dermatically we always use protonuclein special powder in varying strength). No cases of the above varieties are cited, because their histories are all too well known; we have treated many such, and all successfully but one, and it was an old chronic case, of eczema from rhus poisoning, and did not continue the remedy long enough to decide for or against it.

One case of tubercular dermatitis came under my care; it was treated with daily inunctions (25 per cent. lanolin ung.) and hypodermic, daily, injections of ten to fifteen minims of the standard solution (10 grains special powder to drachms 1 of aqua dest., at 98 degrees F.) and a 3-grain tablet every three hours internally; after several weeks' treatment the diseased surface became smaller and smaller and healthy spots could be seen surrounded by the diseased tissues. At this time we lost sight of the case.

In chronic Bright's disease protonuclein is, therapeutically, without a peer in the opinion of the writer; eleven cases have been treated with it in our experience, and while we know the inevitable end of such cases is an untimely death, yet we are certain that in a number of instances, life has not only been made easier, by insuring more nearly perfect tissue metamorphosis, but actually prolonged by its use extended over a period of many months. We respectfully ask each physician reading this to calmly think what "more nearly perfect tissue metamorphosis" means to a sufferer from chronic Bright's disease, and then ask himself if this can be performed as well with any other remedy.

In tubercular joint affections we have used protonuclein in but one case, and that has the following history: Mother died of pulmonary tuberculosis, and maternal grandfather though meeting death by an accident was in the last stage of phthisis pulmonalis; paternal grandfather died of tubercular phthisis; child, a male, at the time of the first exhibition to him of protonuclein, was $5\frac{1}{2}$ years old, this was two years ago; at 2 years of age the patient had scarlatina followed by infantile paralysis of the left thigh and leg, subsequently tubercular hip-joint and ankle disease developed in the affected leg; protonuclein in 3-grain tablets was given every three hours together with cod-liver oil. Early in the spring of 1896 the hip and ankle required operative measures, and was accordingly referred to Dr. J. W. Hairgrove of Jacksonville, Ill., for operation; Dr. Hairgrove has kindly furnished us with his notes while the case was in his care. We append them below:

"L. A., entered May 22, 1896. Operation under ether narcosis, May 25, followed by but slight shock. Tuberculous abscess extending around the ankle curetted and through gauze drain inserted. Large abscess on the inner anterior aspect of the thigh opened and curetted, counter opening over the head of the femur and through gauze drain inserted. After-treatment was antiseptic irrigations through and through with gauze packing. Temperature ranged about 99.5 preceding and for some time after the operation.

"On June 14, was noted some swelling around the ankle. It is evident that some irritation still exists about the epiphyseal ends of the tibia and fibula. However, nothing operative was done until July 7 so that the patient might have an enjoyable holiday on the 4th of July.

"At the operation three incisions were made about the ankle, some curetting but no pus was discovered. The discharging fistula at the thigh was widened to improve drainage and packed with gauze. Henceforth the discharge rapidly decreased and the patient went home on July 23.

"During the whole course of treatment he took protonuclein and cod-liver oil.

"I regret that I am unable to give more definite notes of the case. While there was no tubercle bacilli discovered at any

time, we must remember how difficult it is to find them in thin pus; it can generally be done by the most patient and exhaustive effort only."

[signed]

J. W. H.

The little fellow is now plump and hearty, no swelling or tenderness of ankle or hip, and though the affected leg is some inches shorter than the other he can use the short one to support his weight without difficulty; he is attending public school and is anything but a picture of tuberculosis.

We claim that such results are unattainable without protonuclein. We further wish to say the child has not taken cod-liver oil for six months, but has been constantly on protonuclein.

Three cases of scarlatina have lately been under our care and throughout the disease were given nothing but protonuclein, with the exception of a simple diuretic on two days only. Two of the cases were light, the other developed a severe cervical lymphadenitis, which under the vigorous use locally (in throat) and tablets internally, was rapidly disappearing, when, at this time we left directions and ceased to make visits; we learned from the grandfather that the mother of the child ceased the insufflations when our visits ceased; the gland again rapidly increased in size and was opened several days later by another physician. In this same family were three other children and four adults, who were immediately put upon one 3-grain tablet every three hours; none of these last seven people mentioned contracted the disease.

We can not help commenting that no better prophylactic in acute infectious diseases is known; and, further, that the scope of usefulness to which protonuclein can be put is almost unlimited.

HOW CAN WE INCREASE THE THERAPEUTIC RELIABILITY OF MEDICINAL AGENTS?

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"Without pharmacologic knowledge, the application of remedies must ever be attended with the greatest uncertainty." As a pure science, pharmacology has taken rapid strides during the past few years; but to the physician, by elucidating the manner in which the functions of the various organs of the body may be influenced by the therapeutic agents at his disposal, it has given the greatest gain. Empiricism is disappearing, and ultimately we shall realize the hope of the centuries and medicine may justly claim a position among the exact sciences.

It is not my purpose to show what pharmacology has done in the past, but to call attention to some of the ways in which the science may be of still further service in the future. A physician may be ever so well versed in therapeutics, but if his prescriptions are filled with inert drugs, or drugs varying in strength, his efforts may be useless, or even dangerous. In the past the pharmacist has greatly aided our efforts by improving the preparation of the various remedies. But the time will soon come when he should be held responsible not only for the chemic and botanic purity of his preparations, but also for the physiologic activity of those important medicinal agents which can not be standardized by chemic methods.

I hear some one say this is impracticable, since pharmacists have not been properly educated to carry

out this work; besides, the expense is so great that they can not afford to do it. True, but today nearly all pharmacists buy the bulk of their preparations from some large manufacturing house, which can afford to employ a properly qualified person to make the examinations. Since the retail pharmacist can not do this testing, we should see to it that he supplies to our patients the preparations of some house that does determine the pharmacologic properties of its products. Or, where the retailer prefers to make his own tinctures, fluid extracts, etc., he should obtain his supplies of crude material from such houses as are willing to guarantee the activity of their drugs. It is much more important to the physician that he have a physiologically active preparation than an elegant pharmaceutical preparation. The ideal preparation is the one that possesses the properties of activity and elegance in the highest degree.

Probably to the physician the most important duty of the pharmacologist in his relation to the manufacturing pharmacist is the examination of the crude drugs and active principles before they are made up into fluid extracts, tinctures, pills, etc. Only those crude drugs and active principles should be tested physiologically which can not be assayed by chemical means. But there are quite a number of the most important medicinal agents that the chemist must at present pass, without testing, as no characteristic reactions have been worked out for them. Examples will best illustrate this point. As is well known, ergot, the sheet anchor of the obstetrician in so many hours of peril, loses much of its activity in a comparatively short time after being harvested, and if kept under certain conditions may soon become entirely inert, or if the crude drug was good when it came to the manufacturer the menstruum used may have been such that the more important constituents were left in the improperly exhausted drug; consequently the physician is never quite sure whether the preparation he carries in his obstetric bag can be relied upon to aid him in stimulating an exhausted uterus in a difficult labor, or in checking a much-dreaded post-partum hemorrhage. How much better it is for all concerned to test the ergot physiologically, rejecting the drug if found inert. Then, to complete the precautions, the finished product should be again tested to make sure that it shows the active properties manifested by the crude drug.

Out of twenty-seven samples of crude Indian cannabis, of excellent physical appearance, recently examined by the writer, only thirteen proved to be active when administered to animals; and of a large number of preparations tested, at least one-half were inert. Is it any wonder that physicians have come to believe that hemp is one of the most unreliable of drugs? Or that we occasionally have alarming symptoms following its administration? Digitalis leaves and strophanthus seeds are other good illustrations, and many other examples might be cited if space permitted.

The demand for the active constituents of vegetable drugs is prompted by the physician's desire to administer his potions either in small doses per os or with the hypodermic needle. But many of these active principles, glucosids, alkaloids and others, have thus far eluded the analytic chemist in his attempts to identify them and determine their purity. Since the chemist can not, the pharmacologist ought by all means to examine them before they are made up into preparations for the physician. Neglect this precau-

tion and the manufacturer may, perhaps, obtain a lot of inferior or worthless stock, contaminated possibly by some decomposition product or foreign substance whose action is directly antagonistic to that desired. Of four samples of strophanthin recently tested, three of which were supposed to be chemically pure, there was found such wide variation in activity that one was ninety times as fatal to animals as another. The strength of the remaining two varied between the above limits. No two samples were even approximately the same in strength. What a chance for a sudden, fatal termination of an apparently improving heart case!

Perhaps the most important work of the pharmacologist in relation to medicine is the investigation of new remedies. Synthetic chemistry has developed so rapidly during the past few years that new compounds for medicinal use are constantly being brought to the notice of the medical profession by traveling men, who strive to induce the physician to use the latest hypnotic, antipyretic, etc., promising him that the result will be most gratifying. But it behooves the honest physician to beware of using new remedies until something is known of their physiologic action. When he ascertains the functional changes brought about by the introduction of the drug into the animal economy, he can rationally begin the use of the remedy in his practice, with considerable promise of success.

The examination of medicinal plants for active constituents is greatly facilitated by physiologic testing of the residues obtained by chemical manipulations. By chemical means we can not tell whether a substance crystallizing in an alcoholic extract of a plant is the active constituent of that plant, or whether the amorphous substance dissolved by ether is the principle sought, but we can tell by physiologic methods when we have a substance representing the activities of the crude drug, whether it be crystalline or amorphous—which is the fact of real importance to the physician. Only a few years ago one of Germany's most renowned chemists isolated a beautiful white scillein, which was supposed to be the active constituent of squill. But since then it has been found to be entirely inert, and that the really important constituent of squill is a brown resin-like substance possessing in a very marked degree the characteristic action of the digitalis group.

Heretofore it has been the custom of manufacturing houses, when dealing with a new plant believed to possess medicinal properties of value, to make a fluid extract or some other preparation of the crude drug, and send it out to clinicians, at great expense, in the hope that it might prove of value. How much better it is to have the physiologic properties of the plant examined at the outset! If found to be inactive, the drug may be rejected, thus saving a large item of expense to the manufacturer and much disappointment to the physician and his patient; while if the plant is of value and the physician knows what its effects are upon the various organs of the body, he can use it intelligently, with a good prospect of success. Then, too, human beings are not so recklessly experimented upon, the lives of a few animals being jeopardized in place of so many patients. We can never analyze the action of a drug on the various organs of the human body with such precision as we can on the lower animals, but clinical knowledge obtained after we have a right conception of the physiologic action of the agent used is of very great importance in determining the value of a given remedy.

Until a few years ago nearly all the work done in pharmacology was carried out in the laboratories of the universities of Europe. Recently several leading universities of the United States have fitted up laboratories for the investigation of pharmacologic questions, and for giving the students practical instruction in the action of the more important remedies upon the various tissues of the animal body. To the University of Michigan belongs the credit of being the first institution in the world to give a laboratory course of instruction in pharmacology to undergraduate medical students. Undoubtedly this is a movement in the right direction, and will add to the ranks of the profession year by year men who are anxious to use only those drugs whose physiologic action is known. While we can expect the college workers to add greatly to our knowledge of the action of new drugs and explain the pharmacology of the old ones whose action is not clearly understood, we can not expect them to do the systematic routine work necessary to prevent the manufacturer from unconsciously placing on the market poor or worthless preparations. Neither can the manufacturer rely upon their aid to assist him in materially improving his methods of preparing of his fluid extracts, pills, tablets, etc., a work which demands at each step the careful scrutiny of a practical chemist, frequently supplementing his tests by pharmacologic reactions and not allow the manufacturer to go on year after year, sacrificing physiologic activity to pharmaceutical appearances, as has frequently been done. It should be possible for the workers in a manufacturing concern to work shoulder to shoulder with the colleges, and the result will surely be for the advancement of science and the well being of humanity.

We can not expect too much at first, as very little work has yet been done on quantitative methods of determining the physiologic activities of drugs by reactions on animal tissues alone, and we can never expect the results to be as exact as those of chemistry, but we can expect that a great deal may be done to lessen the uncertainty attending the administration of some of our most important medicinal agents.

COD-LIVER OIL A TIME-TESTED REMEDY.

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If cod-liver oil has been able to maintain its position as a remedial agent from a time "beyond which the memory of man runneth not to the contrary," its present popularity certainly has not resulted from any lack of sharp and sustained controversy. While the literature commending its utility in a wide variety of disorders is very copious, there has likewise been an abundance of articles, papers and discussions, which contended that cod-liver oil was merely a therapeutic fetic; that it possessed no virtue that did not likewise reside in all forms of food fat; that it was no more readily assimilable than good butter; that, indeed, it was a positive bane to the patient in its loathsome taste, its disturbance of digestion, its provocation of biliousness, etc.

In my opinion these dissenting views constitute a most erroneous and deplorable heresy. Quite apart from the colossal volume of clinical testimony which bears witness to the real, genuine and positive utility of cod-liver oil in all wasting diseases, my own expe-

rience in practice sustains the view that cod-liver oil is an agent of incontestable value when intelligently, perseveringly administered. And yet such therapeutic heresies are far from being an unmixed evil. They stimulate thought. They arouse the physician out of any propensity toward routine-prescribing. Our most cherished convictions are all the better for an occasional assault, since we are thus led to examine our ground, weigh our evidence, review the basis of our belief, and place on a substantial foundation of reason and experience the views which we formerly accepted on tradition or authority.

Manifestly, the wide-spread employment of cod-liver oil has not been restricted by the assaults to which I have referred. Not alone in phthisis, but also in a wide category of other disorders, cod-liver oil continues to render substantial service, and beyond doubt it will continue to prove one of the most efficient remedies at the prescriber's command, despite any lack of unanimity on theoretical grounds.

It is commonly supposed that the general employment of cod-liver oil dates from the publication of Professor Bennett's great work in 1841. This is an error. Professor Bennett did, indeed, lend the weight of his authority to a *revival* of cod-liver oil, but it had been previously used in England in the treatment of phthisis; and long before it had been recommended for the treatment of scrofulous and rheumatic diseases. As early as 1771 Dr. Percival had introduced cod-liver oil as a remedy for chronic lithiasis, and it was employed for this purpose at the Manchester Infirmary during a number of years. The fishermen of Norway have from a remote period used it both externally and internally for rheumatic affections. Other investigators soon demonstrated that this remedy enriches the blood, multiplies the number of red corpuscles and produces an incredible increase in weight—an increase which is frequently out of all proportion to the small amount of oil ingested.

The value of cod-liver oil in phthisis pulmonalis is too old and widely known to need comment. Nelligan remarks in his work on *Materia Medica*, "I do not think I am asserting too much for it when I state that its use has to some extent removed tubercular consumption from the list of incurable diseases." Thousands of practitioners will bear out this remark, and a lesser number will join with this author in the regret that the conspicuous success of cod-liver oil in phthisis has caused the profession to lose sight of its utility in chronic rheumatism.

Desiring not to dwell unduly on the diverse applications of this familiar remedy, I content myself with the statement that cod-liver oil is productive of very great service in the treatment of many forms of neuralgia, tuberculous abscesses and chronic arthritis, rickets, strumous ophthalmia, obstinate cutaneous disorders, in chronic ozena, otorrhea and ophthalmia. Among other affections, I lay particular stress on anemia, from whatever cause, and on the obstinate constipation of infants. Brilliant results are occasionally obtained in the tubercular affections of children, especially in glandular enlargements.

For the surgeon cod-liver oil has its greatest value in tubercular affections in association with the indicated surgical treatment of the case. It is an agent which has a curative influence in tubercular disease. Not as a specific, but simply from its ability to increase the body fat, which as Butler says, is a normal and necessary constituent of the body. It is the fuel used