Review of hypothyroidism

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SENIOR THESIS

A REVIEW OF HYPOTHYROIDISM WITH
SPECIAL REFERENCE TO JUVENILE FORMS

UNIVERSITY OF NEBRASKA
COLLEGE OF MEDICINE
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The study of endocrine dysfunction is of very recent origin. The observations of Sir William Gull in 1873 and of Ord in 1877 marks the beginning of the great advancement in those conditions and train of symptoms resulting especially from the dysfunction of the thyroid. (25) Since that time much work has been done in all fields of endocrinology though there are still many questions which are unanswered. Among these are: what can be done to prevent the development of the disrupted balance of the endocrine system produced by the dysfunction of any one of the associated members; Exactly what effect does each member of this group have on the others; What effect on metabolic and other body processes does each one produce; How can we determine which one to suspect in any given situation; am what is the true cause of endocrine dysfunction and how it may be prevented.

In this paper I will endeavor to clear up a few of the questions regarding the thyroid, concerning myself with that phase of thyroid dysfunction of lessened secretion or hypothyroidism, giving special attention to this condition in children and to the best means of detection, prevention and treatment.

For my information I will rely upon those observation made by prominent medical and scientific men who have compiled a mass of material on the subject, and to a limited number of case histories taken from the dispensary.
of our own hospital.

The thyroid gland is developed from a median diverticulum from the floor of the first and second brachial arches. It grows downward and backward as a tubular duct which bifurcates and forms a series of cellular cords which produce the isthmus and lateral lobes. (The thymus bodies develop from the third and fourth brachial pouches as well as the para thyroids. The ultimo-brachial bodies develop from the fifth pharyngeal pouch.) This derivation at times results in embryological pathology in which cysts may originate from unoccluded thyro-glossal duct which is the connection of the diverticulum with the pharynx. This duct normally atrophies, its upper end being represented by the foramen cecum of the tongue, its lower by the pyramidal lobe of the thyroid gland. Normally the organ weighs near thirty gm. and is located at the front and side of the neck. I will pass over other points in anatomy for the sake of brevity. This gives us the general picture of the glandular formation of the thyroid. (#80).

We will define hypothyroidism as that condition in which the clinical and laboratory findings indicate a lowered functional development or a demonstrable absence or lack of the normal internal secretion of the thyroid gland. This may be any condition varying from extreme myxedema or cretinism to imperceptible hypothyroidism commonly seen but not recognized with graduations on the other side of the scale of hyperthyroidism to the extreme cases of exophthalmic goitre.
By myxedema we refer to hypothyroidism developing in the adult after growth has been attained while cretinism refers to hypothyroidism developing in the very young individual resulting in stunted growth with the other accompanying symptoms. (67).

Endemic goitre is merely another form of hypothyroidism based on altered secretion of colloid material which though sufficient in quantity, is sadly lacking in quality so that hypothyroidism essentially exists as far as the body metabolic processes are concerned. This type of hypothyroidism is found in those regions lacking iodine. It is thought by some to be due to a specific or toxic infection of the intestinal tract though this has never been proven. (36) Hypothyroidism may be in combination with lack of secretory power of the anterior lobe of the hypophysis or of any other member of the endocrine system so that exact diagnosis of hypothyroidism is difficult to make. Later in this paper I will try to clear up this question to some degree.

The first study of the endocrine system was that begun by the Brown-Sequard experiments and observations. Later Addison, Oliver, Abel and Opie furnished additional information on the general topic of endocrinology. Opie did his work on the pancreas, especially with reference to diabetes. McCallum and Davidson showed that the life of those with parathyroidectomy could be saved by injecting parathyroid tissue after showing removal of parathyroids to be followed by tetany and convulsions. Also they showed that removal of the
thyroid gland in dogs pronounced symptoms closely resembling myxedema. (1). Experiments tending to show thyroidectomy produced tetany and death (6) probably were due to parathyroidectomy of unintentional origin.

In 1873 Sir William Gull called the attention of the medical profession to the condition he termed "Cretinism" in children which he presented in a paper, "A Cretinoid State supervening in Adult Life in Women". (1) In this paper he also showed a hypothyroid condition in women of later years which was later called myxedema by Ord because of a deposition of a mucoid substance or mucin in the subcutaneous tissues producing a firm swelling.

Reverdin and Kocher noticed a similar condition after complete removal of the thyroid. In later work they found that this did not develop if a small portion of the thyroid gland was left.

Bramwell after his experiments and observations of patients, came to the following conclusions: 1. Myxedema patients invariably had a degenerated thyroid gland at autopsy. 2. This is the only constant lesion to be found. 3. Total extirpation produces similar results in lower animal experimentations. 4. In man, complete thyroidectomy is followed by a myxedematous state. 5. This condition is relieved by injection of thyroid substance. This work definitely connected the disease with the thyroid gland.

In 1877 Ord of England grouped these cases under the term
"Myxedema". Ord discussed the relation of hypothyroidism and associated diseases to the atrophy of the thyroid gland as shown at autopsy and to cretinism occurring in children. (31).

In 1885 Professor Kocher of Germany and Victor Horsley of England showed that myxedema is due to dysfunction of the thyroid gland. Victor Horsley suggested that by transplantation of the thyroid gland of animals into hypothyroid or myxedematous patients that a cure might be affected. This was done by Bettencourt and Serrano of Lisbon by introducing one half a sheep thyroid into the inframammary region of a woman age 36 of definite myxedema symptoms with an immediate improvement in her condition. All symptoms both mental and physical were either relieved or reduced. However the sheep glands would atrophy and treatment was only temporary. (11). In 1891 C.R. Murray of London showed that glycerine extract of the gland also produced relief if given by hypodermic.

In 1888 the Clinical Society of London reported the type signs of myxedema as described by Ord. Fenwick of England in 1892, in a clinic, cited three cases, showing two of them of hypothyroidism which had been treated by thyroid with beneficial results. He showed that injecting thyroid juice hypodermically resulted in an increased urinary output, increased activity and general improvement. He believed the juice had feeble diuretic action due to changes in the blood resulting in easier transudation or secretion from the kidney. This conclusion was founded on the increased growth of hair, increased sweat secretion and a decided improvement in the catamenial
period. He believed the congestion of the kidneys arose from pelvic congestion. (10).

Dr. Ruffer of Paris cited two cases in which myxedema was apparently cured by injection of thyroid juice at about this time. (10). Baumann first isolated what was thought to be the active principle of the thyroid gland but which later proved to be the mother substance of the true active principle. It was a complex organic colloid substance containing about 10% of iodine derived from the thyreoglobulin. He called this thyroidine or icodothyrine. When given to a patient this substance had a beneficial effect or medicinal property similar to that of the administration of the gland itself. (1).

T. R. Brown in 1906 gave a review of the literature and showed that satisfactory results might be expected from the administration of thyroid gland substance to adult or child patients. He also found that administration by mouth of dessicated dried gland was as efficacious as hypo injections of extracts. (1)

Jones in 1913 showed that KI given to a patient produced no increase in the Iodine content of the thyroid juice whereas if the dessicated dried gland was given there was a marked increase in the iodine content with a general betterment of the condition. This gives further proof that it is the complex organic secretion of the gland itself which is of benefit to the organism. Also the serum of hyperthyroid animals acted in a similar manner. (13) In 1914 Kendall isolated the active principle, thyroxin, from the thyroids of slaughtered
animals. (67).

Dr. I. G. Cobb of Middlesex Hosp., England in 1914 reported an apparent cure of a 28 year old man who had been advised to exercise. He had taken up golf and fainted on the golf links. He showed the following symptoms, a low temperature of 97, heart rate of only 44, and fainting spells. His skin was coarse and dry, he had excessive adipose depositions over the shoulders and a general run down appearance. Under gr. one four times daily of dessicated thyroid gland, improvement immediately took place and recovery seemed to be complete with ameliorations of all symptoms. The temperature became normal, skin cleared up and general appearance was better.

When the active principle or thyroxin was isolated from the thyroid glands of slaughtered animals it was found to be a white crystalline substance and biologically its action was similar to that of the glands themselves when administered. About twelve years later Dr. C. R. Harington of England synthesized this substance from coal tar products. However the process is still expensive and impractical from that standpoint.

Thyroxin is active in very minute quantity and appears to have a catalytic action on the metabolic processes of the body. Without it there is a very slow action of the chemical processes of the body with all the disastrous results shown in cretinism or myxedema. There seems to be some special connection with the metabolism of aminocacids though there is probably an involvement of all other processes either directly or indirectly.

There is some clinical evidence that calcium met-
abolism is affected by the thyroid secretion for the X-ray of
the bones of a hypothyroid patient there is a decreased,
irregular density both in children and adults. In children
slight cases can be detected by the late ossification of
the bone centers. In adults the progress of arteriosclerosis
may be arrested and blood pressure reduced by thyroid thrapy.

It is said that there is an intimate relation be-
tween the glands of internal secretion by some and denied by
others. The pancreas is inhibitory to the thyroid and adrenal
glands. The adrenals inhibit the pancreas and increase the
activity of the thyroid. The thyroid inhibits the pancreas
and stimulates the adrenals. The ovarian secretion seems to
be opposed to the thyroid secretion. (36). Therefore if one
gland is thrown out of the normal balance there may be a vicious
cycle set up which is the probable reason for the far reach-
ing effects of thyroid dysfunction. (36)

There seems to be no gland which compensates for
thyroid deficiency. The pituitary gland which acts some-
what as the thyroid gland was thought for a time to produce
a true compensation but at no time could iodine be found in
the pituitary body of any of eighteen sheep after complete
thyroidectomy whether fed iodine or not. This shows there is
no compensation from this source. (7)

Hypothyroidism may show itself in any one of several
forms. In children it exists from slight hypo to extreme
hypo or cretinism. In the adult it exists from slight hypo
with slight symptoms to the myxedematous state resulting from total absence of the thyroid and its secretion. Endemic goitre is another form marked by a hypersecretion of the colloid thyroid substance but a marked deficiency in the active principle thyroxin.

Minor thyroid insufficiency may be present from infancy to old age.

Etiology

Hypothyroidism is the result of an insufficient amount of the normal secretion of the thyroid gland or thyroxin. It may result from either a deficient quantity or quality. Of the various factors involved we find the sexes differing widely. The female is the most commonly affected, hypothyroidism being seven times more common in females than in males due to a lessened function following over action. This overactivity is present at puberty or before as well as at each menstrual period and during pregnancy. (79).

Hyperthyroidism in the mother tends to produce a hypothyroid condition in the offspring probably not as a hereditary factor directly but as a result of a decreased demand on the fetal thyroid with a resulting hypoplasia as occurs in all cases of decreased demand in other body structures. This leaves the child with a gland which is hypoactive at least for a time but which may later become normally functional and results in the child who eventually develops into a normal mental and physical being but who is much later in that development. (2).
There is some evidence to support the view that a direct hereditary factor may be present. For instance the anomalies of the thyroid gland are often accompanied by anomalies of other glands in children. (67) This of course may or may not be familiar for there is no direct evidence that familial precedence has any bearing on the condition of the child's thyroid.

Endemic goitre which is a type of thyroid dysfunction was at one time thought to be due to either an intoxication or to a toxic infection especially of the intestinal tract. (36) However it is really a hypothyroidism resulting from an absence of iodine and is a state of hypersecretion of colloid material deficient in thyroxin. It is found in the Swiss valleys and in certain areas around the great lakes. In these areas even the domestic animals are affected. There is almost a total absence of iodine in these areas. Administration of iodine in these cases often results in a hypersecretion since the thyroid gland is greatly hyperplastic and manufactures an excess of thyroxin with the presence of iodine. (36).

Another type is that resulting from surgical excision of too large a part of the thyroid gland. This happened more frequently in the earlier days of surgery of the neck when the surgeons had not learned to temper their enthusiasm for surgery with a sufficient amount of level headed reasoning. In early surgery of that time there were frequent cases of total excision with the resulting disastrous effects of cachexia.
strumiprivia or surgical cachexia. (31) At first the lack of knowledge of the cause of the results prevented the proper replacement of thyroxin by medication and much suffering followed which at present is relieved by gland therapy.

Other causes of hypothyroidism are such diseases as tuberculosis, chronic infections or general debilitating conditions. Chronic intoxication may be a contributing factor as the thyroid secretion is thought to be a detoxicating agent. The extra demand results in a gradual wearing down of the gland. In such a condition the patient may be greatly emaciated rather than of a fat flabby nature. (19).

Intestinal stasis is either an associated condition or a contributing factor. Though there is rather a constant association this symptom or cause is usually relieved after giving thyroid so that it is probably an effect and not a cause. This is a disputed question which is as yet unsettled.

Gouty rheumatism is often associated though here again we may ascribe the condition to effect rather than cause. (19)

Congenital malformation or absence at times occurs though rarely. Of these there are usually other malformations present which in most cases prevent extrauterine life of the child. At times there is a congenital absence with resulting absolute cretinism. These thyroid absences are of no known origin. (1)

There seems to be no connection of hypothyroidism with familial precedence of birth in the series of fifty-five
cases studied by Dr. M. B. Gordon in 1919. Also there was no connection with syphilis either congenital, in the mother or acquired, thought it might exacerbate the condition if hypothyroidism was already present.

The manner of feeding seemed to have no particular significance, either breast or artificial, as there was no apparent discrepancy on that score. Certainly it was not stopped or even relieved by breast feeding. (26) Infection (acute fevers) such as typhoid and scarlet fever may cause atrophy of the thyroid gland with a resulting hypothyroidism especially in children.

Symptoms

We will now consider the symptoms of the more severe types of hypothyroidism especially of those who have not attained adult life. Since the milder forms all show one or more of the symptoms either objectively or subjectively, the disease can usually be diagnosed by close clinical observation. There are additional indications of the disease which will be taken up later, as well as the more typical signs, in greater detail.

Hypothyroidism may produce any symptoms and attacks all tissue. It is the principle cause of a number of widely varying conditions and is a factor of importance in many others. The thyroid gland is called "the keystone of the endocrine arch." The endocrine system is of great importance in the control of growth and development. It is the principle factor in the regulation of metabolism and dominates the sympathetic nervous system and maintains the physical harmony of the body. The de-
creased activity of the thyroid gland may produce very bizarre results. (22) Instead of being obese like the typical myxoedema the subject of the deficiency is often very thin and even emaciated. In place of the hairlessness which is to be expected from the textbook pictures, one will not infrequently find conditions closely approaching hirsutes since there may first be a hyperactivity of the thyroid gland with its residual effects followed by a hypoactivity resulting from infection or intoxication. The normal secretion acts as a defense against toxic invasion. If the thyroid gland is depressed by severe chronic intoxication, then signs of inadequacy appear. If overcome and the original intoxication causes loss of flesh and the disease is protracted there is both emaciation and hypothyroidism. (19)

Cretinism is marked by a characteristic physical deformity more easily recognized after viewing a case than it is from description. It is due to almost total or complete absence of the thyroxin. This may be the result of atrophy, goitre or congenital absence. The disease may be sporadic or endemic in its appearance. The symptoms are a result of arrested development. The patient is of stunted growth, short and stocky with a phlegmatic appearance and a dull apathetic facial expression. There is a general coarse appearance in those of congenital type. The birth weight is likely to be above nine lbs. and the child develops slowly. Often malnutrition is present and the child loses weight from that
cause. Development of bone is greatly retarded and the ossification centers do not appear as soon as one would expect. (67)

Mental activity is very slow and talking does not begin often until the child reaches two years. At times in severe cases complete imbecility may be present. The child does not lift the head as early as it should and often attempts to walk or stand do not take place until after two years. (17) Sombulence and drowsiness with weakness and loss of memory are often present. (52) In such cases there should be Xrays taken and this will show delayed bone development before other clinical signs lead to a definite diagnosis. Often the fontanelles remain open until very late. (67)

Other clinical signs are, undersize and under weight of the child associated with a dull appearance. The lips and tongue are swollen sometimes tremendously. The child's hair is usually thin and coarse with a brittle dry feel in severe cases. The skin is dry. Usually the cases are not picked up until one to two years though a few may be recognized before six months.

If not recognized early or if the patient is not brought in early, then the symptoms may be increased markedly. The child is greatly undersize with short thick legs, prominent abdomen resulting from tympanitis. The body appears short and squat. The head is rather large and peculiarly shaped with the face puffy and large. The eyelids are swollen though the swelling is not of the pitting type. The nose is flat and the alae are thick, almost negroid in character. Dentation is
delayed and the teeth decay quickly. The skin is of a yellow waxy sallow tint. Often there is a muscular weakness. Supraclavicular fat pads are often present in all forms of hypothyroidism. (67)

Endemic goitre which is the other type of infantile hypothyroid condition, as well as adult form, must be considered as a dysfunction of quality of thyroid secretion rather than of quantity and is a result of a lack of iodine. It makes its appearance usually later and, though it may be present at birth, does not show up until after the second year. It results in very similar symptoms as those of the sporadic form of hypothyroidism with the additional evidence of goitre. In either form early suspicion of hypothyroidism should be evoked by overweight at birth and delay in development both physical and mental as measured by a general normal. An initial weight of over eight or nine lbs. is a signal for close attention. A response to a test therapy of a short rather intensive course in thyroid administration establishes a definite diagnosis. (67) A tendency to chronic infection or to frequent colds or an uncommon susceptibility to all acute infections if often indicative of hypothyroidism.

Adult hypothyroidism or myxedema is easily recognized when fully developed but it does not often occur as a typical case. Ord's description given in England is still accepted as the typical picture. There is an increased bulk of the body, a firm swelling of the skin as distinguished from the pitting edema of nephritis or cardiac disease, the skin is inelastic and closely adherent to the deeper structures, the swelling is not
effected by gravitation, and the dry rough skin with swelling obliterating all expression of the face gives a characteristic blank expression. With the swelling of the skin there is superficial pain due to edema and binding down to deeper parts. The nutrition of the hair is poor, with partial loss especially of lateral 1/3 of the eyebrows. There is a tumefaction of the skin especially in the suboclicular region, also turgescence and infiltration of the mucus membranes with involvement of the teeth in a manner comparable to that of the skin. There is a remarkable physiognomy, slow painful speech with a monotonous voice accompanied by a peculiar nasal explosion. There is a slowness of thought, speech and movement.

Mental disorders are of common occurrence and may take on a depressed phase or be of irritable and suspicious nature. The patient exhibits somnolence alternating with excitability. There may be lack of coordination associated. Low temperature at all times with an aggravation of all symptoms during cold weather is a usual finding. There is a decreased size or a total absence of the thyroid gland. There is a peculiar mental reaction in that there are alterations in temper of unexplainable origin in which the patient may become extremely angry at nothing or be placid at times. There is a curious persistence of a train of thought or actions in which the patient will continue on his own sweet way regardless of protestations or attempts at interruptions by either friends or observers.

The other adult forms of this disease are the endemic goitre which is very similar in symptoms to the above descript-
ion though usually it is of a milder form with the additional presence of a goitre, and cachexia strumpriva or operative myx-oedema which is the result of total or too complete expirpation of the thyroid gland at time of operation for exophthalmic or toxic thyroid disease.

Hutton (42) studied a series of cases in which the results tend to prove that in general there is a decrease in the percentage of polymorphonuclear leukocytes in the white blood cell count. However the total W.B.C. was slightly higher than normal with a relative and actual lymphocytosis of the small variety of lymphocytes. This may be a result of insufficient stimulation of the reticulo-endothelial system by the thyroid gland, although the true cause is not known. This peculiar reaction of the blood may account for the observations (67) made by others that there is a tendency of hypothyroid patients to show chronic infections and which are often relieved by the administration of thyroid gland even though there are only minor demonstrable clinical signs of the disease.

Diagnosis

The definite diagnosis of hypothyroidism in children is based upon a history of overweight at birth with a slightly retarded development. Often the child is known as a "good baby" (67) and does not appear as active as some, rarely cries, sleeps too much, sweats little and appears apathetic. Dentation is often retarded and the fontanells do not close as usual. The child does not attempt to raise the head as soon as usual and walking does not take place for several months.
later than usual in many cases. Often there is chronic infection present and the patient contracts every disease it is exposed to. Mental retardation is often more marked than the physical symptoms would indicate. In extreme cases even imbecility may be present. Basal metabolism is not easily obtainable and is of little value especially in children due to the impossibility of obtaining satisfactory tests. (67)

The diagnosis should be based on the clinical study of the case and even if the symptoms are few and of minor character, therapy should be instituted. If there is improvement, a definite diagnosis of hypothyroidism can be made. This can be used as a diagnostic test.

The fully developed cases are easily recognized either by seeing a case previously or from description. However, this degree of the ailment is so seldom seen that the greatest necessity is an ability to recognize the more obscure cases.

Of the diagnosis of adult form we will say little, for though there is much that can be done in this field in the matter of diagnosis and treatment, most of the things said here of the juvenile forms can be applied to the adult form. In either case a therapeutic test can well be given. A very good point is the constant complaint of coldness and of suffering from the cold especially in the winter time.

Of the list of diseases which must be considered first is nephritis which often closely resembles hypothyroidism in the type of swelling produced if judged only by inspection. However the edema of nephritis is not constant, pitting is
produced on pressure and there are no other clinical signs of hypothyroidism.

There is often a secondary nephritis associated in which case there are symptoms of both conditions. The differential diagnosis of primary nephritis and hypothyroidism are the swollen lips and eyelids with a tougher rather wooden hardness instead of the pitting soft swelling of nephritis. The skin is dry and rough and shows a discoloration with pigment changes producing a waxy yellow color which is rather characteristic. The loss of hair on the body and of the outer one-third of the eyebrows and at edge of the scalp would indicate a hypothyroid condition.

Especially in children one must look for syphilis possible more as a coexisting aggravating factor rather than as a direct cause. As a question of differential diagnosis, syphilis can easily be excluded by the usual type of laboratory tests.

Other causes of mental deficiency in children such as birth injuries must be looked into in many cases for there is usually a history of the child being delivered instrumentally or having fallen out of a chair or of some other injury. But there is no mother of any child who cannot remember one or more such injuries to her child and it is invariably brought up on any case at any time by any mother as an etiological factor in her child's condition and it must be excluded to her satisfaction. Very rarely does an injury of that type account for the condition.
Other glandular dysfunction may at times be confused with hypothyroidism. In face, with an upset of one gland others may be involved. The most common glandular dysfunction mistaken for hypothyroidism is hypopituitary condition. In this disease there is an excessive deposition of fat but it is around the middle one-third of the body in contradistinction to that of hypothyroidism which tends to deposit fat, or appears to, on the upper one-third of the body. There is a similar nephritic condition in both hypothyroidism and hypopituitary cases. In the latter it is more of a decrease in the excretion of water. This may result in an edematous condition which simulates nearer true nephritis than is prevalent in the hypothyroid cases. If the therapy of thyroid gland results in marked improvement it is of thyroid origin. If not, then hypopituitary conditions must either be proven or disproven by further study. (29)

The constant pathological findings in the hypothyroid conditions are either a congenital absence of the thyroid gland or atrophy which is either complete or very extensive. The atrophy may be the result of either an adenitis of the gland or to acute infections often of the specific types. It has been known to follow scarlet fever or typhoid as a complication. Tuberculosis may be responsible by causing an adenitis of the gland. Syphilis has been blamed by a few of the writers but most of them agree that this is merely an aggravation of a preexisting condition with the possible exception of congenital syphilis.
Chronic intoxication may produce an atrophic condition of the thyroid gland as well as debilitating conditions of chronic character. (67)

Goitre which is the other form of juvenile hypothyroidism, as well as an adult form, very seldom shows any normal glandular tissue and the acini are all tremendously distended with colloid material. This material lacks the necessary iodine and is ineffective in its action. The walls of the alveoli are thinned out so that the cells resemble more those of the endothelial lining of blood vessels or of squamous cells than the normal cells of the alveoli. There are few, if any, normal secretory cells left and there is little resemblance to normal thyroid structure.

Associated conditions.

The associated conditions are numerous and we will now take them up in a short review. This gives us some idea of the scope of the field considered and of the things to be thought of in clinical work.

The renal pathology which is almost a constant finding especially in advanced cases is a nephrosis which involves the convoluted collecting tubules with a fatty degeneration of the lining epithelium indicating a metabolic disturbance with an increase of the lipoids of the blood stream. (52). The experiments of A.L. Tatum showed a glandular degeneration of the cortical cells and a dropsical swelling of the cells in the collecting tubules. There may be albuminurea with casts and lowered function especially nocturnal enuresis. (29).
A low basal metabolic rate is found in certain cases of nephrosis especially in female adolescents which indicates hypothyroidism. The skin and hair is dry, the palms and soles are thick, rough and scaly. The urine shows albumin in most of the cases. (52)

Gouty rheumatism is often associated with the disease and indefinite pain of cutaneous character is often present. This is the result of faulty metabolism with the deposition of the offending urates and the deposition of the firm mucoid material in the tissues producing a stretching of the cutaneous tissue which has become firmly bound down by connective tissue. (19)

Hemorrhages from mucus surfaces often take place and may be the result of the chronic infection which often accompanies hypothyroidism. Dr. Hertoghe of Antwerp insists that hemorrhage is one of the most constant symptoms of hypothyroidism. (19) This may be the result of the faulty calcium metabolism which has been noted by other writers. Certain it is that the administration of thyroxin or thyroid gland improves the hemorrhage and the calcium metabolism which is also combated in modern therapeutics by administration of calcium lactate or other calcium compounds. This would bear further investigation as we know there seems to be an association of hypothyroidism and arteriosclerosis which we believe is also a result of calcium metabolism disturbances.

Menstrual disturbances are often associated with the disease and often appear in adolescence. There may be severe menorrhagia in some cases (19) which may be on a basis of
calcium metabolic disturbances. In other cases there may be a very scanty flow or it may be mostly of a mucoid nature or completely absent. It is often involved in ovarian dysfunction. Often there is impotency or loss of sexual desire associated. (25)

Many skin conditions are now thought by some to be influenced by the hypothyroid secretion. Psoriasis, purigo, eczema and herpes may be partly based on this disease as evidenced by improvement in many cases by the administration of thyroid substance or thyroxin.

In the mental cases involving dullness and lack of activity in children, improvement often follows thyroid administration. In the adult there is some connection with many cases of melancholia, neurasthenia and other forms of insanity or psychosis which may be of thyroid deficiency in origin. Migraine is usually present.

Cardiac disorders and vascular changes, as in rheumatism and chilblains, coldness of the hands and feet, seem to have a close connection to hypothyroidism and need closer study to be proven or disproven. (22)

There is evidence that hypertension and arteriosclerosis may be partially of a hypothyroid origin as in many cases administration of thyroid substance brings down the blood pressure and relieves the arteriosclerosis. (79) This may be due to faulty calcium metabolism due either directly to the lack of thyroxin or it may result indirectly due to the upset adrenal reaction as a result of hypothyroidism. Nevertheless there is a reported definite improvement in many
of these cases following thyroid therapy. However this is probably only one of the etiological factors in arteriosclerosis. However we do know there is a calcium metabolism upset present in all cases which is very likely a definite cause as the arteriosclerosis is also known to be based on a disturbed calcium metabolism. (79)

Glandular infections may result from a lack of normal thyroid secretions. Adenitis may be rather general and often results in adenoids, tonsillitis of stubborn character, chronic mastitis and prostatitis. Other chronic infections such as cystitis may be present and of a stubborn character. Often these conditions are amendable to thyroid therapy,(32) and may result from the effect of the disease on the white blood cell picture previously noted.

Prognosis in thyroid deficiency depends on early diagnosis and treatment. The treatment of hypothyroidism whether it be in adult or child, even in the most extreme cases is followed by immediate improvement. The physical disfiguration in children soon disappears and the child develops rapidly if treatment is given before complete ossification takes place. If there is complete ossification, there is no chance of further growth. However even in such cases mental and physical improvement can take place with treatment. The thing which must be done, if complete recovery of the child is to take place, is early diagnosis and treatment.
By use of the X-ray study of the skeletal system, the diagnosis can often be made before six months. Complete recovery can be expected if therapy is begun at that time. Later therapy improves the physical condition more than it does the mental though marked mental improvement does take place. This residual mental deficiency can be prevented by early treatment. The drowsiness disappears, the mind becomes clear and active. The face becomes brighter in appearance and the general mental condition improves. In the adult or myxoedematous patient, immediate improvement takes place and almost complete recovery can be expected. In the emaciated patient who is mentally dull and suffers from chronic debilitating disease, thyroid therapy produces a marked improvement. whereas the usual type of patient loses weight, this type will gain weight markedly under thyroid treatment. (19)

The noticeable physiological improvements are an increased heart rate, normal temperature, thinner and smoother skin. The hair is often regained in part and the body generally loses its grotesque appearance.

Endemic goitre patients show definite improvement with administration of thyroid gland or its extract and the symptoms disappear. At times this type of patient will be thrown over to a hyperthyroidism by an increased normal activity of the gland.

The administration of potassium iodide or of tincture of iodine in these cases is often followed by im-
provement which is probably due to the gland using this iodine in production of normal thyroxin where it had been producing a deficient quality of colloid before. At times they may even become hyperthyroid cases with this therapy.

In chronic debilitating diseases improvement often takes place with the use of iodine either as a tincture or as potassium iodide. This may in ture be due to an increased thyroid activity, with the available iodine present, to produce a greater body activity and increase resistance. Certain it is that either thyroid or iodine administration is such cases is followed by improvement. However, Jones's work tends to show that KI given to a patient produces no increased iodine content in the thyroid gland whereas if dessicated dried thyroid gland is given it will produce an increased iodine content so that the action of the KI may lay elsewhere. (13)

Treatment is at present best accomplished by administering the dessicated dried whole thyroid gland. Extracts, especially glycerine, can be used or the active principle or thyroxin may be given but in any of these preparations the dosage is somewhat hard to gauge. In general the whole gland is just as effective and is much cheaper than the special preparation.

The first attempts at treatment were by transplantation of thyroid gland. However, this foreign tissue would not grow. Later the juice of the gland was injected hypodermically. Finally they injected a glycerine extract of the gland. Each
of these methods was found effective. However it was later found that the active principle was not destroyed by the alimentary tract and that the whole gland is just as effective and much easier to use than the more costly extracts or preparations. (67).

The best treatment is to begin with small doses and gradually increase them until there are symptoms of nervousness and then drop back to a point just below that level. It is best to begin with one-half grain three times daily and increase it up to the desired effect, then drop back. In some cases it is well to give 1/4 to 1/2 grain of whole pituitary gland daily with one-half the dosage of thyroid gland. (22)

Many cases of chronic infection and of hypothyroid conditions of almost imperceptible degree are helped materially by small dosages of thyroid. Many of the dull apathetic children, or children who are slow in development are given a better chance at life with small dosages of thyroid.

The following cases illustrate the points in diagnoses and treatment given in this paper, to some degree. These cases are arranged according to age of the patients.

Case No. 1

Date 4-4-28, Goodwin, Paul, age 6 mos. M. Colored

Came in complaining of chronic cold which gets worse.

Previous history of no significance, whooping cough at age 2 mos. Was in the hospital with pneumonia, 4-4-28 to 4-15-28.
July 19, 1930, came in for chronic tonsilitis and umbilical hernia. Sleeps well and is cross. Respiration difficult.

Feb, 14, 1931, Physical examination shows diastasis recti and umbilical hernia, sluggish reflexes, enlargement of wrists and ankles, large soft abdomen, four years old but mentality low, adiposity.

Treatment, Thyroid extract, gr. 1/2 t.i.d.

Feb 21, 1931, Myxedema, hypertrophic tonsils. Improved.

Physical exam. shows a dull phlegmatic child of low mentality, short, thick makeup with large head and trunk and short extremities. Rx, thyroid as above.

July 11, 1931. Child is apathetic, listless and puggy, is back for checkup on condition. Mother states child plays alright but is quiet, is more alert since treatment.

Case No. 2


Previous illnesses, chicken pox, measles and whooping cough, is subject to otitis media, frequent colds and sore throat, pneumonia and some pain in ankles.

Physical exam. shows bad mouth and teeth.

Rx, codliver oil and milk one quart daily.

March 14, 1929, has been taking codliver oil spasmodically, sleeps abnormal amount, and does not play or talk
much. Walked more last two weeks, is not bowlegged. Has indurated area on left leg just below knee on anterolateral aspect. To use hot packs.

is apathetic and phlegmatic, has a peculiar facies, is fat and chubby. To use codliver oil.

Hair is dry, neck glands are palpable, frequently falls asleep while playing. Given thyroxin 1/2 gr. t.i.d.

March 28, 1929. Improvement is marked, plays and sits like normal. Does not talk much but sleeps less. Rx, codliver oil and thyroid gr 1/10.

Diagnosis, rickets and thyroid disfunction.

April 29, 1929. More active, plays more and sleeps less and walks more. Activities are aimless. Thyroid gr. 1/10.

Physical Exam. tonsils injected.

May 27, 1929. Improved, is bright and active, walks fine, Thyroid gr. 1/10 t.i.d.

June 27, 1929. Improved greatly. Thyroid continued.

October 24, 1929. Tonsils and teeth and adnoids in bad condition, general condition good. Advised hospitalization for cleaning up foci of infection.

November 21, 1929 Cretinism and hypothyroidism is the diagnosis. Medication for headlice and for A.U.N.J.

Ray long bones. Advice - to return in two weeks for tonsils and adnoids.

Case No. 3

2-25-29 Douglas, Melvin, age 3, M. White

Sent in by visiting nurse for Physical exam. Has
had upper respiratory infection for past week. Child is unable to walk and keeps legs crossed most of the time. Has had measles, whooping cough, chickenpox.

Physical exam. shows underdeveloped phlegmatic child.

Rx. Codliver oil and milk

Mar 14, 1929. Condition improved and is active, appetite better and legs improved.

Mar 28, 1929. Child very stuporous, weak, passes large amount of urine. Broad heavy face, body adipose. Rx Thyroid gr 1/10.

April 29, 1929. Improved. Walks better, plays, does not talk but makes sounds. Hair very dry, activities apparently aimless. Thyroid gr 1/10

May 27, 1929. Some improvement but not as bright. Sleepy and irritable. Walks allright. Given no thyroid lately.

Rx Thyroid gr 1/2.

June 27, 1929. Teeth bad, no thyroid lately.

Rx. Codliver oil


Nov 21, 1929. Cretinism and chronic hypertrophic F.A.

Case No 4.

5-29-30 McOlivier, Glen, age 3, M. White

Sat up at ten months, walked at twenty-seven months. Tongue protrudes, says a few disconnected words. One year ago put on thyroid gr II daily, increased to V-VI gr daily for
three months. Began to walk and talk better.

Present illness, scarlet fever, whooping cough, no other diseases. Mother and father living and well.


June 4, 1930. Imbecility mongolian type. Cretinoid, poly gland therapy to be tried after thyroid tolerance is determined.

June 5, Increase thyroid to Gr I t.i.d.

June 12. Thyroid gr I, one day, 2 gr. next.

Oct, 10, 1930 Home untidy, good location.

Jan 8, 1931 Slow and backward in every way, talking, and understanding. Mother wants therapy started again.

Rx Thyroid Gr I daily.


May 21, 1931. Continue gr I thyroid ext. daily.

Case No 5

8-11-26 Hucker, Gertrude, age 7, F. Col.

Came in for tonsils and adnoids.

Sept 5, 1931 Physical exam, palpable thyroid, signs of toxemia not noticeable, slight tremor. Is sleepy all the time.

Recommendation, Lugols sol gtts v q day in milk.

Oct. 3, 1931. Patient drowsy, stupor and slowness both mentally and physically. Grades in school fair. Knee-
jerk O.K. Reflexes O.K. Thyroid much enlarged and patient has not had any menses. Heart has no murmurs, but marked erythema.

October 24, 1931. Complains of tiredness, nervousness, enlargement of neck. Shows course tremor of finger, not abnormal, excessive sweating of hands and feet, pulse 88, bilateral enlargement of thyroid gland not nodular.

Diagnosis. Physical enlargement of thyroid.

Opinion, physical enlargement of thyroid near time of puberty.

Rx Lugol gtts V q day.

Case No 6

3-10-28 Duncan, Mary, age 7, F. W.

Sent in by outcall student for general physical exam. Brother 6, has T.B. Has had flu pertussis, measles, colds and sore throat, otitis media as baby. Heart 50½, T 99° weight 54½ lbs. Mother, father, brother and sister T.B. suspect.

Mar 17, positive V. or Pirquet, H. 50½, weight 53½ T. 98.6.

Rx, fresh air and good food, codliver oil

April 5, 1928. Been having cold, appetite only fair. Marks on arm, bedbug bites.

April 21, 1928, Better appetite, one pound gain. Physical exam. negative.

Rx Codliver oil and rest.
May 26, 1928, appetite good, perspires in afternoon, sleeps well, no gain in weight. Breathing - uses acc. muscles. No rales heard.

Rx Cake of yeast daily.

5-29-28, Tele. report to V.N.A.

8-20-28 Father non-cooperative and will not let patient be brought back to dispensary. Mother does all she can.


1-12-29. Patient comes in for exam. of eye and T.B. suspect. Has slight tremor. Referred to eye and hospital for observation. Has some enlargement of thyroid and prominent eyes.

3-10-29 Enlarged tonsils, injected pillars.

3-14-29. Xray demonstrates old T.B. infection.

3-16-29 B.M.H. plus 17, plus 7, adenoid and tonsillectomy and lugols t.i.d. gtts V


6-20-29 Sits quietly and not irritable.

8-10-29 Feels fine, very active. Takes nap every other day. P. 116. Eyes little less prominent, heart fast rate, no irregularities, no murmurs.
Case No. 7

3-14-29  Jones, Hazel, Age 12, F.W.

Diphtheria eight years ago. Has had frequent colds and sore throat. Has had measles, whooping cough, chickenpox, M.F. and sister, L.&.W.

Physical exam shows badly injected tonsils, enlarged cervical gland. Tonsils and adenoids removed Mar, 1929

4-16-30 Patient sleeps lots, is 5 ft 2½ in, wg 135#. Inactive. Instructed as to diet.

4-26-30 Wg 133½. Still on diet. Give B.M.R.

5-3-30 Wt. 131 3/4 B.M.R. 8% Height 63 in.

5-17-30 Wg 131½, diag. Hypothyroidism with association c. puberty. Urinalysis is negative.

6-14-30 Wg 132½. Menses began last month. Mentally sluggish.

7-14-30 wt. 135. Menses regular. Mental condition unchanged.

Rx. Thyroid gr V, one daily.

7-21-30 As above. Not taken regular. No mental change.

7-28-30 Not sleeping so much, more ambitious. Thyroid Gr V, daily.

8-4-30 Headache, wg 130, take gr V thyroid q other day.

8-11-30 Sleepy, wg 129, take gr V thyroid every day.

Continued Sept 27, when tonsils and ad. removed.

Jan 13, 1931 Regurn to thyroid gr V, discontinued last month. Sluggish and sleepy.
Jan 20, 1931 Restless and frighted, Thy gr II

May 9, 1931 Thyroid gr 1, sleeps well, no palpitation, perspires freely, pulse 96. Has fungus infection between fingers and toes Rx tr. $\text{I}_2$ Iodine

Conclusions

1. There may be any degree of hypothyroidism from absolute cretinism in children to a very imperceptible degree, or from myxoedema in the adult to a very slight hypothyroidism. The degree of dysfunction can be determined by the clinical study of the case.

2. Early diagnosis and treatment is of great importance, especially in children, to save life and to prevent a great economic loss to the individual and to society as well as to prevent suffering.

3. Mental and physical development depends on a sufficient quantity of normal thyroid secretion. If it is not present, it must be supplied. The mentally or physically retarded child who was overweight at birth, who appears apathetic or dull should make one suspect hypothyroidism.

4. Early diagnosis depends on careful clinical study and X-ray examinations of the skeletal structures.

5. Many other conditions, such as depend on sluggish body reactions thought apparently remote from hypothyroidism, may be materially helped by thyroid therapy. For instance, skin diseases, chronic infections, etc. often are amendable by thyroid therapy.

6. There is much correlation in the study of the endocrine system and the effects of the individual glands on each other and
on the body in general yet to be done. Many diseases of a functional character may be based on an upset in one or more members of the endocrine system.
A. G. D.

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