

## THE ENDOCRINE SYSTEM IN INFANCY AND EARLY CHILDHOOD\*

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To the thinking physician, treatment does not consist merely in applying measures of relief. The essence of treatment consists in recognizing the pathological process, in understanding its nature, its cause, the mechanism involved in its production and in the development of its clinical manifestations, in knowing the character, extent, and probable outcome of the resulting functional and morphological changes; in valuing correctly, the significance of clinical and laboratory findings, in ascertaining the indication for, in knowing the action of, and the most effective methods of applying measures for its prevention, abortion, amelioration, or cure.

Eternal as the everlasting hills, metabolism goes on, the basis of life and all its phenomena, while men may come and men may go, like Tennyson's brook, it goes on forever. Species are cast in various molds, generations appear and disappear, youth is followed by age, yet through it all, running along on predetermined lines, goes metabolism. Where there is life, there is chemical reaction and regulating this, are the endocrine glands, the glands of internal secretion.

The review which follows, is intended to cover that part of the literature which especially concerns children. It was found very difficult to separate this from those pertaining to general medicine, and impossible to master all the literature in this fruitful field. It was necessary to leave out much excellent material in the review, for lack of space. I have also purposely omitted for the same reason, a discussion of the sex and glands of the kidney.

### THYROID

By the intensive studies in endocrinology during the past few years, it has been established that the delinquent, backward and mentally defective child is the frequent end result of a disturbed metabolism produced by a derangement of the glands

of internal secretion. In this disorder, as in others due to a disturbed endocrine system, it has been found that there is an intimate co-relationship between the different hormones, that generally no one endocrine substance is at fault alone, but that they are all involved to a greater or less degree in any disease which threatens the integrity of any one, causing thereby a change in the general metabolism. While it may be difficult to state just how much of the deficiency in the delinquent child is due to the thyroid hormone, it is the consensus of the opinion that, in the majority of cases of this type, hypothyroidism is the predominating pathological factor.

This is borne out clinically by the general response to specific thyroid treatment of certain similar developmental defects encountered in children.

It is believed by competent observers that the clinical and experimental evidence exists that the thyroid has bacteriolytic and antitoxic properties.

L. Fasin, at Liege, by experiments on dogs and rabbits, found that the alixin was increased by the subcutaneous injection of thyroid fluid extract of the fresh gland.

The thyroid is the greatest stimulator to metabolism known, acting probably by the effect in increasing muscle tonus through nutrition of the autonomous nervous system. Experiments have shown that the thyroid has an undoubted influence on heat regulation. It also is a potent factor in the development of acidosis, by its influence in increasing oxidation. The thyroid, as you know, also stimulates the pituitary function.

Rachford says, in the whole range of medicine there is no more remarkable example of marvelous curative effect of a therapeutic measure than is furnished by thyroid treatment of cretinism. In this treatment we have a brilliant example of true specific medication.

H. Zondek, of Berlin, tells us that heart disturbances caused by hypothyroidism are characterized by sluggish action, and are benefited greatly by the administration of the thyroid treatment. These cases are marked by dilatation and do not respond to digitalis or other heart tonics.

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McKee, who has had an extensive experience with mongoloids, claims to have attained very good results with thyroid gland extracts.

The dangers attending the use of thyroid preparations depend, to a degree, upon the manner in which the remedy is administered. Beneficial doses, by raising the activity of all metabolic processes, prove tonic, increase the appetite, the strength, and the oxidations, as shown by a slight rise in temperature. When, however, the dose is too large, a weak, rapid pulse and shortness of breath, vomiting, cardiac oppression, a feeling of tightness around the chest, vertigo, and coma may supervene. Excessive doses have also caused anorexia, diarrhea, malaise, lassitude, and pain in the extremities; headache, various eruptions, urticaria, transient and papular erythema and eczema, and, in some cases, nervous manifestations; neuralgia, delirium, convulsions, aphasia, monoplegia, etc. When dried powder or compressed tablets that are not fresh are used, symptoms of ptomaine poisoning may be added to those mentioned. Hence, the observations that these preparations are more likely to produce such effects during the warm weather.

The best guide is the pulse. Any considerable quickening or palpitation should lead us to discontinue the drug until the cardiac action is again normal. There are no dangers in the use of the drug, provided we begin with small doses, from 1/20 to 1 grain, and gradually increase, watching the pulse. It should never be given to a patient who cannot be closely watched.

In some cases, although no other untoward symptom appears, the patient loses flesh. This is apt to occur when 2 grains of the dried gland is exceeded.

As to the length of time the patient shall take treatment, in many cases of hypothermia or arteria, it is necessary for a patient to follow treatment for years or for his lifetime. To be sure, all cases are not cured, but I think it is safe to say that all, when properly managed, are improved.

Dr. S. P. Beebe has used very effectively the human extract, when the animal has failed completely.

It is to be remembered that the dose of thyroid extract is relative to the patient. The dose, to be most effective must be large enough to stimulate metabolism, yet not large enough to cause an increase in catabolism. It appears that the usual dose recommended by pharmaceutical houses is much too large.

The preparations of desicated thyroid on the market vary in strength, so that a small dose of a weak preparation may be practically inert. It has not, as yet, been standardized. It is well therefore, to specify the same preparations at all times, correctly to judge the patient's tolerance. We have found that minute doses 1/20 to 1/10 grain three times a day, has been markedly beneficial to children suffering from infantile wasting, or to children which, for no demonstrable reason would not "grow off" as they should. We have them report at regular intervals, and watch them closely. The following is one of our cases:

Esther B. was seen on June 16 by my brother. Her general condition was good, her intelligence fair, her features inclined to be heavy; she had a noticeably short, thick neck. She was up to grade in school. Her weight was 46 pounds, her height 38 1/4 inches. She was put on thyroid extract gr. 1/2 t.i.d. Her height on the 25th day of October was 42 1/4 inches, a gain of 4 1/4 inches from June 16 to October 25. There was also a marked improvement in facial expression, etc.

We have also found small doses helpful in delayed dentition. But the most pleasing results have been had in mental deficiencies of different degrees and cause. Of course it is not effective in all cases, but you are amply rewarded for your labor by observing the results of even one successful case.

Chronic poisoning, characterized by rapid pulse, emaciation, weakness of the limbs, general debility, and mydriasis have also been observed in individuals who had undertaken, without medical advice, to treat their corpulency, and who had, therefore, subjected themselves to excessive doses.

Children bear thyroid preparations much better than adults and rarely acquire Grave's disease. The reason may be that their active thymus is able to neutralize the excessive or morbid activities of the thyroid gland.

The cause of the manifoldness of the hypothyroidal syndrome may be regarded as in the hyperthyroidal syndrome, as differences in the constitutions of the individual affected.

I will attempt no discussion of the relation of the thyroid and parathyroid, as it is still a much mooted question and time forbids any lengthy delineation of the different views.

Erdheim and his collaborators, on the basis of their investigations, adhere to the view that tetania infantum depends upon a hypoparathyroidism and that the artificial nourishment constitutes only an occasioning factor.

#### THYMUS

It has not been long that the thymus gland has been classed as a part of the hormonopoeitic system. Originally it was regarded as a constituent of the lymphatic apparatus. The nomenclature is still influenced by this classification as evidenced by the following: status lymphaticus, status thymicus and lymphatism. The thymus gland develops as a paired organ from the ventral part of the third branchial cleft. The pair unite very early. At birth the organ lies behind the sternum, backward as far as the pericardium, reaching above somewhat higher than the jugular notch.

The abnormality of the thymus that has attracted most attention is the phenomena called "persistent thymus" and which is supposed to bring about a train of symptoms.

The various conditions caused by an enlarged thymus are well covered by Pfaundler, who states that they are as follows:

- (1) Tracheal stenosis.
- (2) Pressure by the gland upon the circulatory system and nerves.
- (3) Status lymphaticus.
- (4) Laryngospasm.
- (5) Dyscrasias caused by functional troubles of the gland itself.

*Thymic Asthma.*—According to some clinicians, enlargement of the thymus is a relatively rare condition. The conclusion is reached by lack of an examination. It is well to examine for a thymus in any case presenting these definite symptoms: dyspnea, continuous or remittent, suffocative attacks with cynosis and stridor. Very

light or threshold percussion carefully employed in connection with properly executed x-ray work, using both the fluoroscope and photograph, will often demonstrate an enlargement of the thymus gland. I recall one case of thymic asthma seen in consultation, which had escaped the observation of some excellent clinicians. In this case throwing the head backward would cause a violent asthmatic attack. (Case seen by courtesy of Dr. C. J. Carmichael). It has been found that these cases can be markedly benefited by x-ray therapeutics.

This syndrome of enlarged thymus gland and attendant symptoms is sometimes termed status lymphaticus, and these are the class of patients which give the unexpected deaths under trivial hardships. The exact *modus operandi* of these deaths is not understood, and just what role hypothyrmization and pressure on the trachea, pharynx or pneumogastric, or what part they play is not decided. We do know that some of them respond well to skillful x-ray therapeutics. The information as to the physiological function of the gland is very meagre and uncertain, consequently any departure from the normal is very obscure. The influence of the thymus we know bears materially upon the osseous and skeletal formation.

#### SUPRARENAL

The adrenal glands are situated in the epigastric region on each side of the spine close to the upper pole of the kidney. According to Elliott and Armour the cortex of the suprarenal at birth is composed of a narrow outer rim of cells, from which develops the adult cortex. The adrenal glands receive a supply of sympathetic autonomous nerve fibers by way of the splanchnic. The active principle of this gland is epinephrin.

Garmendia tells us that suprarenal insufficiency may cause headache, with attendant symptoms, all of which are benefited by epinephrin, supplemented by recalcification measures.

In diseases where the patient demonstrates a low resistive power as in peritonitis, certain forms of pneumonia, diphtheria, typhoid, etc., when the temperature is subnormal, pulse weak, face dusky or livid, cold and clammy, there appears to

be some deficiency of the adrenal secretion. In diphtheria and peritonitis, investigators by necropsy have found this to be true. It has been suggested that epinephrin be used in these cases. These conditions are relatively common in children in almost any grave infection.

It has been found by Caro, Hoskins and others that the adrenals may be stimulated or excited by the thyroids. Adrenal insufficiency causes children to have the cold mottled skin to which mothers often call your attention, referring to it as "pieded."

It is a well known therapeutic fact that urticaria is sometimes relieved almost immediately by hypodermic injection of solution of adrenalin. Deficient activity of the adrenal due to inadequate development, exhaustion by fatigue, or any other factor, which without provoking organic lesions in the organs or their nerve paths, is capable of reducing secretory activity. Asthenia, accompanied sometimes by cold skin or cold extremities, hypotension, weak cardiac action and pulse, anorexia, anemia, slow metabolism, constipation, psychasthenia, are the many symptoms of this condition.

Adrenal function is of great importance in many ways. Bandler is of the opinion that it influences a child's temperament to marked degree, especially the emotion of fear which is fostered by education, and which, by the way, plays an important part in a child's life. I am sure that the study of the adrenals will bring forth some wonderful discoveries with reference to the growing child and give us a new weapon for the treatment of these unfortunate little ones which are such a problem.

We are told by Sajous, that a close study of the adrenal system would be productive of cures in many of our most fatal and distressing diseases. Many experiments lead us to believe that the adrenals supply, in some degree, the material for the antibodies which cause some children to be more resistive to infectious diseases than others. That there are degrees of deficiency of the adrenal secretions, is a familiar fact to most physicians, when the signs of this condition are brought to his attention. The ruddy, warm, hard romping youngster is not only well nourished

but his skin is warm and red, being well filled with blood. His muscular, skeletal, cardiac, and vascular systems are strong because, in addition to being well nourished, they are well supplied by adrenal secretion, which investigators have shown sustains muscular tonus. The pale, flabby child, with cold extremities and capricious appetite, easily fatigued, apparently has a decided deficiency of the adrenal secretion which causes pallor by lowering the blood pressure. These children are of course more susceptible to disease.

Maranon has demonstrated that it is possible to induce all the phenomena of fright, such as pallor, dilatation of the pupils, acceleration of the heart beat, goose flesh, sweating, etc., without the intervention of the brain, merely by injection of epinephrin in artificially hyperthyroidized or in subjects with latent hyperthyroidism.

Recent investigations have shown that the status lymphaticus possesses a close relation to conditions of hypofunction of the chromaffin tissue. The great interest that clinicians and pathological anatomists demonstrate in this, is due no doubt to the fact that it is associated with sudden and unexpected deaths.

Jump, Beates and Babcock have collected from the literature, seventeen cases of precocious sexual development associated with suprarenal tumor, all of which were confirmed by necropsy. It is interesting to note that fourteen of the seventeen cases were girls. In all the cases there was an overgrowth of pubic hair; in fourteen of them, hair was present on the face; and in five there was axillary hair. Overgrowth of the body as a whole occurred in all. Precocious menstruation and breast development appeared in only one. The majority of the children showed diminished intelligence, but some appeared to be unusually bright. There seemed to be a tendency toward the assumption of the masculine type of the sexual development in all the females and an exaggeration of the normal in the sexual development of the males. The tumor always involved the suprarenal cortex.

Baldwin adds another case, a boy five years old, whose face was like that of a man and had been shaved for some time.

## PITUITARY

The pituitary, like all of Gaul, is divided into three parts: the anterior lobe being typical glandular, the posterior resembling nervous tissue, the "pars intermedia" partaking of both kinds of tissue. Each of these portions produce one or more chemical substances or hormones, the function of which are not as yet clearly understood.

The large or anterior lobe produces a substance which regulates the osseous and muscular development of the body. The posterior is supposed to secrete a series of hormones, which play an important part in the metabolism, especially of carbohydrates.

In pituitary disturbances of childhood, the changes are marked, the skeletal growth may be stimulated or the stature may be small. There is the noticeable change of acromegaly and occasionally, acromicria.

Honax reports two cases of precocious adolescence and overgrowth which came to necropsy. In one there was a pineal tumor, in the other a marked disturbance of the pituitary gland. The clinical manifestations due to abnormal secretions of one or both these lobes, are taken as the chief guide for grouping of these disorders. The clinical syndrome, formerly termed "glandular" symptoms, are named hormonal signs and symptoms, a qualification applying to all endocrine disorders.

The hormonal signs and symptoms are defined as physical or metabolic changes, associated with other endocrine symptoms due to abnormal secretions of the ductless gland. These pertaining to pituitary disorders are divided into physical, metabolic, and other endocrine disorders. Among the general hormonal signs are the well known changes in osseous development, producing disproportion in the measurements, unusual development of the voluntary musculature, abnormal contraction of the striped muscle tissue, pigmentation and hair distribution. Among significant regional signs are, local changes in the head, nose, teeth, chin, hands and genitalia, localized adiposity, pigmentation, etc. Other important pituitary endocrine symptoms are polyurea, changes in the basal metabolism, especially carbohydrate tolerances, mentality, and other

endocrine secretions, temperature, pulse and blood pressure.

However it is well to remember that the function of the entire pituitary body as well as the individual lobes is yet a matter of controversy, and will require much study, both clinical and experimental, for a clear understanding. While it is true that the secretions from the anterior lobe seem to have a definite effect upon the development and function of the osseous and genital system, it is acknowledged that other factors endocrinous and endogenous, undoubtedly, have a considerable influence upon both the growth and development of these two systems. Not all cases of retarded osseous growth and aplasia, for instance, can be attributed to hyposecretion of this lobe of the hypophysis.

Gigantism is supposed to be due to hyperpituitarism; it seems to be acromegaly of the period of growth. Here, organotherapy has been used with reported success.

There has been some wonderful work by surgical interference, but the efforts have been attended by such high mortality that very few evidently have the temerity to undertake it on a large scale.

There is conclusive evidence that the peculiar syndromes observed in children suffering from adiposity, attended by a striking mental torpor are markedly benefited by the administration of pituitary gland. A beautiful example of this is the case reported by Dr. Talbot. In this instance the whole gland was used. Another class, of mental deficiency, one of which was reported in detail by Dr. Haynes, was observed by Drs. Haynes and Kerley for some months, and the results obtained were very satisfactory. This child responded promptly to glandular therapy. The gland used was pars intermedia.

## GENERAL SUMMARY

It is a well known fact that such diseases as Addison's disease, exophthalmic goiter, myxedema, acromegaly, are attended with abnormal psychic phenomena in a great many instances. But mere deficiencies of functional activity, independent of any active pathology in any one of the ductless glands, may inhibit the nutrition of the brain to such an extent that they

produce various forms of idiocy and mental backwardness.

It seems to be characteristic of some families to have a well balanced endocrine system and others have a poorly balanced. These may be demonstrated in a decided tendency to hyperthyroidism showing all the traits of Basedow's disease. As our knowledge grows, these will be explained to a great extent and finally be classified as curable instead of neurotic or hysterical, both of which to my opinion are meaningless. With this wonderful and in some respects unexplored world of medicine, we may find much to balance these unstable and unfortunate individuals.

We are only on the threshold of knowledge of relations of the ductless glands to each other or the clear understanding of the endocrine system, the great role it plays in the development of the growing child, both physically and mentally. But the possibilities are vast for therapeutic measures.

Heredity plays a great part in endocrine dysfunction; as proof we cite you to families who are underdeveloped either physically or mentally, or both. Of course, toxemia and other perverted psychological processes and environment influence these conditions. But mental ills should now be considered just as much as physical ills and when possible, diagnosed.

There is such a close hormone relation between the whole endocrine system that it will require much work on the part of both the laboratory investigators and the clinicians to clarify the situation to the extent that we can say in a given case, that it is this or that gland which is at fault, whether the secretion from the ductless gland is influencing a gonad or a gonad influencing a gland, etc.

In administering ductless glands, one must admit that preparations are abnormal to begin with. The glands used are dried and only the hormones that are relatively stable can be preserved. Even here, we have no absolutely certain method of checking our findings and must usually reason by inference and deductions in the interpretations of results. However, we are on reasonably safe ground when we can by administering preparations of a particular gland, prevent the occurrence

of symptoms that would otherwise result from the extirpation of the gland in question.

It is well to remember that much of the rapid advance of the knowledge of the endocrine system has come about through clinical observation. It is not my intention to belittle the significance of what has been brought to recognition through experimental pathology. This alone has made possible the rapid advance of the clinical side.

Dunn thinks there is an unfortunate tendency in modern medicine to ascribe a great variety of functional disturbances of obscure pathogenesis to a disease of some of the ductless glands, bringing about an indiscriminate prescribing of the glandular extracts for obscure conditions in early life. I heartily agree with him in the extreme, but believe that a closer observation of a patient with discreet and intelligent prescribing of these glands would be of great benefit to the patient, as well as clear up many unsolved problems of medicine. Certainly there is some grasp somewhere to the great system that is so potent a factor in the physical and mental well being of mankind.

Time and space do not permit the consideration of such well known phenomena as cretinism, myxedema, Grave's disease or Addison's disease, etc., except to incidentally mention, but to invite your attention to the less observed and more obscure manifestations of the endocrine system.

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### DISCUSSION

Dr. C. E. Boynton, Atlanta, Ga.—The trouble in dealing with endocrinology at all is that we are liable to become entirely too enthusiastic about it. Personally I believe that the enthusiasm is more than justified. I have been very much pleased in the past year to see the wave which has gone over the country in regard to these endocrine cases. If the general profession continues to be as interested in endocrinology as it has been in the past few years, we are going to know a great deal more about it than we do now. Very few of us are sure whether we know anything about it or not. The fact that the secretions of the glands involve the entire body is true beyond question. We know they make a child grow and develop and if they are absent, this does not occur normally. We know that if they are normally present the child is intelligent; if they are deficient he is not intelligent.

I have been dealing with mentally and physically defective children from an endocrine standpoint during the past few years and have been greatly encouraged by the results. There are many other types of cases which are benefited by gland therapy. At present I have a boy of about ten or twelve years who had been treated by a number of physicians for epilepsy. What epilepsy is I do not know. I know the symptoms. On making a careful examination I also found that the fat distribution on his body would indicate that he had a hypopituitarism. The boy was more or less wrecked from the various treatments. I stopped all bromides and put him on hypopituitary treatment. He was an out-of-town patient and on the way home had a convulsion. That was six months ago, and so far he has had no more convulsions. Now during that six months the boy has changed in shape. The breasts, which were as large as any fifteen-year-old girl's, have been markedly reduced. The excessive collections of fat about the lower abdomen, pubes and hips have about disappeared. In other words, the treatment for hypopituitarism has changed this boy and during the change there have been no more epileptic convulsions.

Dr. L. R. DeBuys, New Orleans, La.—The study of the functions of the endocrine glands is extremely interesting but our information at this time is very wanting. There may be many rea-

sons for this and possibly one may be advanced that because of the complexity of the symptoms produced and the intimate relations of the glands to each other in their function a definite picture may probably be masked.

There is one thing which has occurred to me in connection with the endocrine system and it is this: that patients with endocrine disturbances as we know them at this time are usually not born with them. We may counterdistinguish them from those conditions which are present at birth and which have not been shown to be due to any endocrine etiologic factor, as for example, achondrodysplasias or Mongolian idiocy. A case of endocrine disturbance usually does not show the symptoms at birth, when he is apparently normal, but the symptoms come on later. It is possible that the fetus may be protected through the placental circulation before birth and it may be possible that during the period of lactation the child may receive some substance from the mother to protect him, as it is usually after this stage that we find these conditions developing. It is necessary, therefore, that we should be familiar with the normal growth and development of the child and it is possible that with a thorough knowledge of the normal growth and development we shall be able to recognize the abnormal. With the advance in our knowledge of the disturbances of the endocrine glands we should be able to recognize earlier the symptoms so that by the early instituting of proper treatment we may hope to prevent the tragic pictures later. To illustrate, we know in instances of the cretin, the earlier the existence of the condition is recognized the nearer the normal can we make the ultimate individual. On the other hand, if cretinism exists for a prolonged period not much can be done.

Dr. Hill has covered the symptomatology very thoroughly. We should always bear in mind with the symptoms as he has presented them the possibility of an endocrinopathy existing in the individual. We should, therefore, be careful in our clinical observations to recognize the cases early, be sure that we are right, treat them properly, then expect results. Unfortunately the results that have been recorded have not been as good as they might have been. The lateness in instituting the treatment may in a way be the cause.

In closing, however, I want to sound a definite warning in connection with the administration of things we know very little about. We should be reasonably sure of the diagnosis before introducing into any human being products of the endocrine glands.

Dr. A. A. Shawkey, Charleston, W. Va.—I want to ask one question. Dr. Barbour in his clinic the other morning spoke about the thymus as a factor in acidosis. Personally I recall one child who had a very marked ammoniacal urine from birth, which was unchanged by treatment both medicinal and dietetic. An enlarged thymus gland was found and x-ray treatments begun. The first x-ray treatment reduced the ammoniacal urine and it was further reduced by the second treatment. Notwithstanding that the man giving the x-ray treatments said the gland was not reduced by the treatments, the symptoms disappeared after the second treatment. I have never

heard this feature discussed and should like to ask the speaker to discuss it if he has had any experience with cases of ammoniacal urine apparent of thymus origin.

*Dr. P. F. Barbour, Louisville, Ky.*—The subject of endocrinology has opened up to us a greater field for our study and has taken a step further in the profound mysteries of life. Heretofore, we have traveled along the surface of things and have treated a great many diseases, which the child is subjected to, and sometimes we come to the realization that these fundamental things affect life in a way that we have not sensed. Those of us who have handled many children have many of those unfortunate diseased ones with defective mental development. We realize that we have to go beyond the order of routine of practice and treatment, when the ordinary remedies do not give us results.

The men who put endocrinology on the map, as Dr. Hill has said, perhaps were cranks, but it takes a crank sometimes to wake up the profession and make them realize that there are diseases that the profession know very little about. To say that endocrinology is a complicated subject is true. Anything that affects the foundation of life, and has to do with the deeper physiology of life must be complicated, and so endocrinology is not a simple subject and I think we have merely scratched the surface. When we learn that the pituitary glands have nine different functions, any one of which may be increased or diminished and only one of which may have its effect upon the function of other glands, you can understand at once that the subject is a very complicated one, and one that is very difficult to unravel.

Our attention should be called to the major disfunctions of these glands. I had the opportunity of showing you in the clinic, several definite cases of gland disfunction. These cases were very interesting to me because they represented several different types of trouble, but if we have to wait until we get a distinctive type of cretinism and pituitarism, we will likewise have to wait for an exact type of pneumonia or typhoid fever. We must know that the functions appear in minor or modified form, though many cases of thyroid disturbances are not true cases of cretinism. If you make the proper diagnosis, you can often secure better results by the treatment. If you take a child like the little one I exhibited, who is 14 years old, you cannot now build her into a perfectly normal child, but I think if we had had the opportunity of taking care of her early in life, and recognized this condition when she was a year or two old, we might have accomplished a great deal for her.

Dr. De Buys says these cases do not show evidence of trouble early in life. I think that this is because we have not been on the lookout for them. We are sufficiently familiar with the manifestations, and I am sure with more experience along these lines, we should be able to recognize these very early disturbances. I also think, though I cannot prove it, that many endocrine gland disturbances will be found to be among the impermissible types of disease.

*Dr. Alice Pickett, Louisville, Ky.*—You may be interested to hear of three obstinate cases of enuresis which were successfully treated with

thyroid extract at our Children's Hospital. During my service there last winter we had our usual rather large percentage of enuresis cases to deal with. They were treated along the classic lines, by the giving of atropin solution, care as to diet, the cutting off of fluids after 4 P. M., etc. Out of the number there were three that did not respond. These were cured by the administration of thyroid extract.

We attributed our success to the improvement in general nutrition, brought about by the action of the thyroid, with consequent increase in the muscular tone of bladder and sphincter. All the children were over four years of age, and in no case was the dose more than one-tenth of a grain.

*Dr. W. W. Harper, Selma, Ala.*—There are one or two points I wish to emphasize. We must recognize these cases early. I think we should carry in our minds what a normal child should do—when a child should hold up his head, when he should begin to notice things, when he should reach out for something, when he should begin to talk. When a child fails to do those things which he should do normally, we should begin to search for the cause. For instance, a child does not sit alone at six months, and was unable to hold up its head at four months. A careful examination may show other evidences of cretinism and by instituting early treatment the child develops normally.

Another thing is the difference between diseases of the cortical portion of the adrenals and the pituitary. In diseases of the cortical portion of the adrenals the child grows very rapidly and has abnormal sexual development. For instance, a boy of two years has the anatomical development of a child of five or six years, and his sexual development is that of a boy of 16, 17, or 18. He talks just as a boy passing into adolescence. If the pituitary, on the other hand, is at fault, you have a marked skeleton growth but a real atrophy or shrinking of the reproductive organs. By bearing this in mind, in many cases we shall be able to make a differential diagnosis between diseases of the adrenals and the pituitary gland.

*Dr. H. M. Austin, Laredo, Texas.*—I wish to speak of one point that Dr. Hill brought out, the use of adrenal extract in urticaria. I have used the endocrine gland extract for several years more or less empirically, but I had not read that adrenal extract would have a marked effect on urticarial conditions. I have found that to be so and also that with the addition of pituitary extract the effect was very much more marked and very much more lasting.

*Dr. Hill (closing).*—The object of this paper was not to call your attention to these things that I mentioned, but to stimulate the study of the more obscure conditions.

Dr. De Buys says he does not think these conditions are congenital. I believe they are in some instances congenital. I recall one cretin mother in our institution whose child was a typical cretin. The child was recognized at a month old. Someone suggested that we give thyroid extract to the mother. We did so with marked benefit to the child.

As to the tests that are used to find the disfunction of these glands, there are a number, some of them very accurate. You can find these in the literature on the various glands.