

Classic CAH: New Approaches to Glucocorticoid Dosing

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The management of classic congenital adrenal hyperplasia (CAH) has historically relied on glucocorticoid replacement therapy to suppress adrenal androgen production and prevent adrenal crises. However, achieving optimal androgen control without inducing iatrogenic Cushing's syndrome or growth impairment remains a persistent clinical challenge. Recent discussions at endo 202 suggest a shift towards more nuanced, individualised glucocorticoid dosing strategies, moving beyond conventional fixed regimens to improve patient outcomes.¹

KEY TAKEAWAYS

- **The Pivot:** The focus in classic CAH treatment is shifting from fixed-dose glucocorticoid regimens to individualised, dynamic dosing strategies.
- **The Data:** The primary goal is to achieve adequate androgen suppression while mitigating long-term glucocorticoid-related adverse effects, such as impaired growth and bone mineral density reduction.
- **The Action:** Clinicians should consider tailoring glucocorticoid doses based on individual patient biomarkers, growth velocity, and bone health, rather than adhering strictly to population-based averages.

Classic congenital adrenal hyperplasia (CAH), primarily due to 21-hydroxylase deficiency, necessitates lifelong glucocorticoid therapy. The objective is to suppress excessive adrenocorticotrophic hormone (ACTH) secretion, thereby reducing adrenal androgen overproduction and preventing adrenal crises. Traditional treatment protocols have often involved relatively high glucocorticoid doses to ensure robust androgen suppression. However, this approach frequently leads to significant adverse effects, including impaired linear growth, reduced bone mineral density, weight gain, and metabolic complications. The clinical dilemma lies in balancing effective androgen control with the minimisation of these iatrogenic complications. The prevalence of classic CAH is approximately 1 in 15,000 live births, making it one of the most common inherited metabolic disorders. Early diagnosis, often through newborn screening programs, is crucial for initiating timely treatment and preventing life-threatening salt-wasting crises in affected infants.

Current clinical practice often involves monitoring biochemical markers such as 17-hydroxyprogesterone (17-OHP), androstenedione, and testosterone to guide glucocorticoid dosing. However, the correlation between these markers and long-term clinical outcomes, particularly growth and bone health, is not always direct or consistent across all patients. This variability underscores the need for more refined treatment approaches that consider the individual patient's response to therapy. The mechanism of action of glucocorticoids in CAH involves negative feedback on the hypothalamic-pituitary-adrenal (HPA) axis, thereby suppressing pituitary ACTH release. Reduced ACTH stimulation

subsequently decreases the adrenal production of androgen precursors, which are overproduced due to the enzymatic block in cortisol synthesis.

Refining Glucocorticoid Management

The re-evaluation of classic CAH treatment at endo 202 highlighted the importance of individualised glucocorticoid dosing. The discussion centred on moving away from a 'one-size-fits-all' approach towards regimens that are dynamically adjusted based on a broader spectrum of clinical and biochemical parameters. This includes not only androgen levels but also growth velocity in children, pubertal progression, bone age, and bone mineral density. The aim is to achieve the lowest effective glucocorticoid dose that maintains adequate adrenal suppression and prevents adrenal crises, while simultaneously optimising growth and metabolic health. This individualised approach is particularly critical in vulnerable patient populations, such as infants and young children, where growth is rapid, and adolescents undergoing puberty, where hormonal changes can complicate management.

One area of focus is the timing and distribution of glucocorticoid doses. Administering a larger proportion of the daily dose in the evening or at night may better mimic the physiological diurnal rhythm of cortisol and more effectively suppress the nocturnal ACTH surge, which drives morning adrenal androgen production. This strategy could potentially allow for a reduction in the total daily glucocorticoid dose without compromising androgen control. However, the practical implementation of such regimens requires careful patient education and adherence monitoring. For instance, modified-release hydrocortisone formulations are being investigated to provide more physiological cortisol exposure throughout the 24-hour cycle, aiming to improve androgen control and reduce overall glucocorticoid burden.

The role of adjunctive therapies was also discussed. Mineralocorticoid replacement (fludrocortisone) remains essential for salt-wasting forms of CAH, but its dosing also requires careful titration to prevent hypertension and hypokalemia. For patients with persistent androgen excess despite optimised glucocorticoid therapy, particularly adolescents and adults, investigational therapies are being explored. These include novel ACTH receptor antagonists or modulators, which aim to directly reduce adrenal androgen production without the systemic effects of high-dose glucocorticoids. However, these are still under evaluation and not yet part of standard clinical practice.

Limitations in current management include the lack of robust, long-term prospective studies comparing different glucocorticoid dosing strategies head-to-head, particularly in terms of their impact on adult height and metabolic health. The variability in patient response to glucocorticoids, influenced by genetic factors and individual pharmacokinetics, also complicates the establishment of universal dosing guidelines. Furthermore, the psychosocial burden of chronic illness and daily medication adherence also impacts treatment efficacy and patient quality of life, necessitating a multidisciplinary approach to care. The long-term consequences of suboptimal control, such as compromised fertility in women and testicular adrenal rest tumors in men, further highlight the need for improved therapeutic strategies.

Future directions involve the development of more precise biomarkers to guide therapy, potentially including adrenal steroid precursors beyond 17-OHP, and the integration of genetic profiling to predict individual responses to glucocorticoids. The goal is to move towards a personalised medicine approach for CAH, where treatment regimens are tailored to the unique physiological and genetic profile of each patient, thereby optimising outcomes and minimising treatment-related morbidity.

To further explore the wider field of endocrine conditions, their nuanced management, and therapeutic approaches like those discussed, refer to the Oxford Handbook of Endocrinology and Diabetes.

CLINICAL IMPLICATIONS

The discussions at endo 202 regarding classic CAH treatment underscore a necessary evolution in clinical practice. For too long, clinicians have navigated a difficult compromise between suppressing androgen excess and mitigating the severe iatrogenic effects of glucocorticoids. The emphasis on individualised dosing is not merely a refinement; it is a recognition that a blanket approach to a complex endocrine disorder is suboptimal. Prescribing clinicians should critically review their current dosing protocols, considering whether a more dynamic adjustment based on growth charts, bone density scans, and a broader panel of steroid precursors could improve patient outcomes beyond what 17-OHP alone can indicate.

This shift also has implications for the pharmaceutical industry. The market for CAH treatment has been dominated by generic glucocorticoids, with little incentive for innovation in delivery or formulation. A renewed focus on individualised therapy might spur interest in developing novel glucocorticoid formulations that offer more precise dosing or improved pharmacokinetic profiles, potentially reducing peak cortisol levels while maintaining adequate suppression. Furthermore, the exploration of non-glucocorticoid therapies to directly inhibit adrenal androgen synthesis could represent a significant commercial opportunity, provided these agents demonstrate superior safety and efficacy profiles in clinical trials.

For patients, this evolving perspective offers a glimmer of hope for a better quality of life. The long-term consequences of conventional high-dose glucocorticoid therapy, such as short stature, osteoporosis, and metabolic syndrome, are substantial. A more tailored approach promises to reduce these burdens, allowing children with CAH to achieve closer to their genetic growth potential and adults to experience fewer comorbidities. However, this also places a greater responsibility on patients and their families to engage actively in their care, understanding the nuances of their treatment regimen and adhering to complex monitoring schedules. Education and support will be paramount to successful implementation of these refined strategies.

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REFERENCES

1. Speiser PW, et al. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2010;95(9):4133-60. doi:10.1210/jc.2009-2631
2. Ishii T, et al. Clinical guidelines for the diagnosis and treatment of 21-hydroxylase deficiency (2021 revision). *Clin Pediatr Endocrinol.* 2022;31(3):116-143. doi:10.1297/cpe.2022-0009
3. Nordenström A, et al. Current and Novel Treatment Strategies in Children with Congenital Adrenal Hyperplasia. *Horm Res Paediatr.* 2023;96(6):560-572. doi:10.1159/000522260
4. Sarafoglou K, et al. Future Directions in the Management of Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency. *J Clin Endocrinol Metab.* 2025;110(Supplement_1):S74-S87. doi:10.1210/clinem/dgae759
5. Merke DP, et al. Modified-Release Hydrocortisone in Congenital Adrenal Hyperplasia. *J Clin Endocrinol Metab.* 2021;106(5):e2063-e2077. doi:10.1210/clinem/dgab051
6. Arlt W, et al. Long-term outcomes in patients with congenital adrenal hyperplasia treated with hydrocortisone modified-release hard capsules. *Eur J Endocrinol.* 2025;193(1):76-84. doi:10.1093/ajendo/lvaf130

7. 7. Auer MK, et al. Real-world outcomes with modified-release hydrocortisone in classic congenital adrenal hyperplasia. *Eur J Endocrinol*. 2026;194(6):806-818. doi:10.1093/ejendo/lvag087
8. 8. Neumann U, et al. PERSPECTIVE: Treatment with hydrocortisone modified-release capsules in children and adolescents with congenital adrenal hyperplasia: an expert opinion. *Endocr Connect*. 2025;14(5). doi:10.1530/EC-24-0619
9. 9. Auchus RJ, et al. Phase 3 Trial of Crinecerfont in Adult Congenital Adrenal Hyperplasia. *N Engl J Med*. 2024;391(6):504-514. doi:10.1056/NEJMoa2404656
10. 10. Sarafoglou K, et al. Phase 3 Trial of Crinecerfont in Pediatric Congenital Adrenal Hyperplasia. *N Engl J Med*. 2024;391(6):493-503. doi:10.1056/NEJMoa2404655
11. 11. White PC. Emerging treatment for congenital adrenal hyperplasia. *Curr Opin Endocrinol Diabetes Obes*. 2022;29(3):271-276. doi:10.1097/MED.0000000000000723
12. 12. Goai WH, et al. Pharmacotherapeutic strategies for the management of congenital adrenal hyperplasia. *Expert Opin Pharmacother*. 2026;27(10):979-993. doi:10.1080/14656566.2026.2695099

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