*Endocrine Therapy.** By Louis Minski, M.D., B.S.Durh., D.P.M., Assistant Medical Officer, Bootham Park Mental Hospital, York.

In recent years a large amount of literature has been published dealing with the treatment of mental disorders by means of gland extracts, and I take this opportunity of bringing to your notice some of the results I have obtained while treating patients with these extracts. I shall confine my remarks mainly to the treatment of the psychoses with ovarian extract, as, according to some authorities, the results following the administration of this gland extract have been highly gratifying, and we have therefore made use of it to a great extent in suitable cases. It is a well-recognized fact that there is normally a perfect balance between the various endocrine glands, and that any disturbance of this balance tends to produce a disturbance in the mental and physical states of the person so affected. Thus there is a functional harmony and compensatory interaction between the ovaries, thyroid and pituitary glands, the secretion of one gland helping the action of another. It is also found that if the secretion from one of these glands is deficient, one of the other glands in the same series attempts to take over its function by hypertrophying and pouring out an increased secretion into the blood-stream. Thus, after removal of the ovaries, the thyroid and the pituitary gland tend to increase in size in order to compensate for the loss of the ovarian secretion. It is also a recognized fact that the corpus luteum, placenta and mammary gland secretions tend to depress ovarian function, and, therefore, to diminish the ovarian secretion. This is seen during pregnancy, when the ovarian secretion must be held in abeyance; if this were not so there would be an influx of pituitrin into the blood-stream which would cause uterine contractions and the inevitable termination of the pregnancy.

Now, psychoses following pregnancy are quite common, and some of them may possibly be due to deficiency of ovarian extract as a result of inhibition by the corpus luteum, mammary glands or placenta, depending on the time elapsing after the pregnancy before the mental symptoms develop. Acting on the supposition that if the deficient ovarian secretion be administered to the patient, the hormone balance ought to be re-established and the patient restored to normal mental health, we treated this type of case with ovarian extract, and with very gratifying results.

* A paper read at a meeting of the Northern and Midland Division held at Clifton, York, April 28, 1927.

A typical case in this series is as follows:

The patient was a primipara, æt. 22, who had always been in good mental and physical health until five months before admission. The actual labour was quite easy and normal in every way. A few days after her confinement she became depressed, and, on admission, she was depressed, apathetic and showed psychomotor retardation. She had suicidal tendencies, and suffered from the delusion that she must kill her child. Her physical health showed nothing of note except that her menstrual periods were still absent. Ovarian extract was administered subcutaneously to the patient in the form of 1 c.c. ampoules every fourth day, 1 c.c. equalling 30 gr. of whole fresh ovary, the patient having in all 22 injections. After three or four injections the patient became brighter, took more interest in things generally and menstruation became regular, although scanty at first. She gradually improved, and, after about fourteen weeks' stay in the hospital, she was able to return home completely recovered, and has remained well from that time.

On the other hand, some cases do not respond to treatment, and it is possible that in these cases there is another factor at work, perhaps psychogenic in origin. In cases of this kind—those that do not react to treatment by ovarian extract—it is possible that the pregnancy has acted merely as an exciting factor in determining the psychosis, just as any other mental or physical shock might act.

Another series of cases treated with ovarian extract was the climacteric group.

At the climacteric period the ovaries atrophy, the sexual functions decline, and the ovarian secretion no longer passes into the circulation. As a result of these changes the patient becomes upset, owing to the disturbed hormone balance, and, as the late Sir Frederick Mott explained, the "*joie de vivre*" disappears, or at least is diminished. Probably the internal secretions all contribute to maintain the "*joie de vivre*," and disappearance of the ovarian hormone tends to bring on the depression with the usual delusions as a result of rationalizations. On the other hand, the depression may be due to the fact that the unconscious mind is aware that reproductive life is at an end, the conscious expression of which is depression.

At the menopause the thyroid and pituitary glands enlarge, to compensate for the loss of ovarian secretion, and it may be that mental symptoms arise and continue until the compensation for the loss of the ovarian secretion is established by these glands. Therefore, in these cases presenting mental symptoms, the exhibition of ovarian extract supplies the missing secretion, and tides the patient over the critical period.

Some typical cases in this group are as follows:

The patient, æt. 44, had always been robust, and in normal mental health until about six months previously, when she became depressed and anxious, and also expressed delusions of unworthiness. On admission she was still in this mental state, and, in addition, she complained of a choking feeling in the throat and pains all over the body. There was nothing of note in her physical condition except that menstruation was irregular and scanty. Ovarian extract was administered

as before in 1 c.c. ampoules every fourth day. After about six weeks' residence in hospital the patient had quite recovered and was able to return home.

Another case in this group, although differing in the actual form of mental disorder, was that of a patient, æt. 48, and married. She had been in good health until eleven weeks previously, when she became excited and talkative. On admission she was excited, noisy, talkative and incoherent, and, at times, inclined to be impulsive and violent. Physically her condition was poor; she had intestinal stasis, her eyes were sunken and the skin was sallow. In addition she was menstruating irregularly, and was always worse mentally at her periods. As an initial form of treatment she was given a course of Plombières douches and intestinal disinfectants; the intestinal stasis cleared up, but her mental condition remained unchanged. It was then decided to administer ovarian extract as in the previous cases, and, after about nine months' residence in hospital, the patient was discharged recovered.

About 50% of the climacteric cases treated in this way made a good recovery, and in those which did not respond to treatment it was usually found that there was a tainted heredity, or that the climacteric was not the sole cause.

While dealing with psychoses, presumably the result of the cessation of ovarian secretion, I should like to mention the following case as one of interest:

The patient was a typist, æt. 30, and her previous history was as follows: She was normal as a child, got on very well at school, and later took up "typing," at which she became very proficient. Since the age of 19 she had suffered from pains in the head; these had disappeared latterly, however, and were replaced by delusions. For over ten years the patient had been strange in her manner, but four years ago she became very depressed and had ideas of unworthiness following an attack of influenza. She had recovered from this attack and was in her usual mental health until a few weeks prior to admission, when she became depressed and deluded, and developed suicidal tendencies. On admission she was acutely depressed, looked anxious and said she wished to die. She would not speak unless spoken to, and expressed the usual melancholic ideas of unworthiness. She was also agitated, emotional and confused. Her physical health was poor; she was of small stature, 4 ft. 11 in. in height, and weighed 6 st. 11½ lb. Her heart and lungs were normal, but the abdomen was peculiar in shape, being distended below the umbilicus, and more especially towards the middle line. This was apparently due to the unequal distribution of subcutaneous fat, which was present in excess in this region, and which was verified *post-mortem*. Patient had never menstruated, but, in view of her mental condition, no vaginal examination had been made, and no cause could be found for the amenorrhœa. Her secondary sexual characteristics were well developed.

Whilst in hospital her mental condition remained practically unchanged, although, at times, she was a little brighter, whilst at others she was very depressed, resistive and agitated. After seven months' stay in hospital patient died from exhaustion and pulmonary congestion, and on the day of her death temperature rose to 107° F., with a pulse-rate of over 200.

At *post-mortem* examination the following points of interest were found:

The pituitary gland was normal in size and appearance, and the brain-tissue generally, apart from congestion and small hæmorrhages, was normal. The thymus gland was not persistent, and in the abdomen the kidneys were found to be small, and divided into three lobules by two clefts, one at the upper and one at the lower pole. The uterus and ovaries were in an infantile state, and had never developed. The uterus measured 2 in. by 1⅜ in., but the musculature was well developed; the ovaries were the size of large beans, and the Fallopian tubes were patent and the fimbriæ quite well marked. Microscopic examination of the ovarian tissue showed that it was infantile in type. There were no normal

follicles, although they appeared to be represented by irregularly shaped spaces, which had evidently been lined with cubical epithelium. These were partly filled with a secretion of amphoteric staining properties.

The *post-mortem* findings showed that the ovaries had never functioned, as they were still in an infantile state, and it was probable that the psychosis was the result of disturbed hormone balance following absent ovarian secretion. The patient had been treated with tablets of thyro-ovarian co. (containing ovarian extract 2½ gr., thyroid gr. $\frac{1}{15}$, pituitary whole gland gr. $\frac{1}{8}$, with calcium phos. co. *ad* gr. v), which were given four times a day for some considerable time. No improvement was seen in her mental condition as a result of this form of treatment, and the possible cause of the psychosis may have been an inherent instability in the nervous system.

I wish now to refer briefly to some points in connection with the treatment of the psychosis by means of thyroid extract—a method of treatment which is by no means new, and which is recognized and adopted by most psychiatrists.

Thyroid extract in small doses is used largely in general medicine for various conditions, and also in mental disorders in order to stimulate metabolism by supplying a missing secretion or by augmenting a deficient one. Now in certain cases of mental disorder, *viz.*, those cases which have passed through an acute stage of mania or melancholia and have then drifted into a condition resembling stupor, confusion or secondary dementia, an intensive course of thyroid treatment is often very beneficial. Accompanying the mental state there are usually the following physical symptoms, namely, constipation and faulty digestion, dry skin, feeble pulse, shallow respirations, subnormal temperature, and generally a condition showing sluggish metabolism.

In connection with the technique in this method of treatment it is useful to remember that the patient's weight should be such that he can afford to lose up to about 14 lb. during the treatment, as this often happens. Prior to the administration of the thyroid nourishing diet should be given, *viz.*, eggs and milk in addition to the ordinary diet, and the condition of the intestinal tract should be made as satisfactory as possible. On the first day of the treatment a large initial dose should be given, and, as a rule, 45 gr. of thyroid extract (usually 15 gr. thrice daily) are given.

On the next 5 or 6 days 60 gr. (15 gr. four times a day) are given, provided that the patient's condition is satisfactory. As a rule, reaction to the drug is early and distinct; thus we find that the temperature rises a little and the pulse at once begins to quicken. The pulse-rate must be carefully watched, and any irregularity noted. As long as the pulse remains regular there is no cause for anxiety —no matter how rapid it may be—but any marked irregularity

should act as a danger-signal to stop the treatment. There is often profuse sweating, and the lobes of the thyroid gland become thickened. The patient must be moved as little as possible, and, at the end of the sixth day the treatment is suddenly stopped. Patients who have reacted to the treatment usually look somewhat ill, and have lost weight considerably. It is now necessary to stimulate the patient, and attempt to quickly rebuild the tissues. The diet should be nourishing and liberal, milk being taken in abundance. In addition the patient should be given a strychnine tonic and kept in bed, preferably in the open air.

Two typical cases are as follows:

The patient was æt. 20, had always been dull at school, and was dreamy and forgetful. Two years previously to admission he suffered from influenza with hyperpyrexia, and definite mental symptoms developed. On admission he was noisy, violent and incoherent, and, for a time, was alternately elated and depressed. He also expressed the delusion that he was able to revolutionize the world. He remained in this state for about two weeks, when he became quiet, solitary and would not speak; he was dull and stuporose. As no improvement took place in two months, a course of thyroid was administered. During the treatment he lost 10 lb., but quickly regained this weight. He began to show more interest in things, showed more initiative and talked in a natural manner. Seven months after the course of thyroid treatment he went home recovered, and I saw him two years afterwards, when he was still quite well in every way.

Another case was that of a patient, æt. 21, who had previously been under treatment for acute mania, from which he had recovered. He had a bad family history, as his father was insane, his mother was eccentric and his paternal uncle and grandfather were insane. Since his previous attack he had remained quite well until a day before admission, when he became very noisy and excited. On admission he was confused and disorientated, cerebration was sluggish, his memory was impaired and he was incoherent. Physically he was in poor health; he was flabby, the temperature was subnormal, cardiac action slow and feeble, the skin was dry and the bowels were constipated. He lapsed into a stuporose state, and was given thyroid extract, gr. ½ night and morning, and he became brighter for a time, but again lapsed. He was then given large doses of thyroid, *viz.*, 40 gr. on the first day, and 60 gr. a day for the next five days, and he reacted in the usual way, *viz.*, increased pulse-rate, rise of temperature, loss of weight and profuse sweating. He was kept in bed in the open air and was given nourishing diet, and, after nine months' residence in hospital, he returned home completely recovered and was able to resume his work.

I think these two cases show that the judicious use of large doses of thyroid helps to restore the patient to normal mental health, and, in conclusion, I would like to say that this method of giving thyroid gland—that is, large doses over a period of six days—is always worth a trial in the case of any patient who, after an attack of acute mental disorder, has passed into a stuporose state, and has all the appearance of becoming the victim of secondary dementia and of swelling the numbers of the chronic insane.*

I wish to thank Dr. Jeffrey, Medical Superintendent of the hospital, for permission to make use of the cases quoted, and also data concerning them.

* [This method of treatment was devised by Lewis Bruce some 35 years ago.—Eds.].