Thyroid eye disease

More treatment options

EDITOR,—Donald Munro clearly reviews the pathogenesis and treatment of dysthyroid eye disease.[1] There are, however, alternative treatments which merit consideration.

Lid retraction may be asymptomatic but a considerable proportion of patients benefit from upper or lower eyelid lengthening procedures.[2] These can be very effective in improving the cosmetic appearance and protecting the cornea. These procedures are preferable to lateral tarsorrhaphy because the cosmetic results are better and anterior displacement of the globe is not restricted (thus lessening the risk of optic nerve compression).

High dose steroid treatment is effective in relieving compressive optic neuropathy, but the disease often progresses when the dose is gradually reduced to a more modest level. So, in many cases, long term maintenance treatment is required. Local treatment is therefore preferable and avoids the well known side effects of steroids.

Surgical decompression of the orbit into the maxillary and ethmoid sinuses is a successful procedure for many patients, including those for whom the "eye signs are disfiguring or disabling." Complications include double vision due to strabismus and infraorbital hypoaesthesia.

Radiotherapy is dismissed by Munro: "Britain has few enthusiasts for local irradiation of the orbit." Carefully planned low dose external beam radiotherapy is very effective in patients with progressive disease,[3,4] particularly disease of less than two years' duration. The long term risk of neoplasia is low. It is negligible in elderly patients, for whom this treatment is particularly indicated because of the problems associated with taking steroids long term.

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Patients need joint care

EDITOR,—All of us involved in the care of patients with thyroid eye disease anticipate a fuller understanding of its autoimmunological basis but meanwhile have to manage patients in the light of current practice. Donald Munro's summary of current clinical practice failed to emphasise several important management issues and advances in surgical technique.[1]

We recommend that all patients with moderate to severe thyroid eye disease be under the joint care of an interested ophthalmologist and an endocrinologist. Typical signs of the condition can present months if not years before any endocrine abnormality is detected. The difficulty in making the diagnosis should not be dismissed, and the importance of endocrine review is emphasised.

Patients frequently show signs of thyroid eye disease when the thyroid is overactive. Some may develop "malignant" thyroid eye disease during this phase, and these patients present a particular challenge in clinical management. All types of treatment, be they medical or surgical or depend on the use of radioactive iodine, may cause either improvement or deterioration of patient's orbitopathy. The outcome is unpredictable, and patients require careful counselling.

Munro ignores the many patients euthyroid for 10-30 years, who inexplicably develop severe orbitopathy, and also that, although eye disease is more common in women, its occurrence in older men is often severe.

"Malignant" thyroid eye disease implies orbital apex nerve compression by enlarged extraocular muscles: severe corneal exposure is rare. Patients with active infiltrative orbitopathy without severe proptosis may be most at risk of optic nerve compression, since a tight orbital septum prevents spontaneous decompression in those with significant proptosis. Lateral tarsorrhaphy is often ineffective and has been superseded by many other surgical procedures. If surgical orbital decompression is indicated, the technique used is important, and the usefulness of lateral and superior wall decompression is questionable.

Finally, the cosmetic and ocular motility problems endured by these patients, often for many years, must be appreciated by caring clinicians. The morale of such sadly affected patients may be raised by recourse to self help groups.

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Disfiguring and capricious condition

EDITOR,—We wish to add a few points to Donald Munro's editorial on thyroid eye disease regarding the contemporary investigation and management of this condition. It is surprising to read that "most patients regard the end result of thyroid eye disease as reasonably satisfactory." While severe sight threatening disease is undoubtedly rare, the disfiguring proptosis and periorbital changes that often accompany Graves' ophthalmopathy are an important, if not the most important, consideration to a substantial proportion of patients when they are told that they have thyroid disease. The importance of thyroid eye disease to the patient should not be underestimated.

The statement that "clinical experience suggests that controlling hyperthyroidism usually impedes the development of thyroid eye disease" may have some substance in practice. But the continuing controversy to which Munro alludes over which type or types of treatment may cause deterioration in eye disease, and the not infrequent patients whose eye disease is most active long before or long after their period of greatest thyroid dysfunction, should remind clinicians of the dangers of any generalisations about this capricious condition.

Investigative techniques such as ultrasound scanning and magnetic resonance imaging, which can quantify retro-orbital changes, are potentially important in assessing the occurrence and distribution of structural pathology. Ultrasound scanning, for example, has shown that measurable ophthalmopathy is far more prevalent in patients with Graves' disease than is clinically apparent.[2]

Lateral tarsorrhaphy is no longer considered to be the most appropriate surgical procedure for protecting the cornea unless severe ulcerative keratitis is present. In persistent, less severe disease of the ocular surface lowering the upper lid by recessing the levator palpebrae superioris and raising the lower lid by inserting a scleral spacer graft will produce a better functional and cosmetic result.[3]

Finally, use of Fresnel prisms—easily applied as adhesive plastic sheets to spectacle lenses—is an ideal temporary measure for patients with disabling diplopia who are awaiting stabilisation of extraocular muscle disease before having corrective squint surgery.

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Advice to authors

Priority will be given to letters that are less than 400 words long and are typed with double spacing. All authors should sign the letter. Please enclose a stamped addressed envelope for acknowledgment.

Bad teeth and myocardial infarction

Smokers neglect their teeth

EDITOR,—Frank DeStefano and colleagues point out that the value of their study on dental disease and risk of coronary heart disease and mortality is limited because of shortage of data about smoking habits.[1] According to an extensive literature review by Christen *et al*, there is a strong correlation between smoking habits and oral hygiene or periodontal disease.[2] To quote from their conclusions: "Smokers have more severe periodontal disease (periodontitis) than do non-smokers" and "Adult male smokers have more dental plaque than adult male non-smokers because they tend to have lower dental hygiene standards—that is, they are less efficient brushers, spend less time in oral hygiene care, and tend to be more neglectful in practising general dental health habits." DeStefano and colleagues' paper should be read with this in mind.

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1 DeStefano F, Anda RF, Kahn HS, Williamson DF, Russell CM.

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Biological mechanisms for link

EDITOR,—Frank DeStefano and colleagues report an increased risk of coronary heart disease and mortality in men with dental disease.[1]

There is evidence that immunocompetent cells have a role in initiating and accelerating the development of atherosclerosis and myocardial infarction. In particular, activated macrophages are considered to play a pivotal part. Increased serum concentrations of neopterin are found in patients with atherosclerosis,[2] and in a community based study neopterin was the best single predictor of atherosclerosis—even better than more classic variables like cholesterol, low density lipoprotein, and high density lipoprotein.[3] Large amounts of neopterin are released from human macrophages on stimulation with interferon γ. Increased serum neopterin concentrations have been found in patients with infectious syndromes, malignancies, and autoimmune diseases.[4] Interestingly, among blood donors a substantial proportion with a raised serum neopterin concentration presented with dental diseases.[5]

These data indicate that dental diseases may often lead to chronic activation of the immune system, which may render patients more susceptible to atherogenesis, thus increasing the risk of myocardial infarction. It would be interesting to learn from DeStefano and colleagues whether variables of immune activation are more commonly increased in their patients with dental disease and with increased risk of myocardial infarction.

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Roles of white cells and fibrinogen

EDITOR,—Frank DeStefano and colleagues report that dental disease is associated with increased risk of coronary heart disease and mortality.[1] They note that "the biological mechanism by which periodontal disease or poor oral hygiene could lead to coronary heart disease is not clearly established."

In a recent study of 50 consecutive patients with gingivitis or periodontitis, or both, colleagues and I observed significant increases in plasma fibrinogen concentration and blood leucocyte count compared with values in 50 age matched controls. Multivariate analysis controlling for the effects of age, smoking, social class, and case or control group showed significant correlations between fibrinogen concentration, leucocyte count, and three variables of dental disease (plaque index, gingival index, and the community periodontal index of treatment needs).[2] Both plasma fibrinogen concentration and leucocyte count have been shown to be strong, independent primary risk factors for coronary heart disease and death in several large prospective population studies.[3] The increases in fibrinogen concentration and leucocyte count that we observed in patients with dental disease[2] were consistent with a substantial increased risk of coronary heart disease and mortality according to these studies,[3] in keeping with that observed by DeStefano and colleagues.

I therefore suggest that (*a*) hyperfibrinogenaemia and leucocytosis may be plausible biological mechanisms by which dental disease may directly promote coronary heart disease and death[3]; (*b*) plasma fibrinogen concentration and leucocyte count should be measured in future studies of dental disease and cardiovascular disease to test this hypothesis; and (*c*) oral bacterial infection, which is common in populations at high risk of coronary heart disease, may be an important determinant of variability in plasma fibrinogen concentrations and leucocyte counts in the population, most of which is unexplained.[4,5]

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African drugs slur

EDITOR,—The authors of "Drug smuggler's delirium" consider, among other signs and symptoms, "recent travel in West Africa" as being of diagnostic significance.

West Africa is made up of 15 countries—Ghana, Nigeria, Ivory Coast, Mali, Liberia, Benin, Senegal, Upper Volta, Mauritania, Cameroon, Gambia, Gabon, Guinea, Sierra Leone, and Togo—with a total population of over 175 million. As far as I am aware (and I take a keen interest in these statistics) four Nigerians have died as a result of carrying drugs internally. Travel in West Africa, therefore, seems to be a dubious criterion when deciding whether a patient was suffering from drug delirium.

Articles in the *BMJ* which contain biased statements demean its international stature.

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1 Ramrakha PS, Barton I. Drug smuggler's delirium. *BMJ* 1993; **306**:470-1. (20 February.)

Transgenic pigs under stress

EDITOR,—Claims that human transplants could be revolutionised by success in breeding pigs with "human" organs are inaccurate and misleading.[1] These are not pigs with "human hearts"; they are genetically engineered mutant pigs carrying human genes. There is no evidence that transplanting these unfortunate animals' organs into humans will actually save lives. There is, however, considerable evidence to show that attempts to produce genetically engineered "transgenic" animals of this type often produce physical and developmental abnormalities which inevitably cause pain and suffering to many animals. Transgenic pigs, carrying a human growth hormone gene, produced at the US government's Beltsville Research Station provide a well known example of the dangers of this type of research. The Beltsville pigs suffered from defective vision, arthritis, and muscular weakness and were impotent and very susceptible to stress.

All 35 attempts to transplant animal organs into humans have failed. This new approach using genetically altered animals remains highly experimental. Furthermore, it is clear that this approach cannot provide an answer to the chronic problems of organ rejection.

Only last month the government's advisory council on science and technology recommended the introduction of a new nationwide "opt out" donor scheme which, the committee said, would alleviate the "chronic shortfall" of donors in the United Kingdom. Rather than carrying out bizarre experiments on animals, this country should be investing in health education and taking simple administrative action to save human lives.

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Interferon first in chronic hepatitis C

EDITOR,—Two points warrant clarification in Johnson Y N Lau and Gary L Davis's editorial on chronic hepatitis C.[1] The subtitle of the editorial—"interferon beneficial where steroids fail"—takes out of context the author's statement referring only to patients who have coexisting hepatitis C and autoimmune markers. Even in this group the decision to defer or withhold potentially curative interferon treatment in a chronic infection that may progress to cirrhosis requires careful consideration.

Though there is no doubt that interferon may seriously exacerbate autoimmune hepatitis misdiagnosed as chronic hepatitis C by false positive results of first generation antibody tests, such mishaps are unlikely if a definite diagnosis of chronic hepatitis C is sought with second generation multiantigen tests and confirmatory polymerase chain reaction. Most reported exacerbations induced by interferon developed slowly over weeks and responded to its withdrawal with or without the addition of steroids.

Patients with well documented chronic hepatitis C, as with other forms of liver injury, may have circulating autoantibodies to a range of intracellular antigens, although whether these are merely markers of cell death or play a part in mediating tissue injury is unclear. Varying prevalences of 21% to 41% have been reported.[2] The strong association between chronic hepatitis C and antibodies to liver and kidney microsome type 1 (anti-LKM-1) has given rise to speculation that hepatitis C may precipitate type II autoimmune hepatitis, though recent evidence suggests that the LKM-1 antibodies in the two conditions recognise subtly different epitopes.[3]

Information is scarce concerning the influence of autoimmune markers on the course of chronic hepatitis C. In one study of 102 patients with the disease the 21 patients who had coexistent autoantibodies did not differ from those who were autoantibody negative in terms of age, sex, risk factors, histological findings, or response to interferon.[2] In another study, in which five patients with both chronic hepatitis C and autoimmune markers received interferon, three of the patients responded, one did not respond, and one suffered an exacerbation of the disease.[4]

Overall, the presence of autoimmune markers