# ADRENALECTOMY IN LIPOATROPHIC DIABETIC SUBJECTS: A HUMAN CASE AND A MURINE MODEL (A-ZIP/F-1 MOUSE).

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A 16-year-old female teenager diagnosed with a severe Berardinelli-Seip syndrome had her adrenals surgically removed in 1988 following a successful anti-glucocorticoid strategy with mifepristone alone and in combination with ketoconazole. We presented this case at the 71st ES Meeting in Seattle (Abstract 751,1989), and this author recently published it in full in 2022 (DOI:10.5772/intechopen.102986). There was a striking metabolic amelioration, particularly with the one-week combined therapy. The patient gained 7 Kg and experienced complete regression of her severe acanthosis nigricans and eruptive xanthomas. An OGTT performed two weeks after surgery showed normal serum insulin levels, normal fasting serum glucose levels, and a 2-h serum glucose value in the mild diabetic range. Fourteen years later, Haluzik et al. (Diabetes 2002;51:2113) reported that the A-ZIP/F mouse (a non-leptin responding model of murine lipoatrophy) showed an improvement in hepatic and muscle insulin sensitivity following adrenalectomy. These results suggested that chronic elevation of serum corticosterone contributes to diabetes in this hypoleptinemic mouse and that removing hypercorticosteronemia improves tissue insulin sensitivity. So, both in a human case of lipoatrophy and in this murine model of the disease, adrenal glucocorticoid removal induces a notorious amelioration of the disease. Leptin is well known for its ability to restrain the adrenal axis. However, high serum leptin levels are associated with reduced leptin action (leptin resistance). So, leptin resistance might induce adrenal overactivity in obese and T2 diabetic subjects, leading to adipose insulin resistance, excessive lipolysis, and liver and muscle steatosis. If this hypothesis is proven, we predict a therapeutic role for the emerging, orally available, nonpeptide ACTH blockers (such as Crinetic's CRN04894) in treating these common diseases.