GLAUCOMA AND THE THYROID*

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THE observation of Lagrange (1922) that a glaucomatous eye is "a sick eye in a sick body" is a challenge to ophthalmologists. For some time an association has been noted between hypertension and a high intra-ocular pressure, but Duke-Elder (1940) considers that this relationship is accidental rather than essential. More recently an increased incidence of primary glaucoma has been noted in diabetics.

In the series here reported the development of primary open-angle glaucoma in two cases of Hashimoto's disease first suggested a possible link of this eye condition with auto-immune concepts; a review of the previous illnesses of 100 patients with open-angle glaucoma showed a striking incidence of thyroid disturbances of various types. An assessment of these patients on a clinical and biochemical basis substantiated the initial impression that thyroid dysfunction walked in the shadow of open-angle glaucoma.

The diagnosis of hypothyroidism was made on the basis of the clinical findings, laboratory investigations, and on the results of therapy. Twenty-five per cent. of open-angle glaucoma patients evaluated by Waynes's Diagnostic Index were considered to be subthyroid, with conditions ranging from frank myxoedema to mild hypothyroidism.

The following laboratory investigations were carried out in assessing thyroid function in two groups of 100 patients (100 with open-angle glaucoma, and 100 controls).

(1) *Radio-iodine Uptake Tests.*—The uptake of ^{131}I by the thyroid was measured after 2 hours and after 24 hours. This isotope emits chiefly beta-rays, whose action is limited to a few mm. of tissue, but in addition gamma-rays are also emitted, which ionize negligibly within the body, but which are penetrating and can be measured by an externally placed gamma-ray detector such as the Geiger counter. Of the cases of open-angle glaucoma 54 per cent. showed an abnormally low uptake, irrespective of whether definite clinical evidence of hypothyroidism was present or not. In the control series of 100 cases of closed-angle glaucoma an abnormally low uptake was found in only 13 per cent. In a series of 10 cases of persons without glaucoma taken at random who were suffering from eye conditions such as high myopia, cataract, and senile macular degeneration, the radio-iodine uptake was normal without exception.

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(2) *Agglutination of Thyroglobulin-coated Tanned Erythrocytes.*—The presence of antibodies to thyroglobulin was demonstrated in 30 per cent. of open-angle glaucoma patients and in 10 per cent. of closed-angle glaucoma patients.

(3) *Additional Tests of Thyroid Function.*—These were estimation of the serum cholesterol and electrocardiography.

The age-groups of the two series of patients were roughly comparable, as is shown in Table I.

TABLE I
AGE-GROUPS OF PATIENTS AND CONTROLS

	Age-groups (yrs)			
	50-59	60-69	70-79	80+
Open-angle glaucoma (per cent.)	19	46	32	3
Closed-angle glaucoma (per cent.)	24	50	25	1

The diagnosis and differentiation of glaucoma into closed-angle and open-angle cases was made on the basis of the history, clinical picture, and gonioscopy findings. In the series with closed-angle glaucoma 60 per cent. presented with acute congestive glaucoma, 16 per cent. with symptoms of haloes, 3 per cent. with a unilateral semi-dilated pupil, and in 2 per cent. arterial pulsation was the initial feature. In 8 per cent. cupping of the disc was the first indication of the disease but elicitation of the history and gonioscopic examination allowed these to be considered as long-standing narrow-angle glaucoma. In 4 per cent. the first presenting feature was central venous thrombosis. In the remaining 7 per cent. of cases routine examination revealed raised tension and gonioscopic examination confirmed the diagnosis.

In the series of cases considered to be open-angle glaucoma on gonioscopic examination there were no signs or symptoms suggestive of the disease in 38 per cent., apart from tonometric readings. Cupping of the disc was the initial presenting feature in 42 per cent., central venous thrombosis the first sign in 12 per cent., and in 8 per cent. the diagnosis was confirmed by the water-drinking test.

Table II shows the principal illnesses associated with open-angle glaucoma in these patients; only some 20 per cent. were reasonably healthy and had had no previous illnesses of significance. The inter-connexion so often noted in recent publications between pernicious anaemia, diabetes, and myxoedema is seen in this series, but with glaucoma in addition.

TABLE II
PERCENTAGE ASSOCIATED ILLNESSES IN 100 CASES OF OPEN-ANGLE GLAUCOMA

Nothing of Significance	Thyroid Disturbance	Diabetes Mellitus	Hyper- tension	Pernicious Anaemia	Arthritis
20	45	10	14	7	14

Table III shows the types of thyroid disturbance reported.

TABLE III
THYROID DISTURBANCE IN OPEN-ANGLE GLAUCOMA

Total Number of Cases	Myxoedema	Hashimoto's Disease	Thyro-toxicosis	Thyroid-ectomy	Goitre	Carcinoma of Thyroid
45	16	10	16	15	22	1

A control series of 100 patients with closed-angle glaucoma was also investigated, and a general impression was gained that such patients are fundamentally healthy, with previous illnesses of little significance (Table IV). This would appear to corroborate recent opinion that closed-angle glaucoma is essentially a local eye disease.

TABLE IV
PERCENTAGE ASSOCIATED ILLNESSES IN 100 CASES OF CLOSED-ANGLE GLAUCOMA

Nothing of Significance	Bronchitis	Thyroid Disturbance	Diabetes Mellitus	Hyper-tension	Pernicious Anaemia	Arthritis	Iron Deficiency Anaemia
58	7	Thyro-toxicosis 2 Goitre 1 Hashimoto's Disease 1 Thyroid-ectomy 1	4	12	2	4	4

The sex ratio in this series was 2 : 3, which appears to differ significantly from the sex incidence of 27 per cent. male in open-angle glaucoma. In six cases a glaucomatous crisis had been precipitated by general surgery, either atropine pre-medication or the stress of the operation being the causal factor. Four patients had been treated with such drugs as Artane or Tofranil, which are contra-indicated in glaucoma.

Discussion

A comparison of the clinical history of 100 cases of open-angle glaucoma with that of 100 cases of narrow-angle glaucoma appears to show a significant incidence of thyroid dysfunction in patients with open-angle glaucoma. The raised intra-ocular pressure was not related to any exophthalmos that might be present, as this condition was found in only a few cases and was, moreover, treated with miotics and diuretics, which controlled the intra-ocular pressure whilst the exophthalmos was unaffected.

Although it has been recognized for some time that, in primary glaucoma, there is an impairment of the facility of aqueous outflow, the exact nature of this impediment in open-angle glaucoma has not been apparent. Gonioscopic examination in this type of glaucoma has failed to show why the aqueous does not drain away efficiently. We put forward the speculation that, in some cases of open-angle glaucoma at any rate, a pathological alteration in the trabecular meshwork of the angle of the anterior

chamber is induced by thyroid disease. It is through the spaces of this meshwork that aqueous percolates towards the inner canals of Sondermann and thence to the canal of Schlemm.

Zimmerman (1957) demonstrated an abundance of acid mucopolysaccharide within the inter-trabecular spaces. Davson (1962) suggested that the open holes observed in tangential sections of the trabeculae were full of this mucopolysaccharide jelly, and considered that this jelly, by virtue of its viscosity, exerted the principal restrictive control over the outflow of the aqueous humour. Writing on the pathology of myxoedema, Gabilove and Ludwig (1957) stated that the mucoid substance deposited consisted of an acid mucopolysaccharide in combination with protein. The exact significance of this deposit *vis-à-vis* thyroid function is uncertain because localized deposits of a similar nature occasionally occur in hyperthyroidism.

It is conceivable then that, in thyroid dysfunction, some alteration occurs in either the quantity or the quality of the mucopolysaccharide in the trabecular spaces and that this may play some part in the aetiology of open-angle glaucoma. For some time it has been recognized that cases of nasal obstruction due to localized deposits of this pseudo-mucinous material and referred to our E.N.T. colleagues as "sinusitis or deflected septum", prove to be cases of myxoedema (Boyd, 1958).

Localized deposits are also recognized as an aetiological factor in the carpal tunnel syndrome (Cecil and Loeb, 1963).

Conclusion

It would seem that the sick body observed by Lagrange was that of the open-angle glaucoma patient rather than that of the closed-angle glaucoma patient. Close co-operation between ophthalmologist and physician is clearly indicated, in that glaucoma patients should be investigated with regard to thyroid function, diabetes mellitus, pernicious anaemia, and hypertension.

Alteration in the mucopolysaccharide in the angle of the anterior chamber may be induced by thyroid disorder.

Preliminary results suggest that where myxoedema and glaucoma co-exist it is easier to control intra-ocular pressure with miotics alone once treatment with *l*-thyroxine has been instituted.

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