



REVIEW

Emerging medical therapies for congenital adrenal hyperplasia [version 1; peer review: 4 approved]

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Abstract

Congenital adrenal hyperplasia has traditionally been treated with daily oral doses of glucocorticoids and mineralocorticoid supplements. Such therapy does not precisely replicate the adrenal cortex's circadian pattern. As a consequence, patients are intermittently overtreated or undertreated leading to growth suppression in children, excess weight gain and altered metabolism. Several new treatments are on the horizon. This article will summarize some new potential therapies as adjuncts to, or replacement for, standard therapy.

Keywords

congenital adrenal hyperplasia, treatment

Open Peer Review

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Introduction

Congenital adrenal hyperplasia (CAH) is caused by one of several inherited enzyme deficiencies. The most common form of the classic disorder, found in about 1:14,000 to 1:18,000 births, is steroid 21-hydroxylase deficiency. Mutations in *CYP21A2* (P450c21) impair adrenocortical production of cortisol and frequently aldosterone and lead to the accumulation of adrenal sex steroids¹. Allelic variation accounts for most phenotypic differences. Cardinal features of classic CAH include atypical development of the external genitalia in girls with manifest virilization. Both males and females have salt wasting with failure to thrive and potentially fatal hypovolemia and shock. Newborn screening, now universal in the US² and in many developed countries³, can mitigate these complications (reviewed in 4). Despite life-saving glucocorticoid (GC) and mineralocorticoid (MC) oral therapies, treatment does not precisely replicate adrenal physiology. Individuals with CAH commonly experience adverse outcomes in terms of growth, metabolic, reproductive, and mental health endpoints^{5,6}. This discussion of emerging medical treatments will be restricted to the classic or severe forms of steroid 21-hydroxylase deficiency.

Improved glucocorticoid delivery

Normal adrenocortical secretion has a circadian rhythm quite distinct from that of blood cortisol levels achieved by administering two or three daily oral doses of GC medication^{7,8}. Hydrocortisone (HC) subcutaneous delivery for 6 months via a programmed pump in eight adults with classic CAH produced significant reduction in adrenal androgens with improvement in quality of life and fatigue⁹. Though conceptually attractive and perhaps applicable to highly motivated patients who are inadequately managed by conventional treatment, pump management is complex. An early trial with a once-daily modified-release oral HC preparation (Chronocort, Diurnal, Cardiff, UK) given to 16 adults with classic CAH decreased adrenal androgen precursors despite a slightly reduced daily HC dose¹⁰. However, subsequent phase 3 trials apparently failed to demonstrate superiority to standard HC treatment and this potential new treatment is currently on hold. A different type of modified-release GC (Plenadren, Shire, London, UK) is approved in Europe for adrenal insufficiency but has not been formally tested in CAH.

In the US, the lowest-dose HC tablet is 5 mg, and in Europe 10 mg, excessive for infants and young children. Availability of pediatric-dose formulations would eliminate concerns about improper compounding of HC from tablets^{11,12}. Based on favorable trial results¹³, the European Medicines Agency has approved very-low-dose HC 1 mg granules (Alkindi, Diurnal) for treatment of adrenal insufficiency or CAH in infants and children. A US Food and Drug Administration new drug application is said to be pending.

Androgen/estrogen antagonists and synthesis inhibitors

To ameliorate the effects of adrenal androgen excess, females with CAH often need treatment additional to GC replacement. Such treatments may include dermatologic therapies for acne and hirsutism or additional hormone treatments (or both) to

regulate menses or aid conception. All steroidogenic pathways to androgens and estrogens depend on activity of the enzyme 17-hydroxylase/17,20-lyase (P450c17, CYP17A1). Abiraterone acetate is an orally active, potent P450c17 inhibitor¹⁴ indicated for treatment of castration-resistant prostate cancer^{15,16}. Short-term adjunctive treatment with 250 mg/day abiraterone acetate (alongside standard steroid replacement) normalized the pre-dose serum androstenedione levels in all six women with poorly controlled classic CAH¹⁷. Because abiraterone acetate also inhibits gonadal steroid production and could be teratogenic, its use in CAH would be limited to pre-pubertal children, women using contraceptives, or men who receive gonadal replacement. A clinical trial is under way in pre-pubertal children with CAH (ClinicalTrials.gov Identifier: NCT02574910) with the goal of minimizing exogenous GC and endogenous adrenal sex steroid hormone exposure in order to normalize growth and pubertal development.

Growth-promoting drugs

A systematic review and meta-analysis of adult height in individuals with classic CAH diagnosed before the age of 5 years included just over 1000 children in 35 studies that met the eligibility criteria¹⁸. The pooled data indicated a corrected adult height standard deviation (SD) of -1.0 . The average heights were 169 cm (66.5 inches) for men and 157 cm (61.8 inches) for women, both within the normal range for shorter than average adults in the general population. These data obviate the routine use of growth-promoting medications that are considered only for individuals whose heights were expected to be at least -2.25 SDs. Subgroup analysis revealed that the addition of early MC treatment was associated with increased height outcome¹⁸.

A 2001 report tested growth hormone alone ($n = 12$) or in combination with leuprolide acetate ($n = 8$) to enhance growth in CAH patients with evidence of early puberty. Follow-up over 2 years showed improved predicted adult height, but as of this date, no data have been published to document actual adult heights¹⁹. A proof-of-concept trial demonstrated that co-administration of growth hormone plus an aromatase inhibitor (again, alongside standard steroid replacement) improved adult height in a single adolescent male patient with CAH²⁰.

Since normal adult height may be achieved through judicious use of standard GC and MC therapies, further long-term prospective randomized and carefully controlled studies are needed to determine whether the use of growth-promoting drugs is safe and cost-effective in individuals with CAH. At present, such treatments are not considered standard care in children with CAH.

Other medical strategies

Reducing adrenocorticotrophic hormone (ACTH) production is another mechanism for minimizing adrenal androgen excess. In a small trial of eight women with classic CAH, the selective corticotropin-releasing hormone receptor type 1 antagonist, NBI-77860, was added to conventional therapy²¹, resulting in a more than 40% reduction in the morning ACTH surge and about 27% lower serum 17OHP. Variable reductions of androstenedione and testosterone were observed.

Mitotane, a different type of adrenolytic used for treatment of adrenocortical cancer and Cushing syndrome, was administered to a man with classic CAH and testicular adrenal rest tumors (TARTs) who was infertile for 2 years²². Adrenal androgen precursors were suppressed and TARTs regressed. Paternity was achieved following an increase in sperm count. Mitotane is a potential teratogen (pregnancy category D) and induces CYP3A4, increasing GC clearance, and therefore is not considered a useful adjunct to CAH therapy. ATR-101 (ClinicalTrials.gov Identifier: NCT02804178), which inhibits acyl co-A cholesterol acyl-transferase and shares some mechanisms with mitotane^{23–25}, has been tested in adults with classic CAH; results of this trial have not yet been published.

Adrenalectomy

Adrenalectomy reduces virilization in females and permits decreased GC doses but this is considered a rather radical approach because of surgical risk. Moreover, there is an increased risk of life-threatening adrenal crisis with absolute dependence on exogenous hormone replacement and loss of potentially beneficial hormones—for example, dehydroepiandrosterone (DHEA) and epinephrine—from the adrenal medulla. A final consideration is that adrenalectomy may inadvertently cause the development of gonadal adrenal rest tumors that secrete androgens^{26,27}. For these reasons, the initial enthusiasm has been tempered by long-term complications. Individuals who are known to be non-adherent are poor candidates for adrenalectomy. A systematic review of bilateral adrenalectomy in CAH²⁸ identified 48 cases ranging from infancy to adulthood and most were carried out for uncontrolled androgen excess or iatrogenic Cushing syndrome (or both) caused by administration of large GC doses to achieve control. Post-operative amelioration of these symptoms was noted in most patients, including three women who were able to conceive following adrenalectomy. In contrast, about 40% of patients experienced adverse outcomes, including eight patients with adrenal crisis and one death in an infant. Five males developed adrenal rest tumors requiring surgical removal. Unexpectedly, two males had regression of TARTs²⁸. The conclusion from this review is that adrenalectomy is effective for relief of refractory adrenal androgen excess, but that candidates for adrenalectomy must be chosen judiciously and educated extensively regarding post-operative risks.

Epinephrine deficiency

Individuals with classic CAH have adrenomedullary insufficiency because GCs are required for development and regulation of the adrenal medulla²⁹. The physiologic responses of glucose, insulin, and leptin pathways are dysregulated during exercise among adolescent patients lacking both cortisol and epinephrine^{30,31}. The clinical implications of epinephrine deficiency are not fully known, but it may contribute to hypoglycemia during febrile illnesses, especially in young children, and impair the response to stress^{32,33}. Decreased epinephrine production has been observed in newborns with classic CAH compared with controls; norepinephrine levels were similar³². Epinephrine replacement or supplementation has not been studied. It is not known whether a compensatory norepinephrine response is sufficient.



Gene therapy

In two decades since the initial report that adenoviral gene therapy transiently restored enzyme activity in a mouse model of 21-hydroxylase deficiency³⁴, there have been no human trials. Animal research is ongoing, and intravenous injection of an adenoviral-Cyp21a1 vector in such mice allowed functional enzyme expression in adrenal tissue, resulting in weight gain, near normal progesterone levels, and improved stress response for more than 15 weeks³⁵. However, in another laboratory setting, the therapeutic effect lasted only 8 weeks³⁶. Auto-transplantation of Cyp21a1-expressing fibroblasts into 21-hydroxylase-deficient mouse subcutaneous tissue or direct injection of adenovirus-Cyp21a1 constructs into mouse muscle demonstrated enzyme efficacy for about 4 weeks³⁷. Thus, both adrenal and extra-adrenal induction of Cyp21a1 can temporarily ameliorate steroid metabolism in 21-hydroxylase null mice. It is unclear whether the murine data will be translated into effective human treatments. Permanent correction of mutations causing CAH with gene therapy directed at a patient's own adrenal stem cells would theoretically cure CAH and supplant imperfect steroid replacement. Cell-based therapies and gene-editing technology now in development may be options for disease cure in the future³⁸.

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References

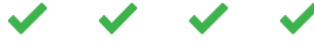
1. Krone N, Dhir V, Ivison HE, *et al.*: **Congenital adrenal hyperplasia and P450 oxidoreductase deficiency.** *Clin Endocrinol (Oxf)*. 2007; **66**(2): 162–72. [PubMed Abstract](#) | [Publisher Full Text](#)
2. National Newborn Screening and Global Resource Center: **National Newborn Screening System.** In: Center NNSGR, ed. *Newborn Screening Reports and Publications.* National Newborn Screening & Global Resource Center; 2006; **2017**.
3. Gidlöf S, Wedell A, Guthenberg C, *et al.*: **Nationwide neonatal screening for congenital adrenal hyperplasia in sweden: a 26-year longitudinal prospective population-based study.** *JAMA Pediatr*. 2014; **168**(6): 567–74. [PubMed Abstract](#) | [Publisher Full Text](#)
4. Speiser PW, Arlt W, Auchus RJ, *et al.*: **Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency: An Endocrine Society Clinical Practice Guideline.** *J Clin Endocrinol Metab*. 2018; **103**(11): 4043–88. [PubMed Abstract](#) | [Publisher Full Text](#)
5.  Arlt W, Willis DS, Wild SH, *et al.*: **Health status of adults with congenital adrenal hyperplasia: a cohort study of 203 patients.** *J Clin Endocrinol Metab*. 2010; **95**(11): 5110–21. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
6.  Finkelstein GP, Kim MS, Sinaï N, *et al.*: **Clinical characteristics of a cohort of 244 patients with congenital adrenal hyperplasia.** *J Clin Endocrinol Metab*. 2012; **97**(12): 4429–38. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
7.  Debono M, Ghobadi C, Rostami-Hodjegan A, *et al.*: **Modified-release**



- hydrocortisone to provide circadian cortisol profiles. *J Clin Endocrinol Metab.* 2009; **94**(5): 1548–54.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
8. Weitzman ED, Fukushima D, Nogeire C, *et al.*: **Twenty-four hour pattern of the episodic secretion of cortisol in normal subjects.** *J Clin Endocrinol Metab.* 1971; **33**(1): 14–22.
[PubMed Abstract](#) | [Publisher Full Text](#)
9. Nella AA, Mallappa A, Perritt AF, *et al.*: **A Phase 2 Study of Continuous Subcutaneous Hydrocortisone Infusion in Adults With Congenital Adrenal Hyperplasia.** *J Clin Endocrinol Metab.* 2016; **101**(12): 4690–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
10. Mallappa A, Sinaii N, Kumar P, *et al.*: **A phase 2 study of Chronocort, a modified-release formulation of hydrocortisone, in the treatment of adults with classic congenital adrenal hyperplasia.** *J Clin Endocrinol Metab.* 2015; **100**(3): 1137–45.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
11. Barillas JE, Eichner D, van Wagoner R, *et al.*: **Iatrogenic Cushing Syndrome in a Child With Congenital Adrenal Hyperplasia: Erroneous Compounding of Hydrocortisone.** *J Clin Endocrinol Metab.* 2018; **103**(1): 7–11.
[PubMed Abstract](#) | [Publisher Full Text](#)
12. Neumann U, Burau D, Spielmann S, *et al.*: **Quality of compounded hydrocortisone capsules used in the treatment of children.** *Eur J Endocrinol.* 2017; **177**(2): 239–42.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
13. Neumann U, Whitaker MJ, Wiegand S, *et al.*: **Absorption and tolerability of taste-masked hydrocortisone granules in neonates, infants and children under 6 years of age with adrenal insufficiency.** *Clin Endocrinol (Oxf).* 2018; **88**(1): 21–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
14. Garrido M, Peng HM, Yoshimoto FK, *et al.*: **A-ring modified steroidal azoles retaining similar potent and slowly reversible CYP17A1 inhibition as abiraterone.** *J Steroid Biochem Mol Biol.* 2014; **143**: 1–10.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
15. de Bono JS, Logothetis CJ, Molina A, *et al.*: **Abiraterone and increased survival in metastatic prostate cancer.** *N Engl J Med.* 2011; **364**(21): 1995–2005.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
16. Ryan CJ, Molina A, Griffin T: **Abiraterone in Metastatic Prostate Cancer.** *N Engl J Med.* 2013; **368**(15): 1458–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
17. Auchus RJ, Buschur EO, Chang AY, *et al.*: **Abiraterone acetate to lower androgens in women with classic 21-hydroxylase deficiency.** *J Clin Endocrinol Metab.* 2014; **99**(8): 2763–70.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
18. Muthusamy K, Elamin MB, Smushkin G, *et al.*: **Clinical review: Adult height in patients with congenital adrenal hyperplasia: a systematic review and metaanalysis.** *J Clin Endocrinol Metab.* 2010; **95**(9): 4161–72.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
19. Quintos JB, Vogiatzi MG, Harbison MD, *et al.*: **Growth hormone therapy alone or in combination with gonadotropin-releasing hormone analog therapy to improve the height deficit in children with congenital adrenal hyperplasia.** *J Clin Endocrinol Metab.* 2001; **86**(4): 1511–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
20. Hawton K, Walton-Betancourth S, Rumsby G, *et al.*: **Growth Hormone With Aromatase Inhibitor May Improve Height in CYP11B1 Congenital Adrenal Hyperplasia.** *Pediatrics.* 2017; **139**(2): pii: e20160730.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
21. Turcu AF, Spencer-Segal JL, Farber RH, *et al.*: **Single-Dose Study of a Corticotropin-Releasing Factor Receptor-1 Antagonist in Women With 21-Hydroxylase Deficiency.** *J Clin Endocrinol Metab.* 2016; **101**(3): 1174–80.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
22. Bry-Gauillard H, Cartes A, Young J: **Mitotane for 21-hydroxylase deficiency in an infertile man.** *N Engl J Med.* 2014; **371**(21): 2042–4.
[PubMed Abstract](#) | [Publisher Full Text](#)
23. Cheng Y, Kerppola RE, Kerppola TK: **ATR-101 disrupts mitochondrial functions in adrenocortical carcinoma cells and in vivo.** *Endocr Relat Cancer.* 2016; **23**(4): 1–19.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
24. LaPensee CR, Mann JE, Rainey WE, *et al.*: **ATR-101, a Selective and Potent Inhibitor of Acyl-CoA Acyltransferase 1, Induces Apoptosis in H295R Adrenocortical Cells and in the Adrenal Cortex of Dogs.** *Endocrinology.* 2016; **157**(5): 1775–88.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
25. Sbiera S, Leich E, Liebisch G, *et al.*: **Mitotane Inhibits Sterol-O-Acyl Transferase 1 Triggering Lipid-Mediated Endoplasmic Reticulum Stress and Apoptosis in Adrenocortical Carcinoma Cells.** *Endocrinology.* 2015; **156**(11): 3895–908.
[PubMed Abstract](#) | [Publisher Full Text](#)
26. van Wyk JJ, Ritzen EM: **The role of bilateral adrenalectomy in the treatment of congenital adrenal hyperplasia.** *J Clin Endocrinol Metab.* 2003; **88**(7): 2993–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
27. Tiosano D, Vlodavsky E, Filmar S, *et al.*: **Ovarian adrenal rest tumor in a congenital adrenal hyperplasia patient with adrenocorticotropin hypersecretion following adrenalectomy.** *Horm Res Paediatr.* 2010; **74**(3): 223–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
28. MacKay D, Nordenström A, Falhammar H: **Bilateral Adrenalectomy in Congenital Adrenal Hyperplasia: A Systematic Review and Meta-Analysis.** *J Clin Endocrinol Metab.* 2018; **103**(5): 1767–1778.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
29. Merke DP, Chrousos GP, Eisenhofer G, *et al.*: **Adrenomedullary dysplasia and hypofunction in patients with classic 21-hydroxylase deficiency.** *N Engl J Med.* 2000; **343**(19): 1362–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
30. Riepe FG, Krone N, Krüger SN, *et al.*: **Absence of exercise-induced leptin suppression associated with insufficient epinephrine reserve in patients with classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency.** *Exp Clin Endocrinol Diabetes.* 2006; **114**(3): 105–10.
[PubMed Abstract](#) | [Publisher Full Text](#)
31. Weise M, Mehlinger SL, Drinkard B, *et al.*: **Patients with classic congenital adrenal hyperplasia have decreased epinephrine reserve and defective glucose elevation in response to high-intensity exercise.** *J Clin Endocrinol Metab.* 2004; **89**(2): 591–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
32. Kim MS, Ryabets-Lienhard A, Bali B, *et al.*: **Decreased adrenomedullary function in infants with classical congenital adrenal hyperplasia.** *J Clin Endocrinol Metab.* 2014; **99**(8): E1597–601.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
33. Odenwald B, Nennstiel-Ratzel U, Dörr HG, *et al.*: **Children with classic congenital adrenal hyperplasia experience salt loss and hypoglycemia: evaluation of adrenal crises during the first 6 years of life.** *Eur J Endocrinol.* 2016; **174**(2): 177–86.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
34. Tajima T, Okada T, Ma XM, *et al.*: **Restoration of adrenal steroidogenesis by adenovirus-mediated transfer of human cytochromeP450 21-hydroxylase into the adrenal gland of 21-hydroxylase-deficient mice.** *Gene Ther.* 1999; **6**(11): 1898–903.
[PubMed Abstract](#) | [Publisher Full Text](#)
35. Perdomini M, Dos Santos C, Goumeaux C, *et al.*: **An AAVrh10-CAG-CYP21-HA vector allows persistent correction of 21-hydroxylase deficiency in a Cyp21^{-/-} mouse model.** *Gene Ther.* 2017; **24**(5): 275–81.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
36. Markmann S, De BP, Reid J, *et al.*: **Biology of the Adrenal Gland Cortex Obviates Effective Use of Adeno-Associated Virus Vectors to Treat Hereditary Adrenal Disorders.** *Hum Gene Ther.* 2018; **29**(4): 403–12.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
37. Naiki Y, Miyado M, Horikawa R, *et al.*: **Extra-adrenal induction of Cyp21a1 ameliorates systemic steroid metabolism in a mouse model of congenital adrenal hyperplasia.** *Endocr J.* 2016; **63**(10): 897–904.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
38. Ruiz-Babot G, Balyura M, Hadjidemetriou I, *et al.*: **Modeling Congenital Adrenal Hyperplasia and Testing Interventions for Adrenal Insufficiency Using Donor-Specific Reprogrammed Cells.** *Cell Rep.* 2018; **22**(5): 1236–49.
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