

Addison Disease: Early Detection and Treatment Principles

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Primary adrenal insufficiency, or Addison disease, has many causes, the most common of which is autoimmune adrenalitis. Autoimmune adrenalitis results from destruction of the adrenal cortex, which leads to deficiencies in glucocorticoids, mineralocorticoids, and adrenal androgens. In the United States and Western Europe, the estimated prevalence of Addison disease is one in 20,000 persons; therefore, a high clinical suspicion is needed to avoid misdiagnosing a life-threatening adrenal crisis (i.e., shock, hypotension, and volume depletion). The clinical manifestations before an adrenal crisis are subtle and can include hyperpigmentation, fatigue, anorexia, orthostasis, nausea, muscle and joint pain, and salt craving. Cortisol levels decrease and adrenocorticotropic hormone levels increase. When clinically suspected, patients should undergo a cosyntropin stimulation test to confirm the diagnosis. Treatment of primary adrenal insufficiency requires replacement of mineralocorticoids and glucocorticoids. During times of stress (e.g., illness, invasive surgical procedures), stress-dose glucocorticoids are required because destruction of the adrenal glands prevents an adequate physiologic response. Management of primary adrenal insufficiency or autoimmune adrenalitis requires vigilance for concomitant autoimmune diseases; up to 50% of patients develop another autoimmune disorder during their lifetime. (*Am Fam Physician*. 2014;89(7):563-568. Copyright © 2014 American Academy of Family Physicians.)

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Author disclosures: No relevant financial affiliations.

► Patient information: A handout on this topic is available at <http://familydoctor.org/familydoctor/en/diseases-conditions/addison-disease.html>.

More than 150 years ago, Thomas Addison described a group of patients with anemia and diseased adrenal glands at autopsy, a condition now known as primary adrenal insufficiency. Autoimmune adrenalitis is the most common cause of primary adrenal insufficiency, or Addison disease, in the United States. Less common causes include infection, hemorrhage, metastatic cancer, medication use, and adrenoleukodystrophy.

Autoimmune adrenalitis is a disorder in which the adrenal cortex is destroyed, resulting in the loss of mineralocorticoid, glucocorticoid, and adrenal androgen hormone production. Addison disease can be part of the autoimmune polyglandular syndromes (type 1 and 2), or it may present as an isolated disorder.¹ This article focuses on the diagnosis and treatment of Addison disease as an isolated disorder, with a focus on the pathophysiology and treatment considerations of autoimmune adrenalitis.

Pathogenesis

Autoimmune adrenalitis can be divided into stages of progression^{2,3} (Table 1). As the

disease develops, individuals lose adrenocortical function over a period of years. In the first three stages, the human leukocyte antigen genes confer genetic risk; an unknown precipitating event initiates antiadrenal autoimmunity; and 21-hydroxylase antibodies are produced, which predict future disease. The production of these antibodies can precede symptom onset by years to decades, and they are present in more than 90% of recent-onset cases.^{2,4-7} In the fourth stage, overt adrenal insufficiency develops. One of the first metabolic abnormalities to occur is an increase in plasma renin level, followed by the sequential development of other abnormalities, including a decreased response to adrenocorticotropic hormone (ACTH) stimulation in the fifth stage. If symptoms of adrenal insufficiency are present but go undiagnosed, an Addisonian crisis can occur.

Clinical Diagnosis

Because the estimated prevalence of Addison disease is one in 20,000 persons in the United States and Western Europe, a high clinical suspicion is needed to avoid misdiagnosing a life-threatening adrenal crisis.⁸ Signs and symptoms can be subtle and nonspecific.

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This guide began as a manual for family medicine residents Over time it evolved into a fairly complete coverage of most of the outpatient issues seen in their training In response to their urging I set out on the journey to convert the manual into the manuscript for this book The book is intended for primary care physicians nurse practitioners and physician assistants It serves three purposes 1 as a quick reference for primary care providers to use in the clinic when seeing patients 2 as a textbook and 3 as a study guide for Board examinations It covers a great number of topics

briefly to allow quick reading To allow fast access the chapters are arranged in alphabetical order beginning with Chapter 1 Allergy and ending with Chapter 27 Women s Health Topics within chapters also are arranged in alphabetical order again to allow quick access Table of Contents Chapter 1 Allergy Chapter 2 Cardiovascular Chapter 3 Dermatology Chapter 4 Electrolyte Disorders Chapter 5 Endocrinology Chapter 6 Gastrointestinal Chapter 7 Hematology Chapter 8 Infectious Disease Chapter 9 Men s Health Chapter 10 Miscellaneous Chapter 11 Muscle Disorders Chapter 12 Neurology Chapter 13 Oncology Chapter 14 Ophthalmology Chapter 15 Orthopedics Chapter 16 Otolaryngology Chapter 17 Pain Chapter 18 Pediatrics Chapter 19 Preventive Medicine Chapter 20 Psychiatry Chapter 21 Pulmonary Chapter 22 Rheumatology Chapter 23 Sexual Disorders Chapter 24 Urgery Chapter 25 Urology Nephrology Chapter 26 Weight Problems Chapter 27 Women s Health

REVIEWS AND WORDS OF PRAISE Dr Milhorn has done a Herculean job to create this textbook for ambulatory primary care providers that is current and comprehensive Each section covers the basics of pathophysiology signs and symptoms diagnosis and treatment The content is presented in a way that is easy to use and understand with excellent supporting photographs and tables Additionally the references are extensive and current I can definitely see using this resource not only in clinical practice but for exam review and preparation Diane Beebe MD Professor Emeritus and Past Chair Department of Family Medicine University Mississippi School of Medicine Past Chair American Board of Family Medicine ABFM If you are looking for a concise informative and well written quick reference for family physician residents physician assistants nurse practitioners or busy family physicians look no further Ambulatory Medicine by Dr H Thomas Milhorn distinguishes itself as the premier reference guide textbook and board review source on the market today it is in a class all by itself Lee Valentine DO Medical Director Mississippi State University Physician Assistant Program and past Program Director of EC Healthnet Family Medicine Residency Program The Philadelphia Medical Journal ,1901 **The Philadelphia Medical Journal** George Milbry Gould,James Hendrie Lloyd,1901 **Pennsylvania Medical Journal** ,1907 Old Dominion Journal of Medicine and Surgery ,1913 *Journal of the American Medical Association* ,1915

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