taking classes of the community, she cannot hope to retain commercial pre-eminence. Such positions should be filled, not according to political influence, but with regard to commercial and scientific knowledge and *savoir faire.*

THE USE OF DRUGS IN DISEASE.*

BY R. G. ECCLES, M.D., BROOKLYN, N. Y.

To how many of your minds has the idea come that pharmaceutical chemistry may be the oldest profession on the earth? The first of living things must have started as a drug compounder. As soon as the early Protozoa began colonial life—*i. e.*, when they changed from one-celled to multi-celled organisms—they must have exchanged with one another those kinds of drugs now known to physiologists as hormones. With progress upward to the higher forms of life we find, on study, that the exchange of drug commodities increased very greatly. Myriads of substances unknown to the lower forms appear among the higher. Prof. Huxley, the great English biologist of the end of last century and the beginning of this, declared that of the many millions of organic substances produced by plants and animals they are all combinations of exactly the same elements as are found in "smelling salts" with a trifling amount of mineral substances. Out of these cells—the primitive pharmacists—produced by their compounding almost the entire array of organic substances found upon your shelves labelled with what laymen look upon as hieroglyphics. While most pharmacists know, in a general way, that the great bulk of their medical supplies are the products of these ancient pharmaceutical chemists few have stopped to consider the fact that their own bodies are miniature drug depots, and that a quite respectable proportion of the drugs found therein vary but slightly from those they sell every day over their counters. The same identical radicals are found in them as are found in the store stock. Your bodies' cells have been licensed by nature, after a proper training in the nature of drugs, to put up the claim that within their membrane walls "Prescriptions Are Carefully Compounded." Within their walls they are constantly at work filtering, precipitating, dissolving, macerating, digesting, percolating, oxidizing, reducing, and hydrolyzing. An inventory of the kinds of goods they carry—not ready made, however, but as chemical radicals—would be astonishingly like those found in a Jersey pharmacy. There are in the cells of a normal human body material radicals for the production, on demand, of some very potent compounds but all so cared for as to be quite harmless. Let us, for a moment, look over part of the list as it occurs to us at first thought. There is phosphorus, phosphoric acid and phosphates; iron, iron oxides, sulphides, sulphates and carbonates; sulphur, sulphides, sulphates, sulphites, sulphurous acid, sulphuric acid, and sulphuretted hydrogen; ammonia, ammonium carbonates, sulphides, sulphates, sulphites and phosphates; nitric and nitrous acids with a host of nitrogen salts, t. n. t., nitroglycerin and dynamite; hydrocyanic acid, cyanogen, cyanates and cyanides; iodine, iodides, iodates, and thyroidine; arsenic acid, arsenic, arseniates and arsenides; formaldehyde, formic acid, formates and many polymers of formaldehyde; glycerin and a host of different kinds of tryglycerides; hydrochloric acid, chlorine and a multitude of chlorides; calcium,

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calcium chlorides, carbonates, sulphates, sulphides, and a multitude of organic calcium compounds; unnumbered substances carrying the benzol ring; fluorine, hydrofluoric acid, and fluorides; alcohol, acetone, acetaldehyde, acetic acid, and acetates of many kinds; citric acid and citrates, oxalic acid and oxalates, oleic acid and oleates; potassium and its salts; sodium and its salts, silicic acid and silicates; copper and its salts; manganese and its salts; etc. In amido-valerianic acid there is the radical for production of valerianic acid and valerianates. The nucleic acid contains the raw materials of phosphorus, phosphoric acid and phosphates, hydrocyanic acid and cyanides, as well as of glucosides. The proteins hold in their structures three amino acids that contain the benzol nucleus, namely, phenylalanin, tyrosin and tryptophane. These are the mother substances of carbolic acid, benzoic acid, salicylic acid, benzaldehyde, aniline and numerous aromatic substances that perfume our drug stores, to say nothing of malodorous skatol and indol. These three amino acids are found in every cell of the human body but are particularly abundant in hair and nails, skin and mucous membrane. Every tissue that is exposed to infection by parasites, to an unusual degree, contains more than those not so exposed. They, with cystin and cystein, that contain oxidizable sulphur, are, strange to say, the first of the amino acids released by trypsin in the bacteria-laden intestine. There they produce the well-known antiseptic substances named and particularly carbolic acid. There the danger of having the cell-foods—the amino acids—stolen by saprophytes and parasites is greatest for these organisms subsist and fatten, as do the cells, on these amino acids. The oxidation of cystin, by bacteria, produces sulphurous acid, an antiseptic about as powerful as carbolic or benzoic acids which it fortifies. It seems as if nature had set a trap for the parasites by which they injure themselves as a cheese-set trap catches mice. Meats, fish, eggs, milk, glutin, and the like, all contain an abundance of these bacteria-inhibitors that only act when being digested or putrefied. The odor of skatol in putrid food is evidence of the fact that the bacteria are, by their depredations, producing antiseptic substances to inhibit their activity. The tyrosin is abundant in melanins, the pigments of the negro's *rete mucosum*, the choroid coat of the eye, and in the hair. With the approach of old age the hair turns gray, the nails brittle, and the eye-sight dim because of a shortage of tyrosin and its oxidizing enzyme, tyrosinase. Skin affections also increase as melanin diminishes. The black skin of the negro accompanies his relative immunity from yellow fever, malaria and trypanosome disease as compared with the lack of immunity in white men. Darwin has pointed out that certain skin diseases of animals attack only unpigmented ones, leaving the pigmented untouched, while piebald animals are attacked only on white spots. The shortage of tyrosin seems to be responsible. Millions of years ago the phenylalanin and tyrosin of plants were buried in the ground with the plants that produced them. We now dig them up as coal and the aromatic radicals of these amino acids constitute the antiseptic substances of coal tar. Our beautiful anilin colors and our many new synthetic remedies have come from these. Their antiseptic powers have preserved them for all these years from the depredations and ravages of time. We, too, like coal, derive our antiseptic radicals from plants as no animal seems to possess the power to produce them, in spite of the fact that none can live without them.

Among the first of well-known men to proclaim the virtues of these substances, as found in coal tar, was George Berkeley, Bishop of Cloyne, Ireland, who died in 1753. You have all no doubt heard his prophetic slogan, that has become a household expression: "Westward the course of Empire takes it way." You probably also know that California has honored him by calling the university city of that State by his name. He extolled tar water as a panacea for many ills and this, together with his then unpopular philosophy, brought ridicule upon him. Pope, the great English poet, however, came to his defense and in one poem says:

"Truth's sacred fort the exploded laugh shall win,
And coxcombs vanquish Berkeley with a grin."

His supposedly erratic defense of tar water has been vindicated by modern research, and the scriptural claim that "The leaves of the trees shall be for the healing of the nations" is also vindicated. In these leaves are, and always have been, produced the world's supply of the best-known parasiticides and antiseptics. All of our food proteins are leaf products, so far as they contain phenylalanin and tyrosin, as are also all coal tars, so far as they contain the benzol nucleus. Through this discovery we are but beginning to see that throughout living nature a battle with parasites is going on in which these constitute the implements of war. To successfully vanquish individual diseases we must pursue the methods of nature in the way it holds in abeyance the countless millions of actual and potential disease-producing parasites that menace all other living things. The way she controls disease we must control it, and the weapons she uses against microbes we must use, in order to be successful. Fifty years ago little was known of these invisible foes, and a century ago only the larger parasites had any place of recognition in our textbooks of medicine. Now we have discovered them to be the constant enemies of every thing that lives. There are now catalogued from 5 to over 20 different kinds for each particular species of plant and of animal. Over sixty have been catalogued and named as enemies of the oak trees. Not a single soul within the hearing of my voice is, at this very minute, free from them. We are all disease carriers. Streptococci, staphylococci, pneumococci, and *Bacillus coli communis* are now waiting upon, and within our bodies, for some favorable opportunity to start disease. They are being held at bay by the antiseptic substances we have named as present in skin and hair, mucous membrane and nails. A scratch of the skin may inoculate the apparently trifling wound with some virulent kind of streptococcus that starts erysipelas and kills us. We stop its multiplication by a free use of exactly the same radicals as the skin that was removed contained. Our supply, however, most likely came from coal tar in which it had lain for many milleniums since the plants that produced it were menaced by still other kinds of parasites. With the advancement of bacterial and chemical knowledge we are, as such cases show, getting rid of empiricism and discovering broad, general laws of treatment that are as sound to-day as they were when, in the carboniferous era, these substances were formed. Unfortunately, there are among us a large number of people who measure progress by the yard-stick of their own ignorance. Knowing nothing of discoveries that lie outside of their studies they look, with unfeigned terror, on any kind of change that does not correspond with the opinions of their great grand-dads. They cling to old fads

and fancies as they do to truth when they happen to possess it. Not laymen alone are guilty of this folly. It is quite common among physicians and pharmacists as well. We are all loath to give up ideas that we took in when babes and sucklings. We have little of the bravery of the pioneer, and dread, with undisguised fear, every innovation that collides with our early impressions. Medical science has entered a new path since our discovery of the cause of disease and we are now being called upon to remodel our ideas in respect to processes of cure. In the confusion that is resulting from this change we are witnessing an intense conflict of opinion between progressive and sessile, or conservative, minds. Remarkable as is the fact, too, the conservatives have chosen for themselves the title "reformer" as they seek, with might and main, to reform things backward.

Among the new so-called reformers are those who seek to stop the use and manufacture of vaccines, those who oppose research in physiology and therapeutics, calling the processes pursued by the name of vivisection and themselves anti-vivisectionists, and those who oppose all drug treatment and condemn it as wholesale poisoning. The creed of the latter is that all drugs are "deadly" poisons and all administration of drugs is poisoning. From their point of view poisons are poisons inherently, and it matters not whether the dose is large or small it poisons in proportion to the amount given, the result being cumulative. This, of course, is a very old notion as well as a very false one, if we can rely on the experimental evidence of modern science. This view, however, has during the last two decades made immense progress in the minds of both laymen and doctors. It has built up a host of therapeutic nihilists, who want to "cast physic to the dogs." It was the inspiring thought among those who demanded the abolition of the use of alcohol in every possible form. It is instigating a crusade against the use of tobacco, tea, coffee, etc. Can you not see where this sort of logic is traveling and what the final result is likely to be unless we can educate the mass of voters to alter their views, in some safe degree, in this craze? Should these emotionalists increase in numbers as fast in the next century as they have done in the past what is likely to happen? Would it astonish you much if, when they feel that they are strong enough, they should raise the cry of "Stop Poisoning the Sick?" They would have no trouble in finding, in medical literature, an abundance of thoughtless utterances, of able medical men, to confirm their contention and win votes enough to close drug stores as they have closed saloons. Take, for example, these two statements, one from *Bulletin* 30 of the Committee of One Hundred on Public Health, p. 88, and the other from a State Board of Health *Bulletin*, as a statement from a leading medical college professor of New York:

"It would scarcely be an exaggeration to say that the first rule of hygiene is to avoid poisons."

" 'ALL POISONS:' All of our so-called curative agents (drugs) are poisons and, as a consequence, every one diminishes the vitality of those who take them."

These views are an echo of the time when men conjured out of their inner consciousness what they called truth. An appeal to nature by actual experiment would quickly have convinced them that so far are they from being true that, under proper qualification, the very reverse is declared by nature to be true. Not one of those who make statements like these has any knowledge of what a

poison is or why it poisons. It does not occur to them that among the most poisonous substances known to man are such foods as beef, chicken, fish, egg, breads, and proteins generally. Notwithstanding their poisonousness we could not live unless our food contained them. In the *Journal of Infectious Diseases*, Prof. H. G. Wells, of Chicago University, tells us that when egg-white, in a perfectly pure condition, is injected into a rabbit's circulation, in two intermittent doses, very minute amounts kill. He says: "One fifty-thousandth of a cubic centimeter of a solution containing but one-millionth of a gramme of protein (egg albumin) sensitizes fatally." (Oct. 20, 1908, p. 456.) That certainly beats strychnine. When these food substances are taken by the mouth the digestive fluids convert them into amino acids that are perfectly harmless. If they enter the circulation partly digested fatal results occur from what is technically known as anaphylaxis. It is now believed that all the various symptoms of different kinds of diseases are due to the anaphylactic poisoning of the body substances by the dead parasites that are being digested in the blood stream. A poison is, so far as we at present know, a substance that has an affinity for some of a cell's molecules and that by union with such molecules produces fatal disturbances in metabolism. The cells are all surrounded by specific membranes composed, as now believed, of protein-like substances. Injury to these, by union with chemicals that damage their function, alters their semi-permeability and leads to cell-death. Egg-white is broken up in the circulation into relatively large molecules of what we may call polypeptids and these have different affinities for different cells but are too large in size to take a proper place in metabolic changes. They act like a monkey wrench thrown between the cog-wheels of a machine. Meat, when partly broken up, has an affinity for a different set of cells from that chosen by egg-white fragments. Fish has still another set of such affinities. The proteins of microbes have, under the same circumstances, still other attractions for different cells and each kind of microbe poisons, with its protein fragments, different kinds of body cells. Hence different diseases display different symptoms. These microbe proteins, so far as we know, behave, when fully digested, exactly as do meats, fish and eggs—they nourish our bodies. Only at a certain stage of partial digestion are they poisonous. The most deadly toxins of disease have been fed to animals by the mouth, in relatively large amounts, without a sign of poisoning. They are digested into harmless and nourishing amino acids. The toxin of botulism is an exception that is probably composed of molecules sufficiently small to be able to pass into the circulation undigested and, therefore, able to produce anaphylactic poisoning. The deadly cyanogen glucosides behave in a similar manner to proteins but they are not digested by the enzymes of the blood if introduced hypodermically. In the alimentary track hydrocyanic acid is released as a poison. In the circulation none of the cyanogen seems to be released and all of the molecules, if in reasonable amounts, are removed by the kidneys. These glucosides, therefore, behave in an exactly reverse manner, so far as their poisonousness is concerned, to that of the food proteins.

All so-called poisons appear to possess specific affinities for different kinds of cells just as do the poisons let loose from foods in anaphylaxis, and these are but particular cases of the general rule in all food substances. The bone cells attract a large share of the lime of the circulation. The liver cells take up most of the

free sugar and deposit it as glycogen. The thyroid cells take charge of most or all of the iodine. The cells of the choroid coat of the eye drag in a large share of the melanin. In the same way the nerves that supply the extensor muscles accumulate lead and produce, thereby, wrist-drop. The neurons of central vision have an affinity for something in tobacco that leads toward dim vision and blindness. Horses that have fed on tobacco leaves suffer, because of this, from amblyopia. Methyl alcohol breaks up, in the circulation, into something that acts on these same neurons producing blindness. Digitalin and aconitine act particularly on the heart muscles. Curarine acts on the termini of the motor nerves. Adrenalin acts on the terminations of the sympathetic fibers. Caffeine has a particular affinity for the kidney and muscle cells. Formaldehyde by linking itself to the aminogen groups of the protein is supposed to arrest metabolism. Ether, chloroform, cocaine, morphine, codeine, and heroine have an affinity for lipoids, being soluble in them, and through this solubility are thought to be able to act on the nerves of sensation, stop their functioning, and abolish consciousness of pain, locally with some and generally with others. In quite small amounts these substances all seem to have but a slight stimulating effect upon the cells that they reach and act upon. A judicious use of digitalis, or of digitalin, strengthens the heart muscles to which they appear to be attracted. A similar use of atropine or belladonna tones and strengthens non-striated muscles, stimulates the respiratory centers and increases intestinal peristalsis. Strychnine is attracted to, and acts upon, the vasomotor and motor centers of the cord, thus increasing the circulation and producing thereby a general tonic effect, through increased supply of arterial blood. These, and all other so-called poisons, when given in proper amounts, act upon special parts of the body—not to injure them—but to increase their physiological tone. When animals, and even unicellular organisms, are exposed to them they acquire immunity to their toxic effects, to a most extraordinary degree. Prof. Roger, in his "Medical Pathology," states that an amoeba "can be gradually habituated to water containing 2 percent of sea salt; it becomes so accustomed to the new conditions that it perishes when again brought back into ordinary water" (p. 79). Parks, in his work on "Pathogenic Bacteria," tells us that bacteria can be habituated to carbolic acid, if administered in sufficiently dilute solutions, so that, in time, they are able to use it as a food (p. 26). Kobert, in his "Practical Toxicology," says: "The smallest snail will withstand more strychnine than an adult man. Many of the stronger cardiac poisons have no action whatever on insects. The rabbit can take more morphine than can a man fifty times the animal's weight. Doses of lead, nicotine, cysticine, etc., sufficient to poison man fatally do not injure the goat. Amygdalin does not affect dogs, but it kills rabbits. The hedge-hog takes with apparent enjoyment a dose of cantharides that will kill several persons under excruciating pains. Whereas, the frog is extraordinarily susceptible to the digitalis poisons, they have no affect upon the toad" (p. 5). The mongoose is not affected by a snake bite. The California oil fly develops in crude petroleum oil. Prof. C. Pichet has shown that in such cases as he has studied "The law is established that in simple analogous substances toxicity is increasingly greater as the substance considered is found the less abundantly in nature" (*Chem. Abs.*, Feb. 20, 1911, p. 714). Habit in the use of the poisons, like habit with arsenic, alcohol,

morphine, tobacco, etc., probably has something to do with such effects. The cells are toned up to a new standard. In vaccination, and serum treatment of disease, the stimulation of cells leaves them able to resist greater amounts of the toxins of such diseases. The anaphylactic effects of different proteins and the susceptibility to most kinds of diseases vary with experience. After one attack of typhoid fever the second attack, if it comes at all, is likely to be very much milder. The cells become more resistant. Prof. H. M. Richards states that: "It has been established that many, if not all, classes of substances which exert a toxic action on protoplasm will become stimulating if presented to the cells in sufficiently small doses" (*Nature*, March 24, 1920, p. 115). Prof. Pfeffer, in his "Physiology of Plants," says: "Submaximal doses of many and perhaps all poisonous substances accelerate respiration, growth, and the production of heat" (Vol. 1, p. 264). Prof. Davenport, Director of the Department of Experimental Evolution, of Carnegie Institute, reporting his many experiments with poisons on plants, says: "It is clear from this table that the addition of even small quantities of innutritious and poisonous substances may so affect the hylogenic processes as to cause twice, or even far more than twice the normal formation of dry substances in a given time, and that this excessive growth increases with the concentration of the poisonous substances up to a certain optimum beyond which growth declines again to below normal" (*Proceedings A. A. Advancement of Science*, 1907, p. 504).

Without the subtoxic effects of adrenalin on the circulation the arteries could not function normally and without thyroidine, growth is arrested and health seriously impaired. Without hydrochloric acid how would gastric digestion proceed? In such cases it is evident that what we call poisons have a very important place in physiology. There is a universal law seen in all living things. It is the benefit derived from normal effort, normal heat, normal electric currents, and normal chemical stimulation. Within proper limits all of these are beneficial. It is only when their stimulation exceeds such limits that they become harmful and this harmfulness is evident in all of them. The muscles are strengthened by massage and by effort. The skin of hands and feet thicken with work. Heat, in proper amount, favors growth as toxic substances do. Just as digitalis strengthens the weakened heart, so all poisons strengthen such parts of the organism as they act upon, provided, of course, that the physiological maximum is not exceeded. When will the world take to heart this lesson and use it for our benefit? When will we all learn that a sick man is always a poisoned man? The anaphylactic effects of the poisons of typhoid give us the clue to the particular parts of the system that need toxic toning against such poisons. The anaphylactic effects of malarial poisons give us a similar clue to the parts of the system that require toning against these poisons. When we know enough to experimentally follow these clues, for all sorts of diseases that we suffer from, and that kill us, we will know how to do by every one of them as we do now with digitalin in weakened heart. Such knowledge will put us on the way to true prophylactic medicine.

To know how, during threatened epidemics, and at other times, to strengthen every susceptible cell against that particular kind of disease, will be to enter into a new era of preventive medicine. To-day we are "locking the stable door when the steed is stolen." Then we will be locking the door before the thief can enter.

Our present efforts in preventive medicine have wrought miraculous results but they are all centered upon environmental prevention. If "an ounce of prevention is worth a pound of cure" in one direction it should be in the other. Nature is showing us many ways by which to resist the poisons of microbes. Let us learn our lesson from her. We must become able to poison our poisoners and to inhibit the effects of their poisons upon our cells. The druggists have a duty here that is as great as that of the doctor. He should discourage all reckless talk about the poisonousness of drugs by teaching his customers, when he has an opportunity to do so, that there are no such things as poisons *per se*, that strychnine, in proper physiological amounts, is no more a poison than is bread or meat, egg or cheese, and that soluble poisons, properly diluted, are more likely to be beneficial than harmful. Unless this is done there may, at any time, arise a wave of ignorant hysteria that will destroy—as it has already hampered and hindered—medical science in its work of aiding the deluded men and women who are sponsors for restricting and troublous laws.

NOTES ON PRIMITIVE PHARMACEUTICALS, SUGGESTED BY THE BRONZE SEALS, OR AMULETS, FROM INDIA, WHICH HAVE BEEN ON EXHIBITION AT THE NEW YORK COLLEGE OF PHARMACY.*

BY ADELAIDE RUDOLPH, NEW YORK.

These seals, originally numbering seven, have given rise to a good deal of speculation. Nobody, yet, has been able to say definitely whether they be wholly religious in character, and the figures which are inwrought in their bases merely symbolic of deities worshipped by certain Hindu sects, or whether they belong to the more general class of amulets, which are still so largely used in India as a protection against witchcraft, sickness, accidents, and other evils and ills of life.

Miss Lucia C. G. Grieve, who lent them to the library, a member of the American Oriental Society and at one time a student of Sanskrit, thinks that they are mostly religious and symbolic in character. It was during a two-year residence at Satara in the Maratha country of the Bombay Presidency of India that she made the collection, buying the seals from time to time of the itinerant fakirs, or "boxwallas." The story told her about these particular seals was, that they had formerly belonged to priests who officiate at the sacred tanks and holy bathing places, to which pilgrims flock throughout the length and breadth of the country, and were, when heated, used by these priests to stamp upon the bodies of the pilgrims, after ablutions, a mark, which could not be lost or stolen, that should protect from the much dreaded "evil eye," and from other disastrous influences.

The two or three Hindus of New York to whom I showed the seals were inclined to support Miss Grieve's opinion—that they are purely religious and symbolic in character, though they discredited the part of the story which relates to branding the flesh. They thought it more likely and more conformable with Hindu customs in general that the stamps should be used to impress symbolic designs on the sandal-paste, or the clay or mud from sacred rivers or bathing

* Read before Section on Historical Pharmacy, A. Ph. A., City of Washington meeting, 1920; seals and amulets were exhibited.