THE DUCTLESS GLANDS AS THEY APPERTAIN TO EYE DISEASES AND TO SURGERY

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Any one associated with a medical organization that has much to do with people who have endocrine disturbances will be impressed by the large number of such individuals who present ocular changes. In the study of these cases it becomes of increasing interest to find that these pathologic changes in the eyes not only can but must be due to the deficiencies of the internal secreting glands.

In only a few cases is it possible to identify one gland as responsible for the ocular condition, for usually more than one is causing trouble. Until better methods of study of the endocrine glands are introduced, and better surgical operations are performed on those which are at fault, disorders of the thyroid and of the pituitary will continue to be considered as the principal causes of diseases of the eye which are amenable to surgery.

In this connection, I wish to record the recent work of Dr. G. W. Crile on the suprarenals. There is a group of cases, the symptoms of which simulate those of hyperthyroidism, in which the condition is frequently called neurasthenia or neurocirculatory asthenia. In these cases the eyes may present all the changes that are associated with hyperthyroidism except exophthalmos. Such cases appear to be benefited by the denervation of the suprarenals. (As a matter of interest, it may be mentioned that studies of the ocular tension in these cases have not as yet revealed any constant rise or fall in intraocular tension.) These cases must be followed further for we have seen but sixty of them and until we know more about them, a definite report cannot be made. Nevertheless as the result of a careful review of these sixty cases, Dr. J. Lehman reports that the best results were obtained in those in which the symptoms of hyperthyroidism were very closely simulated. These patients have a rapid pulse, widening of the palpebral fissures with no exophthalmos, some weakness of accommodation convergence, tremor on closing the eyes, and no difficulty of eversion of the lids. They do tend to have larger pupils, but no true exophthalmos has been seen. The eye signs all disappear after the suprarenals have been denervated. It must be realized that these patients would not be benefited by a thyroidectomy; as a matter of fact, I believe that it is in such cases that postoperative hypothyroidism develops with the progressive exophthalmos which all too frequently accompanies this condition.

Everyone has had experience with cases in which diseases of the eyes have been associated with thyroid disturbance and with the effects of thyroid surgery. The following statements regarding this relation are based on my personal records of approximately 1,500 cases of diseases of the thyroid gland, in 1,000 of which the condition of hyperthyroidism was present when the patient was first examined by me. I do not present this, however, as an isolated report of such observations for there have been many well presented reports of such cases. Those of Dr. Holloway and Dr. Murray, of Minnesota, are excellent examples of the large numbers of these cases which exist throughout the country. The literature presents many case reports, most of them, however, made by surgeons few of whom record the eye signs accurately. Unless actual measurements are made, the eye changes cannot be correctly interpreted. Photographs are extremely misleading.

Before beginning a discussion of the diseases of the thyroid gland that are associated with eye changes, it is necessary to identify the clinical group of diseases of the thyroid which I use here. I consider only cases of hyperthyroidism with or without adenomatous changes, for thyroid disease without toxicity as a rule does not produce eye changes.

In this group of cases, retraction of the upper lid is an earlier sign of eye change than is exophthalmos and is present in a higher percentage of cases than exophthalmos. It is frequently unilateral and frequently unequal. The wide retraction of the upper lid is associated with some orbicularis tension which offsets it. This first and most common eye sign accounts for many of the other eye signs — the staring, the difficulty of eversion, the infrequency of winking, the tremor on closing. Secondarily it accounts for the photophobia, because of the complete uncovering of the pupil and the iris; the excessive tears due to exposure, and the associated conjunctivitis catarrhalis thyroiditis. This is the type of case in which a corneal ulcer may develop. Retraction of the upper lid is the eye condition most helped by thyroidectomy — the wide retraction of the lids is almost immediately benefited and with it the appearance of the patient.

Patients belonging to this group of cases with wide retraction of the lids are frequently photographed before and after operation to show the end-results of thyroidectomy in its effect on exophthalmos. However, in but few cases are any actual measurements given.

Widening of the palpebral fissure is an entirely separate eye sign which occurs frequently unaccompanied by exophthalmos. It is

greater, however, when it is associated with protrusion of the eyes. Exophthalmos also occurs separately with little or no widening of the fissures and in some cases with extreme palpebral spasm on one side, while the other fissure may be narrowed in spite of the presence of definite exophthalmos.

Exophthalmos is present only in cases of hyperthyroidism. If there is no toxicity, there is no protrusion of the eye. We have never had a case of unilateral exophthalmos in a case of hyperthyroidism; all cases of unilateral exophthalmos have been cases of pseudo-exophthalmos due to unequal or unilateral retraction of the lid. In a series of 100 cases exophthalmos developed following thyroidectomy and in one of these cases extreme unilateral exophthalmos was present for a period of three months accompanied by severe hypothyroidism. In another case of postoperative unilateral exophthalmos a large mucocele was found to be present on roentgen examination.

Thyroid surgery has been found to be of great benefit in cases of exophthalmos. The progress of the protrusion is halted; ulcers are healed, and other eye signs due to exophthalmos show improvement. The average amount of decrease of protrusion is between 2 and 3 mm., the amount of protrusion varying slightly in the two eyes — rarely over 2 mm. The degree of protrusion is no indication of the degree of toxicity present and may be as great as 19 mm. over the high normal of 20 mm. which we have established for our series after measuring the protrusion of 1,000 normal eyes. Anterior luxation does not occur when the disease is diagnosed early enough and treated surgically. It may be necessary to operate earlier in the presence of cardiac complication or even in severe disturbances of the nervous system.

That group of cases which is extremely annoying to the surgeon and the ophthalmologist is that in which exophthalmos develops postoperatively. Fortunately, there are not many of these; but, since the exophthalmos progresses slowly, there is a tendency to consider the condition as a recurrence of hyperthyroidism and to perform a second operation whereas these patients already have a deficient thyroid secretion. These are cases of transitory hypothyroidism and they present several other features, such as progressive lowering of the basal metabolic rate, and edema as seen in the case of myxedema (upper and lower lids); no widening of the lids is present except that which is due to the exophthalmos. These patients do not stare; there is no difficulty of eversion; but there is a great deal of weakness of accommodation convergence. Active treat-

ment with thyroid extract offers these patients the greatest relief. In our series the group in which exophthalmos developed postoperatively did not have severe eye signs before operation in the form of exophthalmos due to hyperthyroidism but rather in that form which is noted in association with suprarenal dysfunction or polyglandular disturbance. From my observation, this type of patient does not have an extremely high metabolic rate or a very rapid pulse rate but may present all the other signs of hyperthyroidism.

Disturbances in muscle balance and isolated muscle palsies are common in cases of hyperthyroidism, but whether or not these conditions are due to exophthalmos is a question. There are numerous cases of isolated paralysis, such as that of the external rectus muscles and most frequently the right external rectus. The superior recti, especially the right superior rectus, are most frequently involved. The muscle changes do not clear up to any great extent after operation and may require further operative treatment later on. In six cases in which a squint operation had been performed, after a long period of time the eyes were found to be in maximum divergence or convergence, the opposite of the condition for which operation had been performed.

Weakness of accommodation convergence is the most common muscle disturbance and persists postoperatively, frequently delaying the return of the patient to normal and preventing his assuming his previous occupation. Muscle exercises and prisms for close work are sometimes of some benefit for this condition.

In our series of cases of hyperthyroidism there were eleven cases of increased intra-ocular tension, in none of which were any fundus changes of glaucoma present and in none of which were there any field changes or loss of vision. All but one of these patients returned to normal immediately after operation. This one case was that of a woman with myopia with a persistent tension in excess of 30 (Schioetz). The condition was controlled by the use of physostigmine. In all of these cases a great degree of protrusion was present with severe toxicity; all the patient had severe headaches, which also disappeared postoperatively.

In an ever enlarging group of cases of weakness of accommodation convergence, rapid fatigue, increase in body weight and all other symptoms usually associated with a mild postepidemic encephalitis, a low basal metabolism is found ranging from minus 10 to minus 40. These individuals all are benefited by the administration of thyroid extract replacing the nux vomica and other stimulat-

ing tonics that were formerly used. Disturbances of the eye muscles are commonly associated with general disability, and the possibility that hypo-endocrinism with poor muscle balance is present must always be considered.

With the ever increasing number of thyroidectomies and also the number of severe cases in which surgery is always hazardous though necessary, there may be an involvement of the parathyroid glands — either by their accidental removal or by their involvement in the post-operative scar, or perhaps by the temporary cutting off of their blood supply. There is undoubtedly a group of cases in which tetany is present before operation — those cases in which the patient complains of transitory blurring of vision, or spasm of the ciliary muscle. A large percentage of these patients have refractive errors that have varied several diopters even after a recent examination. Our records show that in over 60 per cent of thyroid cases refractive errors were present for which new glasses had been prescribed three months prior to the necessary surgical operation.

Although routine examination in the following group of cases did not reveal preoperative changes in the lens, postoperatively eye changes occurred as follows: sudden and spasmodic blurring of vision, becoming more frequent in association with some photophobia and then occurring for longer periods and, in some instances, soon accompanied by a haziness of vision. Examination at this time revealed a deposit along the posterior cortex which was granular to flaky in character. This condition progressed and appeared to form spicule-like changes, all posterior, in part as if the lens were thrown in folds. The spasms were of longer duration and lasted from a few minutes to three or four hours. In cases of this type, changes in the lens may progress rapidly to the formation of a complete cataract in one month or they may slowly progress over a period of several years. In all our cases, surgery had to be instituted because the condition was bilateral and because it was necessary in order to save the patient's vision. These patients had low blood content of calcium and an increase of phosphorus, and other signs of parathyroid disturbance.

Just a word of warning in regard to eye surgery in these cases — the condition of the patient must be known before any operation is undertaken. The calcium report should be in the surgeon's hand before he operates; otherwise, he will have to contend with the most severe convulsive type of vomiting. This condition may be controlled by the administration of intravenous injections of 10 cc. of calcium chloride in 5 per cent solution, some sodium chloride

being used before and after the administration of the calcium chloride to make sure that it flows easily and that it is washed in afterward. Dr. McCullagh, who has had these patients under observation, states that his best results have been obtained by the administration of two heaping teaspoonfuls of calcium lactate as often as every two hours, the dose being decreased as the blood calcium increased. He has found it unnecessary to use any other forms of calcium.

With this knowledge of the patient's condition, the surgical risk of thyroidectomy in these is the same as in other cases. In our own series of nine operations, good results were secured in seven; in two, good visual results were obtained in spite of iris prolapse. In both of these cases, severe vomiting occurred shortly after operation. All our patients were women under 50 years of age except two, one of whom was 52, the other 60. In all the cases in which cataracts formed, the condition developed directly after thyroidectomy. The question arises whether the cataracts are due to spasm or to low calcium content. These patients must be kept under medical observation and an attempt must be made to transplant parathyroids, although to date in cases in which this procedure has been attempted satisfactory results have not been secured. In 150 cases of deficient parathyroid secretion, cataract has been present in 10 cases, or 7 per cent.

Eye disorders are probably an involvement of disturbances of the pituitary gland as often as of disturbances of the thyroid gland, but on account of the inaccessability of the former the lack of proper methods of examination makes it difficult to find out whether this gland is responsible for the eye condition.

In a group of children with progressive myopia but otherwise normal, we found a very low dextrose tolerance curve and a low basal metabolic rate. We do not believe that enough time has elapsed for a complete report to be made of these cases. There is some constant factor in the production of the high degree of myopia and of hyperopia of the corneal disturbances, which range from high astigmatism to irregularities and keratoconus. These cases belong in the hypopolyglandular group. We have found two cases that were exceptions to this rule — both in women. In one, marked corneal irregularity was present. This patient had suffered from severe hyperthyroidism; her basal metabolic rate had fallen from plus 86 to minus 40. This condition was associated with a general glandular dysfunction. The other patient, in whom marked keratoconus was present, was in the hyperglandular state although she did not present a typical case of hyperthyroidism.

In a family of five boys, whose father and mother were second cousins, four of these boys (ages varying from 5 to 11 years) were blind. They were affected by hypopituitarism. In two of these cases the low basal metabolic rate indicated the presence of hypothyroidism. The blindness was due to a granule-like pigmentary degeneration of the retina (not a retinitis pigmentosa type). In two other cases, in both of which pituitary disturbances were noted, similar granular degeneration was present. These changes were more marked well out in the periphery.

The difficulty in the study of the endocrine glands has been the lack of accurate measurements, the passive interest of the general practitioner and the too aggressive interest of the endocrinologist.

Conclusions

The following facts are noteworthy:

1. Frequently it is found that patients who are examined for glasses have a muscle imbalance which may be due to hypothyroidism or other glandular dysfunction.

2. Hyperthyroidism produces definite eye changes, which in most cases are benefited by surgery; namely, wide fissures, ulcers and exophthalmos. Associated muscle changes are little benefited by any treatment, medical or surgical.

3. In parathyroid tetany, lens changes are sometimes present, probably the result of a combination of spasm with a deficiency of calcium and an increase in phosphorus.

4. Dysfunction of the pituitary gland is a causative factor in certain retinal disturbances and is an associated factor in other eye changes probably of polyglandular origin.

5. The recent work of Dr. Crile also brings out a group of cases in which suprarenal dysfunction is associated with eye changes.