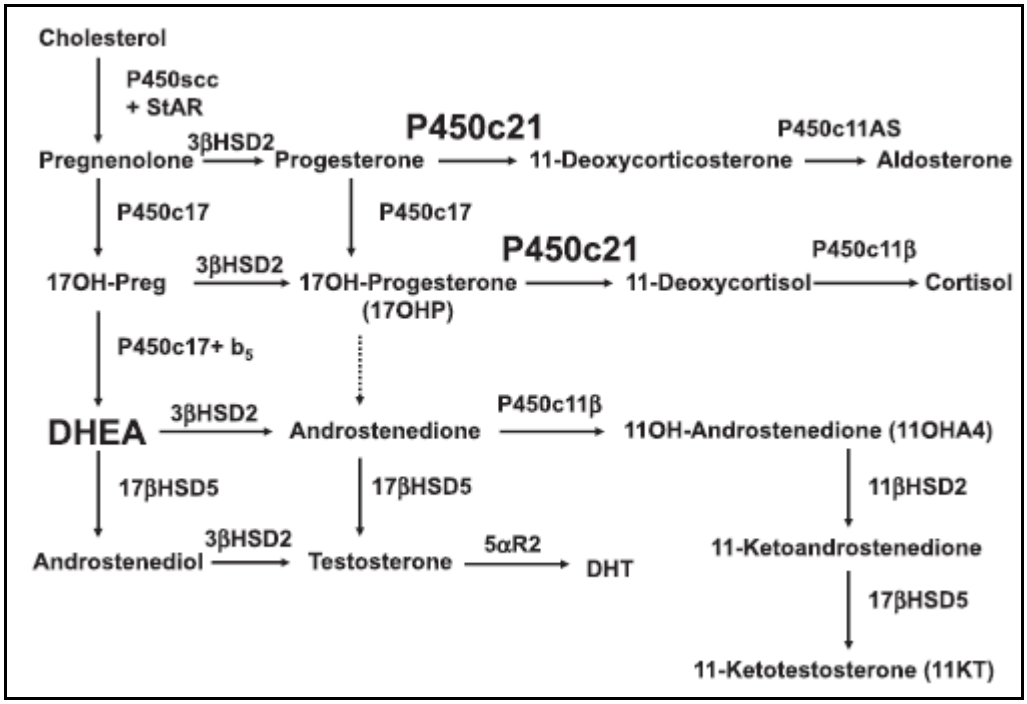
The Association for Clinical Biochemistry & Laboratory Medicine

Better Science, Better Testing, Better Care

Summary of Endocrinology Society Guidelines

Title	Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: An endocrine society clinical practice guideline.
Journal Reference	Speiser PW, Arlt W, Auchus RJ, Baskin LS, Conway GS, Merke DP, et al. Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2018 Nov 1;103(11):4043–88.
Date of Review:	September 2018
Summary of Condition	***Introduction*** Genetic mutations in the enzymes responsible for the production adrenal hormones can result in the development of Congenital Adrenal Hyperplasia (CAH). Patients with CAH are usually identified at birth through screening and the associated signs and symptoms, however rarer or milder forms can occasionally be diagnosed later in life.  ***Figure 1: Normal fetal adrenal steroidogenesis.*** The most common form (classic) is characterised by mutations in the 21-hydroxylase (21OH) enzyme, which normally converts 17-OHP to 11-dexoycortisol and progesterone to deoxycorticosterone. Loss of this enzyme activity results in the re-direction of this pathway leading to an increase in androgens.

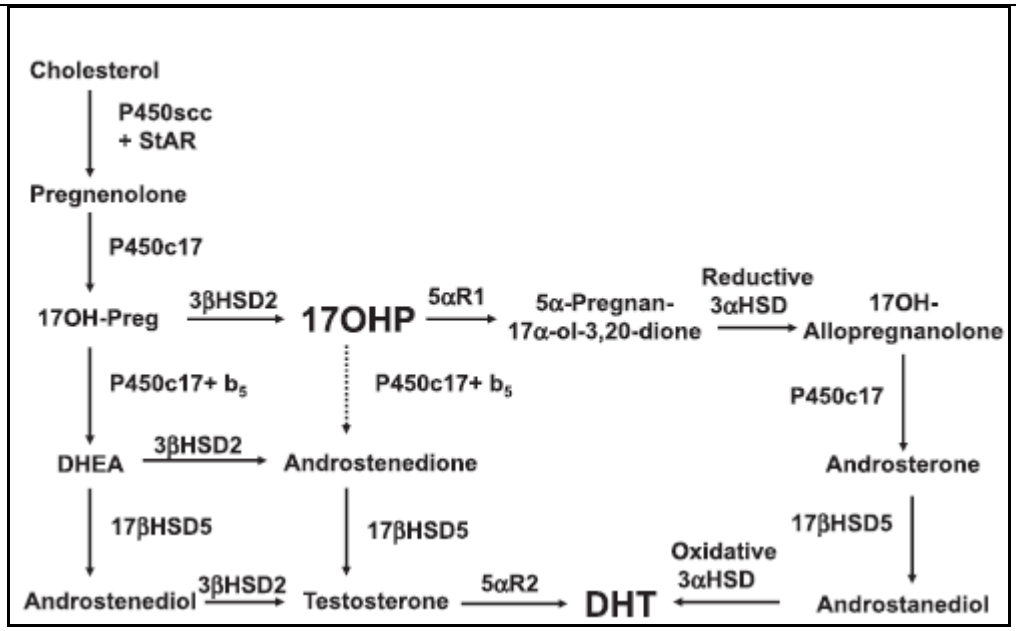


Figure 2 The steroidogenesis pathway in the absence of 21-hydroxylase activity.

Signs & Symptoms

A. Classic salt wasting – inadequate aldosterone production can cause salt wasting, failure to thrive, hypovolemia and shock (Addisonian crisis).
B. Classic salt wasting or virilising CAH – In newborn females the development of external genitalia with varying levels of virilisation. This is due to the increased production of androgens. NB: difficult to determine in males as only sign is early genital enlargement.
C. Non classic CAH – milder form, features of postnatal androgen excess but can be non-symptomatic (it will depend on the type of severity of mutation in the steroidogenesis pathway).

Screening

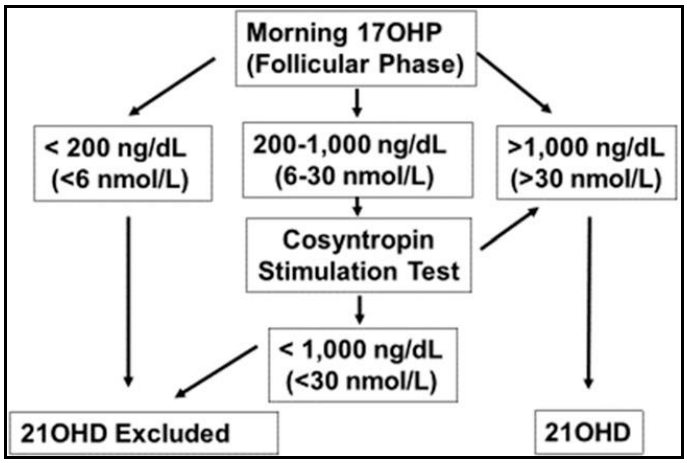
There is currently no screening programme for 17-OHP in the UK (*2019 update*).

Diagnosis & Monitoring

Referral to a paediatric endocrinologist is recommended for a positive test result. Post-infancy, symptomatic patients are suggested to have an early morning 17OHP. Borderline results should warrant a full steroid profile with genotyping only being offered when these results are equivocal.
Monitoring involves assessment of growth, weight, BP and physical examinations. Bone age assessment should be performed until near-adult height is achieved. Adults should have BP, BMI and replacement therapy monitored accordingly.

Treatment

Treatment can include the use of hydrocortisone, fludrocortisone and sodium chloride replacement; however treatment will depend on the sex, age, duration (short, long term and stress dosing), pregnancy status and type of CAH. Care should also be taken to avoid under and over-replacement of steroids.
Surgery can be offered, particularly for virilised females, however parents should be informed on all options available prior to making a decision. Genetic counselling, lifestyle advice and further appropriate support should also be offered.

Overview of assays	A confirmatory method by LC-MS/MS should be used on 8am samples in preference to all other methods (including genotyping) to help improve both the sensitivity and positive predictive value of screening (Figure 3). Laboratories who offer an LC-MS/MS service should be registered in an appropriate quality assurance programme. To fully differentiate between the various enzymatic defects potentially causing CAH, clinicians should ideally send samples for measurement of 17-OHP, cortisol, 11-deoxycorticosterone, 11-deoxycortisol, 17-OHpregnenolone, dehydroepiandrosterone, and androstenedione. **NB** In other countries new-born screening programmes are recommended to use standardised 17-OHP assays for first-tier screens, but to keep in mind those immunoassays can be susceptible to false-positive results. 17-OHP levels are normally high at birth and should decrease rapidly during the first few postnatal days in healthy infants.  ***Figure 3. The flowchart taken from the guidelines on the investigation of 21OH deficiency.*** Genotyping should be offered when all other results are equivocal.
Lab professionals to be made aware	✓ Chemical Pathologist ✓ Clinical Scientist ✓ Biomedical Scientist
Impact on Lab	☐ None
Please detail the impact of this guideline (Max 150 words)	Infants who are being investigated for CAH, or have been diagnosed with CAH will require additional monitoring in the form of automated and specialist biochemical analysis. Analytes such as U&E's and cortisol can be sent directly to the automated lab; however more specialist tests including urine steroid profiles and genotyping may also be required. These more specialist tests would take longer to perform as these are sent away to referral laboratories. Management of older patients should have a less urgent impact on the laboratory providing the patients care is managed effectively. Healthcare scientists should be aware of the importance of handling, analysing and reporting patient results, as acutely unwell patients who are at risk of an Addisonian crisis can deteriorate rapidly. It is therefore paramount that laboratory turnaround times are adhered to in addition to all urgent results being phoned where necessary.

Impact on Lab

- **None**: This guideline has no impact on the provision of laboratory services
- **Moderate**: This guideline has information that is of relevance to our pathology service and may require review of our current service provision.
- **Important:** This guideline is of direct relevance to our pathology service and will have a direct impact on one or more of the services that we currently offer.

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