Prescience of a Surgeon in 1980

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Dear Editor:

A photocopy of a page from an unpublished document, entitled "The Thyroid and the Thymus" by Selwyn Taylor, was recently given to me by Dr. Boris Catz. Mr. Taylor, as is well-known in the thyroid field, was a surgeon and Dean of the Royal Postgraduate Medical School, Hammersmith Hospital, London, until his retirement in 1978. (Incidentally, surgeons are addressed as "Mr." and not "Dr." in the United Kingdom.)

The page begins with Mr. Taylor's address in 1980 at the end of his year as the first president of the International Association of Endocrine Surgeons. Because it is inscribed "Not for publication" accompanied by his signature, I have paraphrased it. Mr. Taylor says he has chosen to discuss a subject that has interested and worried him for most of his medical life. The subsequent paragraph, concerning characteristics of the thyroid in Graves' disease and its implications for treating or resolving exophthalmos, provides remarkable prescience.

Mr. Taylor describes intriguing unpublished experiments involving autoradiographs (after radioactive iodine administration) from thyroid glands of patients with hyperthyroidism, presumably due to Graves' disease or toxic nodular goiter, treated with propranolol. He observed two categories: glands with extensive lymphoid infiltration and those without. In the latter group, the autoradiograph demonstrated a greater degree of "blackening." More extensive blackening in autoradiography implies a greater uptake of radioactive iodine by thyrocytes in glands with fewer lymphocytes. Had we been aware of Mr. Taylor's experience, my British colleagues and I would have cited his observations in our comparison of thyroid autoantibody synthesis by thyroid-infiltrating lymphocytes from Graves' patients treated before surgery with propranolol versus antithyroid drugs (1). This and other studies (some cited below) were possible because of the invaluable collaboration my colleagues and I enjoyed with another inquisitive surgeon, Mr. Christopher Pegg, University of Nottingham, United Kingdom. It was initiated at the 1983 Madrid meeting of the European Thyroid Association. In the lunch break, while several ETA members were sunning themselves at the swimming pool, I heard Chris ponder aloud, "I wonder what all those lymphocytes in the thyroid are doing?"

Mr. Taylor also mentions the possibility of a role for the thymus in relation to thyroid-infiltrating lymphocytes. This comment recalls early observations of differences in Graves'

thymic tissue compared with nontoxic nodular goiter or chronic thyroiditis, namely the presence of medullary thymic follicles and thymic hyperplasia (2). Medullary thymic follicles are also found in patients with myasthenia gravis, and thymectomy has long been associated with clinical improvement of this disease (3). Thyroid antibodies were not detectable in Graves' patients with small thymuses, and prolonged (up to 18 months) antithyroid drug therapy was associated with thymic involution (2). Taken together, such findings suggested a role for the thymus in Graves' disease pathogenesis and prompted us to investigate thyroid autoantibody synthesis by thymic lymphocytes. We found that thyroid autoantibodies are rarely synthesized by Graves' thymic lymphocytes and only after mitogenic stimulation, unlike the spontaneous production observed for thyroid-infiltrating lymphocytes (4,5). Although not a source of thyroid autoantibodies, the thymus plays a critical role in central tolerance: intrathymic expression of the thyrotropin receptor (TSHR) is reduced in individuals homozygous for the single nucleotide polymorphism (SNP rs179247) associated with Graves' disease versus thymic expression in individuals without this particular SNP (6).

Finally, Mr. Taylor suggests that the removal of these "important lymphocytes" may be useful in preventing or resolving Graves' exophthalmos. He links his suggestion with the proposal made many years ago by Dr. Boris Catz (7) that thyroid ablation (total thyroidectomy followed by radioactive iodine treatment) would be an effective therapy for Graves' ophthalmopathy. Mr. Taylor indicates that a lot more work would be required to substantiate such a theory. Indeed, extensive investigations have been performed to elucidate the role of TSHR expression in the orbit in Graves' ophthalmopathy (8). Moreover, these studies demonstrated the presence of orbital infiltrating lymphocytes that may secrete TSHR antibodies and are undoubtedly a source of critical inflammatory cytokines in Graves' ophthalmopathy (8). To Mr. Taylor's "kangaroo leap" speculation, subsequently supported by clinical studies (9,10), I would add that thyroid ablation removes the bulk (albeit not all) of the inciting and ongoing culprits of the disease, the TSHR-specific T- and B-infiltrating lymphocytes and the TSHR.

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