Editorial: Graves' ophthalmopathy

'One of the most puzzling syndromes in ophthalmology is the variable and capricious exophthalmos which is associated with endocrine disorders. The cause and nature of the orbital changes . . . are still unknown.'¹ Duke-Elder, if he were with us today, might be excused for feeling that we had not made much progress since his comments of 1952, and even Graves² and Basedow³ might not be particularly impressed. Our ignorance is certainly not for want of trying, as Duke-Elder tells us in the chapter referred to above that there had already been over 3000 papers on the subject by 1909.

Before the arrival of the concepts of immune responses (and autoimmunity in particular) much of the theorising concerned possible effects from various hormones, especially pituitary, but no one seemed to have much idea how they could produce such peculiar effects, apparently specific to the extraocular muscles. I well remember an embarrassing interview with an examiner during one of my attempts to obtain the fellowship of the Royal College of Surgeons of England, when it was apparent that he was just as confused on the subject as I was.

Teaching it to medical students was always a challenge. How do you explain that something which is associated with Graves' disease is even more likely to occur after thyroidectomy or even in hypothyroidism, where there has been no prior evidence of Graves' disease? I used to try and get around the teaching problem by telling students a bit of a fairy tale. I taught that some unknown substance, in the old days probably a hormone, leaked out from the pituitary and entered the orbit by some form of local

diffusion. Once in the orbit it caused inflammation of the muscles, irritating the levator at first, hence the lid retraction, but eventually causing swelling and therefore exophthalmos, and finally sinking to the bottom of the orbit, where it caused fibrosis of the inferior rectus muscle. Although this story probably sounds naive to aficionados of the subject, of whom there appear to be a considerable number, nevertheless it is quite useful as a means of helping students to remember the sequence of events.

The paper by Weetman, Fells and Shine in this issue is an altogether more serious contribution to our understanding of the problem. In pursuance of the theory that the mechanism of Graves' ophthalmopathy is an autoimmune myositis with a specific expression in extraocular muscles, they have sought human eye muscle membrane binding antibodies in patients. However, as usually seems to be the case in this tantalising condition, the results only give rise to more questions. For example, why are the antibodies found in patients with thyroid autoimmunity regardless of eye signs, and how is it that the antibodies bind equally well to skeletal muscle? In other words, they are not site specific. Perhaps the fairy story I used to tell the students had some truth in it after all.

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References

- 1 Duke-Elder WS. *Textbook of ophthalmology*. London: Kimpton, 1952: 5: 5478.
- 2 Graves RJ. *Collected clinical lectures*. Philadelphia: Waldie, 1838.
- 3 Basedow CA. Exophthalmos durch Hypertrophie des Zellgewebes in der Augen Hohle. *Woch Ges Heilkunde* 1840; 13: 197-204.