The War and Navy Departments are entitled to special mention in connection with the utilization of the moving picture. Orders are about to be placed for more than 100 projecting machines which will be installed in numerous forts, in the field and on several battleships. Soldiers and sailors are to enjoy the same films which to-day are viewed in every city and

town in the world, the service to be obtained through the regular exchanges. Films will be used also for educational purposes in connection with the training and fitting of the men for their various duties.

Excellent film was obtained last summer by several bureaus of the Department of Agriculture, by the Bureau of Mines, the Geological Survey and Life Saving Service.

The activities of the Government in Alaska are quite fully portrayed on several thousand feet of film.

The presentation of these films at the Panama-Pacific Exposition, and later, before popular audiences throughout the country is bound to make the general public more familiar with our Government and its many active functions.

The Therapeutic Uses of Preparations of the Ductless Glands—I*

Notes on Experimental Investigations of Undoubted Future Value

By Robert G. Torrey, M.D.

IN the recent work in the realm of physiology there are few efforts which stand out as possibly of striking importance. Some years ago the theory of anaphylaxis was advanced by Poirier and Richet, and their hypotheses have to a large extent been supported by subsequent investigation. The benefit already attained by the practical application of their theories is incalculable. More recently the work in the von Noorden clinic, particularly by Eppinger and Hess, holds a wealth of suggestion and has already borne fruit in the clinical field. Countless investigators are now working on the problems presented by the ductless glands—their interrelationship and the physiological effect of their activity in health and in states of disturbed function. The relationship of the ductless glands to the nervous tone is not as yet well understood. It seems definitely established that the pancreas produces an internal secretion which acts as a sympathetic depressant; that the chromaffine system as a whole acts as a sympathetic stimulant, or at least as an activator of certain portions of the system; and that the thyroid and hypophysis both in some way inhibit the activity of the pancreas in its nervous effect. This whole subject is so shrouded in doubt, however, that the theoretical side will not be considered here, this paper being limited to a discussion of the therapeutic experimentation which is being attempted with the ductless gland preparations.

Much of this work is pure speculation, much of it doubtless altogether useless, but time and experience will certainly extract some facts which are valuable and which can be shown to rest on a solid foundation. In attempting to put these theories to practical therapeutic use, the broadening of the field of endeavor depends on the practicing physicians. Those who are acquainted with these theories will be on the alert to recognize many interesting conditions which would otherwise escape observation.

THE ADRENAL GLAND.

The adrenal gland or suprarenal body is of all the glands the one about which the most accurate information has been acquired. The isolation of an active principle of a definite chemical nature has made possible experimental work which is more exact than is usual in dealing with animal substances.

The suprarenal body is composed of two portions, morphologically, chemically, and physiologically distinct. The medullary portion contains chromaffine cells related to the nervous system, while the cortex contains cells which stand in relation to certain cells of the sex glands. It is possible that in administering extracts or preparation of the suprarenal gland we have two distinct effects produced—one the result of a medullary substance which activates or stimulates the terminals of the sympathetic nerves. Most of the known action of the glandular extract can be attributed to this factor, including vasoconstriction, hyperglycemia or glycosuria (due to action on the sympathetics of the liver), pupillary reaction, and relaxation of the bronchi. Apart from this action, which may be directly chemical in nature, we have to consider the action of the cells of the cortex.

Animal experimentation is a rather uncertain index of the physiological effect of adrenalin on the human being, as the results of its administration vary a great deal in different species; also the effect is subject to wide variation, depending on many factors, such as nerve depression, as by drugs, muscular relaxation, etc. For instance, adrenalin will cause a marked contraction in a vessel which is relaxed or dilated, while if the vessel is already in a state of good tone there will be little or no effect shown. A small dose may produce a result entirely different from that produced by a larger dose.

As is well known, in the human body adrenalin administered intravenously causes a marked but transient rise in blood-pressure due to contraction of the peripheral arteries. It does not, however, constrict the coronary arteries, but probably dilates them. Its effect on the heart depends on the activity of the vagus, and this is an important factor in determining the extent

of the blood-pressure rise. The bronchi are markedly relaxed by its action, and peristalsis and digestive activity are decreased. The mobilization of sugar is increased with a resulting hyperglycemia or glycosuria. Cannon calls the service of the adrenal secretion to the organism an emergency function, increasing the efficiency of fatigued muscle and decreasing the clotting time of the blood. He also points out that strong emotional disturbances stimulate the discharge of epinephrin, continued worry leading to exhaustion and insufficiency of the gland.

In therapeutics its chief employment has been as a local vasoconstrictor, particularly in dealing with the membranes of the nose and throat. Injections of adrenalin have been found very useful in combating the vascular relaxation incident to shock, and while its action in this regard is very brief, it may prevent collapse in emergency. It is of value as a palliative measure in certain asthmatic affections, when an injection of from three to ten minims of the one-to-one-thousand solution either into a vein or deep in a muscle may terminate an attack almost immediately. While it gives prompt temporary relief in a number of these cases of bronchial asthma and of so-called cardiac asthma, it seems to have no permanent curative effect; but fortunately the susceptibility to the drug is not lost by repeated use, and increased dosage does not appear to be necessary. In antitoxin rashes, which are sometimes of serious moment, particularly if accompanied by edema of the glottis, it has been shown that an injection of adrenalin may altogether relieve the patient of symptoms within five or ten minutes. Here again the effect is not permanent and repeated doses may be necessary. I have seen acute circumscribed edema of the lip and of the tongue practically disappear within ten or fifteen minutes after the injection of ten minims of adrenalin solution into a vein on the back of the hand.

Adrenalin is recommended in the vomiting of pregnancy. Zuloaga has continued the administration of adrenalin in severe and otherwise uncontrollable vomiting from the second month of pregnancy to term, starting with ten drops every eight hours and later giving five drops every twelve hours, alternating with calcium. He is enthusiastic regarding this treatment.

Cavazzani has collected forty-seven cases in which a cure of osteomalacia is claimed to have been effected by systematic adrenalin treatment. He refers particularly to the assumption that deficient functioning of the adrenals interferes with normal skeletal growth, and discusses the question of etiology of rickets in this connection.

In the preparation termed adrenalin we have to deal with not only the chemical substance adrenalin or epinephrin, the product of the medullary cells, but also with an extract of the cortical cells, the nature and functions of which are totally distinct from those of the medullary portion of the gland. In some lower forms of life the so-called interrenal body, which corresponds to the cortex of the suprarenal gland in the higher animals, is indispensable to life, while the adrenal representing the medulla of the gland may be removed without fatal results. It is probable that in Addison's disease the destruction of the cortex is largely responsible for the condition, and also the cortex may be in question in osteomalacia and rickets. In the matter of influencing growth and development of the skeletal tissues and of the sex glands, the cortex is probably more important than the chromaffine cells of the medulla.

Many writers have considered the question of a general myasthenia, distinct from but frequently confused with neurasthenia, which is due to adrenal insufficiency and which yields to organotherapy (thyroid, pituitary, and adrenal being recommended).

I have noticed patients showing various grades of general myasthenia, low blood-pressure, poor skin circulation, and slight pains which seemed referred to the heart, who seemed benefited by the dried adrenal gland administered by mouth; also the pituitary gland has seemed of service; but thyroid must in these cases

be tried with great caution and carefully watched for bad effects.

In summarizing our present knowledge of the use of the adrenal gland as a therapeutic agent, it may be said that certain immediate and direct actions for which the medullary portion is responsible may be granted; on the other hand, there is probably an action due to cortical substances which has an effect on the nutrition of muscle and bone, and in certain diseases, as suggested, its effect may be sought by gland administration. In Addison's disease, where its use is theoretically indicated, the reports of success with adrenalin are not frequent or convincing.

Adrenalin is generally sold in one-to-one-thousand solution, which is reliable if fresh. It deteriorates rapidly, particularly if exposed to the light. The average dose is from five to ten minims of this solution injected well diluted into a vein or deeply into a muscle. The dried gland is also sold and seems to have a certain value when the cortical effect is desired.

The intravenous use of adrenalin is said to be contraindicated in organic heart lesions, nephritis, and arteriosclerosis. In animals it has been shown by Pearce that it is possible by large dosage to produce arterial degeneration, but its use in the ordinary dose subcutaneously has not to my knowledge been shown to be harmful, even when employed frequently and over long periods, as in cases of asthma.

THYROID.

Next to the adrenal, the thyroid is the gland of which we have the most knowledge chemically, though this knowledge is limited to very narrow boundaries. We know that iodine is a constituent of the gland and that in a measure its physiological activity corresponds to the amount of absorption of metabolized iodine. Iodine is held in combination with the colloid substance of the gland. Whether this combination forms a definite chemical substance is not established. Also the effect of this so-called iodothyronine in hyperthyroidism and Graves's disease is not thoroughly understood. Hyperplastic and hypertrophied glands contain as a rule less iodine than normal glands or colloid goitres. This does not mean, however, that less is present in the system, as the iodine content varies roughly with the amount of colloid substance, while the symptoms produced increase as the absorptive power due to the epithelial elements of the gland increases and with the power of taking up and metabolizing iodine, which seems greater as the epithelial cells are increased.

Different disorders due to variations in the gland are attributed to an excess or lack of combined iodine and the excess of uncombined iodine in the system. Thus iodine poisoning bears a certain resemblance to thyroid disease. Iodine which has been found to be beneficial in endemic goitres is distinctly injurious in acute goitres of the hypertrophic type, giving many of the symptoms of Graves's disease, including gastric and intestinal derangements, tremor, emaciation and muscular weakness. The administration of iodine subcutaneously or by absorption from the skin, will markedly raise the iodine content of the thyroid gland. Administered by mouth its effect seems to be less marked.

Histologically, the normal thyroid gland is composed of acini lined with a layer of epithelial cells. The acini are filled with a colloid substance. In a purely colloid goitre the acini are greatly enlarged, the cells flattened or atrophied, and the colloid greatly in excess.

In cases with a thyroid giving marked Graves's symptoms, we are apt to find a proliferation of the epithelial cells, and, instead of a single layer of lining cells, a thyroid adenoma with papillomatous outgrowths into the acini and proliferation of the lining layer. This overgrowth later tends toward atrophy. Thus in a patient with enlargement of the thyroid, even with exophthalmos and marked tremor, we may have to deal with a case of hypothyroidism, as truly as though we had a subject of myxedema or a cretin in question.

It is worthy of note that the hypertrophy of the gland may come on acutely and probably as a result of one

* *The Therapeutic Gazette.*

of several influences. Intestinal intoxications, acute infections, certain mineral poisons, also strong emotional strain, all have been shown to be causative factors.

Thyroid activity may be checked by rest (bodily activity greatly augmenting the effect of the secretion); by x-ray treatment, which causes a rapid epithelial degeneration and atrophy; and most markedly, of course, by operative removal of a part or the whole of the gland. It is not, however, with this phase of the subject that we have to deal.

The size of the gland is no index of its symptomatic activity. We must remember that an enlarged gland need not mean an overactive gland, and that a relatively small gland may induce marked symptoms. The tendency of all goitres is toward resolution. It may be stated that the tendency of Graves's disease is toward spontaneous cure if the storm of symptoms may be weathered, that normal thyroidism will be reached, but that unfortunately the individual may not without aid weather the storm of symptoms; and further, if the normal point is reached, the condition does not remain stationary at the point of normal secretion, but the patient passes to a condition of hypothyroidism. Were this condition simple and uncomplicated it could easily be identified by the physician, but the bodily structures have suffered during the storm and the circulatory apparatus and nervous and muscular systems all show serious damage, causing symptoms and signs which obscure the picture.

Exophthalmos does not altogether disappear after it is once established. Tachycardia may persist from muscular weakness of the heart, caused by damage to the heart muscle, but the tremor, while it may be noticed, will, however, usually depend on muscular weakness and will disappear under conditions of more or less complete rest.

In considering the milder grades of hypothyroidism we find that signs vary greatly in the adult and in the young, and that there is a difference in appearance depending on whether or not the patient has previously suffered from severe hyperthyroidism which has left permanent damage.

In general, thyroid deficiency must be considered in cases showing mental apathy and muscular weakness with fatigue on slight exertion, particularly if there is no loss of weight. A dry skin and pale appearance point further in this direction. In adults particularly, an enlargement of the thyroid gland which has existed for some time is suggestive. There is faulty metabolism and the carbohydrate tolerance is increased. Albuminuria is frequent. Obesity does not occur with any degree of constancy. Indeed, many extremely thin subjects will be noted, particularly when the hypothyroidism is the result of exhaustion of the gland by a chronic infection or intoxication.

There is reason to believe that in a hypothyroidism there is a deposit of a mucin-like substance, a product of tissue degeneration in all the structures of the body. These deposits of foreign material in the muscle fibres of the heart, in the kidneys and liver, and in the brain and nerves, give rise to a variety of symptoms which may be accounted for on purely mechanical grounds.

Skin affections are very common, as might be expected, the mucin deposits making the blood and lymph supply of the skin insufficient and preventing the action of the sebaceous follicles.

The heart's action may be seriously interfered with and the intestinal tract hampered in its action, producing the digestive symptoms which frequently form such a marked feature of this condition. Kidney disturbance has been accounted for by the same theory. Various neuralgic pains and so-called myositis, also migraine, are encountered in hypothyroid subjects, which yield promptly to thyroid therapy, and which seem explicable on these grounds. By direct observation of the bladder and ureters it has been shown that the administration of thyroid extract has a marked effect in combating congestion of the bladder wall and urethral orifices.

In the young we note occasionally extremely nervous subjects of faulty mental and physical development who are benefited wonderfully by thyroid administrations. Extreme diffidence or sulkiness may be the most marked feature of their condition, or an exaggerated nervousness and almost choreic appearance. Sexual development is delayed. It must be admitted that not all of these symptoms can be established as due primarily to thyroid deficiency, but deficiency in one gland influences other secretions and metabolic activities, and we are describing here a type of case which is favorably influenced by thyroid administration. The use of iodine in inorganic combination does not have a parallel effect, while thyroid medication may influence very strikingly the growth, muscular strength, development and mental capacity. Attention was called by Thompson to the good results following the treatment by thyroid gland in a series of cases of enuresis in children. Following this suggestion, I have noted not

only a clearing up of this disagreeable symptom but a remarkable improvement in the general physical and mental condition in several cases.

A case in point is that of a girl of seventeen, referred by a neurologist on account of constant and distressing headaches, general poor health, and menstrual difficulties. This girl was so nervous that it was difficult for her to talk to strangers without attacks of weeping. Menstruation was extremely irregular and accompanied by great mental depression. Enuresis had been frequent for years, and headaches of severe degree were almost a daily occurrence. The use of thyroid in this case was suggested only by the symptoms of enuresis. Not only was this symptom cleared up, but the headaches ceased, and she rapidly improved in her nervous and mental condition to such an extent that she was able to take a business position after completing her studies as a stenographer. I had her under observation for about three years, during all of which time she was more or less dependent on thyroid medication.

In summarizing the condition in which thyroid extract has been credited as an efficient therapeutic agent, we find an alarming long list of diseases and symptoms, but the following demand attention, either through the number of reports of success or by reason of the reputation of the clinician advocating the treatment:

Chronic skin diseases, particularly eczema, psoriasis, and alopecia.

Certain cases of chronic arthritis. Delayed union after fracture.

Anemia, particularly of the chlorotic type, in young women and particularly if associated with metrorrhagia. Albuminuria, especially of the orthostatic variety, and in the young.

Enuresis in children.

Menorrhagia. Habitual abortion.

Various mental and nervous conditions, particularly where apathy and depression are marked and where somnolence is a feature. Melancholia, migraine, various neuralgias.

The possibility of thyroid exhaustion and deficiency may be considered in cases showing a chronic enlargement of the gland, or presenting evidence of long-continued infection or intoxication. It must be looked for at some period in most cases of recovery from Graves's disease. The indiscriminate use of thyroid preparation as a treatment for obesity is certainly inadvisable, but the carefully observed administration in the obese subjects will frequently be found to be beneficial.

In thyroid therapy certain rules should be observed, the chief of which is to always start with small doses, and, save in very exceptional cases, to continue with small doses. One-quarter to one-half grain of the dried gland three times daily is a sufficient dose to begin with, and the latter amount may be too large. One effect of thyroid administration is to liberate rapidly from all the tissues the deposits of mucin-like material, and the toxic effect of this flood may be serious if not accomplished gradually. This effect is often mistaken for hyperthyroidism, resulting primarily from the gland administration. The central nervous system and the heart may be seriously affected by this toxic action and the kidneys placed under a severe and sudden strain. As Leonard Williams emphasizes, the greater the need of thyroid extract, the greater the danger in large dosage. Calcium is frequently indicated in connection with thyroid therapy. Children tolerate thyroid well.

The signs of overdosage are easily identified. Tachycardia, flushing, tremor, nervousness, insomnia, and diarrhea are the chief ones. It might be well to say that if after a brief trial of thyroid, carefully administered and closely observed, good results are not apparent, its use should be discontinued. As far as we know its bad results are readily noted, so that a careful and judicious trial of this treatment cannot be said to be contraindicated in any case in which it appears that it might be of value. Patients will be found in whom a hypothyroidism is temporary and in whom treatment may be discontinued. This is particularly so in the young, but in many cases, of course, occasional or continued medication may be required for years.

Thyroid therapy has, I think, been rather generally neglected. In certain suitable cases the favorable results obtained are so striking and so nearly impossible of attainment by other methods that a wider field of experimentation with these preparations should be covered by the practicing physician.

PARATHYROID.

The parathyroid glands are small epithelial structures lying in close proximity to the thyroid. They are usually four in number, but accessory glands may be present in different parts of the neck or embedded in the thyroid or thymus tissue.

Their removal results in a prompt onset of general tetany. Their partial destruction causes a condition of latent tetany, which may be chronic and partial as indicated by spastic tendency, or may not become frank

until some other condition, such as pregnancy or some physical disorder, supervenes.

The view was accepted for a time that the removal of the parathyroids increased the calcium output and thus decreased the calcium content of the blood and tissues, but this view is now denied by many.

That the calcium metabolism is disturbed in some way is likely, and it is well known that the administration of calcium to patients suffering from tetany will control the symptoms. Other mineral salts, particularly magnesium, are said to accomplish the same result.

The parathyroid is said to have an exciting or stimulating effect on the secretion of the pancreas, an action opposed to that of the thyroid, which depresses the pancreas.

Extracts and preparations of the parathyroid glands have for a number of years been used in tetany and also in paralysis agitans. It is doubtful whether any good results are obtained which could not be produced in a simpler manner by the use of calcium.

The removal or destruction of the parathyroid glands seems to result in an increased excitability of the muscular mechanism of the body. This condition may be controlled to a certain extent by the administration of the gland, or probably more satisfactorily by simple calcium therapy.

Satisfactory evidence is lacking regarding the influence of these glands on growth and development.

(To be concluded.)

Hospital Efficiency.

In May, 1914, the Philadelphia County Medical Society appointed a committee to consider "ways and means by which the efficiency of the hospitals in Philadelphia may be increased." This committee made an extensive study of the hospital situation in Philadelphia. The three reports of the committee embodying the results of this study, together with an introduction on "The Principles of Hospital Efficiency," by the secretary of the committee, are now issued in pamphlet form. One of the most important findings of the committee is that no standards as yet exist by which the efficiency of a hospital may be measured. The operating expense of one institution may be three dollars a day for each patient, and that of another, little over a dollar a day for each patient. Is the latter figure a credit or a disgrace? One dispensary physician may treat twice as many patients in an afternoon as his colleague working under the same conditions. Which one is accomplishing the most good? Standards of efficiency must be formulated and applied before such questions as these can be answered. Naturally, this lack of standards is reflected in chaotic conditions. For instance, the committee made a careful study of the record systems used in sixteen of the largest hospitals in Philadelphia. In eight of these, some systematic effort was being made to secure the completeness and accuracy of the records, the chief resident physician or the registrar finally checking the records. Four different systems of classification were being used in these eight hospitals. Only three of the sixteen hospitals were maintaining separate files for recording all operations performed in the hospital, grouping together all operations of like character, so that the number of all operations performed during a given period, with the results of each, could be quickly ascertained. The committee states that in 31 per cent of the hospitals visited the records were so kept as to be useless for scientific purposes. A number of recommendations are made for the improvement of record systems, the establishing of social service departments, the prevention of dispensary abuses, etc. In fact, *The Journal of the American Medical Association* is of the opinion that the reports contain many valuable suggestions for those who are interested in the improvement of hospitals, and deserves to be widely read.

Foreign Sources of Artificial Dyestuffs

If the general imports of coal-tar dyes into the United States are analyzed as to country of origin, the following is found to be the case for the imports of 1913: Of alizarin and derivatives, Germany supplies 99 per cent; of synthetic indigo, Germany supplies 96 per cent, and Switzerland 2.4 per cent; of other coal-tar dyes, Germany supplies 81 per cent, Switzerland 12 per cent, the United Kingdom 2.8 per cent, Belgium 2.5 per cent, and France 1.0 per cent.

The import from Belgium is supposed to be largely of German origin. The total value of the German import in 1913 was \$8,538,000. It constituted 86 per cent of the value of imported artificial dyestuffs.

The Swiss import reached \$918,232. It formed 9 per cent of the total value. It will be seen that, apart from the modest contribution of Switzerland, the United States depends almost entirely on Germany for its supply of imported artificial dyestuffs.—*Report of Bureau of Foreign and Domestic Commerce.*