

THERAPEUTICS.*

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The word "therapeutics" is derived from the Greek verb "therapeuein," to serve. Its derived or secondary meaning, hence, is service in the cure of or, failing in that, the lessening of the evil effects of disease. It is the branch of medicine which deals with the treatment of disease. Nature cures, physicians treat, says Lauder Brunton. Nature tries to right her own disordered organs and her power to do this is called the *vis medicatrix naturae*. A proper therapeutics should reckon with and not counteract or destroy this power of nature in the human body.

A cure or successful treatment of disease may be either symptomatic or radical and the essential feature to make it successful, if radical cure is aimed at, is to know the cause of the disease. Thus gout manifests itself in various symptomatic ways in different people, to wit: (1) eczema of skin attended with itching, etc.; (2) neuralgia with severe pain; (3) bronchitis with cough; (4) dyspepsia, with flatulence and intestinal disturbance; (5) inflammation of big toe with redness, swelling and pain. Symptomatic therapeutics aims to relieve the respective conditions, to wit: itching, neuralgic pains, cough, flatulence and swelling. Radical therapeutics aims to eliminate the gout itself. In many cases medicine is ignorant of the real cause of the disease or holds to various theories regarding same, in which case symptomatic treatment is employed to make patient comfortable, or combined with this a radical treatment based upon the theory of the seat of the underlying disease held by the individual physician treating same. This treatment or therapeutics may be either empirical, which means based upon inherited usage not based upon knowledge of the reason of the drug's action; or it may be rational when it is based upon real knowledge of the effects of a remedy. The study of disease from the standpoint of observation and experiment or cause and effect began with John Hunter, followed by Magendie, Claude Bernard, Gaspard, Villemein, Pasteur, Koch, Ehrlich, etc.

Disease may be due to failure of some of the organs and parts of the body to operate normally and properly, thus if the heart action is too strong or too weak, thyroid gland secretions are excessive or insufficient, etc., etc.; these may be individual or personal and may, hence, be called normal causation of disease. By far the most diseases are, however, caused by the invasion of the body by bacteria or organisms of some sort, which either themselves destroy tissues and cells as, for instance, syphilis, or whose excretory products or toxins destroy tissue or poison the host. In disease, usually, certain physiological functions are disordered, and it is the work of therapeutics to endeavor to again have those functions become normal. In general various kinds of therapy are available—suggestion, dietetic-, physico-, pharmaco- and surgical. Each has its field and usefulness. Many patients try out one after the other of these kinds or schools of therapy and finally conclude with the radical use of the knife. A specific therapy or one which strikes directly at the cause of the disease is the exception rather than the rule, the rule being either an empirical or rational therapy of symptoms,

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the exception being such specific therapy as salvarsan, quinine and malefern. Serum therapy is supposed to be specific, but it is only indirectly so, inasmuch as the serum, being an antitoxin, merely destroys the effect of the toxins or products of the specific organism. This, to be sure, removes the danger of the disease which consists in toxemia from the toxic excretory products of the organism. Has it ever occurred to you that of the approximately 1000 official products of the U. S. P. and approximately 850 products of the N. F., there are practically not any specific drugs, they are all agents to restore physiological normality or treat symptoms; thus hypnotics, diuretics, laxatives, anesthetics, diaphoretics, antiseptics, antipyretics, digestives, antacids, etc., by paralyzing nerve centers, stimulating the kidney or bladder, producing peristalsis, stimulating sweat glands, etc., etc., make the patient more comfortable and help him by overcoming some of his physiological abnormalities or disturbances?

Before I take up the subject of remedial agents let me call attention to a matter of therapeutic nomenclature. It is the word "pharmacology." By many, perhaps most people and therapeutists, it is accepted as a general word to cover anything that has to do with drugs, *i. e.*, the science of drugs, from the Greek *pharmacōn*- a drug, and *logos*- a discourse. To the knowing few it means the science of the effect of drugs upon the animal body and subsequently the human body. The pharmacology of digitalin is the observed effect of digitalin upon the heart, blood pressure, temperature, kidneys, liver, blood, etc., of a dog, guinea pig, etc., etc., and thereafter, at times, upon the human body and its organs in the clinic. I feel that some central authority as the American Medical Association should properly define the term pharmacology. Wood says pharmacology is the science of drugs, and pharmacodynamics is the study of the effect of drugs upon the healthy animal organism; Cushny says pharmacology is the study of the changes induced in living organisms by drugs.

In earliest times drugs consisted of animal and vegetable products with a few mineral products. Gradually the animal products gave way to vegetable products entirely until the alchemists took up mineral products, largely, and neglected vegetable drugs, and therefrom emanated the science of chemistry, which began with mineral substances and then later developed the organic side. So remarkable was the interest in carbon chemistry that inorganic chemistry went into almost complete eclipse, due to the easy and manifold changes carbon compounds underwent in the skilled hands of the chemist; especially when coal tar first made its appearance and became the mother substance of an almost endless series of new classes of organic compounds; among these the dyestuffs, first called aniline dyes, but incorrectly so, since the best dyes to-day are in no wise related to aniline. Probably the migration of chemists everywhere to this field caused some reaction in the case of a few more mathematically than experimentally inclined chemists and physicists and induced them to come back to the inorganic side and develop the science of physical chemistry. The discovery of radium and radio-activity helped this reaction and, in consequence, to-day the great advances in the science of chemistry are being made in the field of physical chemistry where the theory of solution, the nature of the atom and the study of colloids is fast causing a return of the carbon chemistry hordes to this fascinating and more important field. In my days as a chemical student we were so anxious about what

resulted by mixing two solutions that we overlooked the solution itself and assumed that it merely was the mechanical solution of the substance in the solvent. Because strong solutions of a ferric salt and ferrocyanides gave a dense crystalline blue precipitate, we did not stop to study why dilute solutions of the same gave only a blue solution and concentrated solutions gave a gelatinous blue mass. In consequence the "world of neglected dimensions," as Ostwald calls colloid chemistry, escaped our attention. One of the results, however, of the migration into carbon chemistry fields was the change of therapy—for it flooded the world with so-called synthetic organic drugs, beginning with antipyrine, which the influenza epidemic of 1889–1890 forced into universal prominence, and running for thirty years through a gamut of new patented organic compounds, used very generally by all and for all ills of the flesh. If there is an ailment or symptom for which aspirin is not used by some one person I have failed to note it. Whether it possesses any real merit for anything I have my serious doubts, but the so-called coal-tar synthetics had to run their course and expend their much-heralded and advertised merits. Their sun has passed its zenith and is rapidly approaching its setting despite newspaper advertising and panacea claims. The night of the synthetic crystalloid is becoming the dawn of the re-birth of the crude drug and the colloid, probably because in the human body and the plant the condition of matter is the colloid condition and results are obtained from opium that are not possible with morphine, and from nux vomica that are not possible from strychnine. The active principle is by no means equal to the drug of which it is a part and particularly is the crystalline morphine sulphate not equal in effect or similar in effect to the colloid opium. To be sure, morphine sulphate has played a very valuable and important rôle in medicine and will continue to do so, but I feel that I will live to see the day when colloid morphine will replace crystalloid morphine, at least for many purposes. Hence, it would seem that we are in another transition period in therapeutics—a period that seems to me a transition in two dimensions. The one is the change from crystalloid to colloid for the therapeutic agent, as an abscissa; and the other the change from a symptomatic to a specific therapy, as an ordinate, and between these two variants the curve of the future therapeutics will be drawn.

Therapeutics has been, because of the absence of scientific foundation, more or less of a hazy subject and hence has not progressed nearly as fast or effectively as surgery, which is based upon anatomy and pathology and physiology, all of which are fully developed sciences. When the time comes that therapeutics will have to deal with specifics instead of symptomatics, if I may coin a word to express the bulk of remedial agents of to-day, then medicine as therapeutics will come into its own and the *vis medicatrix naturae* will not be looked to so generally for positive results. Of course, our knowledge of the causation of disease will have to make some progress before a specific medication can rise to give it battle. We must know the cause of so many of our diseases whose origin is yet shrouded in mystery, such as diabetes, anemia, nephritis, scarlet fever, smallpox, measles, whooping cough, cancer, sarcoma, etc., etc., but these will sooner or later become known; and, above all, we must learn to know what changes and processes take place in the living cell in health and in disease. Even many of those diseases whose cause is known, such as tuberculosis, typhoid fever, pneumonia, cholera, ery-

sipelas, etc., etc., we are to-day perfectly powerless to combat by the agencies of therapeutics. We can and usually do—may I say we always do—treat their symptoms or their effects or the abnormality of physiological processes produced by them. But we practically never are able to treat and either paralyze or destroy the nigger in the woodpile—the bug or beast or enzyme or agent that is the cause of the disease. This rascal escapes our therapy, for with the exception of salvarsan for the spirochete, quinine for the plasmodium, santonin for the worm ascoris, and malefern for the tapeworm, whatever in our therapeutics ends the invader's life process—also ends the life process of the invaded and as the latter is the object of our care and solicitude and the end and the aim of our therapeutics, we call off our therapeutics and trust to the *vis medicatrix naturae*, in other words, let our patient fight it out with the bug and try to make the battle as painless and comfortable as we can, and especially look very wise and hope for the best. Great men in medicine have labored long and hard to learn the cause of disease and the effects of disease, and books upon books have been written upon the subjects of etiology and pathology of diseases. How few men have worked and how few books have been written upon the cure of disease—in fact, medical men so dislike the word cure that we had better use the term successful treatment of disease.

When will therapeutics become the science of the elimination of disease instead of the science of the counteraction of the effects of disease or of the reinforcement of the tissues in their struggles to maintain their functions? As the avenues leading to successful effective elimination of disease after it has manifested itself in the human body appear to be jungles too closely and densely overgrown to admit of a hopeful and ready entrance—or to speak plainly are as yet *terra incognita*—another entrance from quite a different quarter into this *terra incognita* is being now actively chopped with the axe and machete of preventive medicine. If we cannot find a therapy which will destroy the nigger in the woodpile of our jungle let us try to prevent these same niggers from getting into the jungle by destroying them in their native and favored breeding ground. Thus has the great and powerful and ably managed world-wide Rockefeller Foundation undertaken to seek out these breeding places of the yellow fever mosquito, the malaria plasmodium, the hook-worm, the cholera bacillus, the smallpox organism, etc. If this can be successfully accomplished for some of these diseases it will prevent us from being attacked by these diseases and therefore avoid the necessity of subsequently eliminating or destroying them. The success of hygiene and preventive medicine is to-day the most hopeful and important attack at present being made upon the citadel of disease. This attack will, however, probably (and I say probably advisedly, because preventive medicine is in its infancy and no one can foretell what it may be able to do when it reaches adolescence and maturity) not eliminate those diseases whose causative organisms are more or less omnipresent in our atmosphere and vegetation, such as tuberculosis, pneumonia, cancer, influenza, scarlet fever, whooping cough, etc. For these diseases we need specific therapeutics and, as all of them are due to an organism which we can appropriately call a pathogenic organism, the most effective therapy would be a germicidal agent which, while destroying the invading organism, does not destroy or injure the invaded host—our patient. Many scientific men have hoped

they had found such an innocuous internal powerful germicide, but were disappointed by the results of its use by the medical profession. Such a therapeutical agent would prove more valuable in one minute than the major portion of our Pharmacopoeia and National Formulary in its lifetime, for it would be an effective agent in the radical specific therapeutics of most of our diseases as against an endless variety of the more or less empirical symptomatic therapeutical agents that constitute the present armamentarium of the physician.

We, surely, all concede that physicians are doing the best they can and applying in most cases at least the best knowledge that is available in their therapeutics. When one picks up the last edition of "Frankels Arzneimittelsynthese," with its 800 pages of description of effects to produce specific medicines one is astounded to find how little of real value to destroy disease producers has been evolved. Practically all of the *specifics in spe* turn out to be only another *symptomatic in re*. We know the effect of organic groups and inorganic radicals fairly well, thus added hydroxyl groups in aliphatic compounds weaken their effect and the same in aromatic compounds. Halogens in aliphatic compounds increase the depressing effect upon the heart and also make them more toxic; amine groups and nitro groups also increase toxicity; ketone groups, like alcohol groups, produce narcosis and reduction of blood pressure; carboxyl groups as a rule decrease physiological effect; double and triple bonds increase toxicity; esters reduce the toxicity of alcohols and acids, as we see in salol; acetylated amines are less poisonous and depressing than amines, as we see in phenacetine. Amines in general are antipyretic and antineuralgic in their effect, but in order to destroy their toxic effect hydroxyl must be introduced and the amine further weakened toxically by acetylation and methylation or ethylation; a cyclic or ring formation seems essential to physiological effect, as practically the same substances in open chain are devoid of effect, while when the anhydride formation closes the ring—physiological effect appears; side chains are, however, necessary to make this effect of value; hydroxyl groups in such cyclic groups are frequently the cause of narcotic effect; practically all vegetable laxatives are derivatives of anthraquinone, and anthelmintics appear to be derivatives of phloroglucin, etc., etc. In this way we can connect up in some way therapeutic effect with chemical composition in organic compounds in a general way; but unfortunately little of it is of value, because there are few general rules and most cases are exceptions. Besides this they are all synthetic organic compounds and practically all are crystalloids, and the day of this class of compounds is at present on the wane; although doubtless valuable new synthetic organic compounds that will prove to be specifics will yet be discovered.

The future of therapeutics, to my mind, lies in the colloid field, and in this field are the crude drugs if administered in their natural state and preferably in the fresh state, rather than in the cured state—although a drug cured at a moderate temperature has probably not lost its colloid nature and hence should be effective. But besides the crude drugs, which are most complex, we have the possible field of colloid metals, colloid salts, colloid compounds, in fact, it has been stated by Ostwald and others that almost any compound or salt or element can be converted into the colloid state. If the human body is colloid as far as its fluids are concerned and these are the elements of the body that convey medicines and deliver them to the place where they are to act, then the drugs that are

to act and to produce an effect in relatively small quantities should, preferably, also be of a colloid nature. This field has only just been touched and it is rather an unexplored forest in which, however, most marvelous phenomena and discoveries are being made by those who have plunged into it. Most chemists, notably those of us who are entering into the sear and yellow leaf stage of our career, are not yet capable of thinking and reasoning in the syllogism of colloid chemistry and we are yet measuring it with the wrong yardstick. In fact, to tell you the truth, those of us raised in Dalton and Mendelejeff and Beilstein have to relearn our chemistry, just as the school boy does his three R's, if we hope to be in the game of chemical and therapeutic science for the next decade. Our chemistry, which to us seemed so scientific and smooth, is distinctly empirical in the light of the knowledge of to-day and, what we and our teachers thought were careful observations, such as the solution of salt in water, were in reality most superficial observations. The despised amorphous colloid to which we gave not even a passing glance is the real live, hopeful messenger of good tidings of to-morrow. The great problem is going to be to get the physician, as well as the pharmacist, to take us at our word and believe in us when we begin to talk to them in terms and in terminology of the "world of neglected dimensions," as Ostwald now designates colloid chemistry. The chemist who formerly cast shy glances and looked askance at mathematics will, in the years to come, have to learn his higher mathematics if he hopes to be a success in the therapeutics and the pharmacy of to-morrow. Crystalloid gold, silver and iron have but little effect therapeutically, but watch what colloid gold, silver and iron will do to the cells of our bodies in 1925. I have recently had some experience in this field, and from what I have seen and what I know I can predict, I think, with equanimity and calm assurance that great things are on the horizon and great possibilities loom up on that horizon that spell big achievement in the field of pharmacy, chemistry and therapeutics. Prominent among these possibilities is the birth of specifics in therapeutics, and the physician of to-morrow will no longer be satisfied to depend upon the "*vis medicatrix naturae*" with its long list of symptomics, but he will be able to call to his aid a line, which need not be very long at that, of specifics. Specifics that are not merely agents to reduce a fever, open up a constipated bowel, induce an unwilling bladder to micturate, or a sweat gland to perspire, or a pain to be temporarily stifled by a narcotic, etc., etc., and yet let the demon eating at our vitals continue to live in luxury and peace; but specifics that strike home at the bug that is at the root of our troubles and make life so miserable for him that he will pass out of our life and pass up his own as well, thus doing away at one fell swoop with the necessity of adding to the prescription many, if any, of the legion of symptomics which now constitute the major portion of the United States Pharmacopoeia, the National Formulary and the small volumes commonly known as the price lists of manufacturers of pharmaceuticals and chemicals.

The Pharmacopoeia of 1930 will, in all probability, be a somewhat thinner tome than that of its immediate predecessors and it will, probably, also be made up somewhat, at least, of different substances. When this occurs therapeutics will no longer be the art of applying substances used to counteract the effects of disease, as Cushny aptly and correctly defines it, but the art of applying substances used to destroy the cause of disease.