tions, buoys, and navigation aids will continue to use radioisotope power. Through this technology many as yet undetermined missions will be carried out—missions which, without this power, would have been impossible.

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Hazards of New Drugs

The scientific approach is necessary for the safest and most effective use of new drugs.

Walter Modell

No drug, no matter how thoroughly tested by time or trial, is absolutely safe. The size of the problem is indicated by a report in the *Journal of the American Medical Association* (*1*) that one of every 20 patients admitted to a large hospital in New York City was there because of adverse reaction to treatment. Serious reactions occur with all therapies—the safe as well as the hazardous, the useful as well as the useless, the old as well as the new, the folk remedy as well as the modern miracle drug. What seems an innocent therapeutic procedure may have serious unanticipated effects. For example, the age-old program of bed rest for the sick seemed so reasonable, was so well grounded in tradition, so plainly harmless, and, one would think, so well tested by usage that, until about 20 years ago, no one challenged it. Yet William Dock (*2*) called it the most dangerous of all therapeutic procedures, supported his revolutionary view with evidence that it caused venous thrombosis and other complications, and ushered in the present era in which the bed is eschewed if the patient can manage to be up and around. In many cases, as well as being happier, patients are clearly safer out of bed than in it. Nothing must be accepted at face value in modern medicine; modern proof by modern standards is essential. The thoroughgoing scientific experiment and the scientific attitude are the only safeguards against the specter of drug disaster.

The aim with all new therapies is to establish a more favorable ratio between probable adverse effect of treatment and probable adverse effect of untreated disease. Testing new drugs involves developing and pursuing the most effective methods for determining therapeutic effectiveness and reaction hazard. Only with tested drugs is there an index of danger of adverse reaction and of potential for therapeutic usefulness. If the information is substantial, one can elect to use the drug on the basis of a calculable risk; without such information one has no way of knowing whether the clinical use of the new drug is defensible.

Preclinical Testing

If medicine is to progress, the determination of calculable risk and expectation for benefit from new drugs is of the first importance. Why, then, are these factors not always precisely determined before new drugs are used in clinical medicine? The reaction of an animal to drugs may differ qualitatively as well as quantitatively from that of man. Therefore, although essential, animal experiments provide a limited view of the potential danger and usefulness of drugs in man. Much more can be learned from preclinical trials in man, and the more extensive these trials, the more informative they are. This is the information that is largely depended on in introducing new drugs, but unfortunately it does not tell the whole story; at best it provides only the basis for a well-informed estimate of immediate effects. It tells little about what will happen after several years of use. It does not tell much about what has not been looked for, and since what we look for is determined by past experience, it is quite possible that entirely new reactions to drugs will go undetected. It does not tell precisely what will happen when the drug is used by the general practitioner, as compared with its effects in the much more careful studies of preclinical testing. Information from preclinical testing is not often extensive enough to cover the rare occurrence. The full extent of both the risk and the ultimate benefit of the drug is therefore learned only after extensive use in actual practice, usually for 2 or 3 years.

Obviously, testing should be conducted with minimum risk to the subject, but since there is no drug without hazard, there can be no testing of new drugs without risk. The justification for taking this risk is that without it there can be no reasonable basis for introducing and using new drugs, and that the danger involved in using them clinically without such testing would be greater than the danger involved in preclinical testing. Therefore, society must recognize that in its demand for new drugs there is clearly implicit a license for qualified individuals to take certain risks in testing drugs as well as to take calculable risks in using them clinically. Medical science is obligated to keep these risks within reasonable limits. But both the medical profession and society in general must be fully aware of the potentiality of drugs to produce disaster.

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Reactions

Reactions to drugs are not the result of something strange and different in modern drugs. Disasters due to drugs are as old as the history of medicine. New drugs distributed solely on prescription do not often cause large numbers of reactions. If reactions seem to be common now, it is only because there are so many new drugs and because communication is so efficient. One drug removed from the market early this year, which was available only on prescription, caused only eight serious reactions before its removal. The case of thalidomide is unusual; the number of individuals affected was large because the connection between drug and effect was difficult to establish, due to the long interval between the short critical period during which the drug can cause phocomelia and the birth of the defective infant, and because thalidomide is relatively harmless at other times during pregnancy and relatively harmless for all users other than pregnant females.

I emphasize the relatively small number of immediate reactions from prescribed drugs today because this was not always the case. In the distant past, when reactions to drugs developed, huge numbers were often afflicted before the causes of the reactions were identified. When mercury was used for the treatment of syphilis in the widespread European epidemics of the 16th century, intoxication from mercury was a commonplace. We now know, from historical accounts, that diarrhea, salivation, and kidney disease were frequent, yet the connection between these disorders and the use of mercury was not discovered for many years. The reasons for this can only be conjectured. Perhaps examination was less thorough and meaningful in those days. Surely the means for making examinations were more limited; procedures such as blood count, determination of blood chemistry, and urinalysis had not been developed. Nor had the science of pharmacology been developed, and thus reactions could never be anticipated before the fact. Also, there was no preclinical testing of drugs.

Sir William Osler once said, "The desire to take medicine is perhaps the greatest feature which distinguishes man from animals." So irresistible is this urge that man frequently takes medication without the advice or counsel of experts and often modifies or tries to improve upon his physician's instructions. I do not make this point to whitewash the medical profession or to malign the public. It is true. What the physician can do, for good or evil, by direct ministration he can do only for those who restrain the human impulse to meddle with his prescriptions. When physicians are too permissive about the use of new drugs, or do not warn their patients adequately of the dangers, the fault is compounded, and drug taking is apt to get out of hand.

When a patient prescribes for himself, the possibilities for harm are incalculable. If a fad develops, as, for example, one did not long ago for the use of Miltown, it can cause extensive trouble. Addiction is a serious adverse result of the use of drugs. It becomes catastrophic only when the layman undertakes to use drugs without medical advice. The serious problems attributable to the extramedical use of morphine and other narcotics are commonplace, and we tend to overlook the fact that they are community catastrophes resulting from self-medication. Perhaps, because it is of more recent origin, and therefore more striking, our barbiturate problem is a better example. There is no estimate of how many people are addicted to barbiturates, for it is not a reportable condition, but the number is very large. Here, loose use by the medical profession, coupled with self-medication, has created a serious public problem.

The menace of adverse reactions to drugs extends far beyond what meets the eye. It is common to evaluate the hazards of new drugs only in terms of immediate and direct anatomic or physiologic disturbances, prompt damage to liver or kidney, cataracts, palsy, baldness, impotence, blood dyscrasias, or collapse—in terms, that is, of what are usually called toxic effects. But there are other consequences of the use of drugs, sometimes of even greater importance, that are not generally recognized because the connection is not immediate or obvious. While these consequences are often manifested quite subtly, they may be major disasters nonetheless.

Ecologic Disturbance

Society has charged the medical profession with control of the spread of disease, and it also demands that it discover cures for specific diseases. Enormous sums are available from the government and through privately endowed research foundations for direct attack on birth injuries, poliomyelitis, multiple sclerosis, tuberculosis, cancer, cystic fibrosis, muscular dystrophy, and other named diseases. It seems to be relatively easy to arouse interest in the eradication of particular diseases. Sometimes one rich man plus one illness equals one foundation. But society is not interested in, and has not provided a special foundation to examine the influence of these programs, should they be successful, on ecologic balance. Yet strange as it sounds, the attack on a specific disease may not always be for the ultimate good of the community. Patently desirable measures may have strange reverberations. About 15 years ago there was an epidemic of rickettsial pox in the New York area simply because a garbage dump was removed as a sanitation measure. Mice that bore the mites that carried the rickettsia had contentedly used the dump as a sort of ever-normal granary and had not strayed far from it. When the dump was removed, they were forced to seek sustenance elsewhere; they moved into nearby apartment houses, where they started and spread the epidemic.

It is a well-recognized and fascinating biologic fact that when one element of the environment is altered, equilibrium may be upset and the effects can be far-reaching; the new equilibrium may not be as desirable as the old. Too often in medicine this comes as a complete surprise. The need to anticipate these effects applies with special cogency to our marvelous new drugs because they *are* so marvelous, because they are so effective in eradicating particular diseases. Infections which were the important causes of serious disease have been reduced through the use of antibiotics to a less important status; pneumonia is an example. But the increased incidence of previously rare infections, little influenced by these drugs, and the reactions to the ecologic disturbance often more than offset the immediate benefits. Increasing longevity has created problems of dealing with the aged, and the decrease in the death rates in overcrowded parts of the world has resulted in food shortages and more starvation.

Although it has been suggested that public health is purchasable and that, within bounds of obvious natural limitations, communities can determine

their own death rates, a World Health Organization pamphlet recently stated, "as one disease is eradicated . . . others grow in importance." This is by no means a new insight. In 1803 Malthus said, "For my part I feel that, if the introduction of the cow pox should exterminate small pox, we shall find a very perceptible difference in the increased mortality of some other disease." In 1873 William Parr wrote, "Infectious diseases replace each other, and when one is rooted out it is apt to be replaced by others which ravage the human race indifferently whenever the conditions of health are wanting. They have this property in common with weeds and other forms of life, as one species recedes another advances" (see *3*).

In his recent series of lectures Dubos states (*3*), "There is no doubt that, of course, scientific medicine is now essential to our social existence and contributes much to the success of modern societies. The paradox is that, despite the spectacular advances in knowledge and treatment of diseases, the need for hospital facilities and the cost of medical care continue to increase. This results in part from the much more exacting criteria of health that prevail in modern societies, but other reasons are also apparent. While a few of the old disease problems are being solved, new ones are constantly cropping up, and make modern man increasingly dependent on medicine for his survival. . . . [The] task is never finished because some problem is solved. Another soon appears which requires attention. Nature always strikes back. It takes all the running we can do to remain in the same place."

Dubos says again (*3*), "The study of specific pathological problems requires the use of laboratory techniques and contributes to the advancement of laboratory knowledge. But the field of medicine transcends this kind of knowledge because it deals with man as a spiritual being and also with the future of the human race. Medical science is concerned not only with the control of individual diseases, but also with the long-range effects of its products on the total performance and happiness of the individual, on the social problems of the community, and the adaptive powers of the race."

But Dubos is the spokesman neither for medicine nor for society. The fact is that society continually presses for cures for specific diseases, and regardless of how much vision the Duboses have, there is as yet no organized concern beyond the development of attacks on selected diseases.

Resistant Diseases

Preventive medicine is accepted today as the most effective means of keeping the community healthy. Drug prophylaxis seems to be a keystone in this program, yet many deplore the unrestricted use of antibiotics, because of a well-founded fear that their wide use may lead to increased incidence of diseases that are less responsive and less well understood than those they are used to combat, and because, also, of the fear that diseases now effectively treated will become resistant to antibiotics. An example of critical importance is the case of the staphylococcus infection, which in pre-penicillin days produced what the surgeon then happily called "laudable pus". It is no longer laudable. Although at first the staphylococcus was highly susceptible to penicillin, there has been a rising incidence of penicillin-resistant strains of staphylococcus. While this resistance was probably not directly induced by exposure of staphylococci to the antibiotic, the wide-scale use of penicillin has resulted in the elimination of susceptible strains and the fostering of resistant strains. In addition, other pathogens which are responsive to penicillin have been replaced by resistant strains of the staphylococcus.

Careless use of penicillin has also led to an increase in the number of human carriers of resistant staphylococcus, while wide use of penicillin and other antibiotics has led to a sharp increase in the incidence of the serious but once rare staphylococcus infection of the intestine. There have also been many deaths directly due to sensitivity to penicillin—sensitivity acquired through needless exposure. It has been stated (*4*) that, in the course of a lifetime, 10 percent of the population of this country may, through contact with food, drugs, cosmetics, or other substances that contain penicillin or other antibiotic become sensitized to it and be unable to use it safely thereafter. A sharp reduction in the usefulness of penicillin (*5*) is therefore a real possibility; it could be a major catastrophe, costing more lives than I care to count. It would dwarf the thalidomide catastrophe.

There is always the chance of harm through the interaction of drugs. Because the possibilities are unlimited, in preclinical testing it is usually impractical to attempt to examine the effects of a new drug on all the other drugs patients may be taking at the same time. Reserpine, until recently an important drug in the treatment of hypertension and mental disease, was found to cause a sudden and extreme drop in blood pressure in patients receiving general anesthesia. Now all anesthesiologists demand that patients stop taking reserpine 2 weeks before surgery.

Ethical Obligations

Much has recently been said of the ethical obligations of both the experimenter and society to the subjects of experimentation with drugs, and of course the obligation is real. But there is a related ethical problem which is not commonly appreciated, even though it has more far-reaching significance, and that is our ethical obligation to the nonsubject, to the ultimate object of research, to the patient who will receive the new drugs in clinical practice (*6*). Subject or nonsubject, inescapably we are all guinea pigs (*7*).

If the trial on the experimental subject is not carefully planned and executed—if, because of concern over ethical obligations to the subject, the discipline of experimental research is not strictly adhered to in the investigation of drugs in man—many nonsubjects may suffer, because the experiment was faulty and provided spurious answers (*8*). Nonsubjects may suffer because a toxic drug is unwittingly used in clinical medicine, and this, of course, is what excites all the attention, despite the fact that it does not occur very often. But what goes almost unremarked, and is even more important and not uncommon, is that the bad experiment may indicate that an ineffective drug is useful, with the result that a useless medicament is established in our therapy. This is a more insidious menace than the introduction of a toxic drug, because toxic effects attract more attention than failure to produce effects and are usually promptly noted. It is much more difficult to identify the ineffective drug once it is in actual clinical use, because it is usually used in combination with a number of other therapeutic measures, and because it is very

difficult to make a careful, thorough, experimental examination of a drug once it has been accepted. Thus archaic drugs like strychnine continue to be used 50 years after it has been established that they have no use in medicine. The adverse effects of the useless drug are more subtle than those of the toxic drug. The useless drug is harmful because it engenders a false sense of security which may lead to a lessening of attention and failure to look for and observe critical features of the progress of the disease. If such a drug is substituted for more effective measures, widespread ineffective therapy, when better measures could and otherwise would have been used, may result.

Today a large number of patients with coronary artery disease, including our most recent ex-President, are being given anticoagulants on a life-long basis in the belief that this prevents the formation of clots in the coronary arteries and thereby prevents extension of the disease. Anticoagulation is an expensive, unpleasant, and, unless carefully watched, dangerous therapy. Its effectiveness has never been scientifically established and is presently being seriously questioned in great medical centers throughout the world (*9*). If it should turn out that the therapy is useless, a large number of patients who have troubles enough will, at the very least, have been exposed to needless expense and nuisance; in some the therapy will have caused reactions of varying degrees of seriousness, and in a few it will have caused death. Should it turn out that the therapy is a useful and effective one, then the patients of the doubting Thomases may, as the supporters now claim, have suffered unnecessary complications and have had shorter lives because the drug was withheld.

For years adrenalin was used for traumatic shock because it raises blood pressure, and raising blood pressure seemed a reasonable thing to do for patients whose blood pressure has dropped as low as it drops in shock. No controlled experiment was made to prove the validity of this reasonable assumption; this was not thought necessary, even though there was a small and barely audible group who felt that the assumption was not even reasonable, let alone a basis for effective therapy. In current therapy norepinephrine and similar drugs are used, all congeners of adrenalin. The basis for this change is not only the belated admission (made when something new appeared) that results with adrenalin in the treatment of shock were generally poor, but also the finding that norepinephrine is an even more potent elevator of blood pressure than adrenalin. The disenchantment with adrenalin, which is a less potent, but nonetheless a potent, elevator of blood pressure did not lead many to question the reasonableness of the assumption that the thing to do in shock is to elevate blood pressure by any means possible.

Those who do question the assumption are growing in number and becoming more articulate (*10*). They support a complete reversal in therapy—the use of ganglionic blockaders, which, if anything, tend to lower blood pressure. This approach is also based on an assumption that seems reasonable—that the blood supply to vital organs should be increased—but it is to be fervently hoped that the experiments to test its validity will be properly controlled. Otherwise we will end up by having two diametrically opposed methods of treating so common and so serious a condition as traumatic shock, not knowing which, if either, is the correct one. If the two divergent therapies are used by different medical groups for a large number of cases, the probability that shock will be improperly treated with drugs will become a certainty.

There will always be losers when dilemmas of this type develop. Yet the dilemmas can be prevented if the experiments which lead to clinical use are ironbound, if the publication of results is withheld until the proof is in, and if general use is not initiated and pressed until the critical questions have been decisively answered through extensive trial in clinical practice.

Those who like real French cooking, or bacon and eggs for breakfast, or prime beef, must be saddened by the rumor, which is rapidly spreading despite efforts by the dairy and cattle industries to silence it, that saturated fatty acids may lead to sclerosis of the arteries. The use of oils rich in polyunsaturated fatty acids in large doses is being pressed as effective prophylactic medication. There is no irresistible proof that saturated fatty acids either do or do not cause arteriosclerosis. As yet, no threat to life has been found in the polyunsaturated fatty acid diet, but it is a threat to good eating, at a time of such great public anxiety that, for some, eating may be one of the few undiluted pleasures. Why undermine it with shaky contentions when all that is needed is the well-controlled experiment in man?

A hazard in drug testing that does not excite the press is the loss of the good drug through inadequate testing or through improper, inexpert early use, so that its potential for adverse reaction in relation to its benefits is misjudged: it is thought to be less effective than it is, or more toxic. As with the people we meet, bad first impressions are often hard to erase. It is not possible to determine how many good drugs have been lost in this way. It is conceivable that there may even have been major losses. And if an effective drug for a serious disease has been discarded, this is a drug catastrophe indeed.

Outside Pressures

Interference with scientific procedure by outside pressure groups tends to keep any discipline from being truly scientific, tends to muddy both the aim and the validity of its research, and tends to keep society from looking upon it as an independent scientific discipline. This is, of course, true for medicine, and in the case of modern pharmacotherapeutics such interference can be dangerous as well.

A dramatic example of what happens because of interference with the scientific process is to be found in the Salk vaccine story. It was a strange coincidence that several manufacturers had sunk fortunes and incalculable effort into processes for the extensive production of vaccine and were busily stockpiling the Salk vaccine at a time when the Polio Foundation was claiming in the press that positive results with the vaccine in the field trials had not yet been established. It was a curious coincidence that the public announcements that the Salk vaccine had been proved effective and that a large supply of commercial vaccine was ready for general use were made on the same day —12 April, date of the death of the late President Franklin D. Roosevelt. Here was interference with scientific procedure in the interests of the dramatic gesture. What were the effects? A large number of cases of paralytic polio developed during the first days of use of the stockpiled vaccine. Modification in manufacture was instituted as quickly as possible, but not before the calamity was substantial—more than 120 cases in recipients of the vaccine

and still more cases in individuals who had come in contact with these 120.

The blame lay in rearrangement of the normal steps in drug development in order that large stocks of vaccine might be accumulated and suddenly made available. In the normal course, the vaccine would not have been made commercially until the results of the field trials had been established. When these results had been announced the manufacturing process would have begun promptly, for there would have been a great demand for the vaccine, but at first the supply would have been short. Larger amounts would have been provided as production processes were developed and improved, but no large, relatively untried batch would have been dumped on the market at one time. Thus, a serious defect in the vaccine would have been discovered long before it was in mass production and before large amounts of vaccine had been administered and a large number of reactions had been induced.

The pharmaceutical industry finds the prompt establishment of its new drugs essential (*11*). It cannot afford to wait. These days, drugs are copied so easily by the astute synthetic organic chemist that rival concerns soon produce near-duplicates of most successful drugs. In the space of 2 years as many as a dozen very close relatives of some new drugs have appeared on the market.

In this kind of rat race it is simply sound business practice for industry to attempt to recover a large portion of its investment in a drug immediately after the drug is introduced. To do this, it attempts to establish a new product so quickly that no Johnny-come-lately can seriously impinge on the firm market that it has created for itself. The pharmaceutical industry uses the same promotional devices that other businesses use to make sure that its new product is used as widely and as soon as possible. It does not allow time for the practicing physician to learn about the drug through the scientific journal, which is slow to publish, or through experience, which is even slower. The drug is promoted from the very first as if its use were a part of standard and accepted practice. The physician is besieged with advertisements and elegant brochures about the drug. He is spoon-fed information by the manufacturer's detail man.

A genuinely insidious practice in drug promotion is the planting in the nation's press of what appear to be news items, informing the public of the development of the new drug and giving details of its hoped-for use in medicine. These salted items lead the patient to bring the existence of the new drug to the attention of the physician before very much is known about it, and to press him to use it instead of other therapy he may have been contemplating. Through these several measures the physician is urged to abandon the therapy he knows well and to use therapy he has had little or no experience with.

Hasty Publication

Knowledge of the extent of usefulness of a drug, of its specific advantages and limitations, of the rare as well as the common adverse reaction—in fine, knowledge of the art of using it—is gained slowly. Estimation of the effectiveness of the new drug in relation to that of other drugs used for the same condition takes experience. Such experience comes only with time; it does not come directly from books and it certainly does not come from advertisements or detail men. After a new drug has been prescribed for two or three years its effectiveness is never the same as it was in the beginning: it is either more or much less useful. Only after it has been widely used does information become available which enables the practitioner to prescribe the drug with wisdom. With rare exceptions, it is only then that a new drug should be incorporated into standard therapy.

Hasty publication and overenthusiasm are understandable in one who feels or hopes that he has made a major discovery, but such is not the behavior of the scientist, and in the case of new drugs it may be dangerous. The story of the origin of the cocaine habit in Europe is well authenticated. Sigmund Freud was largely responsible for its development in Europe (*12*). Freud was, by his own account, the first European to take cocaine after it had been isolated. He liked the effect it had on him, and he continued to take it from time to time thereafter, and even boasted to his fiancée about its effects on him. He assumed that he had performed a valid experiment with his own trials on himself, although he had not applied the safeguard of setting up rigorous controls. Without further ado he proclaimed cocaine to be a treatment for a large number of ailments and attested to its harmlessness. The habit quickly spread in Europe and hooked, of all people, Sherlock Holmes (with, of course, the blessing of Dr. Conan Doyle). Eventually Freud was publicly condemned for his role in bringing about what was then called the third scourge of mankind.

About 30 years ago a new analgesic, meperidine (known under the proprietary name of Demerol), was introduced as a morphine substitute with the claim —and there was no hedging, it was categoric—that it was not addictive. The work on which the claim was based was shoddy, yet use of the drug was vigorously promoted. Experience soon proved that meperidine was highly addictive, and that in this respect it certainly had no advantage over morphine.

In the medical profession, as in any other, it is very difficult to dislodge firmly entrenched notions. Even now, 30 years later, few physicians seem to accept the fact that meperidine is highly addictive. Many seem to assume that the original contention must have had some validity, and they continue to use meperidine as though it were less hazardous than morphine. The medical profession uses morphine with great respect and, as a result, a very small number of patients become addicted to it as an accident of therapy. But this is not the case with meperidine. As a result, many more victims are admitted to the hospital for addicts at Lexington, Kentucky, as a result of meperidine therapy than are admitted because of morphine therapy.

Here, then, is the pattern for disaster with new drugs: a short-sighted view of all effects; faulty experiments; premature publication; too-vigorous promotion; exaggerated claims; and careless use—in brief, a break in the scientific approach somewhere along the line.

Safety with the new drugs, which are both potent and numerous, therefore demands the attitude and skill of the scientist; any thing less is clearly dangerous. Events have proved it. I hope I have indicated why. I contend that the rules of safety demand that the healer be a scientist (*13*), but the question is, can he be? Will that role be acceptable to him or to the patient?

Image of the Doctor

The image of the doctor is important, for it directs both the physician and the patient in their approach to new drugs. There are perhaps four images of the physician. There is the omnipotent witch doctor; there is the Dr. Christian type, who substitutes love, sympathy, and dedication for omnipotence; there is the businessman-doctor; and there is the scientist-doctor. The witch doctor is not acceptable today. The Dr. Christian image has elements which are valuable in the doctor-patient relationship, therefore valuable in therapy. From what I can gather, however, today as few patients believe in Dr. Christian as believe in Santa Claus.

What I fear is the increasingly prevalent image of the physician as the businessman. I do not argue that there are more businessmen-doctors than there used to be; there are probably no more. I am speaking of a change in the doctor image, for although the doctor has not changed, there is no doubt the patient sees him differently. The businessman-doctor must please his customers if he is to keep their trade, and if they apply pressure for a new drug, the businessman's ethics are not sufficient to keep him from giving way. The businessman listens to the salesman peddling "the latest thing." The businessman's ethics are dangerous when applied to today's drugs. If the public believes that *caveat emptor* has been substituted for the oath of Hippocrates, the whole physician-patient relationship changes. The businessman-doctor does not command the respect and does not have the authority that a physician should have.

The old Dr. Christian will not do today. If we are to avoid the dangers and have the fullest possible benefit of modern medication, we must have the scientist, for only he can deal safely and effectively with the output of today's pharmaceutical chemist. It is interesting that the public will not accept his image. The scientist image is all right for physicists and chemists, but the image of the doctor as the dispassionate scientist is shunned even more than the image of the businessman-doctor.

Perhaps the "experiments" of the Nazi scientists at Dachau and other concentration camps had something to do with this. Perhaps it was, as I believe, because the Nazi doctors increased the fear of the physician-scientist that already existed in the mind of the public that codes never before considered necessary for human experimentation with drugs were established at Nurenberg. Yet modern drugs can no more be well or safely handled by a nonscientist Dr. Christian than a nuclear reactor can be safely handled by an untrained do-gooder. The modern physician cannot sidestep the problems that science has created for him, and he must deal with them as a scientist. Progress in medicine—or even, as Dubos suggests, standing still in medicine—demands it.

But there is more to the practice of medicine than dispassionate science. The physician can do much good with effective drugs, but even with ineffectual medication the compassionate physician did a great deal for his patient. We cannot disregard the beneficial effects of compassion, interest, good care, and the communication of hope to the patient. The effects are authentic. The medical scientist must recognize them as well as the pharmacologic effects of his new drugs. The public must be shown that a scientific attitude is not incompatible with sympathy and compassion and a genuine concern for the patient as well as for the outcome of the therapeutic experiment.

Conclusion

Oliver Wendell Holmes (*14*) said 100 years ago, "I firmly believe that if the whole materia medica as now used could be sunk to the bottom of the sea, it would be all the better for mankind—and all the worse for the fishes." This is still true for the fishes; in fact, with our more potent drugs, it would be even worse for them. So far as mankind is concerned, however, I disagree; I need point only to our vastly improved mortality and morbidity rates. But mankind would be still better off if the physician treated the products of modern science with due regard for the principles of science; if there were no pressures distracting him from these principles; and if, in attacking disease, he viewed the large problem, with its long-range implications, as well as the immediate effects on a number of dissociated diseases. I think that the physician must transcend the businessman's ethic, and also that the safe and effective clinical use of new drugs requires a new and acceptable image of the physician, one which combines the qualities of Dr. Christian and the discipline and special skill and logic of the scientist.

Failing this, if new drugs continue to be marketed, we may have even more trouble. A negative attitude toward drugs may develop. Even now there are indications of movement toward therapeutic nihilism. There might have been some justification for such an attitude 50 years ago, but it would be an unforgivable disaster today, for never before has our ecologic balance been so dependent on drugs; never before in its history has medicine had so many useful, effective drugs on hand; and never before has there been such promise of even better ones to come.

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