



Factsheet 5

Endocrine Issues in CHARGE

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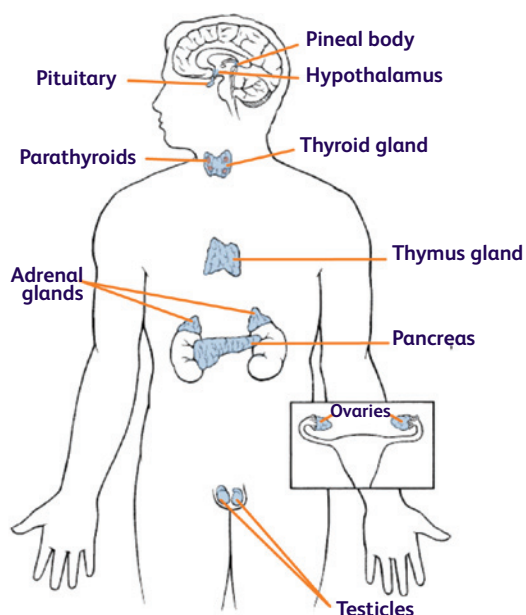
The original acronym for CHARGE syndrome included two potential endocrine (hormonal) problems, namely:

C
H
A
Retarded growth (and development)
G
Genital abnormalities
E

Figure 1 shows the specialist (endocrine) glands which secrete hormones (chemical messengers) into the bloodstream. A number of these are affected in CHARGE syndrome, and predominantly affect growth but also genital development and puberty.



FIGURE 1 THE ENDOCRINE SYSTEM



Growth

A child grows in three separate phases, which merge into each other, but which are under different controls. All of these can be affected in CHARGE syndrome.

Growth:

- in the first 2–3 years, is predominantly under nutritional control
- during childhood, is under hormonal control (mainly growth hormone but also thyroid hormone) and also nutrition
- during puberty, this is under the control of both growth hormone and also sex hormones acting together.

About three-quarters of children with CHARGE have both heights and weights at, or below, the lower end of the normal range. Although there are no disease-



specific growth charts for CHARGE, we have previously described poor growth in children with CHARGE syndrome (See Appendices 1 and 2).

Whilst most children with CHARGE do have evidence of hormonal abnormalities within the hypothalamic-pituitary system, there is little published evidence of deficiency of growth hormone (GH), nor of the response to GH therapy.

Data from several international growth databases includes data on several dozen children with CHARGE treated with GH, most of whom were GH deficient. Patients have been only treated for short periods of time however, with variable responses to treatment, which make it difficult to draw overall conclusions.

Hypogonadism

CHARGE patients commonly have delayed/defective production of sex hormones from the gonads (testicles in boys and ovaries in girls). The main reason for this is reduced central pituitary hormone drive from the pituitary gland (a small pea-sized gland lying underneath the brain) – so-called ‘hypogonadotropic hypogonadism’. The two affected pituitary hormones are luteinising hormone (LH) and follicle stimulating hormone (FSH).

In boys there may also be reduced testicular hormone production because of undescended testicles.

Genital abnormalities

In boys, undescended testicles (one or both) and small penis (micropenis; less than 1 inch (2.5cm) stretched length) at birth. About three-quarters of boys with CHARGE will have micropenis, and approximately half undescended testes.

In girls, the clitoris and labia minora (inner vaginal lips) are often smaller than usual, but this does not require treatment (Sanlaville and Verloes, 2007).

It is likely, though not inevitable, that CHARGE children with these genital abnormalities will also have pubertal problems, as the hormones produced from the pituitary are the same.

Puberty

Puberty problems may include:

- delayed puberty (absence of signs of puberty at 13 years in girls, and 14 years in boys)
- arrested puberty; only getting part way through puberty.

Our experience is that pubertal problems are more common in boys than girls. Most boys do need

assistance with puberty, whereas some girls may have normal or even early puberty.

In children with CHARGE, there are often potential concerns about administration of sex hormones, as they may produce problems – including inappropriate sexual behaviour, menstrual bleeding in girls and erections in boys. These concerns must be balanced against the long-term risks of osteoporosis (brittle bone disease) – as much of the bone strength is laid down in the teenage years under the influence of sex hormones (Blake *et al.* 2005).

Unfortunately there isn't a dose of sex hormones which will protect against osteoporosis but not produce unacceptable behaviour. In girls, a gradually increasing dose of the female hormone oestrogen given by mouth is commonly used. Once full pubertal development has occurred, medication can be changed – either to hormone replacement therapy (HRT) or the low-dose oral contraceptive pill (OCP). To avoid frequent and distressing periods when using OCP, the packs can be run into each other, with two-three withdrawal bleeds only a year.

In boys, gradually increasing doses of testosterone are given by monthly injection, daily capsule or gel. The advantage of the daily capsule or gel is that if there are behavioural problems, then the dose can be rapidly cut back.

It is likely that hormone replacement in both sexes will need to be given long-term.

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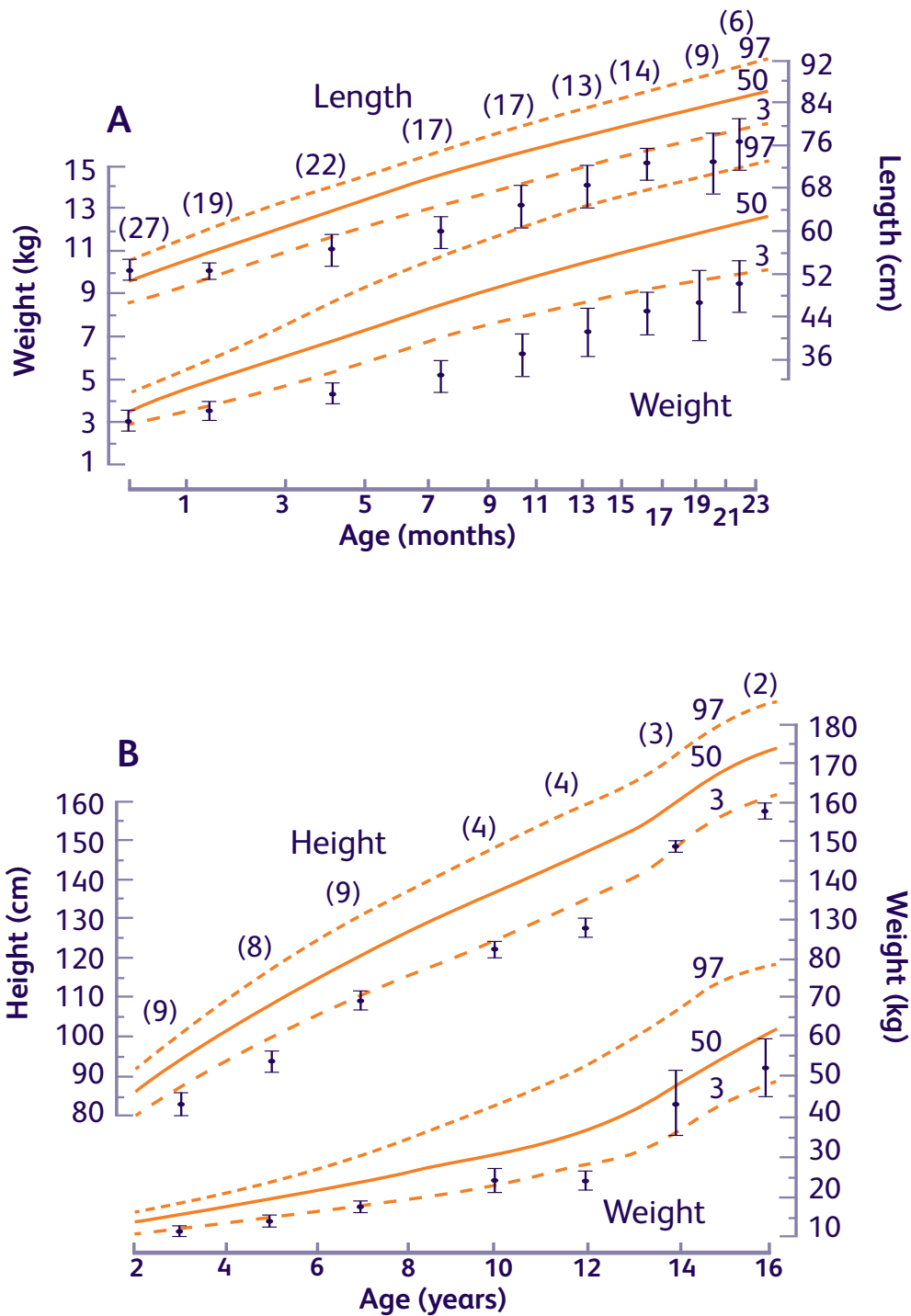
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APPENDIX 1

FIGURE 1 GROWTH IN CHARGE (BOYS)

Mean (SD) length/height and weight for boys with CHARGE association compared with normal boys (A) in the first two years of life and (B) aged 2–16 years. Number of children shown in parantheses.





APPENDIX 2

FIGURE 2 GROWTH IN CHARGE (GIRLS)

Mean (SD) length/height and weight for girls with CHARGE association compared with normal girls (A) in the first two years of life and (B) aged 2–16 years. Number of children shown in parantheses.

