

**Duration** August 2007 –August 2008 (13 months).

**Research Questions** Specific aims of the project are to:

1. Determine the incidence of clinically presenting CAH in children under the age of 16 years in the UK, and to report its distribution by age, sex and ethnic group.
2. To report the clinical features at presentation.
3. To report the proportion of cases who become clinically unwell by 5-8 days of life
4. To report early clinical management and morbidity and mortality to one year post diagnosis, including the proportion of girls with initially incorrect sex or sex reassignment.

**Case Definition** A child will be considered to have a diagnosis of CAH:

**IF AT LEAST ONE** of the following clinical features is found:

- Adrenal crisis or adrenal insufficiency
- Virilisation of female genitalia
- Precocious puberty
- Accelerated skeletal age
- Short stature
- Hypertension
- Incomplete masculinisation of male genitalia
- Positive family history in first degree relative

**AND AT LEAST ONE** of the following criteria are met:

- Elevated 17 OHP in blood test
- Positive synacthen stimulation test
- Test result diagnostic of rarer form of CAH, e.g. 3 $\beta$ -hydroxysteroid dehydrogenase (3 $\beta$ -HSD deficiency) or 11 $\beta$ -hydroxylase (11 $\beta$ -OH) deficiency

The diagnosis of CAH may be made following clinical presentation, investigation of a sudden unexpected death, or diagnosis in a sibling or other affected family member.

**Reporting Instructions** Please report any child, aged up to (but not including) 16 years of age, with suspected or confirmed CAH seen by a paediatrician for the first time in the last month. If a paediatrician is uncertain or awaiting confirmation, the child should still be reported.

**Methods** Paediatricians reporting a case through the orange card system will be asked to complete a questionnaire seeking information on diagnosis, management and outcomes. A further follow-up questionnaire will be sent when the child is one year of age. Notifications will also be sought through biochemical and genetics laboratories concurrently reporting cases directly to the investigators.

**Ethics Approval** This study has been approved by the Thames Valley MREC (Ref: 07/MRE12/25) and has been granted PIAG Section 60 Support (Ref: PIAG/BPSU 1-05(FT4)/2007)

**Funding** Department of Health.

**Support Group** CLIMB-CAH UK Support Group: [www.cah.org.uk/](http://www.cah.org.uk/)

#### Reference(s)

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## CONGENITAL ADRENAL HYPERPLASIA

**Abstract** Congenital adrenal hyperplasia (CAH) is a recessively inherited deficiency of cortisol production with an estimated birth prevalence of 1 in 10,000 to 20,000. Just over half of those affected have a salt wasting form which can present in newborns with an acute life threatening adrenal crisis. CAH is also often associated with accelerated growth and excess androgen production, which may result in girls being incorrectly assigned as boys at birth. Early detection by newborn screening combined with cortisol and mineralocorticoid replacement can prevent life-threatening episodes, and ensure normal growth and sexual development. Screening for CAH has not been introduced in the UK, reflecting inconsistent information about disease burden and it is now timely to obtain better epidemiological data on CAH in the UK. In view of this a BPSU study of CAH incidence and short term outcome is proposed to inform future newborn screening policy.

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**Background** Congenital adrenal hyperplasia (CAH) refers to a group of recessively inherited disorders caused by a deficiency in one of the enzymes necessary for cortisol production in the adrenal glands. The most common form, representing 90% of cases, is due to 21-hydroxylase (21-OH) deficiency resulting in reduced aldosterone (mineralocorticoid) and cortisol (glucocorticoid) synthesis and increased androgen production (and hence virilisation of female individuals). Lack of cortisol synthesis has wide repercussions on survival, growth, pubertal development and adult sexual functioning. CAH is treated with cortisol and mineralocorticoid replacement and, in the virilising forms, correct sex assignment and corrective genital surgery are required.

The mean estimated birth prevalence of CAH in European screening programmes ranges from 1 in 11612 to 1 in 25,000<sup>1</sup>. In the UK the prevalence of clinically diagnosed CAH ranges from 1 in 13,300 in Wales<sup>2</sup>, 1 in 6,200 in the West Midlands<sup>3</sup>, 1 in 20,097 in Scotland<sup>4</sup> and 1 in 25,000 in the Republic of Ireland<sup>5</sup>.

Newborn screening has not been introduced in the UK, reflecting inconsistent information about disease burden. Recently test specificity has improved and it is now timely to obtain better epidemiological data on CAH in the UK.

**Coverage** **England, Scotland, Wales, Channel Isles only**