

## THE VALUE OF DRUGS IN INTERNAL MEDICINE.\*

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We are now witnessing a cautious revival of the use of drugs in the treatment of disease. During the last half of the nineteenth century pharmacotherapy fell more or less into discredit, owing (1) to a reaction against the scandalous abuse of the "shotgun prescription," (2) to the general therapeutic nihilism that followed the rise of studies in pathologic anatomy, and (3) to the growing recognition of the importance of forms of therapy other than treatment by drugs. Though in some quarters the denial of pharmacotherapy was pushed to extremes, it is now generally admitted that the movement against the indiscriminate and non-critical use of drugs, to the relative exclusion of other and often more efficacious methods of therapeutic intervention, was necessary and timely, in order that the more rational therapy of our period might emerge.

In the therapy of to-day, based on more accurate diagnosis and on enlarged conceptions of pathologic physiology, etiology and pathogenesis, a new hopefulness prevails. We make use of a host of methods that are found to be trustworthy for healing, for palliating and for preventing. Along with diet, baths, climate, air, light, heat, exercise, massage, electricity, Roentgen rays, radium, serums, vaccines, mechanical appliances, surgery, nursing, and psychic and social influence, drugs are gradually finding their proper place in the therapeutic armamentarium of the medical practitioner. For among the drugs of various sorts, including both natural substances and pure chemicals provided by separation or by synthesis, there are agents that can now be employed with great confidence and often with the happiest results.

## DUTY OF THE INTERNIST.

In the management of patients and in the treatment of their diseases, it is our duty as physicians to see to it that we do not neglect to make application of any of the agents at our disposal that may reasonably be expected to help. Briefly, to survey the help offered to the physician in his daily work by modern pharmacotherapy, is the object of the present symposium. The time allotted will, of course, not permit of any detailed discussion as to the use of single drugs. It is, I take it, the intention of those who planned the symposium that it should deal rather with general principles that underlie the use of drugs in therapy, and with certain examples of the application of these principles in practice. Others are to speak of the use of drugs by surgeons and by specialists; this paper has to do with their use by the internist.

Man desiring to help his suffering fellow must not lack—indeed, has never lacked—courage. Think, for example, of the boldness of the surgeon who annihilates the consciousness of his patient and then, without trepidation, cuts into the abdomen, or excises a goiter, or removes a brain tumor. The physician also must have bravery—one might almost say audacity—when he attempts by the use of a drug to intervene favorably in the disturbed physical, chemical and biologic processes of the human body in disease.

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## COMPLEXITY OF CHEMICAL PROCESSES.

Man's body is the most marvelous chemical laboratory in the world, a laboratory made up of several thousands of billions of separate work rooms, in each of which the amount and kinds of work done differ somewhat from those in each of the others. No two liver cells probably are precisely alike in their chemical activities. In a single mucous membrane, the chemistry of the constituent gland cells differs markedly from the chemistry of the constituent nerve cells, connective tissue cells and smooth muscle cells. Within the channels of communication that carry fluids and solids about the great laboratory from work room to work room, chemical changes are constantly going on in the transported materials. Even the walls, the beams and the furniture of the billions of work rooms are themselves constantly undergoing chemical change. We are awed enough by the complexity of the chemical processes that go on in health; but let us not forget that in the diseased body, which is the province of the pharmacotherapist, this complexity becomes manifold. Into this apparent infinite welter of chemical transformations (though, in reality, orderly and ultimately knowable) goes the drug that the physician administers in the hope of curing, regulating or ameliorating. Its administration surely signifies courage on the part of the physician who has such a conception of the body's chemistry. The task he attempts is truly Promethean. Is it not to try "to defy Power, which seems omnipotent?"

## THE DEVELOPMENT OF PHARMACOTHERAPY.

Man's needs have been so urgent, however, that medical men everywhere, and at all times, have not hesitated to defy powers when they seemed malevolent; and drug therapy has, despite its besetting difficulties, become one of the successful methods by which medicine "folds over the world its healing wings."

The clinical experience of the centuries slowly supplied an important body of facts regarding the nature of disease and man's power to control it, but the formation of true guiding principles for pharmacotherapy had to await the rise of modern science. More of the value has been learned regarding rational treatment by the use of drugs in the last fifty years perhaps, than in all the centuries that preceded; for, during the last fifty years, we have gained entirely new conceptions of the nature and course of disease.

Through chemical, physiologic, psychologic, pathologic and clinical studies we have learned much regarding pathogenesis, that is to say, regarding the chains of changes in the body that follow on injuries of various sorts. Synthetic chemistry has supplied us with a host of new substances for trial as remedies. The new sciences of pharmacology and toxicology have revealed to us the mode of action of drugs and poisons, and medical students are observing for themselves, in our pharmacologic laboratories, the physiologic effects that follow the introduction of foreign substances into the animal body, and they measure some of these effects with instruments of precision. Knowing only too well that in the diseased body drugs often act in an unexpected manner, in ways very different from those in which they act in the healthy body, clinicians have wisely seen that the pharmacology of the laboratory, though of great value for the general advance of scientific therapy, cannot take the place of accurate clinical observation. It can do much to guide therapeutic effort and to supply criteria for judging of its effects but the final and crucial test of the value of any therapy is that of actual clinical experience.

The clinic can help the laboratory, and the laboratory the clinic; but each has its independent domain that should be conscientiously worked and zealously safeguarded.

#### THE NEW EXPERIMENTAL SCIENCES.

Recently, laudable attempts partially to bridge the gap between the pharmacologic laboratory and the clinic, in the interests of pharmacotherapy, have been observable in the work of the new sciences of experimental pathology and experimental therapy, especially experimental substitution therapy, and experimental antiparasitic therapy (immunotherapy, serotherapy and chemotherapy).

Workers in these new sciences reproduce certain sharply circumscribed syndromes in experimental animals and then study various forms of treatment experimentally, analyzing the effects of the measures tried. With the advent of the experimental pathology and experimental therapy, we can hope for the rapid development of a systematic science of therapy; and though the transfer of results of experiments in treatment of sick animals to treatment of the sick human being will always mean a leap from the known to the unknown, still this transit will from now on be made with ever-lessened danger. New drugs and chemicals will in the future be thoroughly and reliably tested, not only in pharmacologic laboratories on healthy animals, but, as far as possible, also in laboratories of experimental pathology and therapy on animals in which special diseases have been induced, before we shall feel justified in making trial of them in the treatment of sick human beings.

#### CLASSES OF PHARMACOTHERAPY.

Now that physicians generally understand that, in all diseases of pathologic processes, they have to deal with modifications of normal (or physiologic) processes that depend on definite disease causes, modifications, moreover, that are beyond the self-regulating capacity of the organism to keep within those limits of functional activity that we observe in "health," the internist can classify his pharmacotherapeutic efforts according to the kind of effect he desires to produce. Thus (1) he may try with a drug to remove the cause of the disease or to render it harmless (etiologic pharmacotherapy); or (2) he may use a drug that will help directly to restore a pathologically disturbed function to normal (functional pharmacotherapy); or (3) he may administer substances that will aid the organism in its modes of reaction against the disease-cause (regulatory pharmacotherapy); or finally (4) he may employ drugs merely to relieve single troublesome symptoms (symptomatic pharmacotherapy). Internists who, after thorough and complete diagnostic studies, carefully consider these several indications (etiologic, functional, regulatory and symptomatic) should achieve in their pharmacotherapy the highest possible success.

#### ETIOLOGIC PHARMACOTHERAPY.

Pharmacotherapy is seen at its best when, through the use of a drug, the cause of a disease is removed or rendered harmless (etiologic pharmacotherapy) before the patient has sustained irreparable injuries. The organism can then right itself, so that its activities can resume their normal or physiologic course. As our knowledge of disease-causes steadily undergoes increase, even more maladies will be made accessible to etiologic therapy. Physicians of all times have considered the causal indication when they removed harmful substances from the stomach by

emetics, such as mustard or ipecac, or from the intestine by purgatives, such as castor oil, calomel or magnesium sulphate. The greatest successes in causal therapy have, however, been achieved by using drugs that kill living animal or vegetable parasites within the body, or that drive them from the body into the world outside. The use of oleoresin of male fern against tapeworm, of santonin against roundworms, and of oil of chenopodium against hookworms, are paradigms of antiparasitic pharmacotherapy. The parasites of malaria were killed by the quinine contained in cinchona long before we knew that the malarial fevers were parasitic in origin. Pathogenic amebas in the intestine can be killed off by means of emetine hydrochloride. The fungi that cause blastomycosis and sporotrichosis die when subjected to the influence of the iodides. Noteworthy triumphs have recently been scored also by etiologic chemotherapy directed against certain parasites (trypanosomes, spirochetes and spirilla) that cause African sleeping sickness, syphilis, and relapsing fever. Through prolonged experimental work, parasiticides have been discovered that have a greater affinity for and toxic effect on trypanosomes and spirilla than on the body cells and organs; in other words, poisons that are more parasitotropic than organotropic can now be used to kill certain invading microorganisms without too much injury to the invaded host. Arsphenamine and neo-arsphenamine help us greatly in the fight against syphilis, and are undoubtedly valuable additions to our pharmacopoeia. With further studies of the parasitotropic qualities of various arsenical and antimonial compounds, we can reasonably hope for satisfactory means of control of a series of tropical diseases that up to recent times have defied the efforts of therapists.

In the antiparasitic treatment of diseases of bacterial origin, experimental chemotherapy has thus far been baffled. This does not mean, however, a permanent defeat. There is much to encourage investigators to continue their search for internal disinfectants that may be safely used. The body fluids and the body cells contain and manufacture substances that can kill bacteria. The chemical constitution of these bactericidal substances, we can feel sure, will ultimately be discovered; the substances will, later, be made synthetically and utilized in therapy. Moreover, toxic bacteriotropic substances that are foreign to the organism and innocuous for it will also doubtless be found and used. We already know that ethylhydrocuprein will kill pneumococci, though its deleterious effect on the optic nerve makes it unsafe as yet as a therapeutic agent. But who knows how soon some enterprising experimental chemotherapist may find a related pneumococcidal substance that is less harmful to the body, just as the discovery of the relatively innocuous spirilloccidal arsphenamine succeeded that of the blindness-producing atoxyl?

#### FUNCTIONAL PHARMACOTHERAPY.

Though less ideal and important than etiologic therapy, much good can be accomplished by the internist who, making use of a so-called functional pharmacotherapy, tries to restore to normal some function that, through disease, has become disturbed or abolished.

This can easily be made clear by citing a few examples. Thus, a patient with valvular disease of the heart may get on well for years, thanks to the reserve force of his cardiac muscle. But sooner or later, the function of the heart muscle begins to fail, and breathlessness, tachycardia, arrhythmia, passive congestion and

edema appear. In digitalis, the pharmacotherapist possesses a remedy that, properly used, will often slow the heart rate and increase the contractility and tonicity of the muscular walls of the heart so that the circulatory insufficiency will disappear. Or, a patient in whom atrial (auricular) fibrillation exists may have the normal initiation and conduction of atrial stimuli restored by means of a few doses of quinidine. Or, again, a patient whose arteries are becoming sclerotic may have spasms of the coronary vessels and the severe pain of angina pectoris that can be relieved by dissolving a tablet of glyceryl trinitrate under the tongue, which, by dilating the pathologically contracted coronary arteries, removes directly a responsible functional disturbance. Similarly, we can relax the bronchospasm of a typical attack of bronchial asthma by the injection of a few minims of a solution of epinephrin (1 : 1,000), and we can spur the atonic wall of the intestine to contract in a postoperative case by means of a hypodermic injection of solution of hypophysis (pituitary extract). In all these instances we make use of a functional pharmacotherapy.

Another example may be chosen from the field of metabolism. Thus, in gout, uric acid is not adequately excreted by the kidneys, being retained in the blood or deposited in the tissues about the joints. The function of uric acid excretion by the kidneys can be temporarily increased by the administration of cinchophen or neocinchophen, substances that also exert an exceptionally efficient analgesic effect in acute attacks of gout.

What we know as organotherapy may also be regarded as one kind of functional pharmacotherapy. If dried thyroids, for example, be given to a patient with myxedema (due to absence or defective function of the thyroid gland), the substance administered is capable of substituting for the function in abeyance and, in turn, of restoring to normal function those distant organs whose activities have undergone change through lack of the thyroid hormone.

#### REGULATORY PHARMACOTHERAPY.

Turning next to regulatory pharmacotherapy, that form of treatment in which we administer remedies with the object of "aiding the body to react against the disease-process or the disease-cause," a good example will be seen in the pharmacotherapy of acute nephritis. In a severe glomerulonephritis, water, salt and urea are no longer adequately excreted by the kidneys, being retained in the body. The body attempts to excrete these vicariously, through the digestive tract and the skin. The physician may aid the natural reaction of the organism by using (1) a drastic purgative, like compound powder of jalap, which produces copious watery evacuations, and (2) a powerful diaphoretic, like pilocarpine nitrate, which causes free sweating. Such purgation and diaphoresis support the activities of the normal regulatory mechanisms of the body and are therefore classed as examples of "regulatory" pharmacotherapy.

In the treatment of diphtheria with antitoxin, we also employ a regulatory therapy, for, on injection of the antitoxic serum, we support the normal reaction of the organism in its effort to produce chemical substances that neutralize the toxins of the diphtheria bacilli.

The treatment of a posthemorrhagic by anemia preparations of iron may serve as a third example of regulatory pharmacotherapy. The body reacts after severe hemorrhage by increased activity of the red bone marrow, regenerating red blood

corpuscles rapidly. More iron may be required for this accelerated erythropoiesis than is available in ordinary diet. The reactive regenerative process can be strongly favored by administering ferrous carbonate, say, in the form of Blaud's pills.

#### SYMPTOMATIC PHARMACOTHERAPY.

Symptomatic pharmacotherapy, which neither intervenes the disease process as such nor attacks its cause, is, however, a form of therapy that is by no means to be despised. Though it is directed only toward single symptoms that injure or torment him, this therapy is highly important for the patient, and, when successful, is the ground for much gratitude on his part. There is scarcely a symptom that is complained of by patients that physicians have not attempted to influence by pharmacotherapeutic methods. And the relief that can be afforded in many instances thoroughly justifies the attention that is given to the *indicatio symptomata*.

It is above all in the relief of pain and of the various forms of mental and bodily discomfort that this is true. We would not willingly neglect the administration of morphine in renal colic; of acetylsalicylic acid in the arthralgias; of wine or beer to paralyze certain pathologic inhibitions and to bring needed relaxation; of heroine and codeine in the racking cough of pneumonia; or of the various analgesics that are effective in migraine, in neuralgias, and in the lancinating pains of tabes. Though we may deplore the abuses of alcohol as a beverage, of purgatives in habitual constipation, of sedatives in the neuroses, of the hypnotics in insomnia, we all will admit that after causal, functional and regulatory indications have been fully met as our science permits of, there will be occasions when the merely symptomatic indication dare not be ignored.

#### CONCLUSION.

It will be clear from what I have said that the internist looks on the use of drugs in therapy more hopefully now, perhaps, than ever before. Available drugs are of real value in curing, in ameliorating, and in preventing disease, and new drugs that are useful are steadily being discovered.

Adequately to make use of the pharmacotherapeutic means at his disposal for meeting etiologic, functional, regulatory and symptomatic indications, the internist must, it is true, have mastery over a large body of facts. He must be well trained in normal and pathologic physiology and should have become acquainted with the known facts of etiology and pathogenesis. He should have learned in the pharmacologic laboratory the effects of the more important drugs on the normal animal body; and he should have had the opportunity in the hospital wards, and in the laboratory of experimental pathology and therapy, to observe the changes that can be produced by drugs in disease. Very few have as yet had opportunity for the latter, but the medical schools should provide for it in the future.

Our teaching hospitals at present are, perhaps, more diagnostic institutes than institutes of therapy. It might, possibly, be wise to divide our medical clinics in two parts, patients entering one division, for the general diagnostic study and emergency measures, to be transferred afterward to the other division for full treatment, the effects of which could be carefully observed by the students.

The internist with such a training in the medical school as I have outlined will be prepared to institute a rational therapy wherever this is possible. He will know how to make a judicious use of empiric therapy when a rational foundation

is lacking. As a matter of fact, pathology and therapy have of late years made such rapid strides that the physician can, in the majority of instances, give reason for the therapeutic faith that is in him. For this we have to thank both the research activity of the scientific laboratories and the keen and critical observations of our better clinics.

The introduction of new therapeutic methods and new drugs can scarcely be expected from now on to be arrived at by accident, or through pure empiricism. Every new therapeutic agent should, as Magnus<sup>1</sup> has emphasized, be thoroughly tested in the laboratories as regards its activity and its dangers, and, later, in the organized clinics, before it is introduced into general medical practice. Best results in clinical experience must ever remain the final and crucial test of every form of therapy.

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## CONTRIBUTIONS TO THE KNOWLEDGE OF FOREST PRODUCTS.

### INTRODUCTION.

BY ROLAND E. KREMERS.

It seems generally true that a people's interest in forests and the care which they bestow on their available timber is in inverse proportion to their national resources. As the history of our country repeatedly shows, our former abundant forests have been largely wasted until now we face an acute shortage at no very distant date.<sup>2</sup> But even while the wanton destruction of our forests was at its worst, there were far-sighted men who warned the nation of inevitable consequences, and who appealed to European conditions and experiences for their justification. Through such men the now well-known conservation movement was established. This resulted not only in the awakening of general interest, but also in the strengthening of remedial tendencies, notably the development of National Forests and of the present Forest Service, better forest management, and more active reforestation. But whatever the means employed, the chief end of the conservation movement as applied to forestry was timber. In certain sections there has been compromise with other interests and resources, especially in the West where mining and grazing have striven with forestry for priority.

The need for forest conservation is quite generally admitted at present, but there is not the same agreement as to how it shall be practiced or as to its urgency. Yet it seems not at all unlikely that in no very distant future there will be important problems other than timber supply connected with forest areas. These regions will have to do their share in giving employment to labor and in the distribution of population; more and more they will become important as recreation areas and as health resorts. In fact, it is stated that silviculture in the broadest sense is the first and highest development of land utilization, closing the progression of hunting, lumbering, grazing, tillage especially for grains, and tree crops as civilization develops.<sup>3</sup>

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<sup>1</sup> R. Magnus, *Allgemeine Pharmakotherapie*, in Krause and Garré: *Lehrbuch der Therapie der inneren Krankheiten*, Jena, 1, 71-143, 1911.

<sup>2</sup> For a comprehensive statement of the politico-economic phases see "The United States Forestry Policy," by John Ise, Yale Univ. Press, New Haven, 1920.

<sup>3</sup> J. Russell Smith, "Industrial and Commercial Geography" (Holt & Co., New York, 1913), p. 656.