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Influence of Hormones on the Nervous System

Influence of Hormones on the Nervous System

Edited by D. H. FORD, Brooklyn, N.Y.

159 figures and 86 tables



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Preface

The International Society of Psychoneuroendocrinology was formally started at the 2nd meeting of the International Society for Neurochemistry in Milano, 1969. The purpose of the Society was stated as being directed toward bringing together the basic and clinical aspects of neuroendocrinology and related disciplines with psychiatry for the purpose of better understanding the interactions existant between structure, chemistry, function, normal brain behavior and psychosis. There seemed to be several pathways by which this could be achieved. One, the promotion of multidisciplinary research studies may perhaps be the most usefull in the long run. However, this aspect of our intentions appeared somewhat over ambitious for a newly born society, necessitating a large financial support. A 2nd method of bringing together our various disciplines through the membership is to circulate an annual list of the titles of publications of the members, incorporated with a listing of those members who would welcome and could support fellows working in their laboratories (this would be done as soon as it is completed). Finally, there is the concept of the multidisciplinary symposium.

For a new society, the last proposal has turned out to be the easiest to initiate. The selection of the type of program was also relatively simple, since the 'Influence of Hormones on the Nervous System' (other than related to feedback control) is a topic of interest to behaviorists, psychiatrists, neurochemists and neuroendocrinologists alike. It is also a rather timely subject inasmuch as no or few reviews of neuroendocrinology have examined the subject in this manner in recent years. Further, the role of endocrine imbalance in mental retardation and mental disorder is beginning to become increasingly apparent.

The planners of the conference are indebted to the Downstate Medical Center for the use of its facilities and support as well as to the Department of Preface X

Anatomy and the Department of Continuing Education of the Downstate Medical Center of the State University of New York for their support. We would also like to acknowledge the financial support of the Ciba Pharmaceutical Corporation, The Waterman-Bic Pen Corporation, The Warner-Visiter-Pharmaceutical Corporation of Como, Italy, the Eli Lilly Company and of Organon, Inc. Without the timely help of these organizations, this meeting would never have reached fruition. Last, but far from least, we are grateful for the secretarial services of Mrs. Barbara Ginsberg and Mrs. Carol Steig and all the other persons at the Medical Center who have in one way or another assisted in the creation of this program.

Dedication

For a great many years it has been the hope of Dr. M. REISS that the failure of the medical profession to successfully treat the multiple problems of the mentally ill might be resolved. From early in his long, productive career, it was apparent to Dr. Reiss that both mental retardation and psychosis were often associated with a variety of endocrine disorders and that a wedding of neuroendocrinology and psychiatry might lead to a more rapid understanding and resolution of these problems. In an effort to promote such cooperation in treatment and research Dr. REISS evolved the concept of a multidisciplinary society which would incorporate within its ranks psychiatrists, neurologists, neuroendocrinologists, neurochemists, psychologists and other persons interested in the general area of basic and clinical neurobiology. This society was ultimately born in Milan, Italy in 1969 and named the International Society of Psychoneuroendocrinology. It was his hope that by frequent international multidisciplinary meetings and workshops a degree of unity would develop between the various neurally oriented groups which would culminate in more intelligent treatment of the mentally retarded and psychiacally ill patient. The current symposium on the Influence of Hormones on the Nervous System represents the first attempt of the society to bring at least some of these groups together.

We, the members of the Society are certainly greatly indebted to Dr. M. Reiss for persevering in his dream of a united society whose fundamental role is to further our understanding of the functions of the brain. Thus, it is with regret that we must note that on the eve of fulfillment of a dream, Dr. Reiss has passed away. Philosophically one might argue that man should indeed be permitted to leave this world when he is at his pinnacle. However, I cannot believe that a scientist as enthusiastic as Dr. Reiss would have willed matters in this way. He was too much of a fighter to have wanted to

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bow out before the ultimate solutions to the clinical problems of treatment of the mentally ill were in hand. Therefore, I believe that we, the members of the society should dedicate our own studies toward the further resolution of these problems, attempting to better understand how the mind works and what factors influence it. Further, as Dr. Reiss has counselled us, we should work together to utilize our energies in a more productive manner than we might if we continue to follow our separate paths in teaching and research.

DONALD H. FORD Editor

In Memoriam to MAX REISS, M.D., D. Sc.

Dr. Max Reiss, one of the truly great medical research giants in the combined areas of mental illness and mental retardation, passed away July 27, 1970, at age 70.

All of mankind and all of medicine lost a most dedicated and conscientious physician-teacher-researcher and true guiding spirit by his unfortunate passing. His provocative research contributions covering a time-span of close to a half-century to the fields of endocrinology and later neuro-endocrinology and still later psychoneuroendocrinology number in the hundreds. At the time of his death his fertile mind was at work on other and still more penetrating research matters in brain physiology and metabolism. His was a most creative and imaginative mind.

An Austrian by birth, Max Reiss completed his M. D. degree in 1925 followed three years later by the D. Sc. granted in 1928, both by the German University of Prague. A student and later colleague of famed pioneer Endocrinologist Professor Arthur Biedl of Prague, Max Reiss was to remain at the German University of Prague the next fifteen years, working himself up from Assistant, later Dozent and Professor Extraordin in Pathophysiology and Endocrinology.

Professor of world-renowned researcher-scientist Hans Selve, currently Director of Experimental Medical Research at the University of Montreal, Max Reiss was to see many of his medical students and research colleagues continue in his pioneering efforts. Emeritus Professor of Experimental Medicine at the University of Vermont, Dr. Wilhelm Raab; Professor H. Heller, Chief of the Department of Pharmacology, the Medical School, Bristol, England; Dr. R. Gjessing and his Psychiatrist-Researcher son, Dr. L. R. Gjessing, of Oslo, Norway; and Dr. Otakar Poupa, currently Visiting Profes-

sor in Clinical Physiology at the University of Goteborg, Sweden, were among his many associates.

Just prior to the Hitler invasion of Austria and Czechoslovakia, Dr. Reiss managed to relocate in Bristol, England, where he was to devote his next twenty years as Director of the Burden Neurological Institute. While in Bristol, Max Reiss also played a dominant role directing Biochemical and Endocrinological Research Units at various Bristol Mental Hospitals, acting as Chief Consultant to Mental Health Agencies throughout Southwestern England and later Consultant Endocrinologist at St. Ebba's and the Royal Victorian Hospital in the London area.



MAX REISS † DONALD H. FORD ABEL LAJTHA DIXON WOODBURY

While in Bristol Max Reiss was to meet and marry Jeanne Fulkerson, RN, who was to continue to work with and later co-author with her renowned husband a number of significant studies in the fields of mental illness and retardation. Their research work and writings were to carry over to the United States where they had next settled. While in England, Max Reiss was chosen by the Commissioner of Mental Hygiene for the State of New York to become Director of Psychiatric Research at the Willowbrook State School on Staten Island. During the next dozen years Dr. and Mrs. Reiss were to see

a number of Max Reiss' pioneering efforts in psychophysiology and neuroendocrinology bear fruition via his experimental studies with mental retardates. Max Reiss long ago established the thesis that what applied to the mental retardate could and often did have concomitant bearing on the mentally ill and the physical and mental aberrant abounding in the clinical fields of medicine.

Max Reiss was a big man-both in stature and in standing-with his patients as well as his colleagues. He proved himself a humanitarian at heart. He was a man of principle and character. He was forever creative and imaginative in his research. Often he would be the first to arrive and the last to leave his medical research laboratories. Nothing appeared too big nor too small for him to deal with. Jewish by birth, Max Reiss appeared to personify the tragic pains and sufferings his race suffered and endured over the ages, particularly during the Nazi reign of terror in Western and Central Europe during the 1930s and first-half of the 1940s. He possessed the rare gifts of goodness and kindness-of empathy and sympathy-without being overtly showy or gushy. He despised sham and hypocrisy. He demanded much from others, of himself most of all.

I had been a neophyte medical research writer with a strong leaning toward neuroendocrinology and neurocardiology when I first became acquainted with the research contributions of Max Reiss. I had been visiting endocrine research centers and hospitals in the British Isles and on the Continent gathering material for writing purposes when I began hearing and seeing the name Max Reiss more and more frequently. It was not until several years ago, however, that I was to make Max Reiss' personal acquaintanceship. It occurred interestingly enough at an Endocrine Society banquet. I remember the occasion well, for I had just returned from the University of Montreal where I had been visiting with Dr. HANS SELYE and his co-workers, and remarked to Dr. WILLIAM TINDALL, Medical Director of Organon Laboratories of Amsterdam and London, who happened to be seated on my right side, how impressed I had been with SELYE's prolific outpouring of scientific treatises, and such well-written ones at that. If you were that affected by HANS SELYE', Dr. TINDALL remarked, 'you should become acquainted with his former Professor from Prague University days, Dr. Max Reiss. He happens to be sitting directly opposite you.' Thus began my initial meeting with Max Reiss. In the intervening years scores of letters, meetings, and long periods of daily telephone calls ensued. In the process I could not help but admire his breadth and depth of insight and knowledge. Above all, I could not help admire the man.

The one penetrating theme which Max Reiss most deigned to talk about was his long-felt dream to place the study of mental illness and retardation on a firm scientific footing. He long since had perceived the shortcomings of psychiatry and more especially psychoanalysis. His innovative research and clinical testing and follow-ups over a near half-century of study in neuro-endocrinology and neurochemistry and neurophysiology placed him far ahead of his time. Around him gathered a coterie of like-minded researchers and clinicians. Together they would search and explore, forever testing and retesting one hypothesis after another until equanimity had been reached. His early training and research in endocrinology during his early years in medicine disciplined his mind but not his outlook. 'One of these days...' and 'Long after I am gone...' were two popular prefatory statements he was fond of uttering.

The formation of the International Society of Psychoneuroendocrinology one year ago and its culmination in the more recent Symposium at the Downstate Medical Center-Brooklyn were two highwater marks in Dr. Reiss' long struggle to establish a scientific basis for studying mental illness and retardation. Based on the tri-partite disciplines of psychiatry, neurophysiology, and neuroendocrinology Clinician-Researcher Reiss believed he and his followers were finally beginning to penetrate into the more important aspects or layers of brain chemistry and pathophysiology. Though he was the first to admit much further research and clinical testing needed to take place, the Psycho-neuro- endocrine Society, he felt at last had taken that all important leap forward.

It is tragic and unfortunate indeed that so soon after its highly successful opening session, Max Reiss was to depart this earth. His long-felt dream of such an 'international' and 'multi-disciplined' Society having been fulfilled, fate was not to allow his sharing in its future accomplishments. His faith and trust in its purposes, however, shall remain. Then, too, his faith and trust in his coterie of co-workers and followers was such that his dream of the formation of an 'International Psychoneuroendocrine Society' could very well form the stuff by which dreams are both made and fulfilled. Max Reiss was a humanitarian at heart, and it will be his deep concern for people which will be most missed and certainly most difficult to replace.

JOHN MARQUARDT Medical Research Writer

Welcoming Address

Ladies and Gentlemen,

It is for me a great honor and gives me great pleasure and satisfaction to open this 1st meeting of the International Society for Psychoneuroendocrinology. For years many of us have recognized the vital necessity for such an association which to some degree differs from other research societies which are based on much more established, solid and completed knowledge. The branch of research with which we are concerned in our Society differs from that of other Societies, since our field is more comprehensive and a multidisciplinary approach is essential. The work of clinical and basic endocrinologists and neuroendocrinologists is needed, together with biochemical, physiological, electrophysiological and biophysical investigations. Last, but not least, the various branches of psychological concomitants must all be combined in order that the somatic and psychological changes can be realistically evaluated and lead to the improvement in treatment of both psychiatric and somatic diseases. It may be added that in the last decade many conceptions in general have changed. The strict separation made originally by the classical German workers between clinical and basic research has lost its welldefined frontier lines. This is particularly the case when we consider how often observations, made during clinical research, have initiated and encouraged work in the field of basic research. Of course the converse is equally true; that is that the findings of basic investigation medicines are being put to use in the clinic.

The organization of our Society is more or less based on the example of the Collegium Internationale Neuro-psycho Pharmacologicum and the American College of Neuropsychopharmacology. These Societies have already realized the necessity for comprehensive multidisciplinary investigations, a fact which is well-expressed by the multitude of disciplines with which leading committee members of these Societies are associated. However, it has become increasingly clear to many of us from reading the proceeding of these Societies that none of their efforts will ever lead to a full pathophysiological analysis of a disease. As far as therapy is concerned, it does not appear that a treatment will be discovered which would be specific for the illness of a whole patient group in the way comparable to the manner in which insulin is specific for diabetes. Furthermore, when surveying the proceedings of these Societies, one finds that even in the most careful blind and double blind treatment studies, these improvements never effect more than about 60% of the patients even when only modest improvements are included. It is, therefore, not astounding that at the Annual Meetings of these Societies the section devoted to prediction of drug therapy is increasing in content each year. These drug studies often appear to ignore the excellent basic investigations which are carried out concerning the action of drugs an brain chemistry and various enzyme systems.

The objection that each hormone acts on a multitude of enzymes and that it would, therefore, be more economical to investigate the action of exogenous drugs on the endogenous hormone metabolism than to study the effect of exogenous hormones has not found many followers among the neuropharmacologists. It has been repeatedly shown that many of these drugs have a great influence on the action of endocrine glands, while clinical investigation have demonstrated a far reaching indirect effect on the various functions regulated by hormones. For instance, there is the impotence seen in men and the menstrual disturbances in women after treatment with thorazine. In the present stage of knowledge one might conclude that the result of tranquillizer action depends in part on the endocrinologically conditioned constitution of the patient. This sharp differentiation between neuropharmacological and neuroendocrinological work is not only necessary from the scientific angle but also from the practical angle. From the latter angle it is. of course, necessary in the interest of the suffering patient. But, there is still another important point, namely, that psychoneuroendocrinology has in the last ten years been overshadowed owing to the general preference for psychoneuropharmacology. This is due in part to the interest in the large pharmaceutical institutes where the motivation is partly centered on a monetary return for their labors as soon as possible. The desire for an immediate practical return has also unfortunately influenced various public research grant distributing organizations. In recent years the investigation of the psychotropic action of hormones, for example ACTH, has received only a minute fraction of the grant money given to some newly discovered derivatives of thorazine or reserpine. This is particularly the case in mentally retarded patients where the main indication for the use of tranquillizers is for the control of behavior and has in very many cases simply taken the place of the old physical restraint methods. At the moment there are, of course, in large institutions for the mentally ill or mentally retarded patient few alternative methods of management left because of the overcrowding of wards and acute staff shortages. Moreover, clinical and basic endocrinological investigation results on such patients have been almost completely neglected, attention being paid, superficially, to psychological action of the drug. There are, of course, also a few examples available of rational hormone therapy based on endocrinological investigations of such patients which has improved them considerably.

Our association was named Psychoneuroendocrinological because it emphasizes not only the beginning but also the end of the most important pathophysiological vicious circle in the body. All the stimuli stresses and increased environmental demands start their damaging action from the various receptor areas of the brain, go via hypothalamus-pituitary to the various glands whose function is regulated by the pituitary to the body periphery from which various feedback reactions take place. These depend on the effect of circulating hormones acting directly on the brain or are initiated by various events triggered off in the body periphery, again effecting various receptor areas of the brain. It must, therefore, be clear that the simple name Clinical Neuroendocrinology would not cover the whole field, because various brain areas and their role in behavior are undoubtedly included in this total vicious circle. This occurs not only in the brain role as a receptor area, but also as regulator in an enormous number of clinical conditions.

Endocrinology started with the classical experiments of HUNTER who had the good fortune to discover and describe the enormous behavioral and somatic changes observed after castration of cocks and how these changes could be reversed after reimplantation of the testicles. However, the mechanism of these changes, particularly the fundamental ones in brain chemistry which induce psychological and somatic alterations is still unknown. The final truth will not be found by continuing in the present ivory tower philosophy in our research work. One single scientist, with one single research group working under him, is not likely to produce final conclusions. I realize that it is a difficult task, but without the cooperation of scientists of various contributing disciplines the final truth in caincal or basic neuroendocrinology of psychoneuroendocrinology will not be found. The mounting complexity of

the work demands more coordination and integration of effort, more humility and less fragmentation. Otherwise, the cost of disorganization and lack of collaboration, both in human and monetary terms, will become so high that any research effort will not only be delayed but might even be destroyed. Therefore, it is necessary that a large group of research workers combine their efforts for the final purpose, namely, continuous improvement of methods to promote the health of mind and body. This is the only way by which man can survive in view of the continuously increasing demands of the environment.

M. Reiss †
President of the International Society
of Psychoneuroendocrinology

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