists touches upon the problem of pharmacy as a business and pharmacy as a profession. "As practiced in the United States especially," say Richard Deno and his colleagues, "pharmacy is a truly unique combination of profession and business. We are speaking here of the general practice commonly called retail pharmacy—pharmacy in the drugstores and the prescription shops throughout America."[68] How successful this combination in fact is, or could be, we do not know

[67] *Ibid.*, p. 393.

[68] Deno, Rowe, and Brodie, *op. cit.*

very well. Business enterprises are characterized, sociologically, by a primary orientation to profitability and self-interest. Professional roles and organizations, in contrast, are characterized by a primary orientation to the interest and well-being of the client.[69] In principle there seems no reason why the two orientations cannot be mixed in the same concrete role, in this case the pharmacist's role, no reason why they cannot be more or less successfully accommodated to one another, with some strain and actual conflict remaining, of course. An early paper by Thorner seems to have come to this conclusion.[70] A more recent one by McCormack says that pharmacists must make "a final choice" between being proprietors and being independent professionals.[71] McCormack feels that "fusing the two systems" is an adjustment which "is not capable of providing the satisfactions of either role." Judging from the attitudes expressed in the pharmaceutical journals, which may not be representative of the rank and file of the profession, of course, pharmacists seem to identify quite happily with both business and the professions. On public issues concerning health, for example, they identify strongly both with the drug industry and with the American Medical Association. And from both sides they receive encouragement for this identification.[72]

Individual pharmacists vary, to be sure, in the way they blend their professional and business orientations and norms. In a study of 80 retail pharmacists in the city of Albany, New York, Quinney ascertained their relative orientation to the business and professional sides of their work by various questions about their activities and goals in pharmacy.[73] On the basis of their responses, he could divide his

[69] On this contrast, and other defining characteristics, see Bernard Barber, "Is American Business Becoming Professionalized? Analysis of a Social Ideology," *op. cit.*, and Barber, "Some Problems in the Sociology of the Professions," *op. cit.*

[70] Isador Thorner, "Pharmacy: The Functional Significance of an Institutional Pattern," *Social Forces*, 20(March 1942), pp. 321–328.

[71] Thelma H. McCormack, "The Druggists' Dilemma: Problems of a Marginal Occupation," *American Journal of Sociology*, 61(1956), pp. 308–315.

[72] On relations with the drug industry, see Maxwell James, "We Talk to Each Other—Why Can't We Listen to Each Other?", *New Hampshire Pharmaceutical Association Journal*, 26(1962), pp. 1–3.

[73] Earl R. Quinney, "Occupational Structure and Criminal Behavior: Prescription Violation by Retail Pharmacists," *Social Problems*, 11(1963), pp. 179–185.

sample of 80 cases into four types: the professional, with 16 per cent of the sample; the business, 20 per cent; mixed professional and business, 45 per cent; and, indifferent, 19 per cent. Quinney was also able to show that these different types behaved differently with respect to the norms and laws controlling retail pharmacy. Through the cooperation of the New York State Board of Pharmacy, he was able to learn the record of his eighty pharmacists with regard to prescription violations (violations detected by state or federal investigators in connection with prescription laws) during the previous five years. His chief finding was that such violations occur more frequently among the "business" type of pharmacist. Some 75 per cent of these were violators. None of the "professional" type were violators; 14 per cent of the "mixed professional and business" type were violators, and 20 per cent of the "indifferent" type.

Ironically, in the light of their own potential conflict between professional and business norms, some pharmacists have recently found their business interests under attack from a professional group they very much admire, namely, the doctors. As a result of political agitation by pharmaceutical associations, in August of 1964 the Subcommittee on Anti-trust and Monopoly of the Committee on the Judiciary of the United States Senate, Senator Philip Hart of Michigan, Chairman, held hearings on the problem of doctor-ownership of drug stores. This problem seems to vary widely among the states. For example, the New York State Board of Pharmacy announced that no doctors in New York own drug stores. In California, and generally throughout the Far West, many doctors do. While there were only 39 physician-owned pharmacies in California fifteen years ago, there were 213 in 1962, and 39 more were added in 1963.[74] In 1963 California passed a law prohibiting its Board of Pharmacy from issuing new pharmacy permits to doctors and requiring physicians presently interested to give up their ownership by 1967. While a statement by the Executive Director of the American Pharmaceutical Association to the Subcommittee opposes doctor-ownership, a similar statement by the General Counsel for the

[74] Mimeographed statement by Benjamin A. Kingwell, President, California Pharmaceutical Association, distributed by Senator Hart's office. For full details of the hearings held by Senator Hart's Subcommittee, see *Physician-Ownership in Pharmacies and Drug Companies*, Report of the Subcommittee on Antitrust and Monopoly, Committee on the Judiciary, United States Senate, Washington, D.C., U.S. Government Printing Office, 1965.

American Medical Association supports it on the ground that it is only a potential evil and not bad so long as the doctor-owner does not actually exploit his patients through his ownership of the drug store.[75] Apparently as the pharmacist struggles to blend his professional orientations more successfully with his business interest, he sometimes runs into the highly professionalized doctor moving to increase his own business interests. In other societies than the United States, where professionalism among doctors, in terms of the criterion of primary concern for the interest of the patient, is not so strongly institutionalized or has partly broken down, a large proportion of doctors may have business interests in retail pharmacy. On the island of Mauritius, for example, "about a third of all the private doctors have holdings in chemists' shops. Branded products are prescribed which can be bought only at pharmacies in which the doctor has an interest."[76]

The degree of career-choice satisfaction and the self-conceptions of the pharmacist indicate some of the ambivalence he feels as a result of the mixture of business and professional elements in his concrete role. One study of 430 pharmacists in ten metropolitan areas, including both the city centers and the suburbs, found that 49 per cent of them would not choose pharmacy again as a career.[77] Part of the reason for their dissatisfaction may be that some 20 per cent of this whole group said that they had had a more basic interest in medicine than in pharmacy but that they could not afford to study medicine; pharmacy was a second choice to which they had never become entirely reconciled. Furthermore, in this group, after pharmacy itself, medicine is the profession they say they would be most likely to recommend to their sons. Another study, however, reports somewhat less career dissatisfaction.[78] This study, of a national sample of 450 pharmacists, reports

[75] Both mimeographed statements distributed by Senator Hart's office. See Report of the Subcommittee, cited above. See also Warren E. Whyte, "Interprofessional Problems and the Physician," Annual Convention, National Association Board of Pharmacists, *Proceedings*, April 24–25, 1961, pp. 147–161.

[76] Richard M. Titmuss, "Medical Ethics and Social Change in Developing Societies," *Lancet*, 4(August, 1962), pp. 209–212.

[77] Donald T. Meredith, "Student Recruiting at the Grass Roots Level," *Journal of the American Pharmaceutical Association*, 19, (1958), pp. 34–35.

[78] Wallace Croatman and Paul B. Sheatsley, *The Prescription Pharmacist Today*, Washington, D.C.: Health Information Foundation, Research Series 3, 1958.

that the pharmacist in the large metropolitan area (the type reported in the Meredith study) is less likely than the one in the smaller community to consider pharmacy a good career. Apparently there are more disappointed men, would-be doctors, among the metropolitan pharmacists. Overall, however, Croatman and Sheatsley's respondents agree in considerable majority in thinking pharmacy either a "very good" or a "fairly good" field for a young man to enter. They "shape up," say Croatman and Sheatsley, "as a reasonably well-adjusted, satisfied group." Still, they are "a group with few delusions of grandeur about their place in the health field." They realize that many people do not consider them "really" professional and rank them as inferior to doctors. Some 48 per cent of this group feel that the general public sees them mainly as professional; an almost equal number, some 44 per cent, feel that they were seen as mainly businessmen.

In the professional journals for pharmacists, an important focus of concern is that pharmacists should be accorded professional status. There are, for example, frequent discussions of the proper use of professional terms. One pharmacist objects that too many of his fellows see themselves in "the drug business" rather than in professional practice.[79] He suggests that pharmacists adopt various vocabulary changes indicating their professionalism: they should speak of a "pharmacy" and not a "drug store"; they should call other pharmacists "colleagues" and not "clerks"; they should refer to the ingredients of prescriptions as "supplies" and not "merchandise"; and they should refer to patrons as "clients" and not "customers." Two other pharmacists, discussing what they themselves call "the public relations value" of the college of pharmacy diploma and the State Board certificate, urge all pharmacists to have these two indicators of professional status very prominently displayed so that all patrons will be aware of them.[80] One writer goes farther and suggests that the pharmacist place a wash basin where he

[79] M. Boynoff, "The Pharmacist: Drug Consultant?" Annual Convention American College Apothecaries, *Proceedings*, Sept. 29–Oct. 2, 1961, pp. 10–15.

[80] Robert L. Swain, "The Public Relations Value of a College of Pharmacy Diploma and a State Board Certificate," *American Journal of Pharmacists*, 127(1955), pp. 370–376. William Blockstein, "The Public Relations Value of a College of Pharmacy Diploma and a State Board Certificate," *American Journal of Pharmacists*, 127(1955), pp. 377–383.

can be seen washing his hands frequently, as presumably more professional groups such as doctors and dentists do.

In comparison with the more professional groups to whose established prestige they aspire, pharmacists are not very well integrated in a single professional association for the pursuit of their professional goals and the advancement of their professional prestige. The American Pharmaceutical Association, the oldest of the fifteen national associations which exist, has only one-sixth of all pharmacists as members. Five of the national associations are made up principally or entirely of retail pharmacists, but no one of these has a majority of these pharmacists as members. The continuing professionalization of an occupation often depends on a small group of highly-aspiring members who control a national professional association which has some effective governance over the majority of eligible members of the occupation. This leverage for increasing professionalization does not exist among pharmacists, a fact of which some of them are aware and which they deplore.[81]

Professionalism is not an absolute matter, but one of degree, of more and less. One of the criteria of the degree of professionalism, we have seen, is whether an occupation puts a primary emphasis on the norm of direct serving of the client's interest. Another criterion is the degree of abstract and systematic knowledge which lies behind day-to-day functioning in the occupational role. With respect to both these criteria, recent developments in pharmacy have worked in contrary directions, some developments seeming to diminish professionalism, others to increase it. Pharmacists themselves see the sum of these contrary trends in different ways. For example, in the Croatman and Sheatsley study, when pharmacists were asked whether pharmacy required more professional ability today than it did 10–15 years ago, or less, 60 per cent of them said "more," and 22 per cent "less."[82]

On the knowledge and skill criterion, one of the major developments in the last generation in pharmacy has been the great diminution of drug-compounding activities by pharmacists and the great increase

[81] J. Warren Lansdowne, "For Better Communications—Missionaries for Pharmacy," *Journal of the American Pharmaceutical Association,* 21(1960), pp. 272–275.

[82] *Op. cit.*

in dispensing of prepared and pre-packaged drugs. Today, say Richard Deno and his colleagues, the pharmacist "purchases tablets or capsules, for example, in bottles of 100, 500, or 1,000 and dispenses on prescription a dozen or more, as may be ordered. Such prescriptions are commonly referred to as 'count-outs.' The pharmacist ordinarily purchases liquid preparations by the pint or the gallon and dispenses on prescription 30, 60, or 120 ml., for example. These prescriptions are sometimes referred to as 'pour-outs.' "[83] Counting-out and pouring-out are not very skilled work, nor is the typing of the labels on the individual containers into which drugs are counted and poured. There is no precise knowledge of just how much dispensing as compared with compounding the pharmacist now does, but the consensus is that it is the very largest part of his work, somewhere around 80–90 per cent.[84] The same trend toward dispensing of pre-packaged specialties has occurred in other countries besides the United States, for example, Britain and France.[85]

Even dispensing can consist of somewhat greater or somewhat smaller demands on the knowledge and professional responsibility of the pharmacist. Some dispensing requires the pharmacist to use only the specific brand-name drug prescribed by the physician. In other cases, but apparently rarely, except in hospitals, the physician may give the pharmacist "blanket approval" to substitute another brand name or the generic drug itself. Some recent alleged efforts by the drug industry to write legislation that would restrict the pharmacist to the prescribed brand name, outlawing the right of "blanket approval," have been condemned by at least one pharmacist.[86] In general, however, despite what brand names and prepared products have done to their skills in compounding drugs, pharmacists seem to favor them, partly because they identify with the business interests of the drug industry, partly because they see the guarantees of quality and reliability provided by

[83] *Op. cit.*, p. 59.

[84] *Ibid.*; Martin M. Rosner, "Attitudes Toward Maintaining Family Records on Drug Sensitivities," *Journal of the American Pharmaceutical Association*, NS 4, (1964), pp. 169–172, 175.

[85] Matthews, *op. cit.*, p. 296.

[86] George F. Archambault, "Let Us Look at the Generic Name Situation." American College of Apothecaries, *Proceedings of Mid-Year Conference*, Chicago, 1961.

brand-named drugs.[87] These guarantees are often backed up by assumption of legal liability in case of suits.

In contrast to the increase in his routine dispensing activities, certain of the older, more professional functions of the pharmacist continue, and some new ones are rising. People have always asked pharmacists for what was in effect medical counsel, and this need seems to continue. Koos reports that the pharmacist in the small rural town in the upstate New York community he studied had a quasi-medical status.[88] The pharmacist helped the people to "doctor" at home, though he was careful to "advise" rather than to "diagnose" or "prescribe." In short, the pharmacist had always to be aware of the limitations on his own knowledge and responsibility. According to both pharmacists and public, this pressure from the public on the pharmacist to give a certain amount of medical advice continues. Croatman and Sheatsley found that more than two-thirds of the pharmacists they interviewed said that questions about medical care were asked of them virtually every day.[89] And one of every three members of the public sample they questioned said they had sometimes asked pharmacists for medical advice. The pharmacists seem to be very much aware of the necessity to limit the health care advice they give. When asked if the public should be encouraged to ask them questions about health and medical care, 40 per cent said "yes," but on *minor* matters only, and 46 per cent said "no." With very definite restrictions, there is obviously some place here for professional activities by pharmacists, but it would be good to be able to specify that place as carefully as possible in terms of better research knowledge about just what kinds of pressure the public brings to bear on pharmacists and how they can effectively cope with those pressures. In general, doctors seem to be fearful about the medical information given out by pharmacists. Of the 500 doctors surveyed by Croatman and Sheatsley, only 5 per cent said "yes" when they were asked if the general public ought to be encouraged to ask the pharmacist questions

[87] Newell Stewart, "Why Brand Names Protect the Patient," *American Professional Pharmacist,* 27(1961), pp. 50–54. Linwood F. Tice, "Brand Names or Generic—Four Key Questions," *Journal of The American Pharmaceutical Association,* NS1, (1961), pp. 98–99.

[88] Earl Lomon, Koos, *The Health of Regionville,* New York: Columbia University Press, 1954.

[89] *Op. cit.*

about health and medical care; 70 per cent of the doctors believed that most people are getting "too much" advice from pharmacists now. The pharmacist would like to think of himself as a professional member of a "health team," supplementing the doctor.[90] But just what this supplementary role ought to be is not easy to define.

As a result of the recent discovery and use of many powerful drugs, new professional functions for the pharmacist have been suggested. For example, it has been suggested that pharmacists have a role to play in drug safety. In some cases, patients report adverse reactions to the pharmacist rather than the doctor; he can act as a useful liaison with the doctor in these cases. In addition, some pharmacists have suggested that they maintain records of the drug consumption and sensitivities of the families they serve.[91] When the families use two or more doctors, either jointly or in succession, these records can be of help in forestalling adverse reactions. Finally, it is the hope of some pharmacists that they can help to keep their local doctors informed about new drugs as they appear on the market. In all these respects, the pharmacist may have some larger professional role to play, but this role is not yet well worked out.

Beyond the new professional functions that he may exercise in the conventional general retail store, the pharmacist now has some other and probably more professional options open to him in other areas. Even exclusively prescription stores seem more professional than the ones that sell everything besides drugs. And there is increasing room for pharmacists in hospital pharmacy. There are some 7,000 hospitals in the United States, and about half of them already have their own pharmacies. The hospital pharmacist is more readily accepted as a member of the professional "health team" by doctors. Finally, there is research pharmacy, though this requires additional training beyond the usual four-year pharmacy course. Medical centers, and the drug industry especially, are greatly increasing their efforts in research pharmacy.

[90] See a statement of the "health team" ideology in Eugene L. Parrott, "The Pharmacist-Consultant," *Journal of the American Pharmaceutical Association*, NS 2(1962), pp. 92–93.

[91] Rosner, *op. cit.*, pp. 169–172, 175.

5

Some Social Problems Connected with the Use of Drugs

THE USE OF DRUGS, we have seen, is intimately involved in a variety of social problems. Now it will be useful to consider some of these problems directly and more fully. First, however, it is necessary to say something about what is meant by a "social problem." There is no unanimity on this matter among sociologists, but we can lay out some of the essential characteristics which we need to keep in mind as we deal with some particular social problems connected with the use of drugs.[1]

To say that a social system, either a whole society or some subsystem of the whole society, has "social problems" is to say that there is some malfunctioning in that system, some degree of inability to achieve the goals of the system, or some defect in the way in which the goals are pursued. To be "objective" or scientific in specifying social problems we need an "objective" or scientific theory about social

[1] For some valuable theoretical and substantive discussions of social problems, see Robert K. Merton and Robert A. Nisbet, editors, *Contemporary Social Problems,* New York: Harcourt, Brace & World, 1961. S. N. Eisenstadt, editor, *Comparative Social Problems,* New York: Free Press of Glencoe, 1964.

systems to use as the point of reference. By reference to a theory which states the necessary structures, functions, and goals of social systems, we can be precise about particular forms of malfunctioning. The theory will define both proper functioning and malfunctioning equally well.

At the present time, our theoretical knowledge of the functioning of social systems is still rough. Hence our discussion of social problems in terms of that theory is still rough. We can define certain broad social problem areas, such as "crime," "ill health," or "poverty," but our analyses of specific topics in these areas is often notably lacking in precision. As our theory of social systems improves, so will our understanding of social problems. Hopefully, there will be reciprocal influence here; the analysis of particular social problems could contribute to our general theory of social systems.

One essential component of any social system consists of the values and attitudes of the members of the system. Human values and attitudes are somewhat variable not only between different social systems but also, sometimes, within the same social system. Any theory of social systems has to take this fact into account in a number of contexts, and nowhere more so than in its analysis of social problems. Because of the variability of values and attitudes, the definition of a particular social problem is always somewhat affected by the particular values and attitudes in the social system in which it occurs. Thus "ill health" may be a social problem for all social systems, because it represents an incapacity on the part of some members to perform their roles, but just what will be thought of as "health" and "ill health" will depend in part on the values and attitudes of the members of each particular system. Different societies have different values for "good health," depending partly, of course, on the knowledge of what is possible. And even within a society, values and attitudes on this score may differ in different parts of the population. Social problems connected with the use of drugs are very much affected by the different values and attitudes which people have had toward them in different societies, at different times in the same society, and in different parts of the same society at any given time.

In the light of these basic considerations, we shall consider three social problems connected with the use of drugs: first, the problem of the avoidable unavailability of drugs; second, the problem of addiction;

and, third, the problem of illegitimate control of behavior and mind. Far and away the largest amount of concern and discussion has been with the first two of these problems. Concern with the third is now on the increase.

The Problem of the Avoidable Unavailability of Drugs

We have suggested that "good health" is at least a minimal functional necessity and an irreducible individual right in every society because of its importance for effective social performance. In our modern Western societies, because of the high standards we have set for social performance and because of the importance of good health in meeting those standards, the right to good health and to the means of maintaining and restoring it is perhaps more strongly put forth and more widely acknowledged as legitimate than it has ever been elsewhere. This claim is, of course, a claim to all the means of keeping and getting good health. Increasingly, during the last twenty-five to fifty years, drugs have become one of the really essential means. Any set of arrangements which deprives some people in some measure of the drugs necessary for good health is, therefore, dysfunctional for the society and offends our established values. In both respects, it becomes a social problem.

This is what is being referred to, then, as the social problem of the avoidable unavailability of drugs. There are those who say that there are many people in our society for whom drugs are in some important measure avoidably unavailable. They say that this social problem is due to a number of alterable social circumstances. Poverty in general, they would grant, is partly responsible for this social problem, as it is for so many others. But this, they feel, is far from the whole story, and part of the blame belongs to the pharmaceutical and medical groups. They say that drug manufacturers make excessive profits, that they practice monopoly and collusion on prices, that they have excessive costs for advertising, and that they inflate prices to the consumer by the use of brand names instead of generic names. They also blame others besides the manufacturers for contributing to the problem of avoidable unavailability. They say that doctors have bad prescribing habits which needlessly increase their patients' drug expenses. And finally, they say

that retail costs for drugs are too high. For some of these alleged causes they recommend a variety of reforms. Let us look first at each of these several complaints against the present system of providing drugs to those who need them for good health and then look at the recommendations for reforms. The complaints and the recommendations all raise complicated social and economic issues where neither the essential relevant facts nor the conclusions to be drawn are entirely clear. All of them seem to call for further research and analysis. But we can make a useful start in seeing what is meant by the problem of avoidable unavailability.

The costs of medical care generally and of drugs particularly are quite considerable in the United States today. For medical care as a whole, in 1960 the United States spent somewhere between $20 billion and $27 billion, a sum six times that spent in 1929.[2] From 1929 through 1960 the aggregate volume of medical care costs in the United States increased at an annual average rate of 6 per cent. For drugs alone, the increase in costs was from about $600 million in 1929 to about $4 billion in 1960. This increase in output and costs of drugs has been "overwhelmingly concentrated" in "ethical" as against "proprietary" drugs. Between 1939 and 1963, shipments of proprietaries increased at the rate of 377 per cent, those for ethicals at the rate of 1,200 per cent.[3] In 1963, according to Department of Commerce figures cited by Baehr, the cost of drugs amounted to somewhere between 20 per cent and 25 per cent of the costs of all medical care.[4] This proportion has remained relatively stable since the 1920's. Figures on the composition of the medical care dollar given by Lerner and Anderson indicate that 20.6 per cent of total medical costs in 1929 went for drugs, and 19.9 per cent in 1960.[5] Further evidence on the pattern of relative stability of drug prices has recently been provided for the period 1960–1965 by the President's Council of Economic Advisers

[2] Monroe Lerner and Odin W. Anderson, *Health Progress in the United States 1900–1960*. Chicago: University of Chicago Press, 1963, p. 296.

[3] Jules Backman, "Economics of Proprietary Drugs," in *Annals of the New York Academy of Sciences, Home Medication and the Public Welfare*, Vol. 120(1965), Art. 2, pp. 877–879.

[4] George Baehr, "Drug Costs and the Consumer," in Paul Talalay, editor, *Drugs in Our Society*, Baltimore, Maryland: The Johns Hopkins Press, 1964, p. 179.

[5] *Op. cit.*, p. 298. For the relevant facts, see *Drug Trade News*, February 14, 1966.

in their Annual Report for 1965.[6] The proportion going to doctors has decreased in this same time period from 32.6 per cent to 25.2 per cent, and the proportion for hospital costs has increased from 13.7 per cent to 26.3 per cent. Drug costs are certainly an important part of medical costs as a whole.

Is the cost for drugs too high? Seymour Harris implies that it is. He points out that the United States drug industry gets about 25 per cent of the medical-care dollar, while the National Health Service in Britain uses only 10 per cent of its total resources for drugs.[7] And the same point of view was apparently shared by Senator Kefauver and the staff of his Senate Subcommittee on Antitrust and Monopoly when they pointed out that Americans were paying more for the same drugs than people in Europe were.[8] On the basis of information sent them by United States consuls, the Subcommittee found that Merck was selling its brand of prednisone in Great Britain for less than half what it charged at home. It was not made clear whether this lower price was due to lower manufacturing costs abroad or whether the drug had been manufactured in the United States and then shipped abroad to be sold at a lower price. Apparently the latter was being assumed. The drug industry, however, does not agree that costs are too high. In its defense, through a very forceful spokesman, John T. Connor, formerly president of Merck & Co., now United States Secretary of Commerce, the industry emphasized that "the wholesale price, which is the factor over which the industry has some control has been coming down for years even in the face of rising costs. According to the index prepared by John M. Firestone, the wholesale prices of prescription drugs have declined 12.9 per cent since 1959, in contrast to a 28 per cent increase in the Bureau of Labor Statistics Wholesale Price Index for all commodities except farm and food and a 29 per cent increase in the Consumer Price Index during the same period. The 2.6 per cent decline in 1962 was one of the sharpest."[9]

[6] *Drug Trade News*, February 14, 1966.

[7] Seymour E. Harris, *The Economics of American Medicine*, New York: Macmillan Co., 1964, p. 6.

[8] *The New Yorker*, March 14, 1964, pp. 60ff.

[9] John T. Connor, "The Functions of the Pharmaceutical Industry in Our Society," in Talalay, *op. cit.*, p. 122.

Outside the United States as well, costs for drugs are high, sometimes higher in the under-developed than in the industrialized European countries. Titmuss has pointed out that the island of Mauritius, "like other areas in Africa and the East, is now spending a higher proportion of its national income on the products of the pharmaceutical industry than the United Kingdom."[10] And in Europe itself, it has been suggested, they may be rising as a proportion of total medical costs. William Glaser, a well-informed observer of the European medical scene, suggests that costs of hospitals and physicians are controlled by the governments there under their national health arrangements, and nurses are often low-paid members of religious orders. Drugs, still manufactured by private industry, are the least controlled part of medical costs; hence their relative rise.[11]

How does the general public view the costs of drugs? Unfortunately, on this very relevant set of values and attitudes we have practically no evidence. One study, done by a private advertising agency in the early 1950's on an unspecified American sample, found that 63 per cent of all consumers felt that the prices they paid for drugs were too high.[12] Of the consumers who felt prices were too high, 44 per cent blamed the excessive cost on the drug industry. It would be good to have an up-to-date, national-sample survey of the American people's attitudes toward drug costs. And it would be most helpful if such a survey explored why people do or do not think that drug prices are "too high." Do they think drug prices are too high in comparison to automobiles, or food, or other specific consumer products? What is it about drug costs that influences people's relative judgments? Is it the frequent unexpectedness of the "high" costs of drugs? Is it the greater indispensability of drugs in comparison with other consumption products? No cost is ever absolutely "too high" or "just right." It is always social attitudes and their institutional and cultural determinants which mold the views that people have on matters of "fair" prices. In this respect, drug prices are no different sociologically than prices for any other product.

[10] Richard M. Titmuss, "Medical Ethics and Social Change in Developing Societies, *Lancet,* 4(August, 1962), pp. 209–212.

[11] William Glaser (private communication).

[12] As reported in *American Professional Pharmacist,* 1954, editorial matter.

Criticism is also made of the American drug industry for what are alleged to be its "excessive" profits. Seymour Harris feels that there is "much evidence" that the drug industry's profits are "unusually high." He says, "For example, among the ten firms of *Fortune's* 500 largest corporations with the highest return on invested capital in 1961, three are drug firms. In 1960, return on invested capital for pharmaceuticals was 15.5 per cent, second in the nation of twenty-one industries covering the 500 largest industrial companies; in 1961, 15.8 per cent, first in the nation. The respective returns for all 500 largest firms was 9.1 and 8.3 respectively."[13] And, he continues, a survey made by the Federal Trade Commission and the Securities and Exchange Commission covering all manufacturing corporations "reveals very high profits for drugs in relation to all corporations" up through the first quarter of 1962. "In relation to sales and equity, before and after taxes, drugs experienced the highest rate of profit among all thirty industries and subindustries."[14] Even Markham, whose technical and objective economic research seems to have been subsidized by the pharmaceutical companies, says that the ethical drug industry has been "among the top three most profitable industries in the nation each year over the past decade."[15]

Here again, with regard to the charge of "excess" profits, the drug industry has defended itself through Mr. Connor.[16] Mr. Connor was prepared to admit that the drug industry might be getting higher rates of return on its invested capital than other industries. For his own company, Merck & Co., Mr. Connor reported that during the fourteen-year period from 1949 to 1963 "our profit ratio averaged 11.2 per cent of sales and 13.8 per cent of net worth." But, says Mr. Connor, this rate of return is "certainly not unreasonable for a risk enterprise."

An emphasis on the "hazardous speculation" involved in the

[13] *Op. cit.*, p. 77.

[14] *Ibid.*, p. 78.

[15] Jesse W. Markham, "Economic Incentives and Progress in the Drug Industry," in Talalay, *op. cit.*, p. 175. See also the summary statement in W. S. Comanor, "The Economics of Research and Development in the Pharmaceutical Industry," unpublished doctoral dissertation, Harvard University, 1963, p. 61. "In recent years, the pharmaceutical industry has become one of the most profitable in the American economy." Comanor was Markham's student.

[16] *Op. cit.*

development of drugs has also been made by Mr. Walter A. Munns, President, Smith, Kline & French Laboratories, one of the ten largest ethical drug manufacturers in the United States, in his testimony before the Subcommittee on Patents, Trademarks and Copyrights of the Committee on the Judiciary, United States Senate, August 19, 1965. Mr. Munns, in arguing for the desirability of patents as protection against the "hazardous speculation" involved in the discovery, production, and final marketing of a drug, described the case of a drug recently marketed by his company, "Dyrenium," a diuretic agent. Mr. Munns said that the work on "Dyrenium" took about five-and-a-half years and cost over $2 million. "This," he says, "was a hazardous speculation. At any time during this process the product might have been shown to have some property that would have made it unsuitable for human administration, and our work and expenses to that date would have done for nothing. We could never justify this speculation without the exclusivity provided by a patent." Mr. Munns provided the following table to summarize, in time and costs, the various stages of development of the drug.

Activity	*Months*	*Cost to SK&F*
1. From beginning of animal tests to decision to test in man	15	$ 350,000
2. From beginning of clinical testing to New Drug Application submission	18	735,000
3. From New Drug Application to Food and Drug Administration approval	33	1,014,000
Grand Total	5 yrs./ 6 mos.	$2,099,000

Costs for a "new" drug would, of course, be much lower in those cases, which occur not infrequently, where an American company imports a drug which has been discovered abroad and only manufactures it here on license from the foreign drug firm.

Here is where there is a definite conflict of values about the incentives that should govern the manufacturers of drugs. The manufacturers look upon themselves as a profit-making industry which has been

going through a period of great change and high risk. They feel they have invested large sums of money in new drugs, that they have sometimes lost money on particular drugs as well as making it on others, and that they deserve a higher rate of return for taking these risks. Investors seem to have agreed with the manufacturers about the riskiness of their enterprises and the uncertainty of their success. All during the 1950's and continuing up to the present time, stocks of the pharmaceutical companies have been the focus of considerable speculation by investors, and subject to wide up-and-down swings in their value. The most recent example, during the years since 1963, has been the stock of Syntex, a pioneer in research and manufacture of steroid hormones for oral contraceptive drugs.[17] At various periods in 1965, Syntex was "the most heavily traded issue on the American Stock Exchange." In that year, Syntex stock "rose in price more than any other stock on the exchange, from 64⅜ to 219⅝." Nevertheless, "because Syntex's stock has been so volatile, some Wall Streeters have been skeptical of the firm's future once the pill boom lags."[18] It is hard to see how anybody but a speculator could consider such a company a "risky" investment, but such seems to be the case.

But others feel that the industry has not been taking unusual risks, that there has been an explosion of discoveries of new drugs from which the pharmaceutical industry could only profit. Lasagna, for example, speaks of a "pharmacologic bonanza."[19] "During a recent five-year period," a period which he does not specify, he says, "the industry's growth continued at an impressive rate, with such dollar net increases as these: Abbott Laboratories, 40 per cent; Lilly Laboratories, 91 per cent; Baxter Laboratories, 109 per cent; Merck, 133 per cent; Parke-Davis, 200 per cent; Smith, Kline & French, 324 per cent; Schering, 677 per cent; and Rorer, 2,208 per cent." This bonanza has meant a continuous and high level of profits for the industry, what some charge are "windfall" profits and not earned by any special achievements of the companies.

Critics of the drug industry also assert that if it were truly a high

[17] See especially the *New York Times,* May 29, 1964, for a full story on Syntex.

[18] *Time,* Jan. 7, 1966.

[19] Louis Lasagna, *The Doctors' Dilemmas,* New York: Harper & Bros., 1962, p. 132.

risk area there would be less concentration in the industry, less use of administered prices, and less resort to other arrangements for eliminating or reducing competition. In the matter of concentration, for example, the staff of the Kefauver Committee claimed that 90 per cent of the total volume of business done by the industry was in the hands of only twenty-two out of a total of a thousand or so firms.[20] Moreover, it was further asserted, these few large firms follow the practice of price leadership, in which one firm sets the price for a drug and all the others follow, thus avoiding competition. The absence of competition prevents any lowering of the price. Occasionally, when a small firm or a foreign firm does undersell the established group, one of the leaders attempts to cut off this competition with some kind of legal action. Thus, it is alleged, when Syntex of Mexico offered prednisone and prednisolone at lower prices than Schering and the other big companies, Schering sued Syntex and tried to keep it out of the American market. It is also claimed that the large companies avoid litigation of patents and manufacturing priorities among themselves, though not with the occasional smaller competing company. Instead of patent litigation and open competition, the large companies make private agreements about licensing arrangements and royalty payments, the result being the administration of fixed and unchanging prices.

Lasagna, who says, "It is undeniable that drugs of similar structure or use end up at prices which are often identical, despite the fact that they are made by different companies," has suggested what is a very likely source of price administration among the few leaders of the drug industry.[21] He feels that "today's 'price-fixing' " is the result of the fear of excessive competition in the drug industry, the fear of "mutual throat slitting." The rapid rate of development of drugs, the possibility of rapid obsolescence, the hazards of being second or even later in the competitive race to develop new drugs on which all the companies are working, these circumstances make it attractive to the companies to take steps to reduce competition from what they consider excessively high levels. Note, however, that despite these price administration arrangements, the drug industry still feels that it is a high risk area of enterprise. But to others, even when they do not think there is any

[20] *The New Yorker,* March 21, 1964.

[21] *Op. cit.,* pp. 145ff.

overt, back-room collusion among the companies, the industry seems to be eliminating competition and risk entirely. Even without backroom dealing, says Lasagna, "the result of drug-house price policies is at times the same as collusion: an artificial, noncompetitive market where the consumer cannot benefit from price drops, even after a drug has been on the market for years and has long since returned the costs required for its development and initial promotion."[22]

A quite different view of competition and pricing in the pharmaceutical industry has been offered by Markham and Comanor, based on their technical and comparative economic analysis.[23] Markham says, for example, that "the number and size-distribution of the pharmaceutical product firms generally is consistent with reasonably effective competition." He points out that although the "largest four firms account for 27 per cent of the total shipments, the largest eight for 45 per cent, and the largest twenty for 73 per cent," this degree of concentration "is slightly lower than the concentration in United States manufacturing generally, where on the average the largest four firms account for about 30 per cent" of the product. Moreover, although he agrees that there is a "substantial monopolistic element" in each therapeutic market because of the "virtually complete absence of substitutability among drugs in different therapeutic classes," monopoly tends to be short-lived because of product change. "In each of the product markets," says Markham, "the drug industry demonstrates considerably greater instability of firm position than in most industries." In sixteen of the twenty therapeutic markets for which Markham collected evidence, "at least two of the top five firms in 1951 were not among the top five in 1960." This high rate of turnover "appears to be attributable to competition in the form of new product development rather than price competition." Indeed, this same pattern, competition in the form of new product development, is what also substitutes for price competition in lowering the prices of drugs. Once introduced, a drug has "a remarkable history of price inflexibility," says Markham, but lower prices result anyway because of the introduction of either nearly-similar or entirely new and superior drugs at lower prices. "There can be little doubt," says Mark-

[22] See also, Louis Lasagna, "Problems of Drug Development," *Science,* 145(1964), pp. 362–367.

[23] Markham, *op cit.,* and Comanor, *op. cit.*

ham, "that the search for new and improved drugs is an important means of competition for the pharmaceutical industry." The development of new drugs is accompanied in even greater measure by "molecule manipulation" and the consequent production of "me-too" drugs. In sum, "This would all seem to support the general conclusion that the principal means of competition in the pharmaceutical industry is 'product' competition rather than 'price' competition but that product competition itself consists of two varieties: entirely new drug products (creative) and variations of old products (imitative or duplicative). . . . Firms that would not reduce the price on an existing brand name may often introduce a new brand name at a lower price per standard dosage." A large part of the high research expenditures of the drug industry are devoted to the creative and imitative or duplicative search for "new" products. Since "the vast majority of new products consists of drug combinations," as Comanor points out, most of the research is imitative rather than creative and is devoted to products "which hold reasonable assurance of commercial success."

We have seen in an earlier section that there is considerable criticism of the misleading quality of drug industry advertising. There is a further criticism in the present context of the avoidable unavailability of drugs, namely, that the drug industry spends too much money on advertising, and thus unnecessarily raises costs to the consumer. Goodrich has pointed out, "According to a special issue of *Advertising Age* published in January, 1963, the pharmaceutical industry was spending $225,000,000 a year promoting drugs to the approximately 200,000 physicians of this country. This means that more than $1,000 a year was being spent on each physician to sell him prescription drugs."[24] Goodrich seems to think this is too much, but just how much would be enough is not clear. The Kefauver Committee staff also thought that costs for advertising drugs were too high. They made their point by reporting that the records of the twenty-two largest manufacturers of pharmaceuticals showed that, in 1958, they had spent an average of 24 per cent of gross income on advertising and promotion.[25]

[24] William W. Goodrich, "The Responsibilities and Problems of Government," in Talalay, *op. cit.*, p. 145.

[25] *The New Yorker,* March 21, 1964. See also Karl Folkers, "Drug Research in Industry," in Talalay, *op. cit.*, p. 139.

Connor's defense of the industry against the charge of "spending extravagantly to advertise prescription drugs" is simply to deny that the alleged excessive sums are spent. For example, he says, his own company, Merck & Co., spent only 7 per cent of its sales income for advertising in 1962.[26] Again, in the defense as in the accusation about too large costs for advertising, there is no direct meeting of the essential issues of what the functions of advertising prescription drugs to doctors are, how these functions can be best performed, and how much ought to be spent on achieving whatever the desirable goals of advertising might be. This whole matter calls for further analysis and research.

The last part of the charge against the drug companies for causing the avoidable unavailability of drugs, and one closely connected with the complaint against excessive advertising costs, is the charge that the companies pursue the unnecessary and costly practice of emphasizing trade names for drugs instead of generic names. One critic has said, "This vast promotional effort . . . had, essentially, one purpose, to plant trade names firmly in the minds of physicians. The situation was unique in the world of commerce."[27] The use of trade names is seen as a device for reducing competition in the market and for maintaining high prices. To some extent, large and knowledgeable purchasers, such as hospitals and government agencies, can avoid the added costs of trade-named drugs by establishing formularies of generic drugs and purchasing accordingly. But the individual consumer is compelled to buy the higher-priced, trade-named drug which is written on his prescription.[28]

In its defense of trade names the industry admits that there is an essential place for generic-name drugs. "But we also think," says Connor, "that along with the generic names, it is essential for manufacturers to have the right to use trade-marks, because only in that way can a reputable firm identify itself with its own quality products behind which stand the reputation, the careful manufacturing procedures and quality controls, and the sense of responsibility of the firm."[29] Some support for this quality-control function of trade names has been offered by

[26] *Op. cit.*

[27] *The New Yorker*, March 21, 1964.

[28] See Baehr, *op. cit.*, pp. 181, 183.

[29] *Op. cit.*, p. 129.

Bauer and Field on the basis of their investigation of the Russian pharmaceutical industry.[30] They say that "quality control is not well built into the manufacturing process" either in the Russian pharmaceutical industry specifically or in Russian industry generally. Moreover, "efforts to maintain quality control by policing via an external inspection system have been one of the conspicuous failures of the generally successful Soviet economy." The government, with the desire of making the manufacturer assume the quality control and self-inspection function, has suggested to "manufacturers in many areas" that they adopt trade-marks. No matter what the overall character of the economy in a society, the matter of trade-marks obviously poses the problem of the relative advantages of self-control and external-control in guaranteeing the quality of products. It is likely that some mixture of these two types of control is necessary. If so, there is a definite place for trade names in the pharmaceutical industry as well as elsewhere. How much of a place, however, may be neither so much as the industry itself now thinks nor so little as some of its critics claim.

In addition to the drug industry, two other groups are sometimes charged with some of the responsibility for the avoidable unavailability of drugs. They are the doctors who prescribe drugs and the retailers who sell them. "The average doctor," says Talalay, in reporting the feelings of the members of a recent conference on drugs, "tends to 'over-prescribe': he orders unnecessary medicines, the wrong medicines, and too many medicines for the same illness, and he is too easily persuaded to change to the latest product."[31] The doctor, it was also felt, "needs to consider the patient's pocketbook as well as his health." It has even been asserted that the doctor nowadays does not know the costs of the drugs he is prescribing. There may, of course, be some dysfunctional consequences of the doctor's being aware of the patient's ability to pay and of the precise costs of what the patient has to buy for maintaining or restoring his health. Still, before this kind of economic ignorance is accepted as a greater good than evil, some inquiry should be made. Just how much do different doctors know about the

[30] Raymond A. Bauer and Mark G. Field, "Ironic Contrast: U.S. and U.S.S.R. Drug Industries," *Harvard Business Review,* 40(1962), pp. 89–97.

[31] *Op. cit.,* p. 294.

costs of the medicines they prescribe? And how does such knowledge, or the lack of it, affect prescribing practices?

There can be no question that "fads" for certain therapeutic drugs, as well as for other therapeutic techniques, have been common among doctors. In 1876, Buchheim, the professor of pharmacology and history of medicine at the University of Dorpat, complained of this faddishness among doctors. "We know," he said, "that a great number of physicians, without rhyme or reason, go after every new remedy that is recommended to them. If an industrialist is but shrewd enough to advertise sufficiently, he usually succeeds in increasing the sale of his product."[32] Quite recently, we have seen a tremendous growth in the use of antibiotics by doctors. However, the tendency toward drug fads among doctors is not easy to eliminate. It has its sources in the social-psychological uncertainty that they face in a good deal of their practice. Confronted with diagnostic obscurity and therapeutic uncertainty, they use whatever drugs seem to help them in meeting this uncertainty, and sometimes the presumably helpful drug turns out to be ineffective, or productive of harmful side effects, or too costly. Pressed by drug industry promotion, by their patients, and by their own needs for therapeutic action and effectiveness, doctors are indeed sometimes as "pill happy" as their patients. If they prescribe the more costly trade-named drugs instead of the generic-named equivalents it may be because they have a need for the warranty of quality control and liability protection that they feel is provided by trade-marks.

Retailers, too, are said to play a part in the needlessly high costs of drugs. Somewhat surprisingly, the possible blame of the retailers is pointed out by the pharmaceutical manufacturers, in order to defend themselves against accusations that are often exclusively brought against them. "Not enough attention has been given to the retail side of drug economics, in the opinion of several members of the pharmaceutical industry at the conference table," says Talalay, reporting the discussion at the Johns Hopkins drug conference.[33] These representatives of the drug industry felt it was unfair for the Kefauver Committee to concentrate on manufacturing practices, costs, and profits. These are only part

[32] Owsei Temkin, "Historical Aspects of Drug Therapy," in Talalay, *op. cit.*, p. 12.

[33] *Op. cit.*, p. 293.

of the problem, "since the average retail markup is about 100 per cent, or half of the price the consumer pays. It has frequently been said by the industry that reduction or even elimination of profits will not significantly change the retail price."

On their side, however, the retailers point out that their high markups are required because of the large and slow-moving inventory forced on them by the manufacturers' proliferation of drugs that are not really different from one another and by the physicians' tendency to prescribe some at least of every one of the large inventory marketed by the manufacturers. Some retail pharmacists might agree with those who say there are too many varieties, combinations, and minor modifications of drugs being offered for sale. But so long as this great variety is marketed and prescribed, they have to cover the costs of stocking it with what appear to be large markups.

In connection with the problem of proliferation, incidentally, it should be noted that at least so far as the drug manufacturing firms are concerned, though this does not necessarily alter physicians' prescribing practices, there seems to be some change during the last few years. According to figures compiled by Paul de Haen, leading unofficial record keeper for the industry, the number of new pharmaceutical specialties marketed each year in the United States has been decreasing constantly since 1958. Here are the figures for the number of "new products" each year beginning with 1958: 400, 370, 315, 311, 265, 213, 162, and 119 (for 1965).[34]

Proposals for government controls over the drug manufacturing industry in the United States have been made for a long time, starting in the nineteenth century.[35] Such proposals seem to have had their best chance for realization in legislative enactments when some catastrophe occurred that moved the government to action. For example, the first major control bill, the Pure Food and Drug Act of 1906, was passed as a result of the scandals about impure and poisonous conditions in the meat industry. This Act limited itself to the regulation of the labeling of foods and medicines. The next major bill, the Food, Drug and Cosmetic Act of 1938, was enacted into law as a result of a catastrophe in

[34] See *F-D-C Reports,* the so-called "Pink Sheet," a private trade publication, Jan. 24, 1966.

[35] James Harvey Young, "Social History of American Drug Legislation," in Talalay, *op. cit.*

which over one hundred people lost their lives after using the then-new, "miracle" drug, sulfanilamide, when it was marketed in elixir form in a lethal solvent. This was the first bill to give the Food and Drug Administration powers of review over testing and thereby of control over the actual introduction of drugs onto the market. And the third and most recent major bill, the Kefauver-Harris Bill of 1962, probably passed only because of the thalidomide disaster, in which thousands of babies in Europe and some scores in the United States were born deformed because their mothers had taken thalidomide in the early stages of pregnancy. This law considerably strengthened the Food and Drug Administration's control over the testing of new drugs and its powers of licensure for marketing.

In these bills, the law has concerned itself directly only with accuracy of labeling of drugs, with their safety, and, now, with their efficacy. The law has not sought to regulate costs and profits. But the preliminary legislative hearings on these bills, especially for the 1938 and 1962 enactments, have been filled with just these complaints about excessive profits, too high costs, too much advertising, and administered prices which we have seen make up the set of charges against the drug industry. Probably the assumption of those conducting the hearings and those testifying has been that these alleged defects of the manufacturing industry could be remedied under the provisions of the anti-trust legislation and through the agency of the Justice Department, insofar as there were actual violations of the law. Probably also it has been hoped that the adverse publicity resulting from the hearings would push the drug industry toward greater self-control of their alleged failure to serve the public welfare satisfactorily. The Food and Drug Administration has had great difficulties in exercising the control that legislation has assigned to it, namely, the control over accurate labeling, safety, and efficacy.[36] It has had trouble recruiting good staff, in keeping up with its work load, and in keeping its staff from resigning to work for better pay in the drug industry. It has been under pressure from legislators, other

[36] See Lasagna, *The Doctors' Dilemmas,* pp. 181ff.; and, J. K. Weston, "The New Drug Amendments of 1962 and the New Drug Regulations—Comments from a Drug Industry Physician," in Irving Ladimer and Roger W. Newman, editors, *Clinical Investigation in Medicine: Legal, Ethical and Moral Aspects: An Anthology and Bibliography,* Boston: Boston University, Law-Medicine Research Institute, 1963, pp. 344–347.

government agencies, from the drug industry, the medical profession, and from the general public.

Fortunately, essential moves have recently been taken, especially the appointment of a very able Commissioner, and with the strong support of the Secretary of Health, Education and Welfare (the FDA's parent agency) and perhaps even of the President himself, to transform the Food and Drug Administration from a low-quality, under-staffed, police-action-oriented agency into a high-quality, well-staffed, professional, and scientific agency. These moves are very likely to bring about improvements not only in the agency itself but in all the drug-related activities of the medical profession and the pharmaceutical industry. The FDA, and all groups related to it, will be undergoing a series of changes that promise to mitigate some of the worst troubles that have afflicted the discovery, testing, production, and sales of drugs during the last twenty years. These changes should be of the greatest interest to sociological and political research, both as an opportunity to provide some help and as an occasion to study how beneficial governmental and social changes can best be made.

Problems of government control over the alleged responsibility of the drug industry for the avoidable unavailability of drugs are not limited to the United States. Outside the United States, only in Russia is the drug industry nationalized and therefore directly under the control of the government. And we have seen that control over costs and profits may result in other shortcomings in Russia, such as deficiencies of quality control and adequate supply.[37] In the other countries of Europe, the drug industry is privately owned, even in countries like Britain and Germany where the provision of medical services has been nationalized. The social forces that have resulted in the nationalization of medical services push also, of course, for the nationalization of drug manufacture. It would be useful to have studies of the relations between the drug industry and the government in several European countries, and also of the relations between the medical profession and the drug industry. It would be interesting to know whether the profession and drug industry in the various European countries are as sympathetic to

[37] See Mark G. Field, "Pharmaceuticals, Pharmacies, and Pharmacists in Soviet Russia," *American Professional Pharmacist,* 25(1959), pp. 24–29, 106–110, 174–178; Bauer and Field, *op. cit.*

one another as the drug industry and the organized medical profession have been in the United States.[38] These studies would provide a useful comparative basis for the discussion and planning of government controls over the drug industry in the United States.

The Problem of Drug Addiction

Drug addiction is one of the most highly publicized and most morally condemned "social problems" in the United States today. It is considered to involve large and serious amounts of individual and social system malfunctioning and many people find it a terrible affront to their basic moral values.

John Clausen has found that "the extent of drug use and drug addiction, historically or currently, is known only in very general terms."[39] For the United States, he continues, "an Ad Hoc Panel on Drug Abuse in 1962 reported that discrepancies between estimates provided by federal, state and local enforcement agencies and other sources of data were so great as to preclude any adequate estimate of the number of addicts in the United States." The Federal Bureau of Narcotics has attempted to maintain a register of "active addicts," on which are listed approximately fifty thousand names. But there is no way of knowing how many of these people are actively addicted at any given time, nor indeed how many of them are even still alive. In conclusion, Clausen says, "from various fragments of available data, it appears that the number of persons in the United States actively addicted to opiates within the past decade is almost certainly not less than fifty thousand and probably not more than one hundred thousand."[40] In contrast to the United States, Clausen points out, there are probably no

[38] Lasagna, *The Doctors' Dilemma*, pp. 124–125.

[39] John A. Clausen, "Social Aspects of Drug Use and Addiction," to be published in the *International Encyclopedia of the Social Sciences*, forthcoming, 1968. Another excellent and comprehensive study and analysis of the drug addiction problem can be found in the recent book by the "dean" of American sociologists who have been interested in the addiction problem, Alfred R. Lindesmith, *The Addict and the Law*, Bloomington, Indiana University Press, 1965.

[40] But note Lindesmith's even stronger caution, *op. cit.*, p. 127, that "United States statistics on narcotics are grossly unreliable." This holds for the pre-1941 period as well as for the present. Note also that there is a general consensus among criminologists about the unreliability of statistics on all types of crime.

more than a few hundred opiate addicts in each of the following West European countries: the various Scandinavian nations, Great Britain, France, and Italy. Only in West Germany are there a greater number of addicts than is common in the rest of West Europe; the number there is estimated to be something less than five thousand.

Further, with regard to the amount of individual and social system malfunctioning involved in drug addiction, it would also seem that the seriousness of this social problem in this respect may be exaggerated partly because of the special moral condemnation it receives. In an earlier review and summary of the problem, Clausen said, "In perspective, the problem of drug addiction is not a major social problem."[41] What he means is that, compared with the amount of individual and social system malfunctioning involved in such problems as mental illness, juvenile delinquency in general, and alcoholism, drug addiction is of relatively minor extent and social consequence. In fact, and as we shall explore more fully later when we discuss some of the social and psychological causes of narcotics addiction, it is a useful question to ask whether narcotics addiction should not be seen as but a part of some larger American social problems, the problems of poverty and of poor assimilation of some of our newer migrant groups. Drug addiction today, suggests Clausen, "is, indeed, primarily a symptom of a deeper pathology that derives from our failure to integrate into the social fabric the more deprived migrants to our metropolitan centers, especially those disadvantaged by minority-group status. Subjected to all the stimuli which beckon Americans to participate in the joys of an affluent society, yet lacking the legitimate, socially approved means to achieve the gratifications and material rewards promised by this society, some of these persons turn to deviant and illegal means."[42] In any case, whether it is taken as a problem in itself or as a symptom of a larger set of present-day social problems, it is questionable whether some objective social calculus would assign so great an importance to drug addiction as a social problem as it is often given in political discussion and in the public press. The individual and social system malfunctioning resulting from alcoholism may constitute a much greater social problem.

[41] John A. Clausen, "Drug Addiction," in Merton and Nisbet, *op. cit.*, p. 220.

[42] *Ibid.*

Apart from individual and social system malfunctioning, drug addiction has come to be viewed by many groups in American society as a terrible affront to their moral values.[43] The problem of addiction, because of the special moral horror it arouses, say Chein and his colleagues, "is commonly viewed in the most violently distorted perspective, and the efforts of society to cope with the problem are models of irrationality."[44] Chein thinks that the "grossly exaggerated estimates of the number of addicts," exaggerations which he scornfully calls "a numbers game," are in part the result of the moral condemnation of drug addiction, most notably on the part of the law-enforcement agencies. The overestimates may result in part also from the hope of well-intentioned social agencies that they can thereby get more help for addicts.

Clausen agrees with Chein about the special moral disapproval that drug addiction arouses in many circles. The non-medical use of narcotics in the United States is not only a crime, he says, but "one of the most stigmatized of crimes."[45] The public horror of the addict and of the criminals who sell narcotics has resulted in a scapegoating so severe that it has even been made law by the Narcotic Drug Control Act of 1956 that the death penalty be given to those involved in illegal narcotics activities with persons under eighteen years old. Law enforcement agencies at all levels, from the Federal Government on down, have played upon this scapegoating and moral revulsion. As a result, says Clausen, "the Congress of the United States has repeatedly concerned itself with the problem in recent years, imposing ever more severe penalties on the

[43] But note, again, a caution expressed by A. R. Lindesmith. In a personal communication he says, "With respect to popular attitudes in the United States, it is not clear that the punitive view is or has been as strong as you suggest. For example, we repeated here in Bloomington, with a sample of the town population, the questions which Schur asked his British sample, and found to our surprise that the local sample was slightly more unanimous in viewing the addict as diseased than was the British sample! This raises interesting questions concerning the relationship between public opinion and law. The attitude toward the peddler is unquestionably very punitive." It would be highly desirable to study the attitudes of a representative national sample of the American people toward addicts and non-addict peddlers.

[44] Isidor Chein, Donald L. Gerard, Robert S. Lee, and Eva Rosenfeld, *The Road to H*, New York: Basic Books, Inc., 1964, p. 7.

[45] "Drug Addiction," in Merton and Nisbet, *op. cit.*, p. 181.

addict and the despised 'dope peddler'."[46] Or again, Clausen says, "There is no evidence that *addiction* to drugs is favorably regarded in any society or culture, but the status accorded the addict varies markedly. In the United States he has been defined as a criminal and stereotyped as a 'dope fiend.' In much of Europe, on the other hand, the addict is regarded as an unfortunate person whose problem is primarily psychological and medical."[47] Unexpectedly, and particularly since World War II under the direct influence of American views and policy, perhaps particularly in Japan, the drug addict elsewhere has come to be treated as a criminal as he is in the United States, rather than ignored, or treated as a person suffering from a socio-medical disease.[48] This "prohibition-and-police" policy in the countries of the Far East has resulted in consequences similar to those in the United States: racketeering; high prices (heroin and morphine, now, not the more impure opium); and the excessive recruitment of younger, urban, lower-class male addicts.

Despite the strong value condemnation of drug addiction in many circles in the United States, there are some signs that values may be shifting in some quarters. Some sociologists, psychologists, government officials, and medical groups are trying to remove the special moral stigma that is attached to drug addiction and to transform it from a criminal problem to a socio-medical problem. Schur, who has made an intensive comparison of drug addiction in Great Britain and in the United States, suggests that much of the apparent moral horror of drug addiction in the United States is created by the policy and attitudes of the law-enforcement agencies and that public opinion might shift unexpectedly rapidly from a punitive to a reformative view if law-making and law-enforcement views shifted in that direction.[49] Linde-

[46] *Ibid.*

[47] "Social Aspects of Drug Use and Addiction."

[48] Lindesmith, *op. cit.*, Ch. 7. This is the most thorough and up-to-date discussion of the problem of addiction in the Far East.

[49] Edwin M. Schur, "Attitudes Toward Addicts: Some General Observations and Comparative Findings," *American Journal of Orthopsychiatry*, 34(1964), pp. 80–90. See also Edwin M. Schur, *Narcotic Addiction in Britain and America: The Impact of Public Policy*, Bloomington, Indiana University Press, 1963.

smith concurs very strongly in the view that a very considerable responsibility for this moral horror of addiction in the United States is due to the policy and "propaganda," continued over more than thirty years, of the Federal Bureau of Narcotics. It has treated addiction as a police problem and has resisted any efforts to treat it as primarily a socio-medical problem.[50]

In sum, and before looking at some comparative and historical data in detail, we can make the following generalizations about the use of narcotics and narcotics addiction as a social problem: first, use and addiction are not everywhere defined as a social problem in anything like the same degree that they are in the United States; second, use and addiction were not always a social problem even in the United States as they are today; third, use and addiction by different social groups at different times for different reasons may make it desirable to think in terms of a number of different social patterns and problems here, not just one; and, fourth, social policy is itself one of the major determining social sources of the nature and severity of this social problem.[51]

Patterns of Narcotics Use

We can see the patterns of narcotics use and addiction and the great variation in values about them by noting the following considerably different patterns of *use, attitude,* and *treatment:*

Nineteenth-century United States—All of the social classes took opiates in freely available patent medicines and some members of all social classes became addicted. Women addicts seemed to out-number men addicts three to two, perhaps because more women took patent medicines for "female troubles," which were poorly understood and little helped by the medicine of the time. In the nineteenth century addiction may have been less prevalent among Negroes than Whites,

[50] *Op. cit.*

[51] For a forceful statement of all four of these points, independently arrived at on the basis of a lifetime of research and theorizing on narcotics addiction by Lindesmith, see Alfred R. Lindesmith and John H. Gagnon, "Anomie and Drug Addiction," in Marshall B. Clinard, editor, *Anomie and Deviant Behavior: A Discussion and Critique,* New York: The Free Press of Glencoe, 1964.

and the average age of Negro addicts was between forty and fifty years.[52] Addiction was treated as a medical problem. The rate of addiction may have been higher than it is in contemporary United States.

Twentieth-century England and Western Europe generally—The number of addicts is very small and they come from all social classes. Addiction is treated as a medical problem.

Mid-twentieth-century United States—Especially since the 1930's, the largest proportion of addicts came from the poor, culturally-deprived, psychologically-disturbed groups among the Negro and Puerto Rican migrants to our metropolitan urban slums. Addiction was viewed with moral horror and treated as a police problem.

Twentieth-century United States and England—Because of the easier access that doctors and other medical personnel have to narcotics, there are disproportionately high rates of addiction among these groups. The one striking exception are pharmacists, who do not have disproportionately high rates of narcotics addiction. Addiction among medical personnel is treated partly as a medical problem, partly as a police problem.

Early-modern and modern times in the Near and Far East—The use of opium and rates of narcotic addiction have varied greatly in the different countries of these two vast regions. In the past, opium was used by different social classes for a variety of functions—tension-relieving, recreational, and medicinal. According to recent reports, and despite long and intensive efforts by various international bodies, including the United Nations, there is little evidence that there has been any decrease in the traffic in, use of, or addiction to narcotics in these countries.[53]

A somewhat different picture has been presented recently by Lindesmith, at least for the Far East:

> The history of anti-opium measures in the Far East may be conveniently divided into three periods: (1) the period before 1912, which was the date of the Hague Convention in which agreement was reached by the powers with interests in the Far East to attempt a gradual suppression of opium smoking, a vice which was subject to no serious control before this time; (2) the period from 1912 to World

[52] *Ibid.*, p. 164.

[53] See *The New York Times*, Sept. 17, 1964.

War II, characterized by the prevalence of government monopolies which controlled legal production and distributed opium to consumers, who were often registered or rationed; (3) the third period, after World War II, characterized by the elimination of government monopolies and the triumph of prohibition.[54]

As indicated above, Alfred Lindesmith feels that since World War II the Far Eastern narcotics problem has been "Americanized," with all the attendant evils of a "prohibition" policy.[55]

Now let us look at some of the detailed substantiation of these several patterns, considering first the matter of rates of opium use and addiction in some other countries in the recent past and immediate present. It should be noted that these rates are perhaps even less solidly based on evidence than are the contemporary rates for the United States, and that some of them are especially weak in distinguishing between rates of use and rates of addiction. Indeed, more often than not, no attempt is made to distinguish between the two, because extreme use, or addiction, is not viewed with the special moral horror that it is in the United States at the present time. Mild and sporadic use is viewed as shading into more continual and harmful use.

Opium use and addiction occur throughout the Middle and Far East, but with very great, and unexplained, variations in the rates. Much the highest rates are found in India, Iran, and Egypt.[56] But opium use and addiction occur, though often in much lesser frequency, in Borneo, China, Japan, Korea, Burma, and elsewhere.[57] Of course they occur in the West as well, with probably the greatest frequency in the United

[54] Lindesmith, *The Addict and the Law*, p. 190.

[55] *Ibid.*, Ch. 7.

[56] *Encyclopaedia Britannica*, Vol. 16, 1963, "Opium," p. 814. Sir R. N. Chopra, "The Present Position of the Opium Habit in India," *Indian Journal of Medical Research*, 16(1928). United Nations Economic and Social Council, Commission on Narcotic Drugs, 13th Session, *Incidence of Drug Addiction*, 7 March 1958, E/CN. 7/345.

[57] League of Nations, Commission of Enquiry into the Control of Opium Smoking in the Far East, Volume III, Geneva: *Report to the Council*, 1932. United Nations Economic and Social Council, Commission on Narcotic Drugs, *Report of the 14th Session, Official Records: 28th Session, Supplement No. 9*. October, 1959(a). E/3254; E/CN. 7/376. United Nations Economic and Social Council, Commission on Narcotic Drugs, Ninth Session, 13th Session, *Incidence of Drug Addiction*, 7 March 1958, E/CN. 7/345.

States, but also in the several countries of Western Europe and, in at least some small measure, in the USSR.[58] Contrary to superficial expectation, it occurs in much higher rate in Canada (where it is estimated there are some 3,000 to 3,500 addicts in a population of about 18 million) than in the United Kingdom (where it is estimated that there are some 350 addicts in a population of about 45 million).[59] This higher rate in Canada seems to be due to the fact that the Canadian control system is more like that of the United States than like that in the United Kingdom.[60] Throughout the Western countries, there is a consensus among experts, rates of addiction are disproportionately high among the medical professions, in part because of their ready access to heroin; however, there is an equally firm consensus that "addiction among pharmacists is practically nonexistent," with no plausible explanation being available.[61] The difference between doctors and pharmacists certainly indicates that access is not in itself a sufficient cause of high addiction rates. Age and sex rates also vary among the different Western countries at the present time. One study of drug addiction in the Department of the Seine, France, showed a near absence of juvenile addiction, and practically equal rates of addiction for men and women between thirty and fifty-five.[62] This is in great contrast to the high youthful rates in the United States at the present time and to the much greater prevalence of male over female addicts.

Functions of Narcotics Use

Little is known about the functions of the use of drugs and of addiction in other countries than the United States, but, on a common-

[58] United Nations Economic and Social Council, Commission on Narcotic Drugs, 13th Session, *Incidence of Drug Addiction,* 7 March 1958, E/CN. 7/345.

[59] United Nations Economic and Social Council, Commission on Narcotic Drugs, *Report of the 14th Session, Official Records: 28th Session, Supplement No. 9.* October, 1959(a). E/3254; E/CN. 7/376.

[60] For more recent British figures, showing a slight increase in the United Kingdom, see Russell Brain, "The Report of the Interdepartmental Committee on Drug Addiction," *The British Journal of Addiction,* 57(1961), pp. 81–103.

[61] *Ibid.*

[62] United Nations Economic and Social Council, Commission on Narcotic Drugs, Ninth Session, May, 1954. E/CN. 7/SR232.

sense classification, at least three different functions seem to be performed by drug use and addiction in these other countries. They are diversion, medical therapy, and work support.

The diversionary or recreational functions seem to occur for all social classes, but in somewhat different ways. For the lower classes, narcotics represent a temporary escape from hardship; for the higher classes, they offer relief from boredom and a new and possibly attractive experience. Referring to the lower classes, for example, a League of Nations report says, "The social and hygienic conditions under which a great part of the working classes in the Far East live are of so low a standard that these classes of people strive to find some form of diversion permitting them to forget at least for some moments the hardships of life."[63] While some members of the higher classes also use narcotics "to forget their worries and anxieties," Chopra says, some people in these classes use drugs because of their "stimulant and pleasure-giving effects."[64] He also says that these people use it for its aphrodisiac action. "Those belonging to the leisurely and idle classes start taking the drug for the mere fun of it. Its use among this class may be said to be traditional, as ever since the time of the Moghuls it has been considered to be a luxury habit of the rich classes."[65]

The therapeutic functions for which opium is used and from which addiction may result are very broad. "In the Far East generally, and especially in the tropical countries, where the population often suffers from dysentery, typhoid, malaria, and other fevers, there is a widespread belief that opium taken habitually, whether eaten or smoked, will act as a prophylactic against such diseases and cure them. In addition, pulmonary diseases are believed to be cured by opium."[66] Opium is widely taken to relieve pain. According to another League of Nations report, among the working-class Chinese of North Borneo, "the desire

[63] League of Nations, *Opium and Other Dangerous Drugs.* Commission of Enquiry into the Control of Opium-Smoking in the Far East. Geneva: Report to the Council, 1930, p. 23.

[64] *Op. cit.*, p. 430.

[65] *Ibid.* See also *Encyclopaedia Britannica,* Vol. 16, 1963, "Opium," p. 814, for reference to "pleasure" functions of narcotics.

[66] League of Nations, *Opium and Other Dangerous Drugs, op. cit.*

to obtain relief from sickness is the principal cause for commencing to smoke opium."[67] One discussion asserts that no fewer than 50 per cent of all Indian addicts use narcotics to "obtain relief from their ailments."[68] Opium is sometimes given to ailing young children to quiet them. This was true, incidentally, in Europe as well. An informant has told me that when he was a boy in rural Italy, only a generation ago, a potion of boiled poppy seeds was used in just this way, to quiet young children when they cried continually. Finally, narcotics are sometimes used to allay hunger. This is true both for the chronic hunger of the poor and for the hunger resulting from religious fasts. "There is no doubt," says one writer, "that the spread of the practice [of opium use and addiction] is connected with the ban imposed in Mohammedan countries on the use of alcoholic beverages, and to some extent with the long religious fasts of the Buddhists, Hindus, and Moslems, in which opium is used to allay hunger."[69]

Finally, the use of narcotics has the function of providing support in extremely difficult work situations. "A large number of workmen, especially manual laborers in the jungles and forest and in tin-mines in tropical countries, take to the smoking of opium because, having to perform strenuous work in an unhealthy and hot climate, they believe that opium will stimulate them and increase their working capacity. This belief sometimes makes opium smokers of practically the whole labor force on lumber estates, in tin mines, etc."[70] Chopra suggests that "more indulgence is noted among individuals following lines of employment which necessitate long hours of tedious work."[71]

A brief history also illuminates the *variable* character of addiction as a social problem. The use of opium seems to have been known in antiquity among the Egyptians, the Greeks, and the Assyrians, but no

[67] League of Nations, Commission of Enquiry into the Control of Opium Smoking in the Far East, Volume III Geneva: Report of the Council, 1932.

[68] *Encyclopaedia Britannica,* Vol. 16, 1963, "Opium," p. 814.

[69] *Encyclopaedia Britannica,* 11th edition, 1911, Vol. 19, "Opium."

[70] League of Nations, *Opium and Other Dangerous Drugs.* Commission of Enquiry into the Control of Opium-Smoking in the Far East. Geneva: Report to the Council, 1930. See also, League of Nations, Commission of Enquiry into the Control of Opium Smoking in the Far East, Volume III. Geneva: Report of the Council, 1932, p. 132.

[71] *Op. cit.,* pp. 424ff.

ancient authority mentions the problem of addiction.[72] Nor is addiction mentioned in medieval Western accounts of the use of opium in medical therapy. The use of opium for therapeutic and other functions seems to have become much more widespread among the Arabs, following Mohammed, in part because it became a functional alternative to alcohol, the use of which was prohibited by Mohammed. Until quite recent modern times, indeed until the nineteenth century, since there were very few therapeutic "specifics" available to Western medical practitioners, opium was widely and satisfactorily used for the relief of pain. It was almost treated as a panacea, and there was little fear, and perhaps less fact, of addiction as a social problem. In 1701, for example, a London physician, John Jones, wrote about the excessive use of opium just as one might write about the excessive use of tobacco or wine. "None can argue," he said, "that opium diminishes or disables the spirits any more than wine or bread does, a surfeit of which is most dangerous."[73]

Throughout the nineteenth century, in the West, there was a growing therapeutic use of opium, especially through the medium of various patent remedies which were freely prescribed by physicians or available to the general public without prescription. There seems to have been an especially heavy use of these patent remedies for "female troubles," that is, gynecological difficulties that were either purely physiological or associated with psychosomatic malfunctioning. As a result of the free availability of opium in patent remedies and especially in those for "female troubles," the rate of addiction may have been as high as it is today in the United States, even higher perhaps. Today only one addict out of six is a woman, but in the nineteenth century the ratio of female to male addicts may have been three to two.

Along with the growing therapeutic use of opium and the possibly increasing amount of addiction, there was a growing awareness of addiction and its dangers among medical men and the general public. A

[72] I am here following the historical account by Glenn Sonnedecker, "Emergence and Concept of the Addiction Problem," in Robert B. Livingston, editor, *Narcotic Drug Addiction Problems,* U.S. Department of Health, Education and Welfare, Public Health Service, National Institutes of Health, Bethesda, Maryland, 1963, pp. 14–22, but it should be noted that Sonnedecker speaks of the lack of an adequate comprehensive history of the addiction problem.

[73] *Ibid.*

number of events led to this increased awareness. First, early in the century, there began to appear literary accounts of some strange and uncontrolled experiences with opium. Thomas de Quincy's *Confessions of an Opium Eater,* published in 1821, was perhaps only the best known of these. It brought the use and hazards of opium to the attention of an increasingly large literate public.[74] Second, medical scientists and medical practitioners came to have a much better understanding of both the chemical and medical nature of opium and its potentially harmful consequences. Third, the use of opium was increased as a result of the invention of the hypodermic syringe in 1853. This increased the danger of narcotics abuse, a danger which was very much enlarged as a result of the widespread use of the syringe and narcotics during the American Civil War. After the war, the use of morphine and the hypodermic syringe by veterans of the Civil War became known as "army disease." Fourth, toward the end of the century, the use of narcotics and addiction became associated with various criminal elements, especially in the western part of the United States. The use of narcotics became almost as much associated with gamblers, prostitutes, and "evil and illegal Chinese immigrants" as with therapeutic uses. Finally, the problem of narcotics use, addiction, and traffic took on a world-wide cast. Various national and international bodies sought to control the traffic in opium that originated in the Far East but carried its harmful effects to the "more civilized" precincts of Western Europe and the United States. In the United States, as a result partly of the concern of the American Pharmaceutical Association, several state narcotics laws went into effect as early as 1903. A big turning point came with the international Hague Opium Convention of 1912. The signatory nations to this Convention agreed to pass legislation seeking to control the traffic in opium within their own borders. In the United States, the result was that Congress passed the Harrison Act in 1914.

Because the Harrison Act was passed as a revenue act, its enforcement was vested in a special police unit, the Narcotics Division of

[74] See also, in Robert S. de Ropp, *Drugs and the Mind,* New York: Grove Press, 1960, originally published 1957, pp. 77ff., an account of the case of Fitz Hugh Ludlow, a 16-year-old, middle-class boy in Poughkeepsie, N.Y., who tried hashish for himself in the 1850's and published, anonymously, his *The Hasheesh Eater,* in 1860.

the Treasury Department.[75] Acting as a police-enforcement agency, rather than as a socio-medical control group, the Narcotics Division in 1919 brought legal action against a number of physicians who had written opium prescriptions for addicts. These actions resulted in judicial convictions, which were, unfortunately, sustained on appeal by the Supreme Court of the United States. These convictions resulted in a radically changed social definition of addiction, namely, that it was a crime, and not a socio-psychological-medical problem. This criminal definition has only been strengthened with time, due in no small measure to the endless reiteration of this point of view by the Narcotics Division. In effect this agency has had a much larger share in making social policy than government administrative agencies usually do. The addict has come to be defined as a criminal, a "dope fiend," a degenerate, an enemy of society, and not at all as a sick person. Thus, as a result of judicial decision and the attitudes of the Narcotics Division, not only individual doctors but organized medicine as a whole have been afraid to deal with the addict primarily as a sick person. And this has been so despite the fact that in 1925 the Supreme Court, in the Linder decision, rejected "the interpretation that physicians were prohibited by the Harrison Act from treating addicts."[76] Until very recently, the drug addict has been left to the federal and local police authorities and to the illicit drug peddler; only in the last few years or so have medical practitioners reasserted the essentially medical character of drug addiction.

Definition of "Addiction"

Only very recently, also, have some questions been raised about the basic nature of narcotics addiction. Part of the folklore which has

[75] In the material just preceding, and in what follows, I am depending on the useful accounts in Clausen, "Drug Addiction," in Lindesmith, *op. cit.* and in Harris Isbell, "Historical Development of Attitudes Toward Opiate Addiction in the United States," in Seymour M. Farber and Roger H. Wilson, editors, *Conflict and Creativity*, New York: McGraw-Hill Co., 1963.

[76] For this view, see also Lindesmith, *op. cit.*, and Advisory Council of Judges of the National Council on Crime and Delinquency, *Narcotics Law Violations: A Policy Statement*, New York: National Council on Crime and Delinquency, 1964.

become nearly inseparably attached to American discussions of narcotics addiction, popular and professional discussions alike, is that it is incurable once contracted. The universal belief has been, "once a 'dope addict,' always a 'dope addict'." But Schur has pointed out that even the popular belief that it is easy to detect an addict is not true. "Observable indications of addiction," he says, "vary greatly from case to case, and in some instances may hardly be present at all."[77] There is in fact a very high relapse rate for addicts after the usual quasi-criminal methods of treatment, but this fact does not take into account the existence of a certain number of apparently spontaneous and certainly little-noticed cures. Chopra has pointed out that in India the duration of opium addiction seems to vary considerably. While about half the cases last over ten years, about a third of them last only from six to ten years, and the rest, about a sixth, last less than six years.[78] In the United States as well, according to the very latest review of the matter by Clausen, there is some spontaneous recovery. "Some," he says, "—no one knows what proportion—manage to maintain drug use for a time on an occasional basis and to stop altogether without ever becoming addicts."[79] There does seem to be some special set of physiological consequences which occurs in a great many cases of prolonged use of opium. These consequences show themselves in the violent reactions known as the "abstinence syndrome" when drugs are withdrawn. But under what physiological conditions such consequences occur, or in how many cases, has never been carefully studied. Nor have studies been made to see how these physiological conditions interact with, indeed may be vitally dependent upon, a special set of psychological and social conditions.

As a result of their recent intensive studies of narcotics addiction in New York City, Chein and his colleagues have raised these same basic questions about the nature of narcotics addiction.[80] They attempt to distinguish between "users" and "addicts" on the basis not only of physiological criteria but of various psychological and social criteria. They point out that there are variations in "total involvement" and

[77] *Narcotic Addiction in Britain and America, op. cit.,* p. 27.

[78] *Op. cit.,* p. 418.

[79] Clausen, "Social Aspects of Drug Use and Addiction."

[80] Chein, Gerard, Lee, and Rosenfeld, *op. cit.*

"craving" among narcotics users, that these variations are hard to measure, and therefore that "users" and "addicts" are hard to distinguish from one another. Their research and analysis seems clearly to have established the fundamental points that there are significant differences among the individuals usually and harshly all labeled "addicts" and that these differences have consequences for the ability of the individual to stop using drugs. They feel that "the term 'addicting' is used largely out of tradition" by the various international, federal, state, and local authorities seeking to control the distribution and use of drugs.

During the last ten years, the most commonly accepted and used definitions of drug addiction and drug habituation were those set up by the Expert Committee on Addiction-Producing Drugs of the World Health Organization in 1957.[81] The difficulties with the two definitions were so great, however, that the WHO Committee recommended in 1964 the adoption of a new term, "drug dependence," to replace both "drug addiction" and "drug habituation." In the new effort, "drug dependence" is defined as a state arising from repeated administration of a drug on a periodic or continual basis. Its characteristics will vary with the agent involved, and this must be made clear by designating "drug dependence" of a particular type in each specific case—that is, drug dependence of morphine type, of cannabis type, or of barbiturate type. The description of types of drug dependence is confined to medical aspects only, but the Committee recognizes that "none of the pleasure-giving drugs produce a uniform and consistent effect based on their pharmacological properties. The effect of these drugs, including alcohol, on an individual user, depends on a complex interaction between the pharmacology of the drug itself, the personality of the individual taking the drug, and the social setting in which the drug is taken."[82]

We can see still more clearly the necessity of defining addiction in physiological, psychological, and sociological terms when we consider the meaning of the use of various other substances and drugs than opium. It is widely accepted, of course, that alcohol may be as addictive as opium and that there are probably more alcoholics than opiate ad-

[81] The present discussion follows that given by Joel Fort in Richard Blum and Associates, *Utopiates: The Use and Users of LSD-25*, New York: Atherton Press, 1964, pp. 207ff.

[82] *Ibid.*

dicts. Indeed, so long as he avoids the abstinence syndrome, "the addict probably suffers less organic harm and interference with his normal functioning than the chronic alcoholic."[83] However, there no longer seems to be the same extreme social and psychological stigma attached to alcohol addiction as there still is to opiate addiction. Or consider the officially alleged "addictiveness" of peyote. Although the use of peyote was defined in 1948 by a committee of the American Medical Association as addictive, the anthropologist LaBarre and several of his colleagues, on the basis of their intensive experience, have differed with this view.[84]

Recently, several classes of non-narcotic drugs have been redefined as addictive or dangerously habituating and have come under stringent federal and state control. These "psychotoxic" drugs are the barbiturates, the amphetamines, and the tranquillizers, all of which have been in somewhat uncontrolled prescription sale and use until now. It has been estimated, for example, that some thirteen billion pills and capsules of these classes of non-narcotic drugs are being produced yearly in the United States and that, of this total, approximately one-half have been diverted to the non-medical, illegal market, selling at a premium and often to the great profit of organized criminal groups. The consumption of these drugs has increased greatly during the last thirty years. Between 1936 and 1960, while the American population was increasing by 25 per cent, the consumption of these drugs increased three to four times. Between 14 and 18 per cent of all doctors' prescriptions are estimated to be for sedatives and tranquillizers.[85] Concern about this widespread legal and illegal use of the non-narcotic drugs has increased as evidence has accumulated that they are, in fact,

[83] Schur, *Narcotic Addiction in Britain and America*, p. 23.

[84] Weston La Barre, "Twenty Years of Peyote Studies," *Current Anthropology*, 1 (1960), pp. 45–60. Carroll G. Barber, "Peyote and the Definition of Narcotic," *American Anthropologist*, 61(1959), pp. 641–646. Carroll G. Barber, "Rejoinder to Maurer," *American Anthropologist*, 62(1960), pp. 685–687. Oliver La Farge, "Defining Peyote as a Narcotic," *American Anthropologist*, 62(1960), pp. 687–689. D. W. Maurer, "Peyote is Not a Drug of Addiction," *American Anthropologist*, 62(1960), pp. 684–685. David F. Aberle, *The Peyote Religion Among The Navaho*, New York: Viking Fund Publications in Anthropology, No. 42, 1966.

[85] The Medical Society of the County of New York, "The Dangerous Drug Problem: A Policy Statement, With Recommendations on the Abuse of LSD and Other Non-Narcotic Drugs," mimeo. report, 1966.

addictive or dangerously habituating. The barbiturates by themselves are definitely addictive, and it has also been discovered at the Lexington, Kentucky, center for the treatment of heroin addicts, and elsewhere, that many of these addicts have a concomitant addiction to the barbiturates. As for the plethora of tranquillizers on the market, it has been reported by Dr. Carl F. Essig of the Public Health Service's Addiction Research Center at Lexington that at least seven of the tranquillizers in common use have been found to be addictive and to cause withdrawal symptoms similar to those caused by heroin.[86] Finally, as for the amphetamines, apparently they "produce no true addiction but they are habituating and dangerous. Judgment and intellectual impairment, aggressive behavior, incoordination and hallucinations all may occur during withdrawal. Furthermore, amphetamines are being implicated in increasing numbers of automobile accidents."[87]

Over the last twenty years or so every state but Montana has enacted some form of law restricting the sale of non-narcotic "dangerous drugs." Many states patterned their legislation after not-too-stringent federal codes. In 1960, a Uniform State Barbiturate Code was drafted and became the model for new legislation in many states. The big landmark in legal control over the non-narcotic addictive or habituating drugs is the Drug Abuse Control Amendments of 1965, a federal bill requested by President Johnson which alters the Federal Food, Drug, and Cosmetic Act and which came into force on February 1, 1966 under the administrative responsibility of the Food and Drug Administration. This law seeks to avoid the extreme measures of prohibition that the old Volstead Act imposed on the sale and use of alcohol and that resulted, in that case, in so many evil consequences. Instead, it imposes greater control over illegal and harmful use of these drugs through increased record keeping all the way from their manufacture to their wholesale distribution, retail sales, and medical prescription. Manufacturers and distributors of the drugs will be registered with the Food and Drug Administration. Retail dealers must keep precise inventories and copies of all invoices of shipment and prescriptions for these drugs for three years. Physicians who dispense drugs themselves are subject to the same rules and all physicians must limit the

[86] *The New York Times,* June 23, 1965.

[87] The Medical Society of the County of New York, *op. cit.*

time a prescription remains in effect and the number of refills permitted. Prescriptions will not be valid for more than six months nor more than five refills. To supervise the carrying out of these new regulations, the Food and Drug Administration has been given new investigatory and enforcement power over all parts of the system of manufacture, distribution, prescription, and sale. The amendments impose a set of terms of imprisonment and of fines for various violations. These are not excessively severe; there is a maximum of two years in prison and a $5,000 fine. While it is unlikely that the new laws will effectively eliminate all abuse of the non-narcotic drugs, it is probable that they may reduce it considerably.

Finally, with regard to drugs with possibly addictive consequences, what about marihuana? The consensus of informed opinion seems to be that marihuana as used in the United States is not addictive, nor apparently even dangerously habituating in most cases of its use. Lindesmith states that marihuana is not at all addictive as heroin is, and he recommends that it should be treated by the public and the police in a completely different way from heroin.[88] Lindesmith's view that marihuana is not addicting, and that "excessively harsh penalties at both federal and state levels" are laid upon its use, has also recently been stated by The Medical Society of the County of New York through its Subcommittee on Narcotics Addiction of its Public Health Committee.[89] Although some users of marihuana may "progress" to the use of heroin, the great majority do not and only "fool around" with marihuana for a few times. Nonetheless, the use of marihuana is not something to undertake lightly.

Socialization to Addiction

How have addicts been trained into their harmful practices? In all places and times, addiction seems often to be an unintended byproduct of activities with other functions, such as pleasure seeking or therapy. In the contemporary United States, all the evidence indicates, two widespread notions about socialization into addiction are misconceptions.

[88] For an excellent, comprehensive survey of the marihuana problem—marihuana is also known as and comes in the different forms of hashish, cannabis, bhang, ganja, etc.—see Lindesmith, *op. cit.*, Ch. 8.

[89] *Op. cit.*

First, as Clausen has put it, "addiction is not primarily to be attributed to the drug peddler," or, as it is alternatively expressed by Chein and his colleagues, "the great majority of juvenile regular users are not initiated into drug use by an adult pusher."[90] Most users and eventual addicts are initiated into drug habits by "friends" and age peers, members of their informal social groups or acquaintances whom they meet in their neighborhoods, usually the highly-deprived slum neighborhoods of large cities. And since "drugs are probably smuggled into virtually all of our penal institutions," the spread of addiction seems to occur also among intimates in these places, which are often quasi-extensions of our large-city slum neighborhoods.[91] Second, very few users actively seek the opportunity to try heroin. The opportunity to try it usually comes almost casually, as a chance to experiment with something that will provide "kicks" or excitement in an otherwise dull and futile existence. Even in areas of high drug use and addiction, only a minority experiment in this casual way, and some of this minority is "hooked" to continued use and addiction. Some users of heroin start by "fooling around" with marihuana, but here too the socialization is relatively casual and through friendly age peers.

Induction for medical personnel, of course, follows a different pattern. In this situation, apparently, though we have no studies of the matter, initial use of narcotics is with full knowledge of their functions for relieving pain or fatigue. The medical user who becomes an addict finds the drug effects so beneficial that he becomes physiologically, psychologically, and sociologically dependent on them. Unlike the juvenile user, he remains a solitary and secret user or addict.

Causes and Consequences of Addiction

The several questions surrounding the meaning of addiction suggest, of course, that there are also basic questions to be raised about the causes of addiction. A few basic points may be made. It is perhaps now clear that any discussion of the etiology of addiction has to consider the interaction of the physiological, the psychological, and the

[90] Clausen, "Drug Addiction," pp. 193ff. Chein, Gerard, Lee, and Rosenfeld, *op. cit.*, p. 12.

[91] Lindesmith, *op. cit.*, p. 57.

sociological. It is perhaps also clear that since addiction seems to have different functions in different situations, therefore also it has different sets of predisposing and precipitating causes.[92] The causes of addiction among the adolescent male slum-dweller in Manhattan in the 1950's may be quite different from the causes among middle-aged, middle-class women in nineteenth-century America, and both of these sets in turn may be different from the causes of addiction among people of any age or social class in the contemporary Middle or Far East. As for the first type, the slum-dwelling juvenile, this is the only type on which intensive research has been carried out. The studies by Chein and his colleagues show the following sociological and psychological results:—Juvenile addicts come disproportionately from the most deprived areas of the large city; some 15 per cent of the census tracts containing 30 per cent of the boys had 80 per cent of the cases of known addiction. The users and addicts are boys with a pessimistic, unhappy, futile, mistrusting, negative, defiant, manipulative, and devil-may-care attitude toward life. Among the boys in these areas, they come from the least cohesive families. In sum, they are both socially and psychologically quite disturbed. "The evidence indicates," says Chein, "that all addicts suffer from deep-rooted, major personality disorders."[93] As for other types of addiction, besides this one which is so much at the center of current American attention and investigation, much research remains to be done.

Besides varying considerably in its meanings and social and psychological sources, the connections of addiction with criminality also vary a great deal. Apparently only in the United States at the present time, in Canada, and in various Far Eastern countries under the influence of the "Americanization" of their narcotics policy, is distribution and use of narcotics considered a major social problem and surrounded with a dense social network of legal rules and crime detection agencies. "Indeed, in most civilized countries at the present time," says Clausen, "narcotics addiction is not an important social problem and is

[92] For a recent attempt to state a completely general causal theory of drug addiction, see Alfred R. Lindesmith, "Problems in the Social Psychology of Addiction," in Daniel M. Wilner and Gene C. Kassebaum, editors, *Narcotics*, New York: McGraw-Hill, 1965.

[93] Chein, Gerard, Lee, and Rosenfeld, *op. cit.*, p. 14, *et passim*. See also Clausen, "Drug Addiction."

not primarily a matter for criminal prosecution; it is a medical problem to be dealt with through the doctor-patient relationship."[94] And Lindesmith and Gagnon assert very strongly, "The major factor which caused the drug problem to change from what it was to what it now is in this country, in all probability, was the change in public policy, which has had the effect of making the use of opiates illegal and of outlawing the addict."[95]

But if narcotics use, addiction, and even distribution need not in themselves be defined as crimes, once they are so defined they can set in train a whole set of secondary or derived sociological effects which are in fact criminal in both morality and law. First of all, because the distribution of narcotics is defined as a crime, and as a result drug prices rise very high, male addicts are pushed by the system toward committing an endless series of crimes against property in order to get the money to pay for their drugs. The evidence shows clearly that these are primarily petty thefts for the purpose of obtaining the necessary funds to pay the extortionate costs of drugs sold on the illegal market. For the same reasons, women addicts often resort to prostitution, as well as participating in petty crimes against property, alone or in partnership with some male addict. Despite this evidence, there is a widespread belief among Americans that narcotics addiction "is a virulently contagious disease and that it is a major cause of crime."[96] Apparently a small number of crimes of violence by addicts, widely publicized in the metropolitan press as typical of all crime by addicts, are sufficient to keep confirming the erroneous stereotype that many Americans have about the connection between addiction and violence.

Another criminal consequence that derives from the *definition* of narcotics addiction as a criminal and not a socio-psychological-medical problem, is the emergence of an elaborate illegal system for the distribution of drugs. It would seem that the profits to be made from the illegal distribution of drugs are just very much too large not to attract full-time, "professional," non-addict criminal individuals and syndicates. Nobody has really reliable figures on what the illegal market in drugs amounts to, but there is consensus that it is very large. Schur

[94] Clausen, *ibid.*

[95] Lindesmith and Gagnon, *op. cit.*

[96] Chein, Gerard, Lee, and Rosenfeld, *op. cit.*, p. 328.

mentions the estimate that an amount of pure heroin which would be worth $12,000 on the legitimate wholesale drug market would sell for more than $3,500,000 on the illegal market.[97] It has also been estimated that the total volume of sales on the illegal market, at these prices, amounts to several hundred million dollars a year. It should also be noted that there seems to be no evidence that there has been any effective decrease of the size of this illegal market by the actions of the federal, state, or local narcotics-law enforcement agencies.

Still another derived and at least quasi-criminal consequence of defining narcotics addiction as criminal is the use of illegal control practices by the law enforcement agencies themselves. "In general," says Schur, "it appears that a war-against-addiction mentality has fostered an 'anything goes' approach to narcotics law enforcement."[98] Informers who are themselves addicts are used, procedural safeguards for those charged with narcotics crimes are ignored, and so on through the catalog of known procedures of "illegal" police practice.[99] Although, there is no evidence that this police illegality is very large or that it is any greater than it is in connection with various other crimes, it might be so if the police share, as they seem to, the widespread public notions about the special heinousness of narcotics use and addiction.

Remedies for Addiction

There are no social problems, with the individual and social system malfunctioning and the conflicts of values they imply, that are without their associated attempts at treatment and control by those who define them as social problems. When the Harrison Act was passed in the United States in 1914, it probably did not occur to anyone that treatment of narcotics addiction would pass out of the hands of the medical profession. Indeed, until about 1925, both individual medical practitioners and groups of them cooperatively tried to help addicts who could no longer get legitimate access to the drugs they needed. In this period, in some forty different American cities, clinics were estab-

[97] Schur, *op. cit.*

[98] *Ibid.*, p. 56.

[99] Lindesmith, *The Addict and the Law*, Chs. 2–3.

lished by the medical profession for the treatment of addicts.[100] The clinics seem to have been therapeutically effective in some cases; but, overall, they failed both as organizations and as therapeutic agencies. The reasons for this failure have never been definitely established. Lindesmith feels that one essential reason for the failure of the clinics was the hostile attitude of the new Federal Narcotics Bureau, whose officials had toward the clinics "a new philosophy—that of prohibition as expressed in the Volstead Act," rather than a medical point of view.[101] Here may be an especially valuable area for research, especially if treatment of narcotics addiction is returned to the medical profession in the future and if clinics for such treatment are established. Since 1925, control of narcotics addiction has very largely, almost completely, fallen into the hands of the Narcotics Bureau, who have been willing to share it, ever since, only with other law enforcement agencies. As for treatment of confirmed addicts, the federal government provides two major treatment facilities, the United States Public Health Service Hospitals at Lexington, Kentucky, and Fort Worth, Texas, specializing in the "cure" of addicts, but these have been strikingly unsuccessful in their mission. Their patients have an extremely high rate of relapse and seem to use the hospitals as temporary respites from drugs rather than as opportunities for more permanent cures. This is unfortunately the case in spite of the fact that it is only those cases thought to be more hopeful that are selected for treatment at these hospitals.

Quite recently, a new mode of treatment of addicts has come into existence. This is the Synanon Movement, with interesting similarities to the Alcoholics Anonymous movement.[102] Synanon, which seems to have worked out, on entirely empirical grounds, an intensive pro-

[100] In the present account of treatment and control I am essentially following Schur, *Narcotic Addiction in Britain and America:* Ch. 1.

[101] Lindesmith, *The Addict and the Law,* pp. 140–141. Lindesmith, however, does not favor a return to a program that will be highly individualized, between addict and individual doctor.

[102] See Rita Volkman and Donald R. Cressey, "Differential Association and the Rehabilitation of Drug Addicts," *American Journal of Sociology,* (1963), pp. 129–142. Lewis Yablonsky, *The Tunnel Back: Synanon,* New York: Macmillan Co., 1965.

gram of family-like re-socialization for addicts, has been claiming "cure" and rehabilitation rates that are much higher than those obtained by any other known method of treatment. Synanon deserves the most sympathetic attention and the most careful kind of research investigation.

Another, even newer mode of treatment for heroin addiction abandons the goal of re-education, at least temporarily, and seeks instead to *maintain* the addict on another drug, methadone hydrochloride, which is as addictive as heroin but permits the addict to function socially much more adequately than when he is on heroin. This treatment was hit upon accidentally by Vincent P. Dole and Marie Nyswander while they were attempting to help a group of heroin addicts, all of whom were high-dosage, "mainliner" (intravenous injection) users, and all of whom had a history of failures with withdrawal treatment.[103] Dole and Nyswander discovered that daily oral administration of high dosages (100 mg.) of methadone effectively blocked the "narcotics hunger" which all these addicts had previously experienced after withdrawal treatment and which led them back into "mainliner" use. During the first period of treatment, in which the process of switching over to methadone occurred, the addicts were kept by Dole and Nyswander on an unlocked hospital ward and allowed to leave for school, libraries, shopping, and other activities, but usually in the protective company of a member of the treatment staff. In the second period, the addicts became outpatients, living at home and returning to the hospital every day for methadone medication. The third and final period, an advance in degree on the second period, is one in which the addict "has become a socially normal, self-supporting person," still on methadone and dependent on it, but with no further craving for heroin and its "highs."[104]

Although Dr. Nyswander, a psychoanalyst who has long specialized in the treatment of narcotics addicts, hopes that methadone "may be an important bridge to rehabilitation," she would be satisfied if it

[103] This account is based chiefly on Vincent P. Dole and Marie Nyswander, "A Medical Treatment for Diacetyl-Morphine (Heroin) Addiction—A Clinical Test with Methadone Hydrochloride," *Journal of the American Medical Association*, 198(1965), pp. 646–650; and Nat Hentoff, "The Treatment of Patients," *The New Yorker*, June 26, July 3, 1965.

[104] *Ibid.*

enabled some heroin addicts "to become self-supporting, responsible members of the community," even at the expense of indefinitely prolonged addiction to methadone.[105] "It does not strike me as relevant," she has said, "whether these patients ever get off methadone. Some may want to and that's fine. What *is* relevant is that a treatment can be developed so that the addict can become a socially useful citizen, happy in himself and in society. That's much more important than whether he's on or off medication."[106] Thus, Dr. Nyswander would like to see the methadone maintenance treatment defined as a medical procedure and as a procedure which is as morally justified as the medical maintenance of the diabetic on insulin.

Not everyone agrees with this point of view. In the past, for example, the United States Public Health Service has not accepted any treatment of addicts that left the patient dependent on another drug. And at a recent meeting of the Medical Society of the State of New York, Dr. Robert W. Baird, Director of the Haven Clinic for heroin addicts in New York City, also deplored the treatment of heroin addiction by switching to another addictive drug. Dr. Baird is reported to have said that using methadone was "like giving the alcoholic in the Bowery bourbon instead of whisky in an attempt to get him off his alcoholism."[107]

Nevertheless, the methadone treatment has been encouraged by the City of New York to the extent that it has provided funds amounting to more than $1 million and facilities in four municipal general hospitals for further research and experimental use of the drug.[108] Even with these funds and facilities, of course, experience is still small, amounting to about one hundred treated cases as of early 1966, and with perhaps an equal number coming into treatment. Continued testing of methadone is likely unless prevented by the U.S. Public Health Service in accordance with its policy of disapproving of treatments that "merely" switch from one addictive drug to another. In the case of

[105] Hentoff, *ibid.*

[106] *Ibid.*

[107] *The New York Times,* Feb. 16, 1966. For a full account of the Medical Society meeting, where Drs. Dole and Baird presented their opposing points of view, see *Drug Trade News,* Feb. 28, 1966.

[108] *The New York Times,* August 25, 1965.

methadone, however, the benefits of switching and of medical treatment may be sufficiently great to induce the P.H.S. to change its policy. A functional calculus of costs and benefits as between heroin and methadone "addiction" seems to come out all in favor of the latter.

In Great Britain, in striking contrast to the United States, narcotics addiction is the most minor of social problems (only 350 known addicts) and treatment and control has remained essentially in the hands of the medical profession.[109] As in the United States, opiates were freely available before the early 1920's without prescription. The Dangerous Drugs Act of 1920, like the Harrison Act, controls the import, export, manufacture, sale, and distribution of narcotics, but nevertheless the basic principle has been accepted (as laid down by the Rolleston Committee Report) that addiction is an illness, not a crime, and that treatment of illness belongs in the hands of physicians. The British physician is accordingly given considerable latitude in his power to prescribe narcotics for known addicts. If the addict is defined by the doctor as someone who cannot lead even a minimally useful and normal life without drugs, the doctor may prescribe maintenance doses of drugs that keep the addict in some minimally useful condition. British physicians recognize the high rate of relapse among addicts, the great difficulties of "cure," but they accept nonetheless the principle of maintenance treatment. An essential element in British treatment seems to be the non-punitive and cooperative attitude of all the relevant groups: the medical profession, the police, and the general public. There have been practically no secondary criminal practices associated with drug addiction in Britain. Finally, in great contrast to the American situation, the known addicts are about 50 per cent female, mostly over thirty years of age, scattered geographically, and also widely distributed throughout the different social classes. There is one point of similarity between the two countries: in both places the medical profession contributes disproportionately to the number of addicts.

Because of the humaneness of the British system of treating narcotics addicts, it has been reported recently, substantial numbers of Canadian addicts are migrating to Britain to secure this more satisfactory treatment and to escape the harshness of their own country's

[109] On Britain, see Schur, *Narcotic Addiction in Britain and America;* and Lindesmith, *The Addict and the Law,* Ch. 6.

treatment, which is much like that of the United States.[110] Unfortunately, some of the migrants to Britain from Canada, and the United States as well, may be transmitting the American pattern to Britain. The number of known addicts in Britain has gone up by about two-thirds during the last six years, it is said, and the bulk of this increase is accounted for by younger people.[111] "There is no need for panic measures," says *The Economist,* "such as making addiction, as distinct from traffic in drugs, a police matter. Equally, something should be done quickly to check the spread of the disease among the young."[112]

The differences between American and British rates of addiction and their patterns of treatment and control cannot be attributed to some basic, generalized difference in the law-abiding qualities of the two populations. In Great Britain, for example, where there is the same lack of provision for legal abortion as there is in the United States, there is apparently the very same elaborate system of illegal facilities. The American social problem in connection with drug addiction is definitely in considerable measure a product of a certain social policy and its resulting social system.

What is the outlook for the future for narcotics addiction as a social problem in the United States? It is clear that a basic change in values and attitudes towards addiction is necessary if its character as a social problem is to be changed. Comparison with Britain and other countries, and even with the United States at an earlier historical period, indicates that basically different attitudes are possible. How are these different attitudes to be brought about in the United States? How is what is now defined as a criminal problem to be redefined as a socio-psychological-medical problem? Research that would have both policy and theoretical significance on these questions would be highly desirable. Can the values and attitudes of the medical profession, the public, the Congress, and especially of the law enforcement agencies, federal, state, and local, and notably the Narcotics Bureau, be changed? How? By what combination of the diffusion of information and the bringing to bear of political pressure at the right points? Can what now seems to be a vicious circle, in which social policy helps partly to create the

[110] Lindesmith, *The Addict and the Law,* pp. 184ff.

[111] See *The Economist,* August 21, 1965.

[112] *Ibid.*

social problem which is not wanted, be transformed into a beneficent spiral in which social policy plays a more socially constructive role?[113]

There seem to be a few favorable signs of change. In New York, for example, where the concentration of addicts makes the problem far and away more serious than it is anywhere else in the United States, a state agency has recently been willing to experiment with the possibility of running a clinic in which addicts are medically treated and given maintenance doses of drugs.[114] And it has now been made legal in New York State to conduct research programs in which maintenance doses of narcotics are administered "under medical supervision and control."[115] However, New York legislators are still opposed to maintenance treatment by individual physicians. The Executive Committee of the New York County Medical Society of the A.M.A. has proposed that doctors resume some of their rights to the medical treatment of addicts, specifically that they be allowed to maintain some addicts on drugs under highly controlled conditions.[116] This seems to be the first time the medical profession, despite its being "scared stiff" of the problem, as the President of the New York County Medical Society is reported to have said, has moved significantly toward redefining the character of drug addiction as a social problem. Still, basic progress may take a long time. New legislation in New York State, which prescribes compulsory treatment of narcotics addicts, was recommended by state officials speaking of a "war" on the "evil contagion" of addiction, language which is more expressive of a punitive police policy than a socio-medical policy toward this problem.[117] And although the legislation was opposed by a minority who rejected compulsory commitment as both immoral and therapeutically ineffective, the legislation has now been passed.[118] In this whole area, social scientists have an excellent opportunity to study social change in process.

[113] The best statement of a program for reform, of obstacles to its realization, and strategies for overcoming these obstacles, can be found in Lindesmith, *The Addict and the Law*, Chs. 9 and 10.

[114] *The New York Times*, March 9, 1964.

[115] *The New York Times*, July 21, 1965.

[116] *The New York Times*, January 22, 1965.

[117] *The New York Times*, Feb. 24, 1966.

[118] *The New York Times*, February 27, March 5, 28, 29, and 31, 1966.

The Problem of Illegitimate Control of Behavior and Thought

We have seen a great deal of direct and indirect evidence of the very powerful effects of drugs on behavior and mind. A great many, perhaps most, of these effects are positively valued by most people. But some of these effects, and among these some that are still more potential than actual, are viewed by a certain number of people with alarm and disapproval. These people value negatively, rather than positively, certain actual and possible patterns of control over behavior and mind that drugs provide. Out of such value dissensus there arises the "social problem" of the actual and potential illegitimate control of behavior and mind. Harold Lasswell has called this social problem the problem of "somatarchy, or rule by biochemicals."[119]

The social problem of the illegitimate control of behavior and mind has been raised in at least four different connections. The first has to do with the use of tranquillizing drugs to control the behavior of mentally disturbed people. Thomas Szasz, a psychiatrist, for one, has complained of the "chemical strait jackets" by which hospital patients suffering from serious mental illness are being "controlled" unfairly.[120] Tranquillizing drugs, he feels, may violate the right of the patient, often without his consent, to "the maximal recognition of his right to self-determination, growth, and the working out of conflicts."

All apart from mentally disturbed people, second, fears of illegitimate and undesirable control have been raised in connection with "normal" people. Saunders, for example, has wondered if the new drugs may throw not only patients, but "entire societies," into "a sort of painless concentration camp of the mind, in which people will have lost their liberties in the enjoyment of a dictatorship without tears."[121] And another viewer-with-alarm has said: "Some may maintain that man was not placed on earth to be so comfortable, that he should aspire to something nobler than the placid contentment of a well-pastured

[119] Harold D. Lasswell, "Communication and the Mind," in Seymour M. Farber and Roger H. L. Wilson, editors, *Control of the Mind,* New York: McGraw-Hill Book Co., 1961, pp. 266–267.

[120] T. Szasz, "Some Observations on the Use of Tranquillizing Drugs," *American Medical Association, Archives of Neurology and Psychiatry,* 77(1957), pp. 86–92.

[121] J. B. de C. M. Saunders, Introduction, Farber and Wilson, *op. cit.,* p. xiii.

cow."[122] "It is obviously possible," continues de Ropp, "to tranquillize a man to the point at which he loses not only his anxieties but also his ambitions, ideals, creative urges, everything, in short, that distinguishes him from a contented cow." Our values of activity, of striving, of individualistic rationality, all these seem threatened, at least to some people, in a world in which the use of drugs makes a "cow-like" existence possible.[123]

The third connection in which illegitimate use of drugs for the control of behavior and mind is feared is in the "brain-washing" of military and civilian prisoners. Such "brain-washing" is assumed to make radical transformations in the behavior and thought of those on whom it is illegally used. Striking examples of the apparent success of such use of drugs have been reported, not only in the public press but in more specialized media of communication. Such instances have indeed occurred, and the result is a serious problem for both the training of potential military prisoners and for the guarantees of the civil liberties of non-military prisoners. However, the weight of the expert opinion seems to hold that the amount and depth of "brain-washing" effects by drugs is exaggerated. "Combined with the many other stresses in captivity that an individual may be obliged to undergo, drugs can add to the factors aimed at weakening the resistance of the potential informant," says Gottschalk in a summary article on the use of drugs in information-seeking interviews.[124] "But," he continues, "for many reasons, the use of drugs by an interrogator is not sure to produce valid results." Cautions about exaggerating the possibilities of "brain-washing" have also been expressed by Cole and by Miller.[125]

The fourth and final area where the cry of illegitimate control of behavior by drugs has been raised is in connection with the fluoridation of water as a means of improving dental health by preventing dental

[122] Robert S. de Ropp, *op. cit.*

[123] For a similar criticism by a Norwegian, see Karl Evang, *Health Service, Society, Medicine,* London: Oxford University Press, 1960, p. 124.

[124] Louis A. Gottschalk, "The Use of Drugs in Information-seeking Interviews," in Leonard Uhr and James G. Miller, editors, *Drugs and Behavior,* New York: John Wiley and Sons, 1960, p. 518.

[125] Jonathan O. Cole "Drugs and Control of the Mind," in Seymour M. Farber and Roger H. L. Wilson, *op. cit.* and James G. Miller, "The Individual Response to Drugs," in *ibid.*

cavities. The usefulness of adding minute amounts of fluorine, usually in the form of sodium fluoride, to the public drinking water supply is a well established piece of medical knowledge.[126] A great many laymen accept this knowledge and approve of fluoridation of their drinking water. But many others define fluoridation as not only dangerous to their health but as an illegitimate control of their behavior.[127]

The essence of the charge of illegitimacy against public fluoridation has been that it violates the individual's right to behave as he himself determines, that it is a form of "compulsory medication." This charge taps, of course, a very strong value of individualism in American society. As a result, many local referenda on fluoridation have been won by those who have opposed the measure as an unwarranted encroachment on their liberties as individuals. Despite such widespread opposition, public fluoridation has been gradually extended to ever larger proportions of the population. To many, however, it still remains a "social problem" to be violently attacked, a burning injustice, an instance of illegitimate control of their behavior through drugs administered by those who seek to dominate the public and to abridge individual liberties.

In general, throughout this particular "social problem" area, because of the lack of reliable knowledge of the effects of drugs and because of the great fears that spectacular possibilities for the control of behavior and mind may really exist, there is a certain tendency to uncontrolled speculation and to the crying-up of potential effects, both good and evil. For example, a recent book advertisement asks, "What would happen—to Negroes and whites—if science suddenly discovered a way to alter skin pigmentation and turn Negroes white? Just by taking a pill!"[128] And a news story at about the same time, reporting on the effects that doses of RNA have had on making experimental rats perform tasks more efficiently, refers to the possibility of a "smartness" pill

[126] For an authoritative discussion, see Harold C. Hodge and Frank A. Smith, *Fluorine Chemistry, Vol. 4,* New York: Academic Press, 1965.

[127] Benjamin D. Paul, "Fluoridation and the Social Scientist: A Review," *The Journal of Social Issues,* 17(1961), pp. 1–12. Paul's essay is a summary of and introduction to a whole series of articles in this issue of the *Journal of Social Issues* which are devoted to reporting empirical research and sociological and psychological analysis of recent fluoridation referenda controversies.

[128] *The New York Times,* Dec. 28, 1964.

for human beings being made out of the same substance.[129] Such possibilities are not absurd, by any means, but they are often advertised or reported, sometimes unintentionally, in ways that make "social problem" disasters all but imminent.

In conclusion, the problem of the use of drugs is the problem of the use of all human technology. No matter how beneficial some class of technological substances or agents may be, there is always the possibility that they may be, in part or whole, used for ill as well as good. The control of the uses of drugs, as of all other technology, is a problem which often involves large sectors of the total social and political process and for which there are no easy solutions.[130]

[129] *Ibid.*

[130] Bernard Barber, *Science and the Social Order,* New York: Collier Books, 1962, Ch. 10. (Originally published, 1952.)

6

The Definition and Functions of Drugs

AFTER HAVING SEEN so frequently the desirability of taking a thoroughgoing new look at the meaning and uses of drugs, we would like to go back to some fundamentals. In this last chapter, therefore, we shall take up two fundamental and interrelated problems, first, how to define "a drug," and, second, the very large range of psychological and social functions which drugs have in social systems. The significance of these problems and of the way we deal with them is very important for the study of drugs and society.

"A *drug,*" say Goodman and Gilman in their standard textbook on therapeutic pharmacology, "may be broadly defined as any chemical agent which affects living protoplasm, and few substances would escape inclusion by this definition."[1] So broad a definition indicates that the problem of definition is still with us. Indeed it is, and all the more so since anything considered to be a drug takes on an important part of its significance from the social and psychological meanings attached to it by individuals and by social systems.

[1] Louis S. Goodman and Alfred Gilman, *The Pharmacological Basis of Therapeutics,* New York: Macmillan Co., 1958, 2nd edition.

We may illustrate this point in a preliminary way here with a few very concrete examples. A recent dispute between the United States Food and Drug Administration and Mead Johnson Laboratories, a pharmaceutical manufacturer, originated in the assertion by the FDA that the product "Quell," which Mead Johnson was selling as a "dietary food," was in fact a "misbranded drug."[2] Or again, FDA has held that the ink stain used for diagnostic purposes in cases of fungal infection is a drug. The ink stain is manufactured by a large company producing inks for fountain pens, and the ink stain is essentially no different from the fountain pen ink. "Dial" soap, because of its anti-bacterial claims, is also classified as a drug. Indeed, any item listed in the *United States Pharmacopeia* is *legally* defined by the Food, Drug, and Cosmetic Act as a drug. Included, therefore, as drugs, are certain gauze bandages listed in the USP. The social and psychological definitions of materials of all kinds are highly relevant to their being named "drugs." We might even say that nothing is a "drug" but naming makes it so.

An adequate definition of a drug will start with the assumption that anything involved in human behavior needs to be considered at the physiological level, the psychological level, and the social level, and particularly needs to consider these three levels in interaction with one another. At all three levels, a drug is something to be defined not in terms of its substance, but rather in terms of its functions for the system at that level and for the interaction of the functions of the different systems. And, since systems are most usefully specified by scientific theory, rather than more empirically, functional definitions of drugs will be best derived from the systematic theory that is relevant to each of these three levels of behavior and to their interaction.

The Need for a Functional Definition

A comprehensive and systematically functional definition of drugs has several advantages. One of them is to provide a different and better perspective on drugs than definitions which are limited by their substantive character to partial views, views which are often absolute just because they are limited and partial. Another advantage of a functional definition is that it makes it possible to deal with a whole series of important problems of general concern in theoretical analysis and applied

[2] *Drug Trade News,* June 8, 1963.

policy: the problem of multiple functions at any system level and also at different system levels for different drugs and even sometimes for the same drug; the problem of both functional and dysfunctional consequences from the same drug; the resulting problem of a functional calculus among these positive and negative consequences; and the imprecise and hard choices that remain when no good functional calculus is available. Later on we shall consider these and other important functional problems in their general aspects further. A comprehensive and systematic functional definition has the advantage that it enables us to avoid hidden prejudices and unduly negative judgments in our discussion of drugs.

"The term 'drug,' " John Clausen has pointed out, "refers to a wide variety of chemical substances consumed by man, and not merely to narcotics or 'dangerous drugs.' When applied to substances consumed outside of medical channels, however, the word 'drug' tends to connote something negatively valued. Hence, we do not normally refer to the smoking of tobacco as a 'drug habit' but do so refer to the smoking of marihuana, even though many more persons may be psychologically habituated to tobacco smoking than to marihuana."[3] Nor do we usually refer to alcohol as a drug, although Joel Fort has said flatly, "alcohol is the most widely used and abused pleasure-giving drug in the Western world."[4] And, he continues, "in sharp and ironic contrast to the social and legal response to the other related drugs, alcohol is essentially uncontrolled, freely, albeit expensively, available to all, and considered a harmless beverage rather than a dangerous drug." Fort exaggerates a bit, but his basic point is well taken. Hidden prejudices of this kind may have dysfunctional effects that we would like to avoid. For example, is the prejudice against narcotic "drugs" generalized to all drugs by some people, even those for beneficial therapeutic purposes? When people are being trained to the use of various kinds of drugs, how many of these misleading generalizations from hidden prejudices do they transfer from one type of drug to another just because they are all called by the same name for some purposes?

[3] John A. Clausen, "Social Aspects of Drug Use and Addiction," *International Encyclopedia of the Social Sciences,* forthcoming, 1968. The same point has been made by Isidor Chein, Donald L. Gerard, Robert S. Lee, and Eva Rosenfeld, *The Road to H,* New York: Basic Books, Inc., 1964, p. 336.

[4] In Richard Blum, and Associates, *Utopiates: The Use and Users of LSD-25,* New York: Atherton Press, 1964, p. 208.

If the same drug can have different effects, as we shall see, and if different substances called "drugs" can have many different effects as well, then we can profitably consider the multiple functions or effects that drugs have. We shall limit ourselves to social and psychological functions, and to the interaction of these with physiological effects, leaving the purely physiological level to experts in the medical and biological sciences. As our list of different functions will show, it almost seems as if there is no social or cultural or psychological function at all to which drugs, in one or another form, are not relevant. In the study of drugs, specialization which is not based on a comprehensive view can easily become provincialism.

Since there are so many different functions for drugs, and since there is as yet no widely-accepted general social and psychological theory for behavior in general, and therefore not for drugs, our list is more empirical than we would like it to be. It has somewhat overlapping categories and is not at all exhaustive. To signalize the empirical character of the list, the multiple functions will be discussed alphabetically. In considering the whole list, two general questions can usefully be kept in mind. First, are all the listed functions in fact present in all societies, but in somewhat differing degree in different societies and at different times? And second, have there been any evolutionary trends in the emphasis on different functions, for example, away from magical and religious functions and toward therapeutic functions?

The Multiple Functions of Drugs

AESTHETIC FUNCTIONS

Drugs of various kinds have been used by both "primitive" and modern man in achieving the aesthetic experiences associated with such activities as dancing and music. LaBarre, for example, reports that American Indians have used the drug peyote (active agent, mescaline) for giving strength in dancing, in the playing of music, and in the learning of painting and bead design.[5] Modern jazz musicians have often used marihuana to get "high" and achieve special effects in their music.

The most sophisticated and self-conscious exploration of the aes-

[5] Weston La Barre, *The Peyote Cult*, Originally published as Yale University Publications in Anthropology, 1939, No. 19. Reprinted Hamden, Connecticut: The Shoe-String Press, Inc., 1959.

thetic functions of drugs has been made by Aldous Huxley, for whom the aesthetic and the religious or self-transcending functions are combined in the same experiences with mescaline.[6] Mescaline, Huxley says, permitted him to see beauty not available to the ordinary man but only to the artist. "The other world," he says, "to which mescaline admitted me was not the world of visions; it existed out there in what I could see with my eyes open. The great change was in the realm of objective fact." Mescaline made it possible for him to see "a repeated flow from beauty to heightened beauty." And, "mescaline raises all colors to a higher power and makes the percipient aware of innumerable fine shades of difference to which, at ordinary times, he is completely blind."[7] Various psychiatrists have reported that their patients have had experience with LSD similar to Huxley's with mescaline.[8] And one journalist, reporting on the findings of the studies that have been reported in some of the more than 2,000 papers on LSD that have already appeared, says that "another common reaction to LSD is called synesthesia, a blending of sense perceptions. An LSD subject will often feel that he can smell the music he is listening to, or hear the sound of color, or touch the texture of an odor."[9]

APHRODISIAC FUNCTIONS

Although the importance attached to love as a desirable human experience varies among different societies, it is everywhere valued in some measure, for at least some people.[10] It is not surprising, therefore, that a wide variety of drugs and other aids have been used in the attempt to direct and increase the processes of love. A good deal of magic is mixed in with folk-empirical knowledge so far as aphrodisiac drugs are concerned, and so is a good measure of what modern doctors refer to as "the placebo effect," that is, feelings that are psychologically or socially induced, rather than due directly to chemical substances. None-

[6] Aldous Huxley, *The Doors of Perception,* New York: Harper & Row, 1954. See also Meyer H. Abrams, "The Milk of Paradise," *Harvard Honors Theses in English,* No. 7, Cambridge, Harvard University Press, 1934.

[7] *Op. cit.,* pp. 16, 18, 27.

[8] Sanford M. Unger, "Mescaline, LSD, Psilocybin, and Personality Change: A Review," *Psychiatry,* 26(1963), pp. 114, 123.

[9] Leonard Wallace Robinson, *The New York Times,* August 22, 1965.

[10] William J. Goode, *The Family,* Englewood Cliffs, N.J.: Prentice-Hall, 1964, pp. 39ff.

theless, aphrodisiacs have been, and probably continue to be in some societies, widely used for controlling love relations.[11]

Related perhaps to the aphrodisiac functions of drugs are the love-and-affection winning functions of the new "beauty" drugs, the "wrinkle removers" which have been offered for sale recently by some of the American pharmaceutical manufacturers, usually through their cosmetics subsidiaries, e.g., Pfizer through Coty. The effectiveness of these drugs has been challenged by the Food and Drug Administration and writs issued against their sale.

EGO-DISRUPTING FUNCTIONS

"Through all recorded history and everywhere in the world, men have gone to considerable length," say Barron, Jarvik, and Bunnell, "to seek unpredictability by disrupting the functioning of the ego. A change of scene, a change of heart, a change of mind: these are the popular prescriptions for getting out of a rut."[12] Alcohol has been one common, almost universal, way of achieving this effect, but a number of drugs have provided other means, and knowledge and use of these has been increasing in recent times. Mescaline, which comes from the peyote cactus, psilocybin from mushrooms, and d-lysergic acid diethylamide (LSD) from ergot (a fungus that grows on rye) constitute the chief of these drug alternatives.[13] The use of mescaline in its crude form in the peyote button has been known in Mexico and the American Southwest and Plains areas since at least the sixteenth century; pure mescaline was synthesized in 1896 and is the drug which Aldous Huxley used to open up new "doors of perception." Psilocybin and LSD have been more

[11] For a general survey, see Harry E. Wedeck, *Dictionary of Aphrodisiacs*, New York: The Citadel Press, 1962. A hard cover version was published by the Philosophical Library, 1961. See also R. N. Chopra and G. S. Chopra, "The Present Position of Hemp-drug Addiction in India," *Indian Medical Research Memoirs*, No. 31, July 1939, for the use of hemp in India as an aphrodisiac. The subject of aphrodisiacs, though obscured by a variety of factors, would still repay intensive scholarly study. There seems, however, to be something either unpleasant or trivial about the subject that frighens off scholars.

[12] Frank Barron, Murray E. Jarvik, and Sterling Bunnell, Jr., "The Hallucinogenic Drugs," *Scientific American*, 210(1964), No. 4, pp. 29–37.

[13] Blum and Associates, *op. cit.* This is probably the most comprehensive, scholarly, empirical, and objective discussion of LSD we have. For a report on some very recent experience with LSD in New York City, see the Medical Society of the County of New York, mimeo report, News Conference, 1966.

recently discovered. All are alkaloids related to one another in chemical structure.

These drugs are sometimes called the "hallucinogens" because they produce changes in the ego and in perception that cause what seems to be hallucinations. However, the person under the influence of the drug can distinguish his experiences from reality and can attribute them to the action of the drug. Therefore, they are not like true hallucinations. These drugs have often been called "psychedelic" because they are said to provide "a process of going outside, going beyond learned modes of experience (particularly the learned modes of space-time-verbalization-identity). . . ."[14] The hallucinogens are considered dangerous when not used under medical supervision because they sometimes cause psychosis, as well as more often producing effects that resemble psychosis (hence, also, the term "psychotomimetic" for these drugs).[15] Because of their ego-disrupting functions, mescaline, psilocybin, and LSD are being used by some psychiatrists in novel forms of psychotherapy. As Barron, Jarvik, and Bunnell point out, these drugs "produce a wide range of subjective and objective effects."[16]

Nevitt Sanford, the psychologist who was the sympathetic sponsor of their work, has said in the foreword to the study by Blum and his associates:

> This is a point of great importance: the effects of taking the drug are heavily dependent upon the characteristics of the taker. They vary with the situation in which it is taken, with the subject's psychological state at the time, with personality and background, and with social and cultural group membership.
>
> If the source of the drug is illicit and the setting is one in which the aim is to get high with a group of young people, then the effects will be similar to those achieved with the use of various other substances—orgiastic, artistic, or euphoric. On the other hand, if the drug is taken in a medical setting, the responses are more likely to be in the area of changed perspectives and integrative experiences. Within each of these

[14] Blum, and Associates, *op. cit.*, p. 179. See also p. 175, where there is another attempt at definition and where the coinage of the term is attributed to Henry Osmond.

[15] For evidence on production of psychoses see The Medical Society of The County of New York, *op. cit.*

[16] *Op. cit.*

settings, there will be variations with personality and with sociocultural factors.[17]

It has even been shown by some investigators that the group composition and context of experimental animals has an effect on the way in which they respond to drugs.[18] No direct homologies to human social situations are demonstrated by these animal experiments, but they do indicate the potential fruitfulness of further studies on the way human social situations help to determine drug action.

Although mescaline, psilocybin, and LSD seem not to be physiologically addictive, like the opiates, some individuals do become strongly psychologically habituated to them, especially those who take the hallucinogens regularly or who make the drug-taking experience the center of their activities. It is now obvious that the ego-disrupting functions of the hallucinogens can be good or very bad in their consequences. Research is necessary to understand better the sources of these different consequences, as it is also for improvement of the means of control over the taking of these drugs.[19]

IDEOLOGICAL FUNCTIONS

Drugs may sometimes have ideological functions, that is, serve to express a preference for certain social values as against others. The taking of mescaline in the form of the peyote button, centering on the Peyote Cult and the Native American Church, has such ideological as well as religious functions.[20] It was often the full-bloods among the Indians,

[17] Blum, and Associates, *op. cit.*, p. xiv. In their empirical studies, Blum and his associates divide their total sample into five sub-samples which demonstrate the general points made in Sanford's statement, that the responses to LSD vary considerably by psychological disposition and social and cultural context. See especially Ch. III for a systematic comparison of the five sub-samples, but see also Chs. II and V.

[18] See C. W. M. Wilson and R. E. A. Mapes, "The Relationship Between Group Composition and Drug Action in Mice," *Psychopharmacologia,* 5(1964), pp. 239–254, and C. W. M. Wilson and R. E. A. Mapes, "The Effects of Group Composition on Drug Action," in Hannah Steinberg, A. V. S. de Reuck, and Julie Knight, editors, *Ciba Foundation Symposium Jointly with the Coordinating Committee for Symposium on Drug Action on Animal Behavior,* London: J. & A. Churchill, 1964. These papers refer to other literature.

[19] This need for research is stressed throughout Blum, and Associates, *op. cit.*

[20] La Barre, *op. cit.;* Weston La Barre, "Twenty Years of Peyote Studies," *Current Anthropology,* 1(1960), pp. 45–60; James S. Slotkin, *The Peyote Religion,* Glencoe, Illinois: The Free Press, 1956.

those who were anti-white, expressing their preference for Indian values and culture, who were the peyotists, seeking thereby to resist both the physical and the ideological dominance of white values and culture.

POLITICAL FUNCTIONS

Drugs have also been involved in political functions. For example, speaking of the 1930's, Trevor Williams says that "the Japanese have made extensive use of opium for political purposes. It is well established that they poured the drug into those parts of China which they controlled. . . . In this way they hoped so to demoralize the people that there would be no serious attempt at organized insurrection."[21] Similarly, it is alleged that at the present time the greatest barrier to the effective international control of the cultivation and use of the opium poppy is the various politico-economic interests of several Middle- and Far-Eastern countries where this cultivation is still extensive.

PSYCHOLOGICAL SUPPORT FUNCTIONS

Another psychological function for drugs is to provide support in a variety of more or less severe stress situations which the personality temporarily or more permanently faces. Again, drugs (in somewhat crude form) have been used for these functions for a long time, but, recently, more refined drug therapies have been available. In the last fifteen years or so, the several tranquillizing and energizing drugs have provided stimulant and sedative support for personalities unable to cope with some form of temporary or longer-lasting stress. Psychological support drugs have been used sometimes just to provide support as an end in itself, sometimes as a base for active psychotherapy seeking to remove the sources of the stress.[22]

RELIGIOUS FUNCTIONS

As might be expected from the fact that drugs have social and psychological functions of support and control in the secular world, they also have religious functions, that is, functions connected with the problems

[21] Trevor Williams, *Drugs from Plants*, London: A. L. Atkinson, Ltd., 1947, p. 36.

[22] See, among other references, William Sargant, *Battle for the Mind: A Physiology of Conversion and Brainwashing*, New York: Doubleday & Co., 1957, especially chapter on "The Use of Drugs in Psychotherapy"; Harold E. Himwich, "Psychopharmacologic Drugs," *Science* 127(1958), pp. 59–72: and Leonard Uhr and James G. Miller, editors, *Drugs and Behavior*, New York: John Wiley and Sons, 1960.

of transcendent or other-worldly meaning.[23] For example, among the lower classes of Jamaica, marihuana, or "ganja" as it is called there, is given religious significance and "is said to bring the individual closer to God. The cultivation and use of this substance is defended and justified by reference to biblical passages." The Jamaican upper classes support "laws which provide severe penalties for the use and cultivation of the weed. In the meantime, pious, Christian, lower-class Jamaicans continue to grow and use it in defiance of laws which to them seem misguided, if not positively irreligious."[24]

Perhaps the best-studied case of the religious functions of drugs is the case of the Native American Church among the American Indians, a religion which centers on the worship and use of the peyote button. The peyote button was used in Mexico as early as the sixteenth century and may go back a couple of thousand years before that. Individual or tribal-cult use of peyote diffused slowly northward among the Indians of the American Southwest and on the Plains.[25] Before about 1890, peyote use was limited to an aid in the seeking of individual visions and as a stimulant in tribal dancing rites. But after 1890, with the violent destruction of the Ghost Dance, a messianic movement preaching the return of a Messiah who would rescue the Indians from the social and cultural chaos into which White conquests had forced them, the Indians took up the worship and use of peyote as the answer to their fundamental problems of meaning, their path to salvation.[26] Peyote is defined by this religion as the prime incarnation, as something given to the Indians by God because he took pity on them for their weakness in the face of White force. Ingesting peyote gives one some of the power inherent in it; it is not dissimilar from the sacrament

[23] On the uses of and attitudes toward drugs in various religions, see Richard Thomas Barton, *Religious Doctrine and Medical Practice,* Springfield, Illinois: Charles C. Thomas, 1958; on India, see Chopra and Chopra, *op. cit.*

[24] Alfred R. Lindesmith and John H. Gagnon, "Anomie and Drug Addiction," in Marshall B. Clinard, editor, *Anomie and Deviant Behavior: A Discussion and Critique,* New York: The Free Press of Glencoe, 1964, pp. 161–162.

[25] Bernard Barber, "A Socio-cultural Interpretation of the Peyote Cult," *American Anthropologist,* 53(1941), pp. 673–675; Slotkin, *op. cit.;* La Barre, *The Peyote Cult;* and Robert S. de Ropp, *Drugs and the Mind,* New York: Grove Press, 1960.

[26] Bernard Barber, "Acculturation and Messianic Movements," *American Sociological Review,* 6(1941), pp. 663–669.

of taking the bread and wine in Christianity. Peyote religion, seen from the point of view of the social scientist, is a relatively passive and therefore not unsatisfactory way of adjusting to the problems of meaning faced by American Indians.

Although it is not addictive, unfortunately peyote has come under attack as a narcotic in some states, though the Federal Government has not defined it as a narcotic.[27] With the aid of friendly anthropologists, leaders of the Native American Church have fought a number of legal contests for their rights to use peyote for religious purposes.[28] Just recently, at least in the California Supreme Court, these rights were established as valid.[29] As the American Indians become better assimilated into American society, of course, the Native American Church is likely to decline, and even now it is only one religion among several that the Indians profess.

However, it is not only Indians who see in peyote and its active agent, mescaline, the path to religious salvation. Mescaline has religious as well as aesthetic functions for Aldous Huxley, who thinks that mescaline gives people the power to transcend themselves, to open a Door in the Wall (H. G. Wells' phrase) that stands between man and his salvation.[30] "The urge to transcend self-conscious selfhood is . . . a principal appetite of the soul. When, for whatever reason, men and women fail to transcend themselves by means of worship, good works and spiritual exercises, they are apt to resort to religion's chemical surrogates."[31] For Huxley, a religion based on mescaline would probably be highly individualized and would certainly be more passive than active. Other highly sophisticated persons besides Huxley have seen religious uses for modern drugs. For example, such uses have been attributed to LSD; usually, however, as in the case of Huxley, by individuals who

[27] Blum, and Associates, *op. cit.*, p. 217.

[28] Compare the statement in Blum, and Associates: "The legal status of those who use *LSD* has been unclear to observers and to users themselves", *op. cit.*, p. 24. In New York State, under recent legislation, possession of LSD may be a misdemeanor and sale may be either a misdemeanor or a felony. See the Medical Society of the County of New York, *op. cit.*

[29] *New York Times*, August 25, 1964.

[30] Huxley, *op. cit.*, pp. 62ff.

[31] *Ibid.*, p. 67.

have had strong prior interests in religion and who were therefore looking for religious meaning in their drug experiences.[32]

RESEARCH FUNCTIONS

The administration of almost any drug to any patient or any experimental subject may produce considerably varied effects depending on the social and psychological situations in which it is administered. These effects are usually called "non-specific" by the physiological or medical scientist, but the social and psychological scientist sees them as offering interesting opportunities for research into systems which are of primary interest to him. If these social and psychological determinants of effects could be specified, they would contribute to our knowledge of behavior in general and would instruct us in what kinds of social and psychological responses are forthcoming in particular kinds of social and psychological situations. In their symposium on drugs and behavior, Uhr and Miller say:

> Of prime ultimate importance will be the basic knowledge of human behavior that is bound to be gained with the addition of the psychoactive drugs to our list of experimental tools, as suggested by Russell, Eysenck, Mirsky and Rosvold, and others in this book. Drugs have fundamental advantages over surgical intervention: their time of onset, magnitude, and duration are easily controlled; and their effects are ordinarily reversible. Until now . . . psychoactive drugs have been used primarily in animal experiments. But it has become feasible to use them with human subjects for many new sorts of experiments.[33]

The functions of drugs for behavioral research seem likely to be enlarged in the future.

SOCIAL CONTROL FUNCTIONS

As might be expected from the fact that drugs have various psychologi-

[32] Wilson Van Dusen, "LSD and the Enlightenment of Zen," *Psychologia*, 4(1961), pp. 11–16. For some empirical studies of the religious beliefs in and uses of LSD, see Blum, and Associates, *op. cit.*, pp. 35–37, and all of Ch. X.

[33] Uhr and Miller, "Prologue," in Uhr and Miller, *op. cit.*, p. 2. In the same volume see also the chapter on "Drugs as Tools in Behavioral Research" by Roger W. Russell and remarks by Robert B. Ellsworth in the chapter on "Use of Behavioral Adjustment Techniques in Evaluating Tranquillizers and the Value of Drugs in Social Rehabilitation."

cal functions, they have social control functions as well. That is to say, the manipulation of psychological states by drugs also has consequences for the social system, for possibilities of control and direction of the individual whose personality is being affected. "Public confession of sins in Peyote ceremonies," for instance, "is at once a mechanism for the dissolution of individual anxieties and a mode of social control."[34] Or again, it has been suggested that the use of tranquillizing drugs on the back wards of mental hospitals serves more the function of social control of unruly patients than it does a therapeutic function. There are those who fear the social control functions of drugs; they are afraid that drugs will be used for the harmful direction of individuals in social systems. Intended or unintended, social control functions are indeed an inevitable consequence of the use of drugs.[35]

THERAPEUTIC FUNCTIONS

Since the therapeutic functions of drugs are so obvious and so important, very little needs to be said about them here. Perhaps only one point needs to be made—the apparent universality in time and place of the therapeutic functions of drugs. We can read about the therapeutic use of drugs in the earliest historical accounts of man's activities and in the accounts of a great variety of different societies, non-literate and civilized. On an empirical, folk-knowledge basis, drugs have been used in therapies for what seems to be every kind of human ailment.[36] In the modern world, in addition to drug therapies prescribed by the professional physician, there is still a great deal of home medication with "over-the-counter" drugs as well as with folk-remedy concoc-

[34] Barber, "A Socio-cultural Interpretation of the Peyote Cult".

[35] On unintended social control functions resulting from the psychological functions of drugs, see Henry L. Lennard, "A Proposed Program of Research in Socio-Pharmacology," unpublished paper prepared for the Symposium on Psychobiological Approaches to Social Behavior, Harvard Medical School, April 18–20, 1963 and Henry L. Lennard, "Socio-Pharmacology," a lecture to a joint meeting of the General Seminar and the Mental Health Seminar of the Bureau of Applied Social Research, Columbia University, January 24, 1964.

[36] For a few examples, see La Barre, *The Peyote Cult*, on the therapeutic use of peyote in Mexico and in the United States; Chopra and Chopra, *op. cit.*, on household remedies made from hemp [hashish, marihuana] in India; and Morris Steggerda, "Plants of Jamaica Used by Natives for Medicinal Purposes," *American Anthropologist*, 31(1929) pp. 431–434, on various weeds used by Jamaicans to cure colds, malaria, stomach ache, kidney trouble, heart pains, and so on.

tions.[37] Recently, drugs have even come to have a large place in veterinary therapeutics. In 1963, for example, some $254 million was spent for such purposes in the United States alone.[38]

WAR AND OTHER CONFLICT FUNCTIONS

Since there seems to be no social system without some conflict, it is not surprising that drugs have been used in social conflicts as well as for peaceful purposes. Small, non-literate societies have used poison-tipped arrows and darts in their conflicts with one another; and large-scale, modern societies have in the past used poison gas on one another in war, and they now hold the use of gas or biological drugs as a deterrent against prior use by their enemies. Within societies also, component groups or individuals have used poisonous drugs on one another to gain their ends in situations of conflict.

A general point can be made here. Drugs that are beneficial in a certain amount or dosage are often harmful or fatal in another. So it is with poisonous drugs used in situations of conflict. In different dosages, such drugs as aconite and curare, used by non-literate societies to tip their poisonous arrows and darts, become therapeutically beneficial. For instance, aconite is used to relieve neuralgia and as a heart and nerve sedative; curare can be used to stimulate respiration and relieve paralysis as well as to stop respiration and cause fatal paralysis.[39]

Some General Functional Problems

In their discussions of the methodology of functional analysis, sociologists have been concerned with a number of general problems, all of

[37] On home medication, see the report, *Annals of the New York Academy of Sciences, Home Medication and the Public Welfare,* Vol. 120(1965), Art. 2, pp. 807–1024. One of the chief conclusions of the conference on which this publication reports is that "the self-treatment of the symptoms of a minor and transitory illness is not only desirable, but the results are highly satisfactory." Among the chief self-medication products are headache remedies, drugs for the relief of coughs and colds, laxatives, antiseptics, vitamins, antacids for digestive troubles, sedatives for sleeplessness, and anti-itching preparations. The subject and conclusions of this conference need to be the focus of a great deal more research.

[38] *Drug Trade News,* Jan. 10, 1964.

[39] *New York Times,* March 15, 1964.

which seem to come up in a comprehensive discussion of drugs.[40] As we examine how drugs are involved in these general functional problems, we can perhaps shed light not only on drugs themselves but also on these problems in their general significance for sociology as a whole.

The same general set of phenomena, things called by the same, single, loose term, may have multiple functions.

We have seen this point illustrated several times; it is obvious that "drugs" is an omnibus term covering multiple social and psychological functions. Once posed and illustrated, this point urges the necessity for being as specific as possible in any discussion of drugs, or in any functional analysis whatever. For further example, it will not do to describe opium, heroin, and marijuana all as narcotics. Opium and heroin are physiologically addictive; marijuana is not. The neglect of this specific and important difference has resulted in bad mistakes in public policy.

Even the same drug substance may have different functions in different dosages and in different social and psychological circumstances.

This is true for poisons like curare and aconite. It is also true for opium, which is variously, in different circumstances, an addictive narcotic, an effective pain-reliever, and a form of recreation and escape. In India, for example, different uses of opium and hemp (hashish, bangh) are made by different social classes.[41] The hallucinogens have different effects when they are used in a controlled hospital-research setting and when they are used by groups actively seeking mind-releasing, transcendent, psychedelic experiences.[42] Again, the need for specificity is strongly apparent. Of course, specificity, whether physiological, psychological, or sociological, is a characteristic of scientific analysis of which there is only less and more; it does not exist as a final absolute. Thus, it has been pointed out, "The precise manner in which the digitalis leaf alters the irritability of the heart remains obscure despite 200

[40] Robert K. Merton, *Social Theory and Social Structure,* Glencoe, Ill., The Free Press, 1957. (Revised and Enlarged Edition.) Ch. I.

[41] Chopra and Chopra, *op. cit.*

[42] See Blum, and Associates, *op. cit.* In Chs. 2 and 4 systematic comparison is made among five sub-samples of a larger sample studied by this group.

years of practice with clinical digitalization."[43] Similarly, "insulin therapy was used for 40 years before there was any satisfactory knowledge about its chemical structure or action."[44] The specificity of our functional physiological knowledge with regard to both agents has been considerably increased, but could still stand improvement. As Chauncey D. Leake, the eminent pharmacologist and historian of science, has put it:

> Pharmacology remains chiefly a descriptive science. It is largely a matter of accurate observation and ingenious experimentation, with an analysis of the actions of chemicals on living material in whatever terms are appropriate in current physics, chemistry, and physiology. . . . Certain it is that chemical agents may produce wholly different results at different organizational levels of biological material.[45]

The different functions which the same drug or class of drugs has may be partly positive, or eufunctional, and partly negative, or dysfunctional.

This variance of effect has a long history. The historian of medicine, Owsei Temkin, has noted:

> In the Homeric epics the term *pharmakon* connotes a charm or a drug that can be used for good and bad purposes . . . its action for good or bad does not depend on its natural qualities alone. The favor of a god, the observance of ceremonies, the absence of demoniac enemies, the healing intent of the dispenser—any or all of these factors are needed to make it therapeutically effective.[46]

This mixed-effects usage has persisted into modern Greek, where the word "pharmaki" means both medicinal drugs and poisons.[47]

The drug thalidomide, for example, which was responsible for the highly dysfunctional and widespread teratological defects in babies born to mothers who had taken the drug during the first few months of

[43] Francis D. Moore, "New Problems for Surgery," *Science,* 144(1964), pp. 388–392.

[44] *Ibid.*

[45] Chauncey D. Leake, "The Scientific Status of Pharmacology," *Science,* 134(1961) pp. 2069–2076.

[46] Owsei Temkin, "Historical Aspects of Drug Therapy," in Paul Talalay, editor, *Drugs in Our Society,* Baltimore: The Johns Hopkins Press, 1964, p. 3.

[47] Richard Blum and Eva Blum, *Health and Healing in Rural Greece,* Stanford, California: Stanford University Press, 1965, p. 108.

pregnancy, is known also to have functional effects not only as a psychological tranquillizer but as an agent for the reversal of the syndrome of symptoms known as the "lepra reaction" (insomnia, skin eruptions, muscle and joint pains, and high fever) in leprosy patients.[48] It is not known yet whether thalidomide affects the disease of leprosy itself, but it seems to have an alleviating influence on several of its painful symptoms. René Dubos has pointed out the general physiological source of these variously functional and dysfunctional effects, "Even a highly selective drug is therefore likely to react with some structure other than the one for which it has been designed. In other words, absolute lack of toxicity is an impossibility, because absolute selectivity is a chemical impossibility."[49] And there are also sociological and psychological reasons for lack of selectivity and differing functional consequences.

> *One of the reasons for the various functional effects of a given drug agent is that there are always indirect as well as direct effects of its action.*

Again, Dubos has described this functional process for physiological systems in a way that applies equally to sociological and psychological systems. He says:

> Any action exerted on any particular structure or function of any organism bids fair to alter the integration of this organism as well as its relation to the environment. All forms of interference with organismic integration or with ecological relationships are likely to have in most cases indirect consequences, always difficult to predict and often potentially dangerous. . . . A well-documented example of ecological disturbance resulting in various forms of indirect toxicity is provided by the effects that treatment with antibacterial drugs exert on the indigenous microbiota, especially that of the intestinal tract. Most antibacterial drugs destroy many components of the microbiota of animals and man, thereby permitting the multiplication of other microbial agents to which the host is less well adapted. Although this phenomenon has been discussed chiefly with reference to the intestinal tract, it is of equal importance for other organs.[50]

[48] *Time*, July 23, 1965, p. 59.

[49] René Dubos, "On the Present Limitations of Drug Research," in Talalay, *op. cit.*, p. 41.

[50] *Ibid.*

Indirect effects, then, both on the internal structure and integration of a system and on the relation between a system and its environing systems, are always to be looked for in functional analysis.

> *There may be important differences in the short-run and long-run functional consequences from the activity of a drug.*

Once more, we can refer to Dubos for our physiological text, which applies as well in other types of systems. After speaking of indirect functional effects, he says, "Furthermore, these indirect secondary effects often unfold slowly, as the living system under consideration progressively develops, differentiates, undergoes adaptive modifications, or simply becomes older."[51] Thus, effects which are beneficial in the short-run may be harmful in the long-run, again because of changes internal to the system or because of changes in its relationship to its environment. Thorough functional study thus often requires that the agent or system under investigation and those with which it is interacting be kept under close scrutiny over an extended time period to detect differences in their short-run and long-run functional consequences for one another.

> *The functional consequences of a drug may be unintended as well as intended, and unintended as well as intended consequences may be either good or bad.*

So frequent are the unintended and harmful consequences of the use of drugs and other procedures in medical practice nowadays that doctors have come to refer to "the diseases of medical progress."[52] Or sometimes these are called "iatrogenic diseases." In a recent study during an eight-month period on the medical service of a university hospital, the house staff found that 20 per cent of all patients developed some iatrogenic trouble. Of these patients, more than one-half suffered from iatrogenic complications originating in drugs that had been administered routinely.[53] No wonder that the doctor himself is now sometimes metaphorically called "the pathogen."

[51] *Ibid.*

[52] Elihu M. Schimmel, "Editorial—The Physician as Pathogen," *Journal of Chronic Disease*, 16(1963), pp. 1–4.

[53] *Ibid.*

Two other examples of unintended and harmful consequences of drugs have recently been called to public attention by clinical researchers. One is the impairment of performance in automobile driving, which may lead to serious accidents, when people who take even relatively mild drugs suffer harmful side-effects, such as a slowing of reaction time, drowsiness, and itching.[54] Another is the harm of various kinds that may occur to the unborn child because even relatively harmless drugs ingested by the mother during pregnancy may be transformed by the normal "magnifying" mechanism of the human placenta into dangerous agents.[55]

But there are also unintended good effects from drug action, though the bad ones are likely to be more remarked. Gaddum has pointed to these unintended good effects:

> In some parts of the world antimalarial drugs are much used, and this has led to the discovery of various good side-effects. In 1912 a Dutch merchant told Wenckebach that he had found for himself that he could stop attacks of auricular fibrillation with quinine. . . . Quinine has also been found more effective against myotonia congenita and nocturnal muscular cramp. Chloroquine, which is one of the best of the many antimalarials studied in the United States during World War II, is also effective in amebic dysentery, lupus erythematosus, and photosensitization. . . . All these are good side-effects, discovered years after the drugs had been in use for the treatment of malaria.[56]

As in social and psychological systems, the general problem of a functional calculus, or the weighing up of good and bad effects, arises in connection with drugs and their effects on physiological systems.

As Gaddum, again, has put it:

> The bad effects of drugs must be balanced against their good effects. Most drugs, including alcohol and aspirin and penicillin, have toxic effects and cause deaths every year, but no one proposes to prohibit their use, because their good effects are believed to outweigh their bad effects. Chloramphenicol may cause aplastic anemia, but it is generally accepted that its use in the treatment of typhoid fever is justified,

[54] *The New York Times*, February 1, 1966.

[55] *The New York Times*, February 22, 1966.

[56] J. H. Gaddum, "A Perspective on Pharmacology," in Talalay, *op. cit.*, pp. 24–25.

> since the mortality of this disease without it is about 20 per cent and the risk of serious toxicity is much less. A new drug cannot be condemned just because it is found to cause occasional toxic effects; it is sometimes necessary to know how often these toxic effects occur among those exposed to the drug and also how much good the drug does, so that the bad effects may be weighed against the good effects.[57]

Of course, as Gaddum's chloramphenicol example shows, it is sometimes possible to give some quantitative weightings in the case of trying a functional calculus for drugs. This is not so often possible for functional effects of sociological and psychological agents and systems. However, there are difficulties even for drugs and for physiological effects. As Gaddum concludes, "It is, of course, very difficult to get quantitative information of this kind."[58]

Just this difficulty, and the consequent difficulty of making a decision based on some relatively reliable functional calculus, were strikingly manifest in a recent situation confronting the Food and Drug Administration with regard to the antidepressant drug, Parnate. This drug had been on the market for some time and was helpful in some unknown proportion of cases in restoring invalids to a useful life and in preventing suicide. It was then discovered that in a few cases, again in some unknown proportion of the total treated, the drug seemed to have caused fatal strokes. The drug was withdrawn from the market temporarily to permit the FDA's medical director to try to establish what the calculus of functional and dysfunctional effects actually was. In this effort he had the assistance of his own staff and of distinguished outsiders. Finally, despite the lack of precise quantitative data to draw up this calculus, he allowed the drug back on the market, saying, "I believe that the benefit to be obtained from the use of the drug under careful restrictions outweighed the risk from such use." The difficulty of his decision is underlined by the fact that one of the distinguished outsiders who counseled with the medical director was reported as saying that while he "certainly was sympathetic" to the decision that was taken, he could not say for certain whether he would have done the same thing had it been his decision to make.[59] Difficult situations of

[57] *Ibid.*

[58] *Ibid.*

[59] *The New York Post*, June 25, 1965.

this kind are not unlikely to confront the Food and Drug Administration again.

The general problem of a functional calculus is at the heart of many difficult policy decisions about the use of drugs or other functional agents. For example, are the beneficial effects of tranquillizing drugs greater than their harmful effects? One view is that the harmful effects may be greater. For instance, Saunders says, "An increasing number of people are seeking tranquillity at the expense of effective living and are escaping from reality through the medium of tranquillizers."[60] But Aldous Huxley sees the functional calculus in this matter coming out the other way. He feels that the use of mescaline as against other substances and procedures to open "Doors in the Wall" which surrounds men is the "only reasonable policy" for "inducing men and women to exchange their old bad habits for new and less harmful ones."[61] "What is needed," he says, "is a new drug which will relieve and console our suffering species without doing more harm in the long run than it does good in the short."[62] Huxley thinks that mescaline, with possible improvements, is such a drug. In this case, unlike that of chloramphenicol, the possibility of a precise functional calculus does not now exist.

[60] J. B. de C. M. Saunders, Introduction, p. xii, in Seymour M. Farber and Roger H. L. Wilson, editors, *Control of the Mind,* New York: McGraw-Hill, 1961.

[61] *Op. cit.,* p. 64.

[62] *Ibid.*

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for the treatment of drug addicts is based on prejudice and ignorance and that it probably aggravates the troubles it seeks to eliminate. He challenges the adequacy of the training of medical students in the use and prescription of drugs and expresses concern about the ways practicing physicians find out about the flood of new drugs that has been coming on the market during the last twenty-five years. And he judiciously scrutinizes the "avoidable unavailability" of drugs, which some social reformers have alleged to be due to high profits, monopoly pricing, high-pressure advertising, and indifference to prescription costs on the part of physicians.

Policy-makers, social scientists, and laymen will find Professor Barber's book a key to understanding, a guide for action, and a directive for research. Understanding, action, and research are all important in a future which promises only that drugs will become even more important than they are today.

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