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Pointers

Anticoagulants and Infarction: Results of trial in Norway indicate that women benefit as much as men from long-term anticoagulant therapy after myocardial infarction (p. 571).

Dockyard Exposure to Asbestos: Pleural and pulmonary fibrosis and pleural mesothelioma were associated with long-term exposure, even if exposure was intermittent. So far 10 cases of mesothelioma had occurred (p. 574).

Dangers of Chloroquine: Simple scheme for rendering patients ophthalmologically safe; drug's therapeutic value considered to outweigh minor side-effects (p. 579).

Nephrotic Syndrome: Two cases associated with heart disease responded to prednisone (p. 584).

Anastomotic Leak: Neostigmine given to reverse curarization may cause leaking at ileorectal anastomoses. The mechanism may be increased muscular activity of gut or vasoconstriction near suture line (p. 587).

Arteritis of Aorta: Immunoglobulin levels raised in sera from 21 patients, but rheumatoid and antinuclear factor and antibodies to aorta, liver, and thyroid were not raised (p. 589).

Vitamin B_{12} Deficiency: Rapid detection technique suitable for routine laboratories investigating debilitated patients (p. 591).

Asthma: Disodium cromoglycate inhibited usual post-exercise fall in $F.E.V._1$ and may be reason for subjective improvement given by this drug (p. 593).

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Management of Endocrine Ophthalmopathy

"The occurrence of a very common clinical condition which may lead to disastrous consequences, the cause of which is unknown, the pathology obscure, and therapeusis for which is generally ineffective, is certainly no cause for congratulations." That was Sir Stewart Duke-Elder's verdict[1] in 1952. The cause of endocrine ophthalmopathy remains unknown, and it is disappointing that investigations into the association between long-acting thyroid stimulator (L.A.T.S.) and the eye changes have not been very helpful.[2-4] Treatment has remained empirical, and it can only ameliorate the consequences of the pathological process until it spontaneously subsides. Most of the published therapeutic trials have been uncontrolled and difficult to interpret, since the condition is subject to spontaneous relapses and remissions. Furthermore, lack of objective evidence makes the evaluation of any therapeutic measure very difficult.

The nomenclature of the signs of endocrine ophthalmopathy urgently needs revision and clarification, and in particular too many eponymous descriptions are used.[5] In reports of trials the eye signs are often not adequately described—patients who show only lid retraction may be included with patients with conjunctival oedema and progressive exophthalmos. Patients should be assessed for signs of non-infiltrative and infiltrative ophthalmopathy.[6] The former is characterized by lid retraction, lid lag, and simple proptosis, and is usually associated with hyperthyroidism; and the latter by oedema, diminishing visual acuity, papilloedema, and scotoma, and can be associated with the euthyroid state. In the non-infiltrative variety, the patient may have no complaints except on cosmetic grounds, while the infiltrative type may be associated with symptoms of "grittiness" or "sandiness" in the eyes, retro-orbital pain, lacrimation, and diplopia. Apart from treatment instituted for cosmetic reasons active treatment is indicated only where there are troublesome symptoms or obvious progression of the features of infiltrative ophthalmopathy. Once the type and severity of the eye signs have been assessed adequate baseline measurements must be made before any therapeutic regimen is started. These should usually include measurements of exophthalmos, visual acuity, visual fields, ocular movements, intra-ocular pressure, and the width of the palpebral fissure. The integrity of the corneal epithelium can be monitored by regular staining with fluorescein and examination by a loupe or slit-lamp microscopy. Finally, serial clinical photographs provide a permanent record of the eye signs. This is a situation where collaboration between physician and ophthalmologist is essential.

The main aim of treatment is the prevention of corneal ulceration and panophthalmitis. In the presence of retro-orbital infiltration and papilloedema treatment may be needed to avoid optic atrophy. The disfiguring nature of the changes in endocrine ophthalmopathy often produces extreme apprehension in the patient, and much encouragement and moral support must be given by the clinician along with an explanation

that the process is self-limiting. A great deal can be achieved by simple local therapy. When lagophthalmos is present regular instillations of ophthalmic solutions of methylcellulose or liquid paraffin, especially at night, avoids dryness and abrasion of the cornea. Additional protection can be effected by wind shields on the side arms of spectacles or the use of a carefully padded eye patch. Many of these patients have photophobia, and the provision of tinted lenses adds to their comfort. Symptoms are frequently worse in the morning, and elevation of the head and shoulders reduces dependent oedema during sleep. The addition of cold saline or magnesium sulphate compresses may help to reduce oedema, particularly in the lids.[7]

Progression of the infiltrative process and exposure of the cornea with subsequent epithelial changes demand prompt action. Tarsorrhaphy is a simple and effective treatment, but the most desperate cases with boggy oedema of the lids are sometimes unsuitable for suture. Surgical measures may be avoided by local adrenergic blockade using ophthalmic solutions of guanethidine and bethanidine in a methylcellulose vehicle; these have been shown to produce a pronounced ptotic effect with considerable functional and cosmetic improvement.[8-10] Systemic side-effects, such as hypotension, have not been reported. Similar therapy with 1% propranolol has not been shown to have a comparable effect.[11] In some cases of non-infiltrative ophthalmopathy long-term treatment by adrenergic blockade may be considered justifiable for cosmetic reasons.

Infiltrative ophthalmopathy may rapidly progress within 48 hours, and severe conjunctival oedema and exophthalmos may preclude any chance of corneal cover. The rationale for the use of systemic steroids in this situation stems from their anti-inflammatory effect in reducing oedema and the possibility that they act as immunosuppressive agents in a disease which is suspected of having an autoimmune basis. High-dose steroid regimens using intravenous A.C.T.H. and systemic steroids are effective in avoiding serious complications in the acute phase,[12-15] but doses as high as 140 mg. of prednisone daily may be necessary for control.[16] When the steroid dosage is eventually reduced there is usually an exacerbation of ophthalmopathy, and long-term maintenance therapy produces the complications of hypercorticism; but steroid treatment does allow a thorough assessment of the patient to be made. It may provide general anti-inflammatory cover for orbital decompression, and on occasion may even tide the patient over the acute episode.

Local steroid therapy has been advocated,[12] and the introduction of depot preparations such as 6 α-methyl prednisolone has made treatment by subconjunctival or retrobulbar injection a practical proposition. If preliminary reports[17 18] of success are confirmed this method could supersede systemic steroid therapy with its considerable disadvantages.

The postulate that L.A.T.S. is an antibody with a common antigenic stimulus from thyroid and orbital tissues inspired the hypothesis that destruction of all thyroid tissue by surgery or radioactive iodine would allow infiltrative ophthalmopathy to remit.[19 20] The method has been advocated as a useful measure in an emergency. Thyroid ablation is not, however, always easy to achieve, and in one series it was necessary to administer repeated doses of radioactive iodine to a total of over 300 millicuries in one patient.[20] The enthusiastic claims for the effectiveness of ablation therapy have not been confirmed,[21] and there is, furthermore, evidence that the presence of functioning thyroid tissue is not necessary for the persistence of L.A.T.S. in a patient's serum.[21 22]

Metronidazole, a proved antitrichomonal agent, has been reported to have produced appreciable reduction in exophthalmos in 13 euthyroid patients, and one patient also showed resolution of ophthalmoplegia.[23] Increase in exophthalmos occurred in 7 out of 10 patients once the drug was withdrawn. This is an interesting result, which remains to be confirmed.

The co-existence of hyperthyroidism and infiltrative ophthalmopathy complicates the management. The course of the ophthalmopathy in any one patient is totally unpredictable, and it seems prudent not to proceed with destructive forms of therapy for the hyperthyroidism until the eyes are quiescent. Antithyroid drugs provide a flexible and reversible form of treatment and allow therapy to be titrated against thyroid status. Maintenance therapy may be required for many years, but with careful control there should be no need for thyroxine or other thyroid analogues to prevent hypothyroidism. In the case of non-infiltrative ophthalmopathy associated with hyperthyroidism there is no evidence that any treatment will result in serious progression of the eye signs.

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Toxic Substances in Endotracheal Tubes

When endotracheal tubes are inserted skilfully, remarkably few complications result from the contact between the tube and the tissues of the respiratory tract. It is generally assumed that the material, rubber or plastic, from which these tubes are made is non-toxic to the tissues. This may be true of natural rubber, for a British Standard issued in 1962[1] required that "natural rubber compound shall not include in its composition any substance which is known to have a harmful effect on human tissues or to react with body fluids."

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