willing to consider the value of subjects submitted by a candidate who wishes to specialise in psychological medicine.

While care has been taken to make this summary accurate, intending candidates should, of course, consult the official regulations.

(1) See *Lancet*, April 6th, 1912, p. 934; *ibid.*, June 21st, 1919, p. 1092; *ibid.*, August 2nd, 1919.—(2) *Journal of Mental Science*, vol. lxi, 1915, p. 1.—(3) *Ibid.*, vol. liv, 1908, p. 550.—(4) *Ibid.*, vol. liv, 1908, pp. 791-3.—(5) *Ibid.*, vol. lv, 1909, p. 757, and vol. lvi, 1910, p. 374.—(6) *Ibid.*, vol. lvi, 1910, p. 373.—(7) *Edinburgh Medical Journal*, October, 1918.—(8) See *Lancet*, April 27th, 1912, p. 1017; and December 20th, 1919, p. 1167.—(9) Quarterly Meeting of the Association, November 25th, 1919.

Some Mental Cases with Endocrine Considerations. By GUY P. U. PRIOR, M.R.C.S., L.R.C.P., Medical Superintendent, Mental Hospital, Rydalmere; with Reports on Microscopical Findings by S. EVAN JONES, M.B., Medical Officer, Mental Hospital, Callan Park, New South Wales.

IT is well known that with the grosser lesions of many of the ductless glands there are profound alterations in the subject's mental powers. There are doubtless many less pronounced mental alterations due to slighter lesions of these glands which are for the most part unrecognised—in fact difference in character and disposition in different individuals and in the same individual at different times may be due to the variation in the balance of the internal secretions.

Those alterations due to lessened action of a gland have been brought about experimentally by removing the gland in question, with constantly recurring results.

The mental changes due to over-secretion of a gland are not so well understood, and the effect produced by prenatal or congenital gland disease upon the cerebral development has hardly been studied. Congenital thyroid disease in the form of myxœdema and cretinism and the results of treatment with thyroid are known, but the effects of early or congenital failure of the other glands are not, and it is possible that the changes in the central nervous system caused by these may be as far-reaching as those in thyroid failure. It is likely that early changes in gland tissue may be a potent cause of imbecility. Many an imbecile bears unmistakable signs of glandular dystrophy. An Editorial article in *Endocrinology* refers to an unpublished paper, which states that of 1,000 defective children 17 *per cent.* were recognised as of endocrine origin (1). The same article also states that the Binet-Simon age of defective children has been advanced many years after a few months of treatment with thyroid or pituitary. It is possible that there is a large class of ill-defined cases of want of endocrine balance seriously affecting both physical and mental development, which, if

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capable of early diagnosis and treatment, might enable some imbeciles to attain a fair, if not average, degree of intelligence.

The cases 1, 2, 3, 4, 5, 8, 14, 15, 17, 18, 23, 26, 27, 28 and 29 of our series are congenital or of early development, and show evidence of glandular irregularity.

Their condition in the present state of knowledge cannot be diagnosed until there is structural deformity or want of mental development. Did it lend itself to an earlier diagnosis their future outlook might be very different.

The glandular influence on physical development and structural change is better understood than is its influence on the mental development. The large formation, with its increase in bone growth of acromegala and its opposite condition of dystrophia adiposa genitalis, is well known, as also is the difference in the conformation of a myxœdemic and a case of Graves's disease. The changes in an animal after castration, both in character and structure, and the eunuchoid condition due to lack of secretion of the interstitial testicular cells, and the changes in the secondary sex characters and the early sexual development due to lesions of the suprarenal or pineal, present no difficulty in recognition.

Feeding of Tadpoles and Guinea-pigs with Glandular Extracts.

The tadpoles were taken from the pond when about two weeks old, and, as near as possible, were selected of the same size. They were fed every morning with a tabloid of the respective glands. They had no other food except bread-crumbs and water-weed, but this was a mistake, as it would have been better to have given them some animal food, as the controls received none, while the others did in the gland. The fact that the controls did not develop detracts from the value of the observations, but the results obtained from the gland-fed tadpoles, compared with each other, may be of some interest. The tadpoles were taken on October 27th and put into separate bowls, and fed upon thyroid, parathyroid, thymus, didymin, suprarenal, anterior pituitary, and another lot received no gland.

Those fed upon thyroid were all dead by November 19th. They were extremely small, in fact no bigger than on October 27th; they had four legs, and their tails were nearly absorbed before dying. Some day or two before they died they would suffer from syncopal attacks, would swim very quickly round the bowl, suddenly turn on their backs, and drop to the bottom of the water, where they would lie as if dead for ten minutes or more, and then get up and repeat the performance.

Those fed on thymus were, on November 15th, four times as large as the controls; one had hind legs, another none; they were pale in colour and translucent. By December 12th three had died. One had changed into a frog and escaped. The others were large tadpoles, with small hind legs; their bodies were of more triangular shape than those fed with other glands, and they were more translucent. By January 12th three were still tadpoles with hind legs and no fore-legs. One had a hæmorrhage into his abdominal cavity, and was so transparent that his heart could be seen beating and his viscera could be distinguished. That thyroid feeding hastened metamorphosis and retarded growth of tadpoles, and that thymus has the reverse action, causing the tadpoles to become of abnormal size, was pointed out by Gudernatsch (2).

Of the others, those fed with parathyroid remained very small, and by January

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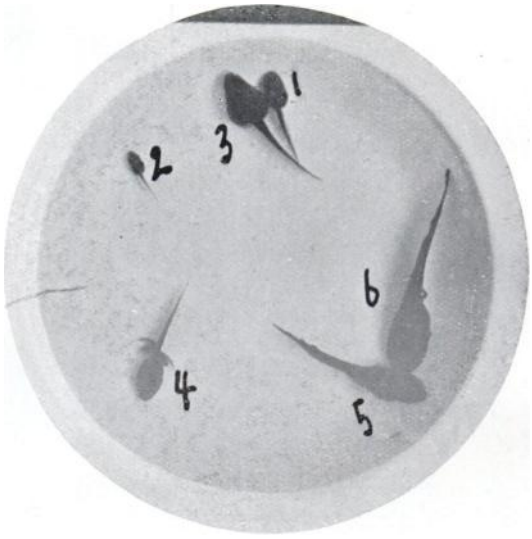


FIG. 1.



FIG. 2.

1. Control. 2. Parathyroid. 3. Thymus. 4. Didymin.
5. Suprarenal. 6. Anterior pituitary.

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12th there were still several tadpoles not much bigger than at the commencement. One had become a small frog by December 18th, and died two days after. By December 30th two more had become frogs, and were also very small, dying almost immediately.

Those receiving didymin were the most inconsistent. Some had become frogs by December 12th, and quickly escaped. By January 12th one was very large, pale and translucent, and of the shape of those that had received thymus, and others were darkly pigmented and with hind legs.

The suprarenal tadpoles were more forward with their legs than any of the others except the thyroid, and were also darker in colour. They were of more slender build and their limbs longer and finer than the anterior pituitary ones.

The anterior pituitary tadpoles showed the most definite changes, though these were not uniform. On November 19th it was noted that they were much larger than any of the others. On November 25th two were of extreme size, with very long, thick tails, no legs, and their companions had small, thick legs and abnormally large bodies. On December 18th five survived—three frogs and two tadpoles; these latter were the largest and heaviest of the collection. The frogs were also larger than the others, the legs being shorter and thicker and the skin markings more distinct.

By the end of the time of our observations none of the controls had changed into frogs, though some had hind legs. They were smaller and more backward than any except the parathyroid, of which they were about three times the size. The lack of animal food in their case may have kept them back. On December 18th the largest tadpole in each bowl was weighed, with the following results: Control, 1,220 mg.; thymus, 3,330 mg.; parathyroid, 900 mg.; didymin, 2,320 mg.; suprarenal, 4,106 mg.; anterior pituitary, 5,520 mg. Fig. 1, taken in January, shows the relative size of the tadpoles at this time. Fig. 2, taken at the same time, shows the most advancedly developed. It will be seen how much larger the anterior pituitary tadpoles are than the others and the undeveloped condition of those being fed with parathyroid. It is, of course, impossible to draw any definite conclusions from these observations, but they bear out the observations already made upon thyroid and thymus feeding. It also seems that parathyroid delays both metamorphosis and growth and that suprarenal stimulates both, but without the far departure from normal caused by anterior pituitary, which stimulates growth and causes bone changes.

In reference to a paper by McCord and Allen on feeding tadpoles with pineal gland they found a marked reaction of the pigment-cells, so that in thirty minutes those of the pineal-fed tadpoles were much larger than the controls. (3)

We have also made feeding observations upon guinea-pigs. The does were fed with the gland the day their young were born, the mothers being removed a week later and the young continued to be fed with the gland for from five to six months, their weight being taken weekly and the time of reproduction noted. Where several guinea-pigs in the same pen have grown at about the same rate only one is recorded; where there has been much difference two are shown on the chart. The controls steadily increased throughout. Those fed on thyroid lost weight towards the end and never grew to the same degree as the controls, and were all the time of thin, sickly appearance. One, when a month old, fractured a leg from unknown cause, but disturbance of his calcium metabolism may have had something to do with this. The parathyroids, for a time, remained stationary and at one time lost weight, but at the finish were as heavy as the controls. Those fed on thymus, whole pituitary, anterior pituitary and suprarenal developed about normally except that the last two did not reach to within two or three ounces of the controls. The pigs taking didymin were much inhibited and those taking varium were inhibited to a lesser degree. In these two pens no buck was born; the effect of the feeding applies only to does. A buck was put in with them when they were a few weeks old, but as they were not fed from the first with the gland a record of them was not kept. The pineal pigs grew very slowly for the first five weeks, but by the twenty-second week were well up to the normal.

At the end of our observations the young guinea-pigs varied in age from 22 weeks to 28 weeks. They normally reproduce at from five to six months. (4) Our control was 23 weeks old and was in young. The parathyroid had one young when 22 weeks old, the whole pituitary one at 24 weeks, and the anterior

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pituitary one when 20 weeks old. The pineal doe at 25 weeks was heavy in young. The pineal pigs had long, straight and silky hair such as we do not remember seeing before in a guinea-pig, but we cannot say that this was the result of feeding and not of breeding. In the thyroid at 22 weeks, thymus at 25 weeks, suprarenal at 23 weeks, didymin at 25 weeks and varium at 27 weeks there was no pregnancy. It is stated that animals fed upon extracts of the glands strike a fresh balance of glandular activity after a time and no great change is brought about by such feeding. The results are also said to differ with the age at which the animal is commenced to be fed.

The thyroid is the gland about which most is known as to its relationship to the mind. A myxœdemic patient is depressed, dull, slow in thought and action, with diminished reflexes, often with hallucinations of hearing due to the swelling of the aural mucosa or of central origin, and not rarely finds her way into a mental hospital, where she is generally found to be a melancholic and irritable patient, indifferent to her surroundings, idle and without interests, with a more or less marked degree of dementia. Case 16, referred to in detail later, was such a one.

In cases of hyperthyroidism there is the reverse mental picture. She is often of cantankerous disposition and ever ready to take offence, but she thinks and talks quickly, her movements are rapid, and her energy abundant. Should she become insane, she generally suffers from acute or subacute mania unless the condition passes from hyper- to hypothyroidism, when the condition becomes one of melancholia.

Of the congenital mental conditions accompanying diseased states of the thyroid we have cretinism—sporadic and endemic—Mongolism and infantile myxœdema. With these there may be all degrees of weak-mindedness—from the most extreme idiocy to a high-grade imbecile. Mongolism is probably not entirely an athyroid condition and does not improve to any extent with thyroid treatment, though Case 17 livened up after receiving thyroid in small doses for some months, while her hair-growth also improved somewhat.

Cretins and infantile myxœdemics make great improvement with thyroid therapy. McCarrison records the case of a cretin, æt. 9, who could neither walk nor talk, but who, after treatment with thyroid, was able to walk, and learned to say a few words. (5) As a rule the earlier the treatment is begun the better the result.

The mental symptoms of an adult myxœdemic are greatly improved, if not cured, by taking thyroid. Hertoghe says that nerve-cells are not destroyed in myxœdematous infiltration, but become infiltrated and depressed, and that transmission of impulses, though delayed, is not abolished. (6)

The thymus gland has some influence upon mentality. Sajous states, " Removal of the thymus in dogs is followed by clear evidences

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of idiocy (Morel). The thymus was present in all of 61 autopsies performed by Katy on mentally normal children. In 28 mentally weak children examined by Bourneville it was absent. In another series of 408 autopsies on non-myxœdematous children of from one to five years of age the thymus was present in only 104 cases." Sajous attributes this to the presence of thymus being necessary for the proper carrying out of the phosphorus metabolism, which is important for the development and maintenance in health of nerve-tissue. (7)

In our series of 46 *post-mortem* examinations from which the glands had been taken for examination, 25 cases had a definite thymus gland. Twenty-three of these were confirmed by microscopic examination, and 6 were not sectioned. Among these 46 cases were 32 epileptics, 22 of these latter having the thymus present, of which 18 were sectioned and examined with the microscope. The largest glands were found among the epileptics. Eight epileptics were cases of sudden death, 7 being under our care, while 1 of great interest was from a neighbouring hospital, and at whose autopsy we were allowed to be present. All these cases had enlarged thymuses. Two may be described as being as large as the palm of the hand; of the others, one weighed $3\frac{1}{2}$ oz., another 2 oz., and a third $1\frac{1}{2}$ oz. The youngest of these 8 patients was 20 years and the oldest 53 years. Two of them were found dead at night, having been seen previously to within half-an-hour, and both having been in their usual health the day before. One was Case 5, to be described later under the apituitary cases, where a description of his glands will be found. Case 31, the other patient who was found dead, was of eunuchoid type, an imbecile and a sexual pervert, whose epilepsy had commenced at 15 years of age, and who was 22 years at the time of his death. He had a very large thymus, reported to be a persistent infantile one. The suprarenal, both cortex and medulla, showed degenerative changes.

Case 32 was æt. 46. His epilepsy had commenced ten years previously. He died immediately after taking a fit—the third within eight hours. An attendant was standing beside him at the time. A *post-mortem* examination was made, and the heart, lungs and kidneys were found normal. There was a considerable amount of thymus tissue, reported to be very vascular and of a regenerative type. The suprarenals showed degenerative changes, both of cortex and medulla. The thyroid showed vesicles small and irregular, the lining epithelium cubical and actively proliferating. The intermedial tissue was increased and the blood-vessels congested. The pituitary was in a condition of over-activity. There was a small and normal parathyroid.

Case 33 was a girl, æt. 25, an epileptic of ten years' duration. She did not have an epileptic attack on the day of her death, but after going to bed became very restless, wandering about the dormitory. On

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being put back to bed by the nurse, for the third time, without any resistance or struggling, she collapsed and died. An autopsy was made nineteen hours after death. There was slight active tuberculosis of both lungs. The heart was soft and flabby; the aorta was small, admitting only one finger. There was thymus tissue present: it was reported to be a retrogressive infantile one, and to contain numerous Hassall's corpuscles and also particles of lime. The ovaries were fibrotic, and the vessels in process of obliteration. The spleen contained numerous small hæmorrhages. The pancreatic cells were shrunken and very few islets were to be seen. The suprarenals were reported to be normal.

Cases 34, 35 and 36 all died shortly after taking a fit, and were under different observations at the time of their death. Case 34 was a man, æt. 20; was heard at night by an attendant to be in a fit, and was in the convulsion when the attendant went to him, but died immediately the convulsion had ceased. A *post-mortem* was made six hours after death and there was venous engorgement of all organs. The thymus was much enlarged. In this case also the aorta would only admit one finger, otherwise the heart was normal. The report on his glands stated that the thymus was of persistent infantile type, that the testes showed interstitial fibrosis and diminished activity, that the thyroid was quiescent, there was advanced vacuolation of the suprarenals, and that the section of the pituitary showed an effusion of serum into the pars intermedia.

Fig. 3 shows a thymus of infantile type. Note the dilated capillaries and large Hassall's corpuscles.

Fig. 4 shows a thymus of a regenerative type showing small masses of fine thymic tissue containing Hassall's corpuscles scattered through the fatty areolar tissue.

Case 35 was æt. 31 and had suffered from epilepsy since he was twelve years of age. He had had five fits the night previous to his death, and three on the afternoon on which he died, dying immediately after the last. Before this he was conscious and fairly well. An autopsy was held eighteen hours after he died. The heart was dilated, the muscle being flabby; the aorta would admit two fingers through the orifice from above. The thymus weighed $3\frac{1}{4}$ oz., the thyroid 1 oz. and the spleen 6 oz. From the microscopical examination of the glands it was stated that the thymus was a persistent infantile one, that the testicles were normal, also the pituitary and spleen. The thyroid was of increased, and the pancreas of diminished, activity. Of the suprarenals, it was stated that the cortex showed advanced degeneration and that the medulla stained normally, but was intensely congested.

Case 36 was a male patient, æt. 53 years, 6 ft. $3\frac{1}{2}$ in. in height, and deficient in secondary sex characters. He had suffered from epilepsy

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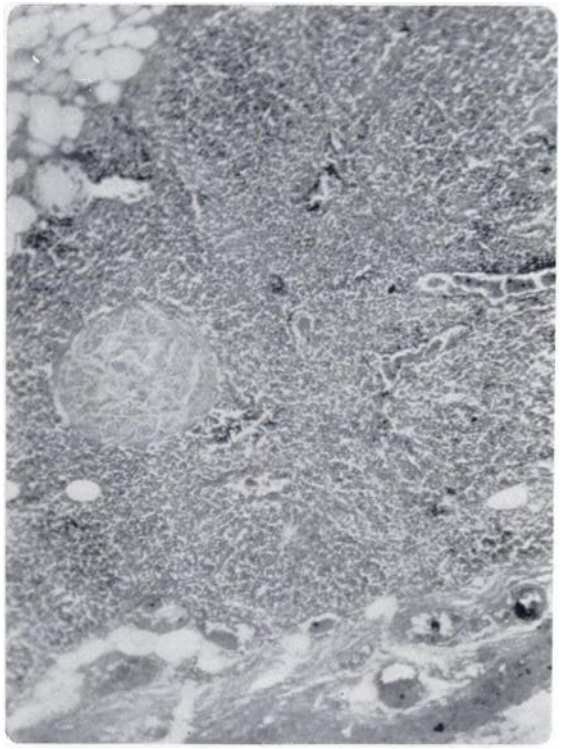


FIG. 3.—Thymus. × 80. Infantile type.

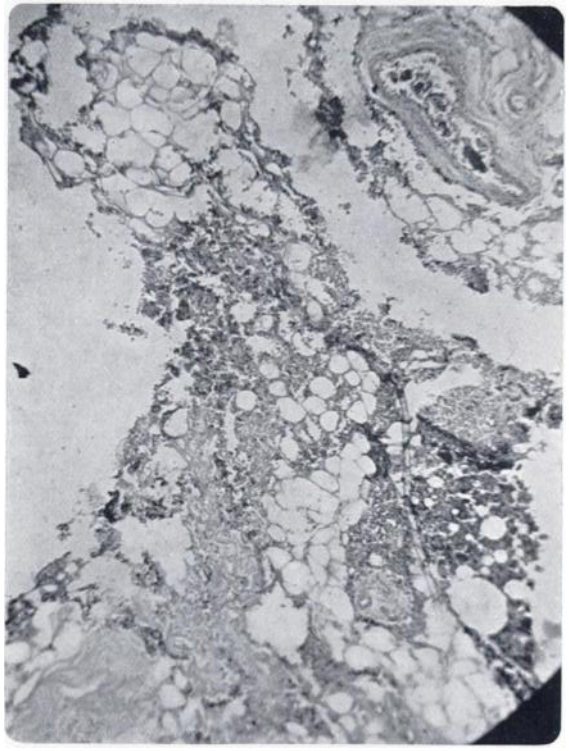


FIG. 4.—Thymus. × 80. Regenerative type (epilepsy).

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for many years. He had eight fits within half-an-hour, and did not recover consciousness between them. He was being given a soap-and-water enema when he collapsed and died, before the enema had acted. A *post-mortem* examination was made twenty hours after death. The body was very fat and the skull very thin. The brain weighed 48 oz., and the ventricles were moderately dilated. The heart weighed 14½ oz. the aorta being normal. The spleen weighed 6½ oz., the thyroid 2 oz., and the thymus 2 oz. The two suprarenals together weighed 1½ oz. The pituitary was large, the sella turcica being broad and deep. The pineal gland was noted as being large. This is one of the cases in which the thymus was not sectioned. The thyroid was over-active, the pituitary and testicles normal, and there was fatty infiltration of the liver.

Case 37 died four hours after being given an injection of typhoid vaccine. He was æt. 30 and an epileptic since early childhood. A few minutes after receiving the vaccine he had a rigor and a little later his temperature rose to 105° F., and he died within four hours with signs of acute pulmonary congestion. He had not at this time had any fit. The *post-mortem* examination was made twenty-three hours after death. The brain was found slightly congested, the sella turcica was small and shallow, the posterior processes were bent forward, and the pituitary was smaller than normal. The heart was dilated, the muscle flabby, the aorta small, admitting two fingers. The lungs were acutely congested. The thyroid was large, the thymus weighed 1½ oz., the pancreas was acutely congested, and the liver and spleen were also congested. The following is the report of the microscopical examination of his glands: The thymus of persistent infantile type. The suprarenals—the cortex exhibits well-marked vacuolation. The testes normal. The pancreas showed extremely acute congestion—the alveoli and islets were disorganised. The brain showed nothing abnormal except extravasation of blood-cells from small capillaries. The heart-muscle appeared normal and the kidneys intensely congested. This man had received typhoid vaccine twice previously, at two-yearly intervals. He had been trephined, operated upon for appendicitis, also received "606" intravenously three times.

Taguichi records the case of a healthy man, æt. 57, who died within an hour of receiving 1 c.c. of typhoid vaccine. On *post-mortem* examination evidence of *thymus lymphaticus* was found (8). All our 7 patients above described, together with others who have evidence of enlargement of the thymus, have been given typhoid vaccine without ill-effects. Case 36 had many opportunities of dying suddenly, in ways common in *status lymphaticus*, and why these causes should act at one time and not another, it is not possible to say.

The ductless glands in epileptics show a far departure from the

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normal. Including the 8 cases of sudden death, we have made *post-mortem* examinations and sections of some or all of the glands upon 32 epileptics, of which 20 were male patients and 12 female.

Of the male patients, 15 had enlarged thymuses, and in 5 the gland was not present.

The suprarenals showed degenerative changes in 15 cases, were found to be normal in 3, and in 2 they were not examined. The changes in the suprarenals were mostly found and more marked in the cortex. The cells of the cortex failed to stain, the nuclei stood out well, but the cytoplasm was coarsely granular or represented by a fine network enclosing clear spaces. In 4 cases the degenerative changes were well marked in the medulla as well as in the cortex.

The testes from 4 patients were not examined; from 12 they were found to be normal, and from 4 there was a deficiency in the interstitial cells, one of these being Case 5—an apituitary one.

The pituitary showed no constant change in 11 cases; it was either normal or of slightly increased activity. In 5 cases it was not examined, in 3 it was stated to be of diminished activity, and in 1 case, dying suddenly, there was a serous effusion into the pars intermedia.

The thyroids were mostly of the two types, 6 being taken as being quiescent and 7 as of over-activity. These we equally divided, there being 7 of each in our series; in 4 cases the thyroid was normal, and twice it was not examined.

The pineal was only examined twice. In one case it showed degenerative changes and in the other it was normal.

The liver was examined from 10 patients. Once it was found normal; all the others showed signs of fatty degeneration or fatty infiltration.

The pancreas was reported upon from 8 patients. In 3 it was normal; in the other 5 the islets of Langerhans were few in number and showed degenerative changes.

The spleen was examined from 7 patients. From 1 case it was reported normal, in 1 there were small hæmorrhages, in 1 waxy degeneration; the rest showed fibrotic changes.

In the 12 female cases an enlarged thymus was found in 7 cases, the condition being confirmed by the microscope in 6, in 1 case not being sectioned. The gland was absent in 5 cases.

Of the ovaries, in 1 case these glands could not be found at the *post-mortem* and were presumedly congenitally absent, in 3 cases they were not examined, and in 8 cases the fibrous tissue was much increased and the organs were shrunken and atrophic. In 3 instances small Graafian follicles were seen.

The thyroid in 4 of the 12 cases was not sectioned; in 2 it was stated to be normal, in 5 showing signs of over-activity, and in 1 case of under-activity.

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The pituitary was normal in 9 of the series, said to be of minus activity in 1 case, and was not examined in two.

The suprarenals were normal in 5 cases, showed degenerative changes in 6, and were not examined in one case.

The pancreas from 6 cases was examined. In 2 it was normal, and in 4 the same degenerative changes were found as described in the male cases.

The spleen from 4 patients was examined, 1 being normal; 2 showed fibrotic changes and 1 was the subject of waxy degeneration.

The liver was examined from 9 patients. Once it was found normal; the other 8 had fatty degeneration.

What strikes one as most worthy of note in these results is the large percentage of cases in which the thymus is found to persist, and the great number of times in which there is found degenerative changes in the suprarenal cortex. That the liver, spleen and pancreas are seldom reported to be normal is suggestive, but the number of times these organs have been examined is not sufficient to say that changes are constant. The fibrotic and atrophied ovary appear to be almost invariably present, and the fact, as we have shown, that the menstrual function is most irregular in epileptics (9) may depend upon this. A corresponding change is not found to the same persistency in the male sex gland.

Kajima describes similar ovarian changes as we have found in epileptics in two cases of dementia præcox, but he found no testicular changes.(10) Writing on the Abderhalden reaction, Orton says that the majority of dementia præcox cases react against brain or sex-gland, or the two combined, showing a dysfunction of this gland.(11) Dr. Kate Hogg, in an unpublished paper written ten or twelve years ago, claims to have found changes in the uterus or ovaries in 21 out of 30 cases of dementia præcox examined. She came to this conclusion from pelvic examinations made under an anæsthetic. She describes the ovaries as being sometimes atrophic, sometimes subject to fibroid degeneration, and sometimes as hypertrophied with loss of function. She concludes the paper by saying, "A condition exists which indicates the unfitness of the organism to reproduce its like, which is the final phase of degeneration." It would appear from the condition of the epileptics' ovaries that also in them Nature is endeavouring to eliminate the unfit.

Over-activity of the thymus has been described as causing eunuchoid-like growth, *i.e.*, tall individuals with long bodies and long limbs, and deficient in secondary sex characters. Bandlier (12) and Sajous (7) both speak of an infantilism as being due, among other causes, to a persistent thymus. Among our *post-mortem* cases, in which we have found a large and active thymus, have been men of 6 ft. or over as Cases

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31, 36 and 38, the first 2 being of eunuchoid appearance, others being of all degrees of size and weight, including two dwarfs as cases 5 and 18.

There are, in the series, three other cases not epileptics in whom an enlarged thymus was found. Unfortunately only one of the three glands was sectioned, this being from Case 18, which is described under the cases; her thymus was a persistent infantile one. Of the remaining two, one was from an imbecile lad of 18 years, who died from pulmonary tuberculosis. His thymus weighed 2 drachms, thyroid 6 drachms, spleen 6 ozs., heart 8 oz., with an aorta that would only admit one finger. The other was from an old lady æt. 73, who died from intestinal obstruction. Her adiposity was rather in excess, and the hair on head and pubes very scanty. At the *post-mortem* a cyst of the pituitary was found, the pineal and thyroid were small and some thymus tissue was present.

Diminished suprarenal activity may be accompanied by mental symptoms. Acephalic monsters are said to have no suprarenals. It is stated in Osler and Macrae that "hypoplasia of the suprarenals" has been noted in the hemicephaly and other failures of brain development. Czery reports absence of medulla in 5 cases of hydrocephalus, and Hanseman 8 cases of anencephaly with atrophy. They described the mental symptoms in Addison's disease "as a tendency to fatigue from mental or physical exertion. Constant apathy associated with depression, insomnia or an increased tendency to sleep. Yawning, loss of memory, delirium, dizziness, tinnitus and headache."(13) Falta says that in the later stages there may be delirium, convulsions and coma.(14) An over-action of the suprarenals in either sex is manifest, by an increase in male sex characteristics and in the female with amenorrhœa in addition.

"Wiesel believes that the *status thymico-lymphaticus* is equal, or almost equal, to the chromaffin tissue in the pathogenesis of Addison's disease. He suggests that adrenal inadequacy prevents the involution of the thymus, the lymphatic glands undergo hyperplasia, the vascular and genital systems hypoplasia."(15) If this is so it explains the common association in epileptics of over-active thymus glands and under-active ovaries and degenerative suprarenals.

Extracts of ductless glands of late have been found of service in a wide variety of diseases and disorders. It is an extremely old method of treatment. Harrower mentions Egyptian writings of about 500 B.C. in which orchitic substance is advocated for the treatment of impotence.(16) Probably the first reference to organotherapy is in the *Apocrypha*, where Tobias is commanded by an angel to take the heart, liver and gall from a fish. The heart and liver were to be changed into smoke and used as an inhalation for the purpose of driving away evil spirits.

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The gall was useful to anoint one who suffered from "whiteness of the eyes."(17) This was written between 625 and 700 B.C., but it is our purpose to limit our remarks upon the use of these glands to our own experience, which has been mainly with epileptics and primary dements. The glandular treatment of mental cases has its definite uses without doubt, and it is certain that the scope of this usefulness will be greatly extended with larger experience of their use. A patient may be not far removed from idiocy, or apparently advanced in dementia, and may, by appropriate administration of gland extracts, be rendered quite unrecognisable from what he was, and who can say but that if treatment could be undertaken much earlier, some congenital deficients might be saved from being classed as such?

We have found thymus useful in epilepsy in some cases, but, as in all things in epilepsy, it appears harmful in others. One case, which has been taking thymus for some years, averages many more fits if this is suspended for a time, and takes some months to fully recover the ground lost when the gland is resumed. Thymus causes a retention of calcium, has some control over the formation of acids, and is largely concerned with the phosphorus metabolism, by any of which means it may influence epilepsy. We have also found thymus useful, as regards both sexes, in cases of increased sexual irritability; here it probably acts by diminishing ovarian, thyroid, or pituitary secretion; an over-action of any or all of these will excite the sexual organs.

Thyroid, in addition to its well-known action in cases of athyroidism, has been proved of extreme benefit in cases of primary dementia, chiefly those of hebephrenic type. When given as advised by Drs. Davidson and Johnson (18)—*i.e.*, in rapidly increasing doses up to 80 gr. *per diem*—remarkable results have been obtained. The authors do not say how the changes come about and many of the cases cured are certainly not of the athyroid type, and it is probably not the thyroid *per se* that does the good. Thyroid is a stimulant to most of the other glands, especially of the sex-gland, which has been shown to be often of diminished activity in primary dementia; it also stimulates the suprarenals and pituitary, and it is likely that in this way the beneficial results are brought about. This mode of treatment is not altogether safe, as it may light into activity an undetected and unsuspected tubercular lesion. Smaller doses of thyroid combined with suprarenal and perhaps sex-gland may in some cases bring about the same result, as is instanced in Cases 14 and 21.

Suprarenal combined with thyroid has been of great use in the cases just mentioned. We think the partial disappearance of the œdema in Case 30 must be attributed to adrenalin; the doses given were large and long-continued and there were no persisting toxic symptoms. It has been of value in some cases of epilepsy of asthenic type and in

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some old cases of alcoholic origin. It appeared to be of special value in Case 61, who was a lad, æt. 9. Six years previously he had been given a dose of diphtheria antitoxin because there was diphtheria in the family. Two months later epileptic fits commenced; the attacks for the first four or five years averaged from five to seven a week. For eight months before admission he had from fifteen to forty attacks daily—mostly minor ones—but had an occasional major attack. On admission he was mentally fairly bright and he had several scars on the back of his head from falls. He had a well-marked white dermographic reflex; the hands and feet were bluish and cold, otherwise the physical signs were normal. In the first month after admission he had 562 fits, would lose consciousness and fall if not supported, but did not often convulse. He was given suprarenal gr. v daily and bromide and calcium. He had 303 attacks during the first month of treatment and eleven during the second month and has had none since, now twelve months. During the first three months he gained 14 lb. in weight.

We have found parathyroid very useful in some epileptics and in some its continued use seems necessary for their well-being. One of our cases, while taking this together with bromide, had but one fit a month, and without the parathyroid the number of fits rose to seven or eight a month. This gland has proved useful in all cases of myoclonic epilepsy in which we have used it.

We have entered into the uses of pituitary when describing apituitary epileptics, but we have not given it an extended use in other mental cases. We gave it with calcium to two primary dements with prolonged periods of amenorrhœa with the idea of stimulating the ovarian function. One of these girls menstruated after a month's treatment, the other after several months. Both made considerable physical improvement, but neither improved mentally.

We have had some cases of temporary—but no lasting—benefit from varium and didymin.

Cases 1, 2, 3 and 4 are all epileptic patients of apituitary type. Cases 1, 2, and 4 are about 5 ft. 2 in. in height and weigh from 13 st. 11 lb. to 13 st. 8 lb.; Case 3 is 5 ft. 5 in. in height and weighs 12 st. 9 lb. Cases 1, 2 and 3 show deficient growth of body and face hair, their maxillary hair is absent or extremely scanty, the hair about pubes is of effeminate formation and there is no hair growth otherwise upon the body or limbs. In Case 4 there is a more abundant hair growth both on face and body. In all four the mammary glands are large and pendulous, the hands and feet are rather small and clubbed, the genital organs are undeveloped, the supra- and infraclavicular spaces are obliterated and the fat distribution generally is as in the female. Their blood-pressure is rather low, the highest in the standing position being 115 mm. Hg. in Case 1 and the lowest was 95 mm. Hg. in Case 2. In their dermographic reaction Case 1 gives no reaction; 2 and 4 show a distinct white reflex, continuing for seven minutes in Case 2 and for three and a-half minutes in Case 4.

Of their blood examinations Case 1 gives an average of 7,800 leucocytes per c.mm., with a differential count of polynuclear leucocytes 71 *per cent.*, large mononuclear

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cells 5 *per cent.*, small mononuclears 24 *per cent.*, hæmoglobin 90 *per cent.* Case 2 gave an average leucocyte count of 12,000, of which the polynuclear leucocytes were 64 *per cent.*, large mononuclears 5 *per cent.*, and small mononuclears 31 *per cent.*, a hæmoglobin content of 80 *per cent.* Case 3, leucocytes averaged 11,300 per c.mm.; the polynuclear leucocytes were 74 *per cent.*, large mononuclears 4 *per cent.*, small mononuclears 22 *per cent.*, hæmoglobin content 80 *per cent.* Case 4, leucocytes averaged 10,500 per c.mm., with polynuclears 76 *per cent.*, large mononuclears 8 *per cent.*, and small mononuclears 16 *per cent.*

Falta, in describing the blood condition found in apituitarism, says the red-cell count is slightly reduced and hæmoglobin about normal. Leucocyte count often reduced, sometimes increased. Of the differential count he says that the neutrophilic cells are reduced and the mononuclears, especially the small, are increased (19).

Cushing states that there is in these cases a low temperature, which can be raised by an injection of pituitary extract (20).

In Cases 1 and 2 the temperature was taken twice daily for four days. In Case 1 it varied between 97·4° and 98·2° F. On the fifth day they both had an injection of pituitrin. Four hours after the temperature in Case 1 registered 98·6° F. The temperature of Case 2 varied between 97·4° and 98° F., the latter being recorded only once. He rose to 98·2° F. four hours after the injection.

Although these four patients are by their general make-up and contour typical of apituitarism, and the fact that they are epileptics rather bears out the diagnosis, for this disease is often accompanied by epilepsy, the results of examinations of their metabolic processes is not altogether consistent with this.

Falta says that in hypophysial dystrophy the carbohydrate assimilation limits are raised and that there is no inclination to glycosuria, but, on the contrary, an abnormally high tolerance to carbohydrates; he states that Cushing found an abnormally low amount of blood-sugar. In two cases mentioned by Falta the amount of blood-sugar was normal. He obtained no sugar urinary reaction after injections of adrenalin (21).

Our four cases gave a glycosuric reaction in their urine after an injection of ♏ x of adrenalin. On a second occasion Cases 1 and 3 were given an injection of ♏ v of adrenalin and their blood-sugar examined before and two and a-half hours after the injection. Case 3 showed a trace of sugar in his urine before the injection and a large amount after. His blood-sugar was ·11 *per cent.* previous to the injection and ·14 *per cent.* two and a-half hours after, both being greater than would be expected in a case of this type. Case 1 gave no urinary reaction to this lesser dose of adrenalin, but his blood-sugar rose from ·1 to ·12 *per cent.*

Case 3 was found to have a persistent glycosuria, which varies from a slight trace to ·37 *per cent.* His blood-sugar in ten estimations varied between ·13 and ·21 *per cent.* His glycosuria rose after a fit in all times observed but one. On five examinations his urine was found to be free from sugar; on four occasions this immediately preceded a fit, and the fifth time was after a fit. The changes in his blood-sugar apparently bore no relationship to the epileptic attacks. His general condition is good; he has no polyuria. Twenty-four-hour specimens having been collected for fifty days, during which time the largest amount passed being 1,278 c.c., there generally being in the twenty-four hours between 500 and 800 c.c., with a specific gravity in the neighbourhood of 1,020. No glandular treatment influenced the daily quantity of sugar. He was given pancreatin under the idea that the pancreatic secretion might be deficient; he also received pituitary and thyroid without benefit to the glycosuria or epilepsy. The glycosuria is easily controlled by diet.

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Case 5 was a case of similar kind except that he was more dwarfed and fatter, showing the same physical conformation and very undeveloped genital organs. He was æt. 28, and died suddenly shortly after taking a fit and without any apparent cause that could have been thought sufficient to cause death. A *post-mortem* examination was made about twelve hours after death. The brain showed nothing appreciably abnormal, the sella turcica was ill-defined and shallow, the pituitary body was very small, and the pineal gland was described as being small. The heart was small and fatty, but showed no fatty infiltration. The abdomen, inside and out, was very fat. The spleen, liver and pancreas appeared normal; both kidneys were small and lobulated like that of a horse. A persistent thymus gland was found in the midst of fatty tissue. Some of these glands were examined microscopically, but unfortunately the pituitary was lost. The testicular interstitial cells were reported deficient, the thymus to be acutely congested and the suprarenal to show signs of under-activity. The thyroid was normal.

Case 6 is one of interest on account of her history. She is a female patient, æt. 18, is well nourished, with small hands and feet, smooth skin, hair smooth but has been falling out for the last twelve months, pulse 80 per minute, blood-pressure 115 mm. Hg. There is a tendency to hairiness on the lower limbs, and on the abdomen there is a dark line from the umbilicus to pubis. The thyroid gland is distinctly enlarged. She had convulsions in infancy; suffered from minor epilepsy from five to fourteen years of age; at sixteen, at the time the menses should have occurred, she had a major epileptic attack, and has suffered from these at increasingly shorter intervals since. Menses appeared at twelve years of age, was always irregular, but since the recurrence of the epilepsy the periods of amenorrhœa have been longer, and sometimes persist for four months. If the period does not occur somewhere about the proper time she has epileptic attacks, which are preceded for about two days by a feeling of "illness and heaviness." Her mother has exophthalmos, and had a large thyroid removed three years ago, and which was not noticed until four years after the birth of the patient. A paternal cousin is an epileptic. The points of interest in this case are the fact of the mother suffering from glandular affection, and the fact of the menses becoming more irregular as the epilepsy became more established. This might point to the two having a common cause.

McKinnon, Johnson and Henninger, after describing alterations in the clinoid processes observed in many epileptics, say that it is probable that a moderate degree of hypopituitarism exists in all epileptics, and that epileptic attacks are probably precipitated by sudden cessation of practically all secretion from the posterior lobe.(22)

The pituitary gland has a stimulating effect upon the ovarian function, and irregular menstruation is common in apituitarism.

Cases 1, 2, 3, 4 and 5 are of weak intellect, but fairly bright, and occupy themselves usefully. Case 4 is, and 5 was, extremely irritable, and will fight and quarrel with the slightest provocation. Case 6 might be considered of normal mentality; she was smart at school, good at games, and said to be thoughful of others, but occasionally irritable with children.

Cases 1, 2, 3 and 4 have been treated by us for epilepsy, and 6 was removed from our care to be treated by Christian science. There are several cases of epilepsy that have been reported as having been cured, or greatly benefited, by anterior pituitary extract, the doses being from gr. viii to gr. xxx daily.

Cushing mentions 13 cases of apituitarism associated with epilepsy; 7 of them presented uncinate symptoms. All of these suffered from a cerebral tumour. Two followed upon a fracture; the others were considered to be primary glandular hypoplasia. The traumatic cases did well on glandular treatment. He treated some of these cases with

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whole-gland pituitary, giving as much as from 36 to 300 grains daily. They improved mentally, lost weight, and the epileptic seizures were either suspended or greatly diminished.(23) We have had no success in treating these patients either with pituitary extract or with glands that might act indirectly upon the pituitary. We have not given the pituitary in the larger doses above recorded.

Case 7 is an occasional epileptic, dull and demented, upon whom no special observations have been kept. His general conformation is much the same as in the preceding patients except that he is taller. He was not admitted to a mental hospital until he was seven years old, and was then too demented to give any reliable history; probably the failure of his pituitary action and his epilepsy are of late development, and due to arterial change in the neighbourhood of the pituitary gland.

Case 8, an imbecile lad, æt. 15, measuring 5 ft. 2½ in. and weighing 9 st. 4 lb., cannot read. He knows some letters but not others, knows figures, but cannot do the simplest addition. He is quiet and good-natured, but easily led into mischief by others more evil than himself. His general appearance is effeminate, and his palate high and narrow. In three examinations his blood-sugar varied from ·12 *per cent.* to ·14 *per cent.* Two hours after an injection of adrenalin ♏vij it dropped from ·14 *per cent.* to ·11 *per cent.* He gave no sugar reaction in his urine to five hours after the injection; he has no polyuria. In the blood-counts his leucocytes averaged 12,000 per c.mm. The polynuclears were 76 *per cent.*, large mononuclears 6 *per cent.*, and small mononuclears 18 *per cent.*

Case 9, a Greek, æt. 37, 5 ft. 6½ in. in height, weighed 16 st. 4 lb. He has vivid hallucinations of hearing and delusions of persecution. For the most part he is depressed and quiet, but subject to certain attacks of impulsiveness and violence. His genital organs are much atrophied. In this respect the photograph is not much good, as the penis is almost imbedded in fat, and cannot be recognised as such. His skin is smooth and hair-growth abundant. He is a difficult case to place from a glandular aspect, but might be considered a mixed one, in which an apituitary and athyroid action play a part, with perhaps an over-suprarenal action, accounting for the excess of hair-growth, and his blood-pressure being as high as 140 mm. Hg. In 1913 he greatly improved on the thyroid treatment, as advocated by Drs. A. Davidson and H. H. Johnson, but lapsed back after a few months, and since then it has not been possible to renew the treatment as any attempt to do so greatly accelerates his pulse. Treatment with thyroid and pituitrin and pituitrin alone has been without results.

Case 10 was a lad, æt. 13 when admitted. Two years previously he had been knocked down by a motor-car. He was unconscious for five days, and when he regained consciousness he had a double internal strabismus, and complained that he could see one object several times at once. Before the accident he had been a normal boy of gentle disposition, obedient, and generally amenable, and well up to the average at school. After recovery from the accident he became absolutely untruthful and quite irresponsible, and it was found impossible to further educate him. Twelve months after the injury he had fifteen epileptiform fits in one series. After this his mental failure was more noticeable; he would wander away and forget to return, became cruel to animals, committed male sexual practices and his memory failed greatly. He was admitted in June, 1916, was then nicely spoken and of attractive appearance, but absolutely devoid of moral sense; would thieve and lie in a most pleasant and natural manner. His memory was very deficient. He had a remarkable chest development, with an expansion of 3 in. His hands and feet were rather large, and the development of his organs of generation out of all proportion to his age, otherwise he was about normal physically. About six months after admission he became less alert and less talkative. His hair, which had been fine and glossy, became coarse and thin, also his eyebrows became much finer. His skin reflex, which had been red, continuing for several minutes, changed to a distinct white, also lasting some minutes. He has, about every six months, a series of four to five fits within a few hours, which leave him mentally dull and confused for some days. Blood-counts made in February, 1917, gave an average

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leucocyte number of 7,637 per c.mm., of which the polynuclears were 61 *per cent.*, small mononuclears 26 *per cent.*, and large mononuclears 13 *per cent.* Another differential count made a month later gave polynuclears 51 *per cent.*, small lymphocytes 27·5 *per cent.*, large lymphocytes 12·5 *per cent.*, eosinophiles 3 *per cent.*, large hyaline 5 *per cent.*, mast-cells 1 *per cent.* The blood-sugar ranged from ·07 *per cent.* to ·11 *per cent.*, and a slight trace of sugar was found in the urine one and a-half hours after subcutaneous injection of adrenalin ♏vij. After receiving thyroid gr. ½ twice daily for four months a great improvement was noticed in his condition generally; he became brighter and the memory improved, though his moral character became no better. The change in this lad followed a severe head injury. It is probable that by this injury he received damage to the pituitary body, the sexual over-development activity and perversion being explainable by an irritative lesion of the anterior lobe, the effeminate *ensemble* to a want of secretion of the posterior lobe, the symptoms of the athyroidism being secondary to those of the pituitary. An X-ray picture of his skull was taken, and it was reported to show no abnormality in the region of the sella turcica or elsewhere.

Case 11 is another apituitary patient, a woman, æt. 32, and congenitally weak-minded. She was at school for three years and can only read and write but little. She is 5 ft. 1 in. high and weighs 15 st. 10 lb. Her chief characteristic is her irritable temper. There is here some resemblance to an athyroid case, but her hair is thicker and more glossy, her skin is smooth and moist, and in spite of her weight she is an active worker and fairly quick in her movements. Her menstrual function is normal and regular, commencing at eleven years of age. For four months she took thyroid, gr. x. daily, her weight dropping to 13 st. 10 lb. For the last twelve months she has been having from 2½ to 5 gr. of thyroid daily; while on this she is brighter mentally and less quarrelsome and her weight keeps at about 14 st., and rises to over 15 st. if the thyroid is discontinued. The thyroid acts in these cases by stimulating the patient's own pituitary gland action.

The next two cases show signs of over-suprarenal action. Case 12, an old lady, æt. 78 at the time of her death, was of very masculine appearance and possessed a deep male voice. She had been an asylum patient for twenty years, and all that time in a condition of chronic mania and constantly pugnacious. On *post-mortem* examination her heart was found to be enlarged and fatty, with soft muscle and atheroma of its vessels, the aorta being free from atheroma. The kidneys were cystic and granular. The pancreas was large with a great deal of fat, and no definite division between the gland and the fat. The ovaries were almost completely atrophied. The thyroid weighed 2 dr. and each suprarenal 3 dr. It was reported microscopically that the thymus showed no glandular elements. The pancreas was extensively atrophied and the suprarenals degenerated. The thyroid was inactive. Her masculine ways and appearance could be explained by over-action of the suprarenals, which had probably lately atrophied from age, and this would account for the extreme atrophy of the ovaries and the activity of the thyroid. The pancreas or suprarenals may have been originally at fault, their action being antagonistic. The patient's age was such that degeneration of all glands might be expected, so the autopsy is not of the value it would have been at an earlier age.

Case 13 is a demented epileptic of long standing. She shows fairly well-marked male secondary sex characters. Her condition may have been brought about by an over-suprarenal or a diminished ovarian action.

Case 14 is a small-headed imbecile, æt. 31, with an abundant hair growth over his body. He would lie about all day, could hardly be roused, would not converse, had no interests, was quite indifferent to all things, and was of faulty habits. His blood-pressure was under 100 mm. Hg., his blood-count about normal, but the small mononuclear cells were nearly as many as the polynuclear, the blood sugar was ·05 *per cent.*, and there was no urinary reaction to 5 minims of adrenalin. The dermographic reaction was white. We looked upon him as a case of over-suprarenal activity which had passed into one of under-action. He was given thyroid, from gr. ½ to 1 daily, and an injection of adrenalin ♏v–x on alternate days. This was continued intermittently for three months. The change was gradual but great. He is now lively and bright, will converse freely, is a keen card-player, employs himself usefully and has made two attempts to escape. The glandular treatment has changed him from a vegetative to an active, if not intellectual,

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individual. He is probably now as of good, if not better, mentality than at any period of his existence. After improvement was manifest some estimations were made upon his blood-sugar, when it was found to vary from ·05 to ·16 *per cent.* In three leucocyte counts made at this time the average was 12,000, of which the polynuclears were 62 *per cent.*, small mononuclears 31 *per cent.*, and large mononuclears 3 *per cent.* He now gave a slight urinary sugar reaction to adrenalin ♏x.

Case 15 is an unintelligent woman, æt. 37, whose general appearance is like that of a boy of eighteen years of age. She has no mammary development, no axillary hair, and the hair on her head is thin and fine. The skin is darkly pigmented in the axillæ, around garter lines and on forearms. There is no dermographic reaction; the thyroid and thymus are not detectable. She has never menstruated, and it is reported that her ovaries and uterus are infantile. This is a case of mixed glandular dystrophy, the ovaries and thyroid, as shown by want of physical and sexual development, being primarily at fault, though there is a general want of gland activity.

Case 16 was æt. 58 at the time of her death. She was admitted to Callan Park Mental Hospital in 1889, suffering from melancholia which had followed upon a short attack of mania. Melancholia has been the predominant mental symptom since, accompanied in later years by a progressing dementia. She is a typical case of myxœdema, with rough dry skin, thickening of the subcutaneous tissue, thin scanty hair, absence of eyebrows, the acute susceptibility to cold, slowness of thought and action, and general apathy. She had been taking thyroid gland for many years. It is noted that in 1894 and 1896 she was treated with this drug but that no improvement followed. In 1903 she was again treated with thyroid and with much benefit, becoming less depressed and more lively. From this time to the time of her death she was almost continuously having gr. v–x of thyroid daily. If this was discontinued for a short time she put on weight, became so dull and uninterested that she would not even move of her own initiative, became silent and would be faulty in habits. While taking the gland, although depressed and morose, she would dress, take food, and look after and even occupy herself. In July, 1917, she had four epileptiform convulsions in quick succession and died two days afterwards. At the *post-mortem* examination there was much fat everywhere, which made it difficult to define the limits of some of the glands, which were themselves impregnated with fat. There was very little thyroid tissue, and what there was was ill-formed and degenerate. The thymus tissue was also much degenerated; the spleen was small, weighing 4 oz.; the kidneys lobulated, otherwise healthy. The heart was fatty and the arteries very atheromatous. After microscopical examination it was reported that there was no evidence of active thymus tissue, and that the ovaries, suprarenal and pituitary showed signs of much underaction.

Case 17 is æt. 14 and Case 18 is æt. 32. Both are simple and childish, incapable of being educated, and both delight in playing with dolls. Case 17 is a Mongolian, with the hands and feet, dry skin and scanty hair of athyroidism. She has an insane inheritance. She learned to walk at seven and to talk indistinctly at nine years of age. She was very irritable and dribbled much. She menstruated at 13½ years, and at this time developed secondary sex characters and also sexual inclinations, for which reason she was removed from her home. On from gr. ½ to 2 of thyroid daily she made improvement, she grew and gained in weight, the condition of the skin and hair improved, the dribbling habit ceased, and she became quite talkative and talked more freely and clearly. It has been possible to teach her to scrub, fold clothes, and generally help, which she does fairly well and with much pleasure.

Case 18 was of rather different type, the skin and hair being normal; the hands and feet were small, but not of the stubby formation of the former patient. She was of low intelligence, could not talk distinctly, and could understand but little of what was said to her. She suffered from attacks of tetany which were associated with the menses. She died of cerebral abscess secondary to middle-ear disease.

Case 19 was a case of gonod deficiency. The genital organs are infantile, the breasts are large and pendulous, the fat distribution is of feminine character, and there is a poor growth of face and body hair. The hands and feet are small and

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slender, the pelvis large and well formed, the voice high pitched and of peculiar intonation. He was seventy years of age when his photograph was taken and was admitted seven years previously. His intelligence is very limited and his conversational powers are almost *nil*.

Cases 21 and 22 are both æt. 16, but have developed very differently. Case 21 is 5 ft. 4½ in. in height and weighs 9 st. 8 lb., while Case 22 is 4 ft. 8½ in. and weighs 4 st. 2 lb. Case 21 made but little progress at school but is stated to have been a good industrious girl in the house. Six months before admission she became dull and listless, and talked nonsense to herself in a muttering tone, but otherwise moped about taking no notice of anything. The menses, which had hitherto been regular, became irregular and scanty, and she is said to have lost weight. The symptoms followed upon a "heavy cold." On admission she was very dull, would repeat but would not answer questions, and was quite indifferent to her surroundings. She passed urine apparently unconsciously, wetting her bed during the night and her clothing during the day. She was well nourished, skin smooth, soft and active, hair normal, hands and feet cold and damp. The pulse was 88 per minute, and the blood-pressure was 120 when standing. The dermographic reflex was white, continuing for ten minutes. For six months she was given suprarenal gland gr. v, and made rapid improvement. She became bright and industrious and gained more than two stone in weight. Because of this gain in weight and there being no symptoms of athyroidism she was given pituitrin and varium, but continued to gain weight and weighed 12 st. 3 lb. when she left the hospital eighteen months after admission. Her mental improvement has been maintained, her mother reporting that the patient has never been so well as at present. In this case there was probably some dysfunction of the suprarenals following upon the "heavy cold," this being followed by diminished ovarian action.

Case 22 is a very dissimilar one. She has been a hospital patient since she was six years of age, and at that early age was given to violence. At the present she appears about ten years of age, speech is very imperfect, no axillary hair, mammary development is poor, and skin and hair are normal. The thyroid gland can be felt, but the thymus cannot be detected. Chvostek reflex is present. The knee-jerks are exaggerated and there is left ankle clonus. Dentition is good. Though of childish and pleasing appearance she is a most evil minx. She will attack anyone without reason or malice, will trip up or push down the old and feeble and will come up smiling and spit in one's face. She is filthy in habits, and throws fæces about her room and has not menstruated. There is no special sign of glandular deficiency. She is undeveloped both mentally and physically, the under development in this case being of cerebral origin.

Case 23 was æt. 18 on admission, 4 ft. 8 in. in height, and weighed 5 st. She has but little intelligence, cannot read or write, and, although expressing a wish to learn, on sending her to school it was found impossible to teach her. Physically she is undersized and undergrown; she has a peculiar growth of fine hair all over the body, with but little axillary hair. There is a line of pigment on the abdomen from the umbilicus to the pubis. The mammary development was poor on admission but had increased six months later. Her thyroid gland cannot be felt. The thymus is enlarged and can easily be percussed out. The bones are small and slender, as are the hands and feet. The skin is smooth and soft, the sweat-glands of axillæ being abnormally active. The pulse was 88 per minute. She has a slight intermittent glycosuria, which was found on testing her urine previous to an injection of adrenalin. Her blood-sugar at this time was ·14 *per cent.*; two hours after the injection it had fallen to ·05 *per cent.*, the excretion of urinary sugar being much increased. The hæmoglobin content is about 100 *per cent.*; the leucocyte count averages 10,000 per c.mm., the polynuclear cells being 76 *per cent.*; small mononuclears 11 *per cent.*, large mononuclears 7 *per cent.*, eosinophiles 4 *per cent.*, masts and hyaline cells 1 *per cent.* each.

It is difficult to determine whether a thymus in this, and similar cases, is primarily enlarged, or secondarily, as either compensatory or inhibitory to some other gland. What results the enlarged thymus has upon growth and formation probably depends upon the amount of over-action, the effects upon other members of the endocrine system, and the time of life at which the enlargement occurs. This case was treated for some months with suprarenal extract gr. v and gr. ½

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thyroid daily. Except that she gained 8 lb. in weight and that her mammary development has increased there has been no noticeable change.

Cases 24 and 25 are similar in their mental, but very different in their physical make-up. Case 24, who is æt. 14, is 5 ft. 10½ in. in height and weighs 10 st., while the other case is a year older, 4 ft. 10 in. in height and weighing 6 st. 10 lb. Both these boys had been to school, and although they had not done well, had done fairly, and had commenced to earn their own living, Case 24 on a dairy farm and Case 25 in a boot factory, and both were spoken well of by their employers. After doing well at their work for a while they each took to wandering from home and would remain away for days, seemingly doing nothing but walking the streets and sleeping in empty houses or out-houses. Each would rob their parents before starting from home, but had not been known to rob anyone else, except Case 25, who, living in an orchard district, admits taking fruit for food. In each case the thyroid could be felt, while Case 25 had an enlarged thymus but not Case 24. Case 24, whose bones were large and thick, hands and feet large, and genitals of abnormal development, might pass as one of over-pituitary action and was treated with didymin to lessen this activity. The other lad has a generally diminished glandular activity, with the exception of the thymus, which may be keeping the others in check. Case 24, in three blood-counts, gave an average leucocyte count of 10,000 per c.mm. with polynuclears 52 *per cent.*, small mononuclears 43 *per cent.* and large mononuclears 5 *per cent.* He gave a slight urinary sugar reaction two hours after an injection of adrenalin ♏x. The blood-sugar on two examinations was ·05 *per cent.* while on a third it was ·14 *per cent.* This was previous to the adrenalin injection, after which it fell to ·11 *per cent.* No blood observations were made on Case 25.

The two boys soon returned to their normal mentality and left the hospital after six months' residence. Case 24 has been out more than twelve months and is reported to be doing well. Case 25 was returned after being away a month, as he was inclined to wander and did not settle to work. About a month later his parents insisted on removing him to a Salvation Army home, and to us he has been lost sight of, but he should be doing as well as his companion.

Case 26 is æt. 18, weighs 7 st. 12 lb., and measures 4 ft. 9½ in. His hair and skin are normal, and his bones short and thick. He has a fair amount of sense, is capable of useful occupation, but has no initiative. He has no idea of the value of money, is easily led into mischief, and readily becomes a tool of others, which was the reason of his admission. This is a case approaching achondroplasia. He contrasts with the cases 27, 28 and 29, three Mongolian imbeciles, with the spade-like hands and feet, the rough dry skin, thick lips, and undershot jaws, scanty dry hair on head and deficiency of body hair. Case 29 gives a distinct white skin reaction lasting ten minutes, and passes about 3,000 c.c. of urine in twenty-four hours. His leucocytes average 6,500 per c.mm., the polynuclears being 58 *per cent.*, the large mononuclears 14 *per cent.*, and the small mononuclears 28 *per cent.* In three examinations his blood-sugar varied from ·05 *per cent.* to ·15 *per cent.* After an injection of ♏ x of adrenalin his leucocytes rose from 5,062 to 24,750 per c.mm.; there was a slight rise in the blood-sugar but none excreted in the urine.

Case 28 was 5 ft. 10 in. in height, and died of colitis at the age of 45. At the *post-mortem* examination, made twelve hours after death, his brain was found to weigh 39 ounces; his heart was normal, except that the aorta would only admit one finger. There was a considerable amount of thymus tissue scattered about the mediastinum. The thyroid was small, the suprarenals were large, but were apparently mostly fatty tissue.

Case 64 is one of a peculiar œdema, and follows fairly exactly the description of Milray's disease, but there is no hereditary history. She was first admitted to a mental hospital in December of 1911. Her mental condition had been diagnosed as recent mania, and moral insanity. She had been sent to a reformatory at quite an early age and at eighteen she went into service, and shortly after eighteen had a baby. In January, 1914, she was treated for retroflexion of the uterus, pyelitis and cystitis. She was subsequently treated for a double salpingitis and later a left salpingo-oöphorectomy was performed. Later in the same year she suffered from gonorrhœa. She came under our care in March, 1916, and was then in good physicial health. In April of that year she complained of pain in the right hip-joint, after which for three months she persistently complained of pain in one of the joints of the right leg.

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Towards the end of July the right ankle-joint was swollen and at this time it was noticed that she had a few pus-cells in her urine and some diplococci. In November, 1916, the right leg from the hip to the ankle was swollen and œdematous. The blood was repeatedly examined for filaria, but with negative results. In January of 1917 the leg was very swollen and she complained of severe headache. A lumbar puncture was performed and 17 c.c. of fluid was removed under a plus pressure. Three days after the puncture the leg was almost normal, but had returned to its original degree of œdema within the next week. In October of 1917 the left leg below the knee became œdematous. The next month the left leg and thigh were œdematous, as was the right. A silk-worm-gut drain was put into the inner surface of both thighs, but no benefit followed this, although they drained freely for a time. A lumbar puncture had been repeated once or twice but never with the same result as the first time. In February of 1918 several incisions were made into the legs, which drained freely, but they did not diminish in size. About this time numerous hard round nodules developed; they were very tender to touch. Two were removed and examined under the microscope but no lepra bacilli were found. In this month the right arm became swollen, and there was a tenderness along the course of the nerves. In March she complained of a great deal of temporal headache. Twenty c.c. of cerebro-spinal fluid were removed under increased pressure, after which the headache improved, and the legs became smaller, though nothing like normal. In April of the same year she complained of much abdominal pain and often vomited. The headaches again became severe. A lumbar puncture was repeated with relief to the headache, but it was not followed by any lessening of the swelling of the legs or arm. Injections of adrenalin ♏x and calcium iodide gr. xv were given into the scapular region every second day for a fortnight. The swelling in the legs became much smaller, the decrease being most marked the day after the injection. She then objected to the injections and they were discontinued. Between May and September the injections were repeated several times for about ten days or a fortnight at a time, each time with much diminished swelling of the legs, more especially the left; the thighs at one time became normal. When the œdema was diminished the patient complained of very much more pain in the legs. In October of 1918 six injections of pituitary, 1 c.c., were given on alternate days and after the second dose there was some improvement, but this was not lasting. In December of the same year the right arm began to swell—first the hand and forearm, then above the elbow. Another series of injections of adrenalin and calcium were given, the two drugs this time being given separately. The patient became resistive and the treatment was discontinued. After these six injections there was marked improvement. In January of 1919 the left arm also commenced to swell and the right became bigger still. During the next month both arms and both legs were extremely swollen, and she was unable to move any one of the four limbs. The patient now implored to have the treatment resumed, and this was only consented to on the condition that she would be treated as long as was thought necessary, and that she would take and do all things as told. She was given 1 c.c. of adrenalin, and this was repeated every second day. By February 18th the left arm and hand were normal, the right hand nearly so, the swelling of the left leg had disappeared except of the foot and ankle, the right leg was smaller, and the œdema softer, and would now pit on pressure. Always before, when patient's legs were going down, she had vomiting attacks and severe abdominal pain, but this time these were not so severe, but she complained of a great deal of pain in the limbs as the œdema diminished. In March of the same year both hands and arms were normal, and she had free use of them. The left leg was also normal. From July the adrenalin injections were continued for ten weeks. They then caused giddiness, breathlessness, and much pallor of the face, so they were reduced in frequency and amount, and afterwards discontinued. Suprarenal tabloids gr. xv and gr. i of thyroid daily were substituted. The improvement has been slow but continuous, and there has been no return of the œdema of the upper extremities. That of the lower limbs has persisted, though it has been much more variable, the degree of swelling altering from day to day. The patient's mental condition has undergone a great change for the better. She is now affable and cheerful, whereas formerly she was most morose and taciturn.

The differential diagnosis of this case is by no means easy. The patient at times

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during her illness was extremely resistive both to treatment and examination, for which reason observations upon the chemistry of her blood and urine have not been made. In the earlier stages of her illness she was thought to be suffering from gonorrhœal rheumatism, and finding diplococci in her urine supported this supposition, which could not be maintained when the leg became generally œdematous. The diagnosis then rested between an œdema of venous or lymphatic origin. No filaria could be found in the blood nor could any cause for a venous block be found. It was self-evident that the œdema was not of cardiac, portal or kidney origin, though there was often a trace of albumen in the urine. An angio-neurotic œdema was considered, but as a rule the œdema in these cases comes and goes quickly, attacking first one and then another site. Later when two and then a third limb was attacked, the case exactly resembled one of Milray's disease, which is described as an œdema which first attacks one limb, then another, until all four limbs are affected; it persists until the patient either dies from exhaustion or from some intercurrent disease. According to descriptions, the one essential of Milray's disease is that it is hereditary, but no hereditary history could be obtained in this case either from the patient or her friends, her parents having died when she was quite young, the family separated and were brought up by the State, and so no great reliance can be placed upon the family history. No pathology has been given to Milray's disease.

Œdemas, sometimes persisting, sometimes very transitory and without any apparent cause, or with such insufficient cause as long standing, are not uncommon in the insane, though the pathogenesis of these have not, as far as we are aware, received much attention as yet.

We look upon this case as likely to be due to some lesion of the sympathetic nervous system. We gave her adrenalin under this idea, and the calcium because of its action upon the blood-vessels. Her blood-pressure previous to the adrenalin injections was within the normal range, nor was there any increase after the injections, even when the larger doses were being given. A sign of insufficiency of her own adrenalin system was the fact that only upon about two occasions was there sugar in the urine, even after repeated 1 c.c. doses of adrenalin. It is advised that adrenalin be not given repeatedly even in small doses, but in this case it seemed to be doing nothing but good, and the case appeared so hopeless otherwise. Her menses had been in abeyance for some twelve months, but reappeared at irregular intervals while receiving the calcium iodide and adrenal injections and continued fairly regularly while receiving larger doses of adrenalin.

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[It is regretted that owing to the prohibitive cost of reproduction numerous other interesting photographs which illustrated this article could not be published.—EDS.]

REFERENCES.

(1) *Endocrinology*, vol. i, p. 133.
(2) D. N. Paton.—Ref. *Regulators of Metabolism*, p. 118.
(3) *Endocrinology*, vol. i, p. 344.
(4) Harmsworth.—*Natural History*, pt. 12, p. 605.
(5) McCarrison.—*The Thyroid Gland*, p. 144.
(6) 'Thyroid Insufficiency," *Practitioner*, January, 1915.
(7) *Practitioner*, February, 1915, p. 181.
(8) *Endocrinology*, vol. ii, No. 3, p. 336.
(9) "Epilepsy and the Ductless Glands," *Journ. Ment. Sci.*, June, 1918, p. 58.

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Table showing the Activity of the Ductless Glands of Epileptics as found by Microscopical Examination.

Males.

No. of case.	Age.	Cause of death.	Thymus.	Testis.	Thyroid.	Pituitary.	Suprarenal.	Pancreas.	Spleen.	Pineal.	Liver.
37	31	Fracture of skull	Active	Normal	Inactive	Normal	Inactive	Not examined	—	—	—
38	31	Enteric fever	,,	,,	Normal	,,	Deficient	,,	—	—	—
35	29	Epilepsy	Very large, persistent infantile	,,	Over-active	,,	,,	Under-active	Normal	Not examined	Degeneration
39	59	Acute pulmonary congestion, post-epileptic	*Nil*	Under-active	Ditto	,,	Under-active	Deficient.	Fibrosis	—	—
40	26	Pneumonia	Not examined	Normal	Under-active	Under-active	Normal	Under-active	—	Degenerative changes	—
5	28	Epilepsy	Active	Under-active	Over-active	Very small —lost	Under-active	Normal	Waxy degeneration	—	Fatty degeneration.
41	49	Pneumonia	Active, persistent infantile	Normal	Under-active	Under-active	Normal	Not examined	Capsules and vessels thickened	—	Normal.
42	28	Status	*Nil*	Not examined	Ditto	Not examined	Cortex missing	—	Fibrosis	—	Cloudy swelling.
43	51	Epilepsy	Active, regenerative type	Ditto	Over-active	Normal	Cortex and medulla under-active	—	Small hæmorrhage	—	Fatty degeneration.
44	73	Pulmonary tuberculosis	*Nil*	,,	Under-active	,,	Ditto	—	—	—	Ditto.
32	40	Epilepsy	Active, regenerative type	,,	Over-active	Over-active	,,	—	—	—	—
31	22	Epilepsy, sudden	Active, persistent infantile	Normal	Not examined	Not examined	,,	—	—	Normal	—
45	46	Cardiac disease	Active	Inactive	Normal	Inactive	Not examined	—	—	—	Fatty degeneration.
37	28	After vaccine	Active, persistent infantile	Normal	Not sectioned	Normal	Under-active	—	Extreme congestion	—	—
46	65	Pneumonia	*Nil*	,,	Under-active	Not examined	Normal	Normal	Thickened arteries.	—	Fatty degeneration.
47	19	Epilepsy	Active, persistent infantile	,,	Normal	Ditto	Under-active	Under-active	—	—	—

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36	—	Status	Present, but not sectioned	„	Over-active	Normal	Not sectioned	—	—	—	Fatty degeneration.
48	62	„	Ditto	„	Ditto	„	Under-active	—	—	—	Ditto.
49	34	„	„	„	Normal	„	Ditto	Normal	—	—	—
34	25	Epilepsy, sudden	Very large, persistent infantile	Under-active	Under-active	Serous effusion	„	—	—	—	—

Females.

No. of case.	Age.	Cause of death.	Thymus.	Ovary.	Thyroid.	Pituitary.	Suprarenal.	Pancreas.	Spleen.	Pineal.	Liver.
50	62	Pulmonary congestion	Active	Not found	Normal	Normal	Normal	—	—	—	—
31	56	Malignant disease of pancreas	*Nil*	Inactive, fibrotic	Over-active	„	„	—	—	—	—
52	44	Pulmonary tuberculosis	„	Under-active	Active	„	Under-active	Under-active	Fibrotic	—	Fatty degeneration.
53	39	Status	Not examined	Fibrotic and under-active	Normal	„	Cortex and medulla under-active	—	—	—	Fatty infiltration.
54	50	„	Active, regenerative	Do.	Not examined	Under-active	Cortex under-active	Under-active	—	—	—
55	37	„	Not sectioned	Under-active	Over-active	Normal	Normal	Waxy degeneration	—	—	Fatty infiltration.
56	50	Lymphadenoma	Active, regenerative	Not examined	Not examined	Not examined	Under-active	Fibrotic	—	—	Do.
33	25	Epilepsy	Very large infantile	Fibrotic under-active	Do.	Do.	Normal	Under-active	Normal	—	Not examined
57	31	Status	Active	Very small fibrotic	Under-active	Normal	Under-active	Normal	—	—	Fatty degeneration.
58	46	Enteritis	*Nil*	Not examined	Over-active	„	Not examined	—	—	—	Do.
59	24	Pericarditis	Active, persistent infantile	Small fibrotic	Not examined	„	Normal	Under-active	Not examined	Not examined	Not examined
60	39	Pulmonary tuberculosis	Present; not sectioned	Not sectioned	Over-active	„	Under-active	Normal	—	Normal	—

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(10) Ref. *Med. Journ. of Australia*, June 1st, 1918.
(11) Orten.—*Amer. Journ. of Insanity*, vol. lxxi, p. 579.
(12) Bandler.—*Med. Gynæcology*, p. 157.
(13) Osler and Macrae.—*Modern Medicine*, vol. iv, p. 781.
(14) Falta.—*The Ductless Glandular Diseases*, p. 336.
(15) Osler and Macrae.—*Modern Medicine*, vol. iv, p. 787.
(16) Harrower.—*Practical Hormone Therapy*, p. 2.
(17) Tobias.—Apocrypha, chap. vi, verses 2 to 17.
(18) A. Davidson and H. H. Johnston.—"Use of Thyroid Extract in the Treatment of Mental Disease," *Aust. Med. Cong. Trans.*, 1911, vol. ii, p. 817.
(19) Falta.—*Ductless Glandular Diseases*, p. 305.
(20) Cushing.—*The Pituitary Body and its Disorders*, p. 268.
(21) Falta.—*Ductless Glandular Diseases*, pp. 290 and 291.
(22) Ref. *Practical Medicine Series*, vol. ix, 1914.
(23) Cushing.—*The Pituitary Body and its Disorders*, p. 272.

Regarding the Treatment of General Paralysis. By G. H. MONRAD-KROHN, M.D.Christiania, M.R.C.P.(Lond.), Physician to the Neurological Section of Rikshospitalet, Christiania; Lecturer in Neurology to the Royal Frederick University, Christiania.

WHEN Noguchi found spirochætes in the brain of general paralytics some years ago it seemed as if we were entering into a new era, not only in the pathological conception of the so-called "parasyphilitic" or "metasyphilitic" affections, but also in their *treatment*. In this latter respect most of us have hitherto been somewhat disappointed, and it may therefore be advisable to take up the rationale of the treatment for revision.

The reason why the usual antisyphilitic remedies are of little or no effect in these affections may be found in one or more—perhaps all—of the following possibilities:

(1) *Either* the antisyphilitic remedies or the antibodies—the formation of which they give rise to—do not get access to the spirochætes on account of their anatomical localisation;

(2) *Or* the spirochætes may have acquired an immunity to the antisyphilitic remedies (1);

(3) *Or* the initial spirochæte affection of the cortex may have already started a vicious circle, which *per se* will lead to destruction irrespective of the spirochætes.

(4) Finally the possibility must also be kept in mind that metasyphilitic lesions may be due to a mixed infection of spirochætes and some other microbe or microbes (*e.g.*, Porter Phillips's diplococcus or

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