

Edwin B. Astwood (1909-1976) and the Treatment of Hyperthyroidism with Antithyroid Drugs

“Ted” Astwood did not come to endocrinology by a smooth and easy route but rather as a chance encounter for a mind seeking a challenge. When in 1943 he wrote about an entirely new treatment for hyperthyroidism, namely, medical therapy with drugs that blocked thyroid function, it had come about because his mind sought and found an explanation to a puzzle.

Ted grew up in Bermuda where his father supported the family well and supported Ted for some years into his career. His mother, enamored of the Seventh-Day Adventist (SDA) religion, directed Ted to an SDA college for his higher education. Thinking he would go into mathematics, Ted switched to medicine as his family saw mathematics as suitable for a life in banking and Ted thought otherwise. Still, his mother’s sensibility again directed Ted to the only SDA medical school, the College of Medical Evangelists in Loma Linda, California. He lasted two years before his developing agnosticism led him away from California to Montreal where he finished his medical training at McGill University; he received his MD in 1934. He interned at Montreal’s Royal Victoria Hospital; here is where he seems to have found endocrinology. He met there investigators such as Hans Selye and J. S. L. Browne and his life course was set.

Bright thought he was, Ted did not stay on at the Royal Vic for further training. He had had a run-in with the chief of the medical service, who was an author of one of the widely used textbooks of medicine at the time. On rounds, Ted was asked what he thought was the diagnosis in a patient; he made one. The chief carefully explained why that could not be right. Ted pursued it and found that he had in fact been correct. The next day’s rounds brought a question from the chief and Ted quietly explained that his diagnosis had been correct. The chief went on to point out how it was not so important to get the right diagnosis but to come to a conclusion with a rational explanation even if it might be wrong. Ted thought otherwise (one of his characteristics) and left for Baltimore the next year. He really did not have a plan and was fortunate to land a position in surgical pathology. This was essentially a research position and he now got into endocrine research on his own, examining the hormonal control of the rat mammary gland and of changes in fish color. After two years, he had been recognized as an up-and-coming physician-investigator and won a Rockefeller Fellowship for three years of further training.

Now Ted moved to Cambridge, Massachusetts to work in Harvard’s Biology Laboratories under Frederick Hisaw, the discoverer of relaxin and a powerhouse in the emerging field of pituitary hormone physiology. A PhD degree was forthcoming for Ted after only two years; Ted had invented assays for estrogen and for progesterone and had defined a new hormone that he called “luteotropin” that we now know is prolactin (prolactin had been recognized a few years before but Ted established its relevance to the hormonal support of the rat’s corpus luteum). By now it was the depths of the great depression and he had to find a “real” job. He did so back in Baltimore in Johns Hopkins’

department of obstetrics, mainly as a researcher. He stayed only a bit over a year as the 29-year-old scientist-physician was then called to Boston to join the staff at the Peter Bent Brigham Hospital, one of Harvard's major teaching hospitals, with a joint appointment in the pharmacology department (the latter appointment was fortunate as there was literally no research space in the hospital). His major interest was in adrenal physiology.

But things were to turn in another direction. Sometime in 1941, he noticed a paper written from Johns Hopkins' nutrition department by old acquaintances, Cosmo and Julia Mackenzie. They had noticed that rats fed certain sulfa drugs developed goiter. Because of his knowledge of endocrine feedback loops, Ted quickly recognized that what was happening was that the rats' thyroid glands got larger because the sulfa drugs interfered with thyroid function and so stimulated the secretion of thyrotropin (TSH) which in turn made the thyroid gland grow. Ted proved this by giving the drugs to rats after their pituitaries were removed with the result that the thyroid glands now failed to grow: the goiter was pituitary-dependent. Further, as a physician, Ted saw the drugs' utility: if such a drug could be given to persons with hyperthyroidism, it might lower the excess thyroid function and cure the disease.

In 1942, then, Ted focused on thiourea and thiouracil as possible antithyroid agents. It was reassuring that, given to normal persons, these drugs did not seem to do much. But, initially at least, they seemed not to do much in patients with hyperthyroidism either. Then after a bit more experimentation, the approximately correct dose was defined and three patients with hyperthyroidism had a clear improvement in their disease; this result became his 1943 paper. There were difficulties. He and his colleagues had happened unwittingly to have picked drugs that had a fair number of side effects. But the answer was, for them, to push on. Ted had moved again in the mid-1940s to the Tufts-New England Medical Center and now his group tested literally hundreds of similar agents for antithyroid activity over the next several years; most of the drugs were supplied by one or another pharmaceutical firm. The result was the recognition of propylthiouracil and methimazole as effective treatments by the late 1940s. They remain to this day the only two antithyroid drugs available in the United States.

Ted went on to other work with his main focus being on the thyroid gland for most of the next 30 years. Honors came his way: the Lasker Award in 1954 and election to the National Academy of Sciences. But he held to the old school of physicians' behavior: he would never patent any of his discoveries. He retired early at age 62 years and died of cancer in 1976. He trained many in his unit; all remember their time with Ted as one of the high points of their lives.