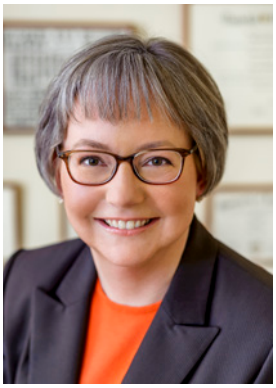
THE GLANDULAR CORNER: THYROID

Linda Isaacs, MD, Discusses Glandular Thyroid Extracts, Their History, and Current Applications



Linda L. Isaacs, M.D., received her Bachelor of Science degree from the University of Kentucky, graduating with High Distinction with a major in biochemistry. She is a graduate of Vanderbilt University School of Medicine and is certified by the American Board of Internal Medicine, completing the recertification process in 2001, in 2011, and in 2019.

The earliest references to the medicinal use of preparations of the thyroid gland go back more than a thousand years. Practitioners in China dried animal thyroid glands, minced them, and mixed them with jujubes to make pills, or powdered them and mixed them into wine.[1] Seaweed was used for the treatment of goiter in China and other cultures. The prevalence of goiter in communities far from the sea was well known in Europe for millennia.

With the development of anesthesia in the 1800s, surgeons began removing goitrous thyroids, precipitating hypothyroidism and myxedema.[2] Meanwhile, other physicians had noted that, on autopsy, the thyroid glands of patients with myxedema were practically nonexistent. In 1891, Murray treated a myxedema patient with injections of thyroid extract, with dramatic improvement.[3]

Soon after, reports came of patients successfully treated with oral thyroid, sometimes prepared as a sandwich with anchovy paste. Patients preferred thyroid in pill form, so medicinal use of thyroid as food was short-lived. However, occasionally thyroid tissue has accidentally made its way into the food supply, causing "hamburger thyrotoxicosis."[4,5] Thyrotoxicosis has also been seen in dogs, especially smaller dogs, after thyroid tissue was included in dog food or dog treats.[6]

A subset of patients have insisted that they felt better on desiccated thyroid, and its use has continued to this day.

Protocols for oral thyroid extracts have been in existence for more than a century. A 1905 issue of *Merck's Manual of the Materia Medica* included "Thyroidin Merck. Dried extract sheep's thyroid; 1 part represents 6 parts fresh gland … Dose: ½–1 grn. (0.03–0.06 Gm.), gradually increased to 2 grn. (0.12 Gm.), 3 t. daily, in tablets."[7]

One of the first patients to receive oral thyroid in the United States began treatment for severe hypothyroidism in 1892.[8] She died in 1943, at age 91; her final years were marked by a balancing act between hypothyroid symptoms (when her dose was dropped) and angina (when it was raised).

Thyroid products were in use well before any reliable methods for checking potency existed. Iodine standardization became part of *The Pharmacopeia of the United States of America: Ninth Decennial Revision* in 1916, but iodine could be present in an unusable form, especially if iodine was provided to a goitrous animal very shortly before slaughter.[9] Iodine would be rapidly taken up by the animal's thyroid, but not have had time to be incorporated into the active hormone.

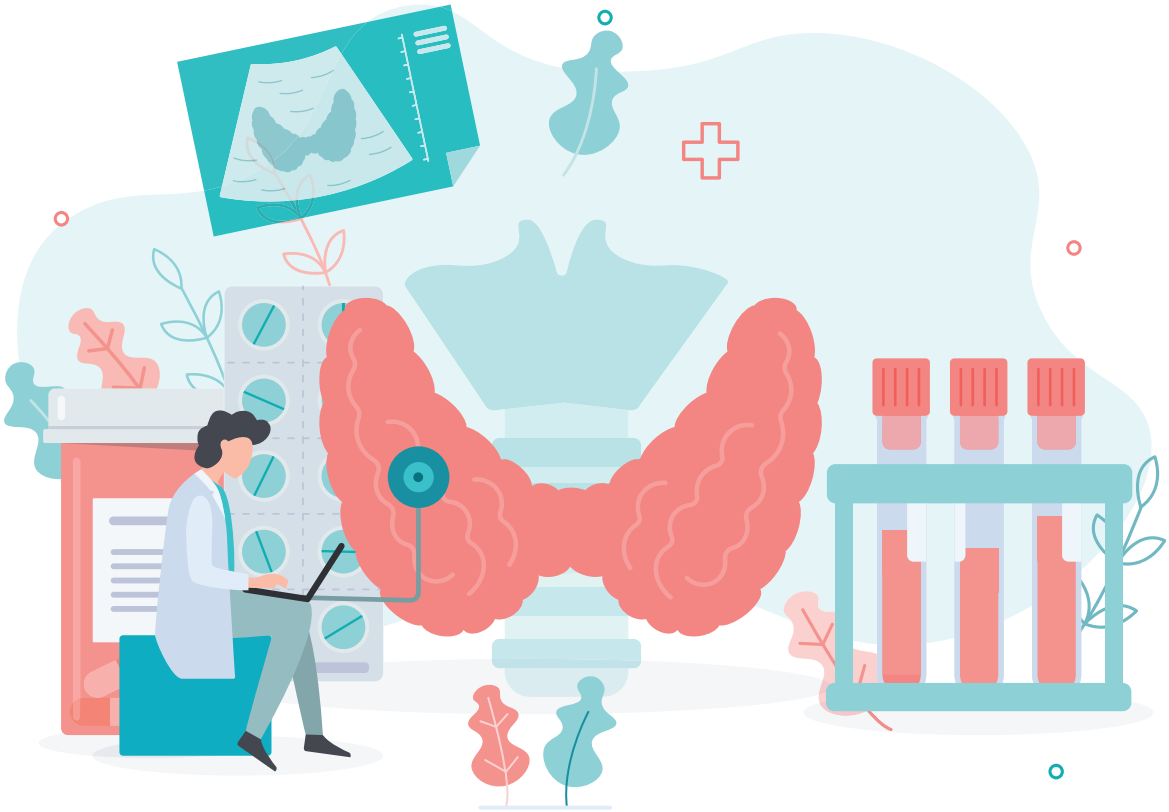
The potency of thyroid products was evaluated through biological testing, such as through research on the effect on the basal metabolic rate of rats, or prevention of goiters in animals rendered hypothyroid by thiouracil.[10] A 1917 article reported a method of testing the activity of thyroid extract by its effect on the maturation of tadpoles.[9] With the tadpole assay of seven products purchased in a drugstore, three had more activity than a standard preparation (in one case, more than 50%), two were equal in strength, one was about half strength, and one was practically worthless. The author recognized that the seasonal availability of tadpoles could limit their usefulness, but suggested that tadpoles could be stockpiled in cold temperatures for later use.

With the advent of synthetic levothyroxine sodium in the 1950s, the pressure was on to gradually steer practitioners away from the use of thyroid extracts.[11] Opponents of thyroid's use emphasized its variability in potency, as demonstrated by various biologic assays and by clinical results in patients. Manufacturers would sometimes switch from one species to another for their raw material; porcine thyroid was most commonly used in the United States because of higher iodine content and ease of collection.[10] In 1956, Kroc and Stasilli reported that, based on biologic assays, bovine-derived thyroid products were less active.[10] A 1962 publication reported similar findings, using measurements of thyroxine (T4) and triiodothyronine (T3).[12]

As measurement of T4, T3, and thyroid-stimulating hormone (TSH) became common in the 1970s, endocrinologists emphasized that synthetic levothyroxine sodium was the preferred treatment.[13] However, a subset of patients have insisted that they felt better on desiccated thyroid, and its use has continued to this day.

In a 2013 publication of the results of a randomized, double-blind, crossover study comparing desiccated thyroid extract to levothyroxine, a research group based at the Walter Reed National Military Medical Center reported that the extract caused modest weight loss, and that nearly half the participants preferred the extract to levothyroxine.[14] A follow-up study, published in 2021 by the same group with the same methodology, compared T4, a T4 + T3 combination therapy, and desiccated thyroid extract. TSH remained within reference range in all groups; a subgroup analysis of patients symptomatic on T4 alone found a strong preference for the combination therapy or for desiccated thyroid extract.[15] A 2020 retrospective study examined the stability of TSH values in patients on levothyroxine therapy compared with patients on desiccated thyroid and found no difference.[16]

With these recent studies, the medical world seems to be returning to the position found in a 1970 pharmacology textbook: desiccated thyroid extract "is a highly satisfactory preparation for clinical use. Its continued popularity does not derive merely from a reactionary attitude, although at first sight the preparation might seem to be crude, old-fashioned, and poorly standardized. It is evidently uniformly well absorbed unless it has an enteric coating, and the potency is sufficiently standard that variation cannot be detected clinically if the official preparation is prescribed."[17] ■



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