HIV – WHAT THE GENERAL PHYSICIAN NEEDS TO KNOW

Sir,

I was interested to read Dr Tony France's recent CME review on HIV infection in which he refers to rheumatic syndromes.[1] It is worth noting that the rheumatic disorders associated with HIV range from septic arthritis through soft tissue lesions to seronegative spondyloarthropathy. In the past, reactive arthritis, psoriatic arthritis and undifferentiated spondyloarthritis were commonly observed in patients with HIV infection in the West, and nowadays these entities are prevalent in HIV-infected indigenous black Africans, having been rare before the HIV pandemic.[2,3] The introduction of HAART has changed the spectrum of clinical manifestations with septic and malignant complications now being the most common.[4]

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AN ORIGIN OF THE TERM AUTOANTIBODY

Sir,

Understanding of the immune system has changed profoundly in the last decade; Dhillon and Gray[1] in their recent review in the *Journal* describe how work on the rheumatoid factor has lead to the detection of antibodies to citrullinated peptides, anti-CCP2, clearing the way to early diagnosis and tighter control of the rheumatoid process. They suggest that in patients with susceptible genes, an inflammatory response may be generated by 'up regulation' of the inflammatory milieu. Here lies the connection with the work of Fehervari and Sakaguchi[2] who describe a subpopulation of CD4+ T cells which, acting through the transcription factor Foxp3, are able to turn T-cells into regulatory cells, profoundly influencing tissue responses. This world of molecular immunology sets us apart from the scene of seventy years ago, when the tools of investigation were histopathology and classical serology. This letter describes the use of 'reagents' produced in much the same way as the rheumatoid factor in the first investigations of thyroid immunology and the finding of precipitating antibodies in thyroid disease.

In 1936, a paper was published by C Picado and W Rotter[3] with the auspicious title 'Précipitines Sériques Antithyroidiennes chez les Goitreux'. They examined the serum of patients admitted to the thyroid service of the Hospital San Juan de Dios in Costa Rica. They found an increase in thyroid precipitins much above that of the normal population of patients of similar age, and in some, anti-pituitary and anti-adrenal antibodies were noted. These findings suggested that diseases accompanied by hypothyroidism were those with an extraordinary rise in thyroid antibodies.

> 'Faits qui semblent indiquer que dans les malades où il y a hypothyroidism, celui-ci s'accompagne d'une augmentation inusitée des précipitins anti-thyroidiennes et souvent aura des précipitins antihypophysaires.'

This extraordinary story now begins to go off the rails. They decided to correlate the antibody titres and histopathology of excised thyroid glands of individual patients which they divided into macrofollicular nodular, diffuse parenchymatous and nodular tubular goitres. This writer has concluded that this foray was unsatisfactory due to the small number of cases. They found no antibodies in thyrotoxicosis, in contrast to the work of MacGregor[4] in Edinburgh many years later; furthermore, there is no mention of either lymphocytes or plasma cells in their descriptions of the histopathology.

So what happens next? The pair travel to Saarbrucken in Germany where they again publish another auspicious title, 'Über Modifikationem der Schildrusenfunktion bei verschiedenen Immunitätsreacktionen'.[5] Reviewing their earlier work, they noted that in cases of hypothyroidism, the greatest increase in serum precipitin was found. 'Im fallen von hypothyroidism (endemic Kropf, myxoedeme, Kretinismus) bei denen wie gesagt eine starke vermehrung der antithyroidalen serum-prazipitine gefunden wird'. This prompted the question whether thyroid function was secondary to an anti-hormone effect or simply due to the cytotoxic action of the antibody.

They approached the subject experimentally by studying the effect of rabbit anti-human thyroid serum (ATS) on the thyroid gland of guinea pigs. They found that injections of ATS caused hyperplasia and hypersecretion, although long continued injections caused hypoplasia. Another property of ATS was the enhancement of the activity of thyrotrophic hormone as judged by its effect on the histology of excised glands. They claimed that thyroid secretion working as antigen, induced an immune response with the formation of serum precipitins whose short term function resulted in hyperthyroidism, and chronically a suppression of thyroid function as judged by low flattened thyroid epithelium.

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