THE GLANDULAR CORNER: ADRENAL

Linda Isaacs, MD, Discusses Adrenal Glandular Therapies, Including Their History and Current Clinical 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.

She and her long-time colleague, the late Nicholas J. Gonzalez, M.D., collaborated on two research projects, three articles published in scientific journals, and a book, The Trophoblast and the Origins of Cancer. Since his untimely death, she has continued the work they shared. Her website is www.drlindai.com.

In 1855, Thomas Addison, MD, combined his observations of patients with weakness, fatigue, hypotension, nausea and abdominal pain, skin pigmentation, and eventual death with autopsy findings of abnormal adrenal glands to describe the condition that is now named after him, Addison's disease. In subsequent decades, it became clear that the adrenal glands are essential to health, based on clinical history and autopsy results in humans, as well as experimentation with adrenal removal in animals. As Addison's disease became more widely recognized, many physicians came to believe that there could be milder degrees of adrenal fatigue.

With the discovery in the 1890s that dried thyroid gland could resolve symptoms of hypothyroidism, a wide variety of glandular products began to be used. A 1905 issue of Merck's Manual of the Materia Medica included "Suprarenal Capsule, Dried, Merck. 1 part represents 5 parts fresh capsule," used for the treatment of Addison's disease, hay fever, and neurasthenia. 1 Clinicians used adrenal glandular

material, either raw or dried and formed into a tablet, to treat various conditions with some success. Here is an example by Francis M. Pottenger, Jr., MD:

"In August, 1932, we began feeding whole beef adrenal glands to a group of patients suffering from asthenia. These were administered within a few hours from the time they were removed from the animals. Our reason for this was because of the various reports connecting this condition with adrenal deficiency. The improvement in their energy and sense of well-being was very definite. In September, 1932, a child whom we were treating had been suffering from continuous asthma for several months and was completely exhausted. With the idea that we might at least relieve his exhaustion we gave him seven grams of whole raw beef adrenal gland, which was first ground and then mixed with peanut butter. That night the child became free from asthma and remained so for three days."2

Researchers tried to find the active hormone in the glandular material, as had been previously done for thyroid hormone. Adrenaline was purified from the adrenal medulla well before the hormones from the cortex were isolated. A pharmacology professor with Addison's disease devised his own treatment, called the Muirhead method, which required 1,200 mg of dried whole gland orally per day. Since no one was sure whether the cortex or medulla made the component that would prolong life, adrenaline injections were also included. Muirhead was bedridden before beginning this treatment

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and improved substantially on it, but, after several months, he deteriorated and died.³ In a series of patients treated at the Mayo Clinic in the 1920s, the Muirhead method was described as beneficial for half the patients treated.⁴

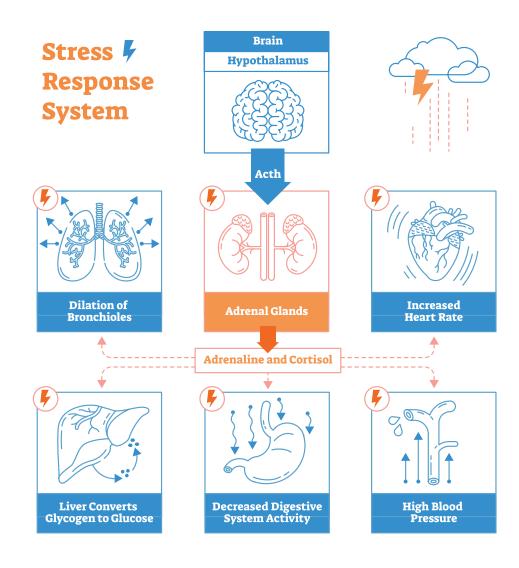
As it became clear that the adrenal cortex made the crucial component, whatever it might be, various solvents were used to make extracts of the

adrenal cortex. However, they were expensive and difficult to produce, especially in the volume that would be needed to support life in a patient with no adrenal function whatsoever. The extract made by Swingle and Pfiffner in the early 1930s brought about remarkable improvement in patients who were bedridden, nauseated, and hypotensive, but it required 600 g of bovine adrenal cortex (from roughly 20 cows) to produce enough for a daily dose for such a patient.⁴ Two physicians in Australia reported success in managing patients with 3 g per day of oral dried whole adrenal gland supplement, along with a highsalt diet, using the expensive adrenal extract only when the patient was in crisis.⁵

Oral glandular materials fell out of use by the medical establishment when methods of large-scale corticosteroid production were devised in the 1940s. The side effects of corticosteroids were recognized fairly quickly; as early as the 1960s, caution was advised in their use.⁶ This may be why the orthodox world has come to frown upon a diagnosis of "adrenal failure" that is not supported by testing they recognize—the side effects of corticosteroids are not trivial, and they should be reserved for those who unequivocally need them.

One of the most striking observations I made, as I reviewed the early literature, is how little corticosteroid there actually may have been in the glandular products and crude adrenal extracts used, with some success, in treatment of Addison's disease in the 1920s and 1930s.

The 7 g of raw adrenal gland that Dr. Pottenger gave an asthmatic child? It had no more than 0.028 mg of cortisol in it. Perhaps that child's recovery could be attributed to the adrenaline in the raw adrenal, though such an effect would wear off too



I USED THE FOLLOWING INFORMATION TO MAKE THESE CALCULATIONS:



ACCORDING TO THE MERCK PUBLICATION, 1 PART DRY = 5 PARTS WET¹



quickly to explain the three-day improvement described by Pottenger.

In the Mayo Clinic series, half of the patients with adrenal failure on the Muirhead regimen improved on a product that could have contained no more than 0.024 mg of cortisol. The crude extract that was used in the 1930s with dramatic effect in moribund Addison's patients required 600 g of bovine adrenal cortex to make a daily dose. That would work out to 870 g of whole adrenal, which would at most contain 3 mg of cortisol. The extract probably contained less, given inevitable losses in processing.

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These calculations serve two points. First, while an Internet search on adrenal glandulars will produce alarming documents about adrenal suppression, there isn't enough corticosteroid present in dried adrenal material to cause such suppression. A 200 mg capsule would require roughly 1 g of raw material to produce, which would contain 4 to 5 mcg of cortisol—orders of magnitude less than the amount the body makes each day.

Second, given that these clinicians saw improvement in seriously ill patients with products that could not have contained a significant amount of cortisol, I believe there is something other than cortisol in the whole gland, whether raw, dried, or crudely extracted, that is beneficial to patients. This stands to reason, given all the various hormones naturally present in both the adrenal cortex and medulla. I know I see the benefits of adrenal glandular in my clinical practice. And it does not produce dependency; in many cases, patients who initially find adrenal glandular capsules helpful for fatigue eventually do not need the product. As for side effects, it can cause nausea or headaches, especially if taken away from food. In my experience, it rarely causes problems in an exhausted patient, but as the patient recovers, the dose may need to be decreased or the product discontinued.

References

- 1. Merck & Co. Merck's 1905 Manual of the Materia Medica. New York (NY): Merck & Co.; 1905:109.
- 2. Pottenger FM Jr., et al. The Treatment of Asthma: With Special Reference to the Oral Use of the Adrenal Hormones and Sodium Chlorid. Cal West Med. 1935;43(1):10-3.
- 3. Rowntree LG. Subsequent Course of a Case of Addison's Disease. J Am Med Assoc. 1922;79(7):556-7.
- 4. Rowntree LG, et al. Addison's Disease: Experiences in treatment with various suprarenal preparations. J Am Med Assoc. 1931;96(4):231-5.
- 5. Hicks CS, Mitchell ML. The Treatment of Addison's Disease by Whole Adrenal Gland. Proc R Soc Med. 1935;28(7):932-40.
- 6. Benedek TG. History of the development of corticosteroid therapy. Clin Exp Rheumatol. 2011;29(5 Suppl 68):S-5-12.
- 7. Wagner WC, et al. Reproductive physiology of the post partum cow. II. Pituitary, adrenal and thyroid function. J Reprod Fertil. 1969;18(3):501-8.
- 8. Howes JR, et al. Adrenal Gland Weights of Hereford and Brahman Cattle. Proc Soc Exp Biol Med. 1960;104(2):322-4.