21 Hydroxylase Deficiency

21-hydroxylase deficiency is the most common cause of congenital adrenal hyperplasia and results in the inability to produce cortisol. 21-hydroxylase is embedded in the smooth endoplasmic reticulum of cells in the adrenal cortex. This enzyme catalyzes the hydroxylation of 17-hydroxyprogesterone to 11-deoxycortisol in the glucocorticoid pathway and also catalyzes the hydroxylation of progesterone to 11-deoxycorticosterone (DOC) in the mineralocorticoid pathway. Due to this enzyme defect, cortisol and aldosterone synthesis is compromised. Loss of aldosterone causes severe hypotension and hyperkalemia. Loss of cortisol causes loss of feedback inhibition to the steroidogenesis pathway and leads to hyperplasia of the adrenals. Defect also causes backup of the precursor 17-hydroxyprogesterone. Because this substrate is also a precursor for sex hormones, it is shunted to the androgen synthesis pathway. Increased sex hormones cause masculization and female pseudohermaphroditism.



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Pathophysiology

Decreased Cortisol
Down-arrow Court-judge-sun
21 hydroxylase catalyzes the hydroxylation of 17-hydroxyprogesterone to 11-deoxycortisol in the glucocorticoid pathway. Deficiency of this enzyme compromises cortisol production, leading to loss of feedback inhibition to the adrenals and resultant adrenal hyperplasia.

Increased 17 Hydroxyprogesterone
17 Hydra-jester on Stilts
21-hydroxylase is embedded in the smooth endoplasmic reticulum of cells in the adrenal cortex. This enzyme catalyzes the hydroxylation of 17-hydroxyprogesterone to 11-deoxycortisol in the glucocorticoid pathway and also catalyzes the hydroxylation of progesterone to 11-deoxycorticosterone (DOC) in the mineralocorticoid pathway. Deficiency of 21 hydroxylase causes buildup of the substrate 17-hydroxyprogesterone.

Decreased Aldosterone
Down-arrow Aldo-stereo
21 hydroxylase also catalyzes the hydroxylation of progesterone to 11-deoxycorticosterone in the mineralocorticoid pathway. Deficiency of this enzyme causes decreased aldosterone production, leading to hypotension and hyperkalemia.

Signs and Symptoms

Hypotension
Hippo-BP
Aldosterone stimulates the conservation of sodium, secretion of potassium, and increased water retention in the kidneys. Therefore, decreased aldosterone leads to life threatening volume loss with severe hypotension.

Increased Renin
Up-arrow Wrenches
Severe volume depletion caused by loss of aldosterone causes increased renin levels in the body as the body attempts to compensate for volume loss.

Hyperkalemia
Hiker-banana
Aldosterone stimulates the conservation of sodium, secretion of potassium, and increased water retention in the kidneys. Therefore, loss of aldosterone causes severe hyperkalemia.

Female Pseudohermaphroditism
Masculine Queen-card
Deficiency of 21 hydroxylase causes buildup of the substrate 17-hydroxyprogesterone, which is diverted to synthesis of DHEA, androstenedione, and testosterone, leading to masculinization. Females with 21 hydoxylase deficiency can present with female pseudohermaphroditism due to increased androgen synthesis.

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