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# Psychoendocrinology

*Edited By* MAX REISS



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# Psychoendocrinology

*Edited By*

**MAX REISS, M.D., D.Sc.**

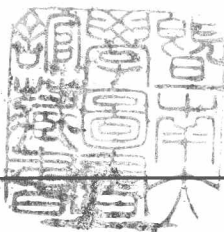
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*Endocrinology Association*



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## FOREWORD

THE SYMPOSIUM on Psychoendocrinology was arranged, within the frame of the 2nd International Congress for Psychiatry at Zurich, to correlate the progress made in the study of endocrine function in psychopathology during the seven years since the 1st International Congress.

The role of endocrine function in psychopathology has been considerably clarified in the last ten years. The chaos which existed then in the conception of endocrine psychiatry led first to disillusionment and then to the realization and appreciation of our ignorance of the influences of endocrine function in psychiatry. Finally, however, new life has started to grow on the ruins produced by the many misconceptions which we are only now beginning to understand. We are closer to the truth. The body and the adaptability, depending upon hormone equilibrium, have finally found their place in the discussion between psyche and mind.

This Symposium represents the first attempt to combine the views and results of clinicians and pure research workers concerned with the psycho-neuroendocrine interrelation. They are working in their hospitals and laboratories in all parts of the world.

Clinicians naturally are most concerned with the value of psychoendocrine investigations in therapy, while laboratory workers are interested in discovering the significance of any correlation that they may have found. The papers in this book were arranged with the clinical lectures first, followed by those more devoted to experimental analysis. Both groups, however, are unanimous, when examining their therapeutic results, in not accepting any results as the final solution but only as one more valuable link in the pathogenetic analysis of mental disease.

THE EDITOR.

## **Psychoendocrinology**

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# I

## PSYCHOENDOCRINOLOGY\*

MAX REISS

- I. EARLY MISCONCEPTIONS AND DISAPPOINTMENTS.
- II. ANALYSIS OF PREVIOUS FAILURES AND NEW APPROACH TO THE PROBLEM.
- III. THE SIGNIFICANCE OF THE HORMONE EQUILIBRIUM, THE PERSONALITY PATTERN, AND EMERGENCY SITUATIONS FOR THE PRECIPITATION OF MENTAL DISEASE.
- IV. THE NEUROENDOCRINE INTERRELATION.
- V. THE PATHOGENESIS OF MENTAL DISEASE IN THE LIGHT OF A PSYCHO-ENDOCRINE CONCEPT.
  1. The hormone equilibrium during mental breakdown and the acute disease.
  2. The hormone equilibrium after one year of the disease process and in chronic patients.
- VI. THE HORMONE EQUILIBRIUM DURING RECOVERY FROM MENTAL DISEASE.
  1. Hormone equilibrium during spontaneous improvement.
  2. The hormone equilibrium during and after treatment with conventional routine methods.
    - (a) Electropexy.
    - (b) Deep coma insulin therapy.
    - (c) Pharmacotherapy.
    - (d) Psychotherapy.
- VII. THE SCOPE OF HORMONE THERAPY.
- VIII. CONCLUSION.

*\*This paper is based on the following previous publications by the author:  
Application of endocrinological research methods in psychiatry: J. Endocrinol., 7, 236, 1951.*

*Psychological changes connected with spontaneous and experimentally produced alterations in steroid hormone metabolism: Ciba Foundation Colloquia, III, 128, 1952.*

*The neuroendocrine relationship. J. Ment. Sc., 1944 (January).*

*Investigations into psychoendocrinology: Int. Record of Med. 166, 196, 1953.*

*Die Entwicklung der Psychoendokrinologie: Berliner Gesundheitsblatt, 20, 517, 1955.*

*Psychoendocrinology: J. Ment. Sc., 101, 683, 1955.*

*The Changing Concepts of the Role of Endocrine Function and Treatment in Psychiatry, a paper read by J. C. Batt and M. Reiss during the Symposium.*



PSYCHOENDOCRINOLOGY is a name used for the study of the interrelation between the functions of the brain and the endocrines. Neither my friends nor I liked this name, but after many discussions we could not decide on an alternative. We even went further, when in 1956 we decided to call our whole research group, consisting of psychiatrists, psychotherapists, psychologists, biochemists, pathologists and endocrinologists, the "Psychoendocrine Association." The name psychoendocrinology was further established at the International Psychiatric Congress in Zurich. The present psychoendocrine concept has developed during the last ten years on the basis of a good deal of trial and error, and much frustration and disillusionment had to be overcome before we felt certain that we were on the right track.

### EARLY MISCONCEPTIONS AND DISAPPOINTMENTS

The efforts of all the biochemists and endocrinologists who wanted to find a cause for a psychopathological phenomenon are best likened to the labors of the Danaids or of Sisyphus. Labors and efforts including the evaluation of the sometimes "statistically significant" results, could have been saved had all these workers not been the victims of some serious misconceptions. These misconceptions were originated by endocrinologists and perpetuated and enlarged by psychiatrists.

From the beginning, endocrinology was connected with descriptions of specific psychological sequels of glandular under- and overfunction. Take for example Berthold's classic experiments, in which he was the first to describe the loss of fighting spirit in the cock after removal of the testicles, and its return after reimplantation of the latter. We have learned, however, that it is often misleading to apply too readily experiences we have had in animal experiments to the analysis of human behavior patterns. We know, for instance, that in human beings sex hormones play a less important role in the development of the fighting spirit, and that this psychological phenomenon depends upon a greater multitude of endocrine, psychological, and genetic factors than in animals. On the basis of his experience with the sex drive of animals, the en-

ocrinologists tried to treat homosexuality in men with male sex hormones, and were extremely puzzled to find the patient becoming, if anything, more homosexual. They tried to treat frigid women with estrogen, and found that the female sex hormone does not influence the female sex drive, while testosterone, the male sex hormone, often does increase it. Incidentally, Freud pointed out the risk of the gonads themselves being overestimated, and added that the chemical mechanisms concerned are probably more diffuse and complex than the consideration of them alone would make one suppose.

Impotence is, in the mind of many endocrinologists, still most readily associated with underfunction of the testicles. Psychological stress factors which can be the cause of many endocrine changes connected with impotence, are barely considered. Careful study, for instance, of the psychological changes during the development of a hypothyrotic state, which may take several years before becoming clinically recognizable, have shown impotence to be an early symptom during the development of hypothyroidism. The text book description of the psychological concomitants of disturbed thyroid function is still so incomplete as to be misleading. Hypothyroidism is always connected with slowing down of mental processes, hyperthyroidism with anxiety neurosis. Only a few endocrinologists have ever taken the trouble to establish, by careful study of the case history, the great variety of psychopathological changes that can occur during the time needed for the development of the final endocrine status, diagnosed as "major endocrine disorder." The clinical endocrinologist has also spent regrettably little time in considering actually why such a great number of patients, showing a major endocrine disorder, are comparatively little deranged psychologically at a time when others show severe neurotic or psychotic disturbances.

The psychiatrists, some thirty years ago, had an entirely open mind about endocrinological psychiatry and accepted the significance of the various claims made by endocrinologists concerning the causative role of endocrine dysfunction in the development of specific psychopathological disturbances. Kraepelin, one of the

founders of clinical psychiatry expected endocrinology to provide the final solution in the pathogenesis and treatment of some psychiatric disease entities. Freud, too, expressed on many occasions, the hope that endocrinological investigations would supply solutions to many psychiatric problems.

However, all the efforts devoted to endocrinological psychiatry were made in vain. Hoskins and Sleeper (1929), for instance, believed that the development of schizophrenia was due to an under-function of the thyroid. Unfortunately, they dealt with a small series of schizophrenics who showed low metabolic rates and reacted well to thyroid treatment. On the basis of these results many psychiatrists all over the world started to treat schizophrenics with thyroid preparations, without, however, making sure that they *were* hypothyrotic. There were even psychiatrists in this country who had a whole ward of schizophrenic patients on thyroid therapy. All these people occasionally had a most convincing success, but in the great majority of cases there were failures which discredited the whole treatment. It would be very difficult to convince a psychiatrist today to begin thyroid treatment again now that his youthful enthusiasm has been so greatly dampened.

It must have been most frustrating for the psychiatrist, when he started thyroid treatment of cases which fell psychiatrically into the same disease entity, to find one reacting nicely and the other remaining completely unchanged or even deteriorating. Their experiences with sex hormones must have been similarly disappointing. Some recommended treatment with sex hormones, others castration, but in the end the results were always the same. After the reports of initial successes the treatments were repeated and the results found to be, in the majority of cases, negative—obviously since the treatment was not guided by proper clinical and laboratory investigations—thus the treatment was discredited and the conclusion reached that the mental disturbance in question had nothing to do with sex hormones.

Most disappointing of all was the work carried out on treatment with adrenal cortex hormones. Originally, before the various hormone compounds of the adrenal cortex were isolated and synthe-

sized, a great number of authors reported very encouraging successes of treatment with adrenal cortex extracts in a variety of psychiatric conditions. These were soon forgotten when cortisone was discovered, and reports were made about the psychopathological reactions of some patients who were treated for rheumatism with mammoth doses of the drug. One ought to emphasize that such psychopathological reactions occur apparently only in patients with a certain pathophysiological or mental predisposition. Otherwise, it is obvious that it would occur much more generally. These results, however, made the psychiatrist forget the encouraging experiences he had with adrenal cortex extracts, which obviously contained very little cortisone. If one wants to make a comparison with incidents in the history of endocrinology, it comes to mind that the use of insulin would never have been discovered for the therapy of diabetes had one not gauged the hormone dose according to the patient's blood sugar concentration and the urinary sugar excretion. Otherwise, one would have killed a discouraging amount of patients, and in others effected not the smallest therapeutic result.

Much of this experimental work was begun before satisfactory measuring methods had become available in endocrinology. In any case the investigations were carried out either by psychiatrists who had little understanding of endocrinology and its methods, or by endocrinologists who had little or no experience with mental disease. This was soon realized, and the belief was that the introduction of more modern and progressive endocrine investigation methods, and the isolation and use of biologically active hormones, would greatly contribute to progress in endocrine psychiatry. It was believed that one might find clearly circumscribed endocrine deviations causing depression, schizophrenia, etc. The investigations were carried out in mental hospitals with exact methods, that were progressively improved from a technical viewpoint. However, a feeling of utter frustration must come over anyone, be he psychiatrist or endocrinologist, who attempts to survey the thousands of biochemical and endocrinological investigations into schizophrenia. M. Bleuler (1954) recently undertook just such a survey, but after he had marshalled all the facts he found them so contradictory

that he could not permit himself to draw any definite conclusions. In fact, he was not even sure whether the classic syndrome of schizophrenia had any sort of causal relationship to endocrinology at all, and at a recent meeting dealing with psyche and endocrinology he was rather inclined to separate entirely endocrine psychosis from real endogenous psychosis. A still more recent review by Richter (1957) on the biochemistry of schizophrenia does not show any recognizable trend towards definite deductions. Mayer-Gross and his co-workers (1954), in their recent textbook wrote: "Thyroid, sex glands, adrenal cortex and pituitary have all been suspected as the primary cause of the disturbance, but with no conclusive evidence."

### ANALYSIS OF PREVIOUS FAILURES AND NEW APPROACHES TO THE PROBLEM

The causes for the existing chaos in the biochemical and endocrine investigation results became increasingly clear to our research group.

A great number of investigations did not deal with psychiatrically homogenous groups. It would be difficult to find, among their published results, some that are not based on biased samples.

Few of the numerous statistical evaluations of deviations found in, for instance, schizophrenic patients, is valid where the disease entity, schizophrenia, is concerned. Various groups of workers investigating quite different groups of schizophrenics, acute states, chronic states, simple schizophrenia and paranoia, were rather surprised when their "statistically significant" results contradicted the equally "significant" results of other investigators. Many workers also did not realize that so-called "homogenous group," owing to the prevailing system of classification, can contain patients in various states of exhaustion, some of which are excited, some very quiet, etc. One cannot expect to find in such groups significant changes, say, in the blood corticoids, or in other chemical, urine, or blood components.

At an early date, we thought that investigations of greater numbers of the same disease entity, or bigger hospital populations,

would render more valid information. In these large scale investigations, however, the arithmetic means are usually identical with, or very near to those of the control groups, but the range of the results is considerably wider, the standard deviation greater.

Figure 1 illustrates such investigative results. It summarizes the results of our large scale investigations on schizophrenics and can

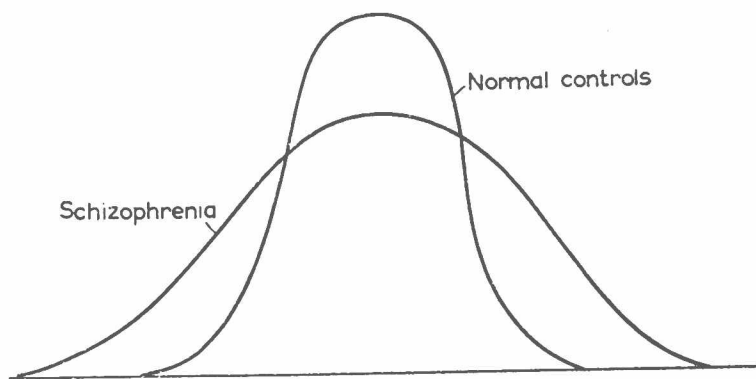


Figure 1

equally apply to blood circulation rate, body temperature, basal metabolism rate, blood chemistry, thyroid activity and excretion rate of adrenal cortical steroids. However, one may draw one final conclusion from these investigative results, namely, that the various biochemical and endocrinological deviations occur much more frequently in mental patients than in the normal population. Such results were achieved by screening the thyroid activity of hospital populations, or a considerable part of them, in Bristol from 1949 to 1953 (Reiss et al.), St. Ebba's Hospital, Epsom from 1954 to 1957 (Sands), the Royal Victoria Hospital, Netley from 1954 to 1956 (Robinson) and Burgholzli, Zurich from 1953 to 1954 (Stoll).

In later investigations more attention was paid to the biochemistry and the endocrinology of the *individual* patient. This change in emphasis evolved from the fact that great diurnal and day to day variations occurred in many patients. In judging steroid hormone production, for instance, these single values were unsuitable

for use in statistical evaluation of cross sections. Further it seemed profitable to investigate the individual patient longitudinally for some time during the deterioration, or improvement, of his mental disturbance. The first results were rather unexpected. It seemed that individual patients with apparently identical psychopathological symptoms showed quite different endocrinological disturbances, under- or overfunction of one gland, or of various glands; alternatively, individuals with the same kind of endocrine disturbance had either no pathopsychological symptoms at all, or quite divergent manifestations of disturbed mentation.

These findings initially shattered every concept we had concerning the role of the endocrines in psychiatry. They later became the starting point of a more productive working hypothesis.

#### THE SIGNIFICANCE OF THE HORMONE EQUILIBRIUM, THE PERSONALITY PATTERN AND EMERGENCY SITUATIONS FOR THE PRECIPITATION OF MENTAL DISEASE

The variety of the endocrine disturbances that can accompany identical psychiatric disease entities brings to mind experiences with groups of individual soldiers during the war, where the same biochemical change and emergency situation could bring about a variety of neurotic and psychotic reaction patterns. For instance, a group of young men about equal age, in a lifeboat after a shipwreck, are all subject to similar conditions of exposure, starvation and thirst, and to the realization of the uncertainty of their fate. A number of them will not show any psychopathological manifestations at all, others may behave in a very hysterical way, while some may have hallucinations or show all the symptoms of a manic or depressive psychosis. Decisive in their behavior are their preformed personality patterns. In view of what has been described above, namely that identical endocrine disturbance can be accompanied by a variety of psychopathological manifestations, we were forced to draw the conclusion that it is not the quality of the hormone disturbance which determines the type of mental breakdown, but the premorbid personality pattern that is decisive.

In later continuation of the endocrine investigation of mental patients, in which particular attention was paid to the early stages, and the stages intermediate between normal status and a fully developed endocrine disturbance, it was found that the disturbance of one function of one gland rarely occurred on its own, but was usually accompanied by a disturbance of other glands. In other words, a single endocrine disturbance was usually only regarded as an indicator for the disturbance of the whole hormone equilibrium. Therefore, to characterize the hormone equilibrium of a patient attempts were made to investigate the function of at least two glands. Investigation of the functions of the thyroid and the adrenal cortex were within the scope of our group. Simple biochemical investigations were postponed at this time, since it was realized that they give us much less information than the investigation of the hormone equilibrium, which is primarily responsible for the biochemistry of the body. The failure, for example, of some of the best biochemical investigations to lead to any final results is due to the fact that the importance of this sequence was not realized in time. Gjessing, in his admirable research into the changes in nitrogen metabolism, ascribed to the thyroid function the whole responsibility for the most characteristic cyclic changes. That, however, happened at a time when the influence of testosterone, or cortisone, on nitrogen metabolism was not yet known, so that the final solution of the problem still awaits an exact repetition of the original Gjessing experiments, but including control of the adrenal cortex and gonadal function. The same can also be said about any other biochemical component, as for example sugar metabolism, which also depends primarily on the interaction of a number of hormones. There is no doubt that the ductless glands are the main regulators of the biochemical equilibrium of the organism, and the more we learn about their physiology the more we can see how even the simplest metabolic functions are finally dependent on the function of the endocrines, and how the body equilibrium which can ultimately be defined as a tendency to maintain a constancy in the chemical patterns of blood and tissue, is dependent on the cooperative effort of various duct-



less glands. It is obvious that a decrease or increase in the functions of a ductless gland will have its repercussions on the width and stability of the biochemical equilibrium. Thus it must be assumed that the homeostasis of the organism is not an unalterable factor. In some individuals, it can be stretched very far, sufficient for the regulatory demands of enormous efforts, while in other individuals a small effort can lead to a failure of homeostasis. This failure may be followed by severe functional disturbance of some organ systems, among which the brain function plays, of course, a predominant role if one considers that about 30 per cent of the total oxygen consumption of the body takes place there.

Selye's stress and adaptation theory, and E. B. Cannon's theory about the body's regulation towards emergency function, described some small part of all the forces of the organism for maintaining biochemical equilibrium. Cannon's theory, however, was based only on the regulation afforded by adrenal medulla and sympathics, and Selye's gives a prevalence to the anterior pituitary lobe-adrenal cortex axis. Considering the knowledge accumulated about factors contributing to the maintenance of homeostasis a very great number of such adaptation theories could be described at present. It would be wrong to restrict the explanation of the adaptability of the organism to Selye's theory alone. Instead of sticking to such presently well introduced phrases as "adaptation to stress," it would be considerably more productive if more attention were paid to the endocrine and biochemical *adaptation to everyday life* and its demands. A better understanding of the functional endocrinology of everyday life, and sufficient methods to measure the changes taking place should become a most essential basis for the pathogenetic analysis of the development of various mental disorders.

Today it can be safely assumed that the endocrine equilibrium is necessary for the maintenance of normal functions during everyday life, and for the adaptability of the individuals to various emergencies, as they are offered by different psychological and physical stress conditions. It has proved useful to characterize the various elements concerned in the development of mental dis-