

EXOPHTHALMOS*

A. D. RUEDEMANN, M. D.

BILATERAL EXOPHTHALMOS IN ADULTS

Bilateral exophthalmos occurs more commonly in adults than in children, offers more difficulty in diagnosis, and, as a rule, is not as easy to treat. Blood disturbances such as spontaneous leukemic and traumatic hemorrhages cause some cases, and a rare type of glandular and blood disease known as Mikulicz's disease, as well as other types of leukemia, may be responsible for other cases. The exophthalmos associated with trichinosis, allergy, and serous tenonitis is mainly due to edema while in hyperthyroidism, malignant exophthalmos, hypothyroidism, and hypertension the proptosis is caused by edema, but the tissue finally becomes fibrotic and solid. Cerebral aneurysms may produce bilateral exophthalmos, as may cavernous sinus thrombosis or lateral sinus thrombosis. Paget's disease and acromegaly cause deformities in the skull which produce exophthalmos analogous to that seen in tower skull and hydrocephalus in children. However, in neither of these diseases is exophthalmos a prominent or important sign. Exophthalmos may result from muscular relaxation due to external ophthalmoplegia, but this is rare.

The most common cause of bilateral exophthalmos in adults, as well as in children, is disease of the thyroid gland. Hyperthyroidism or toxic goiter is a common, devastating, general disease which seriously affects the eyes and is often injudiciously treated by surgeons and oculists alike.

HEMORRHAGE

The conditions that cause hemorrhage producing exophthalmos in children will do the same in adults, and in the latter, arteriosclerosis is responsible for an occasional case of this type. The incidence of exophthalmos from hemorrhage is greater in adults than in children, where in cases of scurvy, hemorrhage may occur.

Spontaneous hemorrhage: Spontaneous hemorrhage in an adult does occur, although it is extremely rare. It usually produces a unilateral exophthalmos, but cases have been reported in which it was bilateral. I have seen one patient who had orbital hemorrhages which produced unequal exophthalmos due to severe and fatal myelogenous leukemia.

Hemorrhage from trauma: Bilateral hemorrhages due to trauma are more commonly due to automobile accidents. However, in several patients who had been "slugged" by hold-up men, there was mild

*This is the second of four papers on exophthalmos and protrusion of the eyeball. The remaining papers will appear in subsequent issues of the Quarterly.

exophthalmos from orbital hemorrhages. These patients may also have bleeding from the nose and ears.

Hemorrhage due to asphyxia: Asphyxia produces hemorrhages in the orbit due to compression of the chest; retinal hemorrhages may also be present. In patients with asphyxia following the Cleveland Clinic disaster, the lids had an edematous, boggy appearance, and exophthalmos, evidently secondary to the venous stasis and tissue edema, was present in many instances.

Scurvy: Scurvy may produce orbital hemorrhage with exophthalmos in adults, although in all the literature only one reference is made to this and then only one eye was affected.

INCREASE IN ORBITAL TISSUE

Leukemia, Mikulicz's disease, lymphoma, lymphoblastoma: A syndrome including enlargement of the lachrymal, salivary, and buccal glands was first described by Mikulicz in 1892. Many reports of the condition have appeared in the literature since that time, and individual instances of the disease present wide variations.

Howard suggests the following classification of the disease: (1) the syndrome as described by Mikulicz, accompanied by no alteration in blood or enlargement of lymphatic glands; (2) Mikulicz's disease, plus enlargement of the lymphatic glands, but with no increase in the number of leukocytes; and (3) the same clinical picture due to leukemia *per se*.

Owen and Hennessey reported a case in which there was tremendous enlargement of the lachrymal glands. Removal of some of the tissue revealed a dense mass of lymphoid cells embedded in a fine stroma; no eosinophils or giant cells were present.

Exophthalmos is one of the signs of this disease, being due to invasion of the lachrymal tissue by the lymphomatous mass. The protrusion is down and in and is not great, whereas the lid involvement may be of extreme degree, and the patient may have difficulty in opening the lids. Removal of some of the tumor mass may be advisable, but roentgenotherapy has been so beneficial in two patients I have seen recently that I feel this treatment deserves a trial before operation is undertaken.

The first patient, an elderly woman, had enlargement of one lachrymal gland with little exophthalmos, but considerable diplopia. The parotid and salivary glands were also enlarged. The other patient, a man, had swelling of both lachrymal glands, both parotid glands, and both salivary glands. In this instance, too, the exophthalmos was not great, only 3 to 4 mm. The blood picture revealed an increase in the lymphocytes. Following the roentgenotherapy, the exophthalmos decreased in both patients.

In the other forms of leukemia, the solution of the problem often

EXOPHTHALMOS

depends upon the type of cell involved in the process. My personal experience has been with two cases in which the clinical diagnosis was chronic lymphoma involving the orbits, usually the anterior portion, and producing more lateral displacement than exophthalmos. One patient died with a large tumorous mass of the brain and the other from a growth which eventually was diagnosed as lymphosarcoma or questionable hypernephroma.

Martin Cohen reports a case of lymphoma and Algernon Reese a case of leukemia in which exophthalmos was the primary sign of the disease, and the blood findings and biopsy substantiated the diagnosis.

The blood picture need not be positive for a diagnosis of leukemia to be made because the tissue is all that is necessary to classify the growth as of leukemic origin. However, from my own experience and a careful review of the literature on the points of differentiation in this disease, it is my opinion that the condition should be diagnosed as to gross type and that general treatment with roentgen irradiation should be attempted in an effort to reduce the size of the masses. It usually is possible to find some lymph glands, either in the groin or axilla, that are invaded, and the questionable blood findings do not alter the indications for irradiation or even the prognosis in most instances.

The protrusion of the eyes is not great and usually is not straight forward. No diagnostic value can be attached to this, however, as each patient presents an individual problem.

Bilateral tumor masses: Bilateral tumors are extremely rare and usually are of unequal size. One patient, whose course was rapidly fatal, had a chondrosarcoma of the sphenoidal sinuses; this rapidly invaded both orbits from the apex. Roentgen examination revealed the destruction of the bone and examination of the nasopharynx showed invasion of the posterior nasal fossa.

Malignant neoplasms may invade the orbit at the apex, posteriorly or mesially, or from below. Our experience has been that most invading growths from the antrum are carcinomas, whereas sarcomas may extend from the sphenoidal, ethmoidal, or frontal areas.

A diagnosis of exophthalmos due to growths of this type is not easy to establish, although by exclusion and careful examination of the nose and throat, one usually can find a clue in the sinus area somewhere.

EXOPHTHALMOS DUE TO EDEMA, VENOUS STASIS, ETC.

In this group of conditions, the exophthalmos is brought about by edema of the tissue due to venous stasis or other local conditions.

Trichinosis: Exophthalmos due to trichinosis is infrequently reported and quite commonly overlooked in making a diagnosis. I have seen two patients with trichinosis in whom the local picture was a fluid

edema with mild exophthalmos and much edema of the lid, and I missed the diagnosis in both instances.

The eye signs precede the general symptoms but do not last so long, whereas the systemic signs are slow in onset and may persist an exceedingly long time. In addition to edema of the lids, there may be some pain in the orbit and slight immobility. Otherwise, the examination of the eyes reveals nothing abnormal. However, the blood picture with the very high eosinophil count, sometimes as high as 65 per cent, with gradual recession and the muscular pain are typical of the disease.

The larval invasion, at the end of three or four days, produces generalized muscular pain, soreness, fever, headache, and orbital edema. The disease can be confused with sinus disease, typhoid fever, influenza, and some other general systemic diseases.

The history may give valuable information as to the time of ingestion of the pork. Equally important, however, is the type of pork eaten as well as the place of purchase. Pork sausage (bologna type) and barbecued pork, and the pork used in chop suey houses are the chief offenders. At present, pork is inspected externally only and no microscopic study is made. Trichinosis is widespread in the pig, and man, as a secondary host, is more commonly infested than would be expected from the number of cases reported in the literature.

In early exophthalmos when edema of the lids, malaise, and leukocytosis, especially with a marked increase in eosinophils are present, the diagnosis of trichinosis should be suspected. A microscopic section which reveals the parasites establishes the diagnosis. These worms become encysted and live for a considerable period of time, and the host may be aware of their presence only because of excessive fatigue.

Treatment of this disease is unsatisfactory from a medical point of view. No known treatment has proved consistently efficacious.

Tenonitis: Tenonitis, either serous or purulent, produces exophthalmos in adults similar to that described under the same heading in children.

Serous tenonitis is fairly unusual; however, its occurrence is sufficiently frequent to warrant attention. Slight exophthalmos, which is usually unilateral, associated with a straw-colored edema of the conjunctiva and pain on movement of the eyes, and severe headaches are the common signs. Increase in the number of white blood cells and moderate increase in temperature are additional findings of significance. The second eye is affected usually within three or four days after the symptoms appear in the first.

The use of diathermy, hot packs, and salicylates are efficacious in treatment. The patients recover fairly rapidly but remissions are not unusual.

EXOPHTHALMOS

Exophthalmos due to purulent tenonitis usually is unilateral and is characterized by severe pain, inflammation, and leukocytosis, which may be followed by protrusion of the globe, loss of the sight or loss of the eye, and eventually, meningitis and death. This is a serious condition and warrants immediate care and constant observation.

Cavernous sinus thrombosis and stasis: Cavernous sinus thrombosis is usually a fatal disease which should not be confused with other conditions around the eyes. In spite of its severity and relative frequency, a diagnosis is not made in many cases almost to the time of the patient's death.

Severe fever and cerebral symptoms, varying from delirium to dementia, are common signs. Venous engorgement, conjunctival edema, heavy lids, proptosis, and intra-ocular lesions are all present in a well advanced case. The history is important, and a boil on the nose, a sty, or a minute skin infection may precede the later complications. Although generally unilateral, it is not unusual for the disease to involve the sinus and orbit on the opposite side shortly before the patient's death.

An excellent book by Turner and Reynolds covers the subject fully and points out the venous channels which the infection follows. There are no criteria for predicting which patient with a minor infection may be afflicted with this complication, and our present knowledge is not sufficient to prognosticate the course of the infection. The advice is needless that all infections of the face which involve the upper lip, nose, and eyes should be carefully watched and treated to prevent extension of the inflammation. The patient should be at complete rest, and general measures in addition to magnesium sulphate dressings should be instituted early.

A number of cases of so-called cavernous sinus stasis have been reported in the literature and I have observed one personally. Transitory edema of the orbit with irregular exophthalmos was present for which no cause could be found. Dr. John Phillips, after numerous observations, concluded that some obstruction of the cavernous sinuses was present. The edema of the disc was severe, as was the vascular stasis. The patient was followed for several years, but eventually could not be traced.

Unilateral exophthalmos has been noted when brain tumors had compressed the sinuses. A severe progressive disease of the orbits associated with fever, headache, pain, and transitory delirium should arouse suspicion of some complications in the cavernous sinus.

Hyperthyroidism: Toxic goiter was first described by Parry in 1825, and later by Graves who listed three cardinal signs—tremor, tachycardia, and exophthalmos. Since that time, other symptoms and

signs have been added such as the increased basal metabolic rate, loss of weight, excessive flushing of the skin, irritability, perspiration of the hands and feet, and nervousness which progresses at times to psychosis and dementia. This is a serious disease and exophthalmos is one of the serious and difficult problems it presents.

Widening of the palpebral fissures is observed more frequently than exophthalmos and usually precedes the latter by at least a month. Widening of the fissures is not a constant accompaniment of exophthalmos, but, when present, may be unequal and unilateral. It is caused by a spasm of the levator palpebrae. A spasm of the orbicularis oculi sometimes offsets to a slight extent the palpebral widening, but this occurs only rarely.

The orbital fissure is usually 9 mm. wide, but measurements as high as 22 mm. have been recorded without proptosis of the eye, and greater widening has been observed in conjunction with exophthalmos. Widening of the fissures is the disorder of the eye most commonly seen in photographs of patients with thyroid disease. In this type of case, brilliant surgical results are achieved and the condition is most distressing if not relieved by operation, since it persists to haunt the patient cosmetically by virtue of his friends' lamentations and his own persistent lachrymation.

A unilateral retraction frequently is responsible for the mistaken diagnosis of unilateral exophthalmos, as well as that of unilateral ptosis, whereas the actual picture is usually a normal anterioposterior position with retraction of the lid on one side and with a partially successful attempt of the orbicularis to overcome the levator spasm on the other side.

The widening of the fissures bears no relationship to the severity of the hyperthyroidism and is a common finding in neurocirculatory asthenia and in cases of paralysis of the superior rectus muscle in which the levator attempts to compensate. When the widening is extreme, the eyeball must be protected, as the cornea dries at night. Lid sutures usually are unsuccessful, especially in conjunction with exophthalmos, although it is sometimes possible to bring the lower lid up (Frost's method), using a collodium skin dressing to help support the skin of the face.

Widening of the fissures is not present in all cases of hyperthyroidism, but it is a frequent and early sign and probably accounts for the following accompanying ocular signs and symptoms.

a. Lid lag which is due to poor coördination between the levator and other muscles of the eye, especially the inferior rectus. A persistent, wide fissure may require operation on the lids, and, of the three procedures advised, tarsorrhaphy is preferable. This yields satisfactory

EXOPHTHALMOS

results, is not difficult to perform, and does not require hospitalization or closing of the eyes.

b. Photophobia is a secondary feature due to exposure keratitis and total exposure of the entire cornea and pupil to light. The levator spasm does not allow the lids to relax, even in the brightest light. Patients so afflicted should wear tinted lenses when they are in the sunlight.

Exophthalmos, originally listed as one of the triad of symptoms in Graves' disease, is not present in every case of toxic goiter, but is observed in the majority of cases. It is not present in cases of large colloid goiter unless some toxicity is present, nor can it be found in patients with thyroiditis, simple adenoma, or carcinoma. When it is present in these types of thyroid disease, there is always evidence of hyperthyroidism. The size of the gland is not indicative of its toxicity, nor is the exophthalmos a sign of the severity of the disease.

Every instance of exophthalmos in hyperthyroidism in my series of over 5,000 cases was bilateral. Using 20 mm. as a high normal value, unilateral proptosis was not evident in a single case. The protrusion may be unequal, but in only a few instances was there more than 3 mm. difference, and in only two cases did the difference in measurements amount to more than 5 mm. The degree of protrusion varies tremendously and may result in anterior luxation of the globe with blindness and, frequently, death. However, extensive protrusion is not always the cause of anterior luxation. There is a decided tendency of some eyes to luxate early, and it must be attributed to a weak anterior fascia and a marked spasm of the levator palpebrae plus the rapid development of edema. These patients, in whom the condition progresses rapidly to luxation, are usually of advanced age—almost always more than fifty years of age. Frequently there is an associated severe cardiac condition (myocardial degeneration) or dementia, or both. Luxation as a rule is followed by death.

The duration of the exophthalmos before operation prognosticates the amount of recession to be expected after removal of the thyroid gland. Definite promises should not be made, however, for in my series, the average recession after operation was only 2 mm. In early cases, the recession is more marked, but in advanced cases there is little if any return toward normal.

In every case of exophthalmos due to thyroid disease, careful measurements should be recorded and, if the condition is progressive, the patient should be subjected to thyroidectomy. Of the three types of treatment, medical, surgical, and irradiation, operation performed early in the course of the disease offers the best results so far as the exophthalmos is concerned.

Exophthalmos which makes its initial appearance following operations on the thyroid gland and exophthalmos which progresses after operation are extremely distressing complications and are caused by several factors. In the first place, the so-called recurring hyperthyroidism may be due to retention of too much glandular tissue and this requires further removal. However, the eyes should be observed carefully, for the condition may be the result of acute hypometabolism with rapid edema simulating the exophthalmos of hyperthyroidism, and, in this event, removal of additional thyroid tissue may be fatal to the patient or at least may cause serious damage to the eyes.

Secondly, exophthalmos coming on postoperatively presents unquestionably the most devastatingly severe type of protrusion to be found in conjunction with thyroid disease. In the first place, it simulates severe myxedema of the orbit rather than edema due to hyperthyroidism, and hence really represents a different process which will be discussed under the heading of malignant exophthalmos. In my opinion, this type is evidence of a true polyglandular disease.

Thirdly, there is a group of patients with truly recurrent hyperthyroidism, in whom the exophthalmos halts for a period, recurs, and becomes increasingly, though slightly, worse after each attack. In my experience, operation offers these patients more than any other treatment although, in some instances, several operations may be required.

A corneal dystrophy occurs in association with the exophthalmos of hyperthyroidism that is not found in retraction of the lids in any other cases of exophthalmos; it simulates that associated with the postsurgical dystrophy of tic douloureux. The areas are rarely infected and the degeneration of the globe is not due to a primary infection. A low-grade iritis has also been noted in several cases. Evidence in some instances points to a vascular embarrassment, whereas in others, the process seems to be of a neuromyopathic type. These patients with corneal involvement respond immediately to removal of the thyroid gland and it is our practice to operate earlier under these circumstances in order to relieve the condition in the cornea. Since instituting this procedure, no eyes have been lost, and the ulcers have responded with no additional treatment.

Keratitis lagophthalmos occurs only in certain individual cases, and many patients with wide protrusion suffer no corneal disturbances.

Lachrymation is a common disturbance in exophthalmos and is due to exposure and stimulation of the lachrymal glands. An irritative type of conjunctivitis also is frequently present and this is relieved by general treatment and relaxation of the lids following operation.

To correct the failure of the lids to close at night, there is nothing so satisfactory as a well-fitted Buller or cellophane shield. Suturing of

EXOPHTHALMOS

the lids and similar procedures are treacherous and illogical because the edema can not be pressed out and the posterior pressure is then magnified against the cornea or the sutures. A more rational procedure is to apply vaselined gauze (super-saturated) over the eyes at night, and most efficacious of all is early operation on the thyroid gland.

In conjunction with these cases of exophthalmos, there have been ten instances of transitory glaucoma and one in which the glaucoma persisted. The tension reading recorded 90 mm. (Schiötz) in one case and all the readings were fairly high. All except one of these patients were relieved by thyroidectomy and that one had myopia with glaucoma, exophthalmos, and postoperative hypometabolism. This patient required eserine over a period of ten years. Changes in the visual fields were not present in these patients, with the exception of the last. I believe that increase in intra-ocular pressure accounted for the severe headaches of which these patients complained. In all these instances, the disturbance was bilateral, all patients were adults, and intra-ocular surgery was not necessary in any case.

No visual field changes of diagnostic importance occur in toxic hyperthyroidism. In all our cases, the fields were normal or the changes observed were merely coincidental. The results of studies of the fields in this group are almost identical with those in a group of normal patients.

Another associated sign of exophthalmos in hyperthyroidism is edema of the lid, usually of the upper lid. The lower lid is rarely affected except in cases of long standing, and, if present, it is a good indication that the exophthalmos has been present for considerable time. In patients with edema of the lower lid, there is very little recession of the eyes after operation. The edema of the lid, however, is exactly the same as the orbital edema—fluid in the early stages, which is followed by lymphocytic infiltration (mild in some cases) and later, by fibrosis not unlike myxedema.

Many of the other ocular signs of thyroid disease are merely secondary and are infrequently observed. However, a disturbance of muscular function occurs quite frequently. The weakness of accommodation convergence (Möbius' sign) is common in exophthalmic goiter, persists long after operation or medical treatment, and may require special muscle exercises or prisms before the patient is able to work and become rehabilitated economically. Of all the eye signs, this one is the most persistent, and years after the patient is "cured" of the disease, the muscle error may lead him a disagreeable chase from oculist to surgeon to oculist.

Other muscles are similarly involved and isolated muscle paralysis is common. The two muscles most frequently involved are the right

superior rectus and the right external rectus. Much of the dysfunction corrects itself in time and from six months to a year should elapse before any operation is undertaken on the ocular muscles. Recovery from thyroid disease is very slow because the disease affects the entire system, and naturally the rebound is not rapid.

Bilateral involvement of the muscles is more than coincidental. At least six cases of bilateral paralysis of the superior rectus muscles have been seen and in these instances, as one would expect, the fissures are exceedingly wide. The patients of necessity carry their heads well back and the muscles of the neck suffer spasm and cause pain.

The internal recti may be weakened but are rarely paralyzed. The oblique muscles are frequently involved. However, cases are on record of involvement of the oblique muscles and of the inferior recti. The head tilts in these instances are similar to those noted in the presence of hyperphoria.

One patient has presented an interesting story. Following operation, he suffered from hypometabolism and is now going through a second remission of myasthenia gravis. Treatment to date has carried him along and his basal metabolic rate has ranged from plus 54 to minus 36 per cent. The myasthenia was discovered when the metabolic rate was low.

Complete external ophthalmoplegia was noted in two patients with exophthalmos, one in whom it was severe, and the other with slight proptosis. Both these patients succumbed before treatment could be instituted. One had definite symptoms and signs of cerebral involvement, and the other was mentally normal the afternoon when his death occurred due to cardiac failure.

Changes in the pupil, iris, retina, and nerve head are diagnostically of no value in hyperthyroidism, because they are rarely involved in true toxic goiter. No significant diagnostic sign can be attached to any changes in these parts.

A study of the capillaries in a number of patients with exophthalmos reveals a definite venous stasis and subconjunctival edema. Another interesting finding is a collection of what appear to be oil droplets along the deeper and larger vessels. In some instances, these are so extensive as to completely surround the vessels although I have been unable to determine what their significance may be. Their presence is constant enough to make one feel that some faulty exchange of tissue lipids may play a part in the production of orbital edema. These oil droplets are especially numerous in cases of malignant exophthalmos.

The description by Moore of the orbital contents is typical for our findings in all cases of exophthalmos of short duration. "I therefore made an incision the entire length of the inferior conjunctival fornix,

EXOPHTHALMOS

exposed the contents of the orbit, and with forceps picked away piecemeal as much orbital fat as possible. I estimate that a heaped up teaspoonful was thus removed . . . In addition, however, the fat seemed edematous, and in particular the inferior, internal and external recti muscles, which were exposed for a considerable distance, and these, instead of being the flat, rubber-like muscles, such as we become familiar with in squint operation, were greatly swollen, fusiform bellies, apparently from edematous infiltration, not quite so stout as the last joint over the little finger."

The importance of establishing a diagnosis of exophthalmos is emphasized in cases of neurocirculatory asthenia. Because the general symptomatology simulates that of thyroid disease so closely, the eyes are an important aid in the differential diagnosis. The patients show moderately high basal metabolic rates, rapid pulse, tremor, and loss of weight; they also are extremely apprehensive. Examination of the eyes reveals a retraction of the lids due to levator stimulation and not to true spasm, some lid lag but no exophthalmos, never any muscle palsies and usually dilated pupils which are absent in true thyroid disease. Furthermore, if these patients are placed in bed at complete rest, the basal metabolic rate decreases 20 to 30 points and the heart rate becomes slower. In this group of patients, an erroneous diagnosis of hyperthyroidism is often made and poor results follow operation on the thyroid gland while some of the most brilliant results are secured following treatment of "exophthalmos." These are the patients who, in my opinion, are afflicted with the most severe type of proptosis with which we have to deal, namely, "malignant exophthalmos" which develops following thyroidectomy.