



Whole adrenal extract for Addison's disease in the 1920s: Where is the cortisol?

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ABSTRACT

Prior to the development of synthetic corticosteroids, Addison's disease was treated with oral desiccated whole adrenal glands or crude extracts. These products could not have contained meaningful amounts of cortisol, yet some patients improved. There may be something in whole glands that can stimulate failing adrenals to make cortisol.

In the 1920s and 1930s, Addison's disease was treated with desiccated whole adrenal gland or crude alcohol extracts. All of these products were abandoned by the medical world when medications like prednisone became available in the 1950s.

In the following discussion, this information is used:

- Whole gland, ground, contains 2–4 µg/gram of cortisol [1]
- The adrenal cortex is about 69% of the gland [2]
- Five parts whole adrenal makes 1 part dried adrenal [3].

The Muirhead method of treating Addison's disease, used at the Mayo Clinic during the 1920s, involved oral administration of 1200 mg of oral dried whole gland daily, along with 1 mg rectally, and injections of epinephrine [4]. On this regimen, Muirhead himself had resolution of pigmentation and improvement of performance status for a time. The Mayo Clinic investigators reported that “half of the patients showed some benefit, a third responded with results that were considered excellent, and a sixth were living after three years.” 1200 mg of dried whole gland would have been derived from roughly 6 g of raw adrenal, which would contain at most 0.024 mg of cortisol.

In the same article, the Mayo investigators describe bringing patients with Addison's disease from moribund to fully functional with the use of an adrenal extract requiring 600 g of adrenal cortex raw material to make enough for one day's treatment. This would require about 900 g of whole adrenal, which would contain at most 3.6 mg of cortisol, probably less with losses in processing.

In another article, physicians in Australia treated patients with 3 g per day of a product they made by mincing and drying adrenal glands [5]. They also recommended a high salt diet, and used an adrenal extract intermittently. Three grams of dried product would be derived from roughly 15 g of raw material, which would contain at most 0.060 mg of cortisol.

In these three scenarios, patients reportedly improved from adrenal insufficiency with products containing amounts of cortisol far short of what are used today. The Mayo Clinic article does not report on salt intake; the high salt diet would certainly have been helpful for the Australian patients, but the article states they were only restored to health with the addition of the oral glandular material.

There are several possible conclusions from this. First, there is something wrong with the above calculations, or the data on which those calculations are based. Second, that the investigators in these articles were not actually treating patients with Addison's disease, since laboratory testing was rudimentary in that era. However, the descriptions of the patients, including skin pigmentation, extreme weakness and unstable blood pressure, sound valid.

The final possibility is that some other entity in the whole adrenal glandular was of value to these patients. Since cortisol is necessary for the treatment of Addison's disease, the substance in the whole adrenal glandular might help a failing adrenal gland make cortisol. This substance could have applications in patients weaning off high dose corticosteroids. MicroRNA might be the substance, since a 2015 article reported the persistence of microRNA in bovine tissue extracts [6]. If there is an animal model of Addison's disease, that could be a way of testing whole adrenal glandular, to see if it delays or eliminates disease progression.

Ethical approval

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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