

A Guide describing the types of adrenal insufficiency

Adrenal Insufficiency (AI) is a general term used when there is a deficiency in the production of glucocorticoid (cortisol = hydrocortisone). A deficiency in mineralocorticoid (aldosterone) may or may not also be present. AI can be caused by a number of different conditions and can be **primary** or **central** (central AI includes both secondary or tertiary).

Primary Adrenal insufficiency occurs due to abnormalities of the outer portion of the adrenal glands known as the cortex. In primary AI, production of both cortisol and aldosterone is dampened. ACTH levels are elevated as the pituitary gland tries to correct the AI.

Some causes of primary AI include:

- Addison's disease (autoimmune adrenalitis)
- Congenital adrenal hyperplasia
- Adrenoleukodystrophy
- IMAGE syndrome
- Congenital adrenal hypoplasia

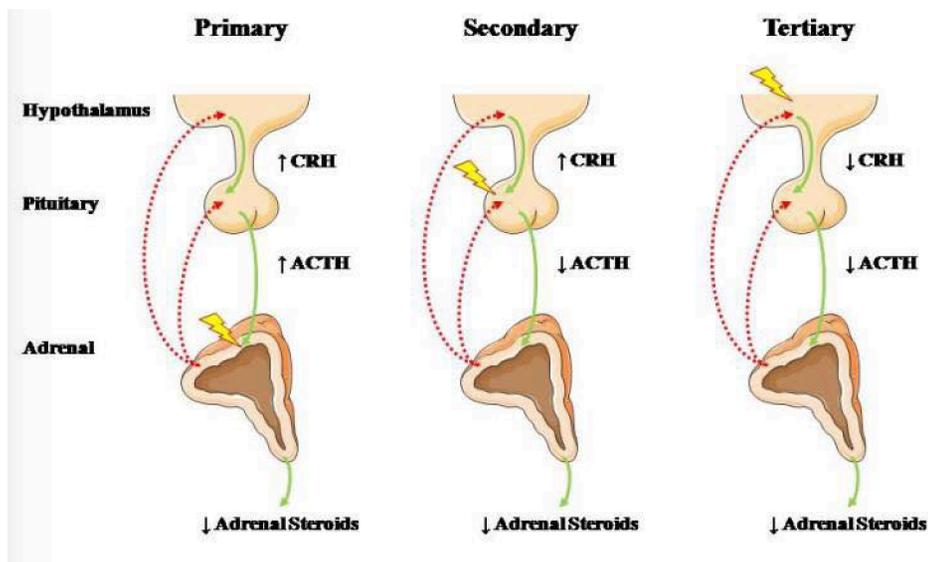
Photo from the National Institutes of Health (NIH)

Lightning bolt indicates where the problem for each originates.

Primary = high CRH and ACTH

Secondary = high CRH and low ACTH

Tertiary = both CRH and ACTH are low



Central Adrenal Insufficiency encompasses pituitary (**secondary**) and hypothalamic (**tertiary**) causes. Corticotropin-releasing hormone (**CRH**) is the hypothalamic (brain) hormone that causes the pituitary gland to secrete the hormone, ACTH which, in turn, tells the outer part of the adrenal gland to produce cortisol. (See NIH photo.)

*A CRH test is typically used to assist with the diagnosis when other less invasive tests fail to provide the necessary answers.

Secondary adrenal insufficiency (SAI) occurs due to damage of the pituitary gland. Morning ACTH levels are generally low in this setting.

Some causes of secondary AI include:

- Pituitary tumors
- Mutations in pituitary transcription factors causing multiple pituitary hormone deficiencies and possibility isolated ACTH deficiency
- Sheehan syndrome (pituitary infarction)
- Trauma
- Iron deposition

Tertiary adrenal insufficiency occurs due to problems with the hypothalamus. Tests may show low-to-normal morning ACTH levels.

Some causes of tertiary AI include:

- Use of glucocorticoids
- Hypothalamic tumors
- Hypothalamic hypopituitarism
- Following cure of Cushing syndrome
- Trauma
- Iron deposition

*A CRH test can be used to differentiate secondary AI from tertiary AI. ACTH levels will increase in hypothalamic disease, but remain low with pituitary disorders.

See our website for more information about testing for AI.
<https://aiunited.org/testing-for-ai/>

Document compiled by AIU using sources from the Lancet 2014 "Adrenal Insufficiency": Evangelia Charmandari, Nicolas C Nicolaides, George P Chrousos.

Additional resources from NIH and Mayo Clinic were also used.

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