Nottingham University Hospitals NHS
NHS Trust

Long term consequences of steroids

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Long term effects of steroid therapy

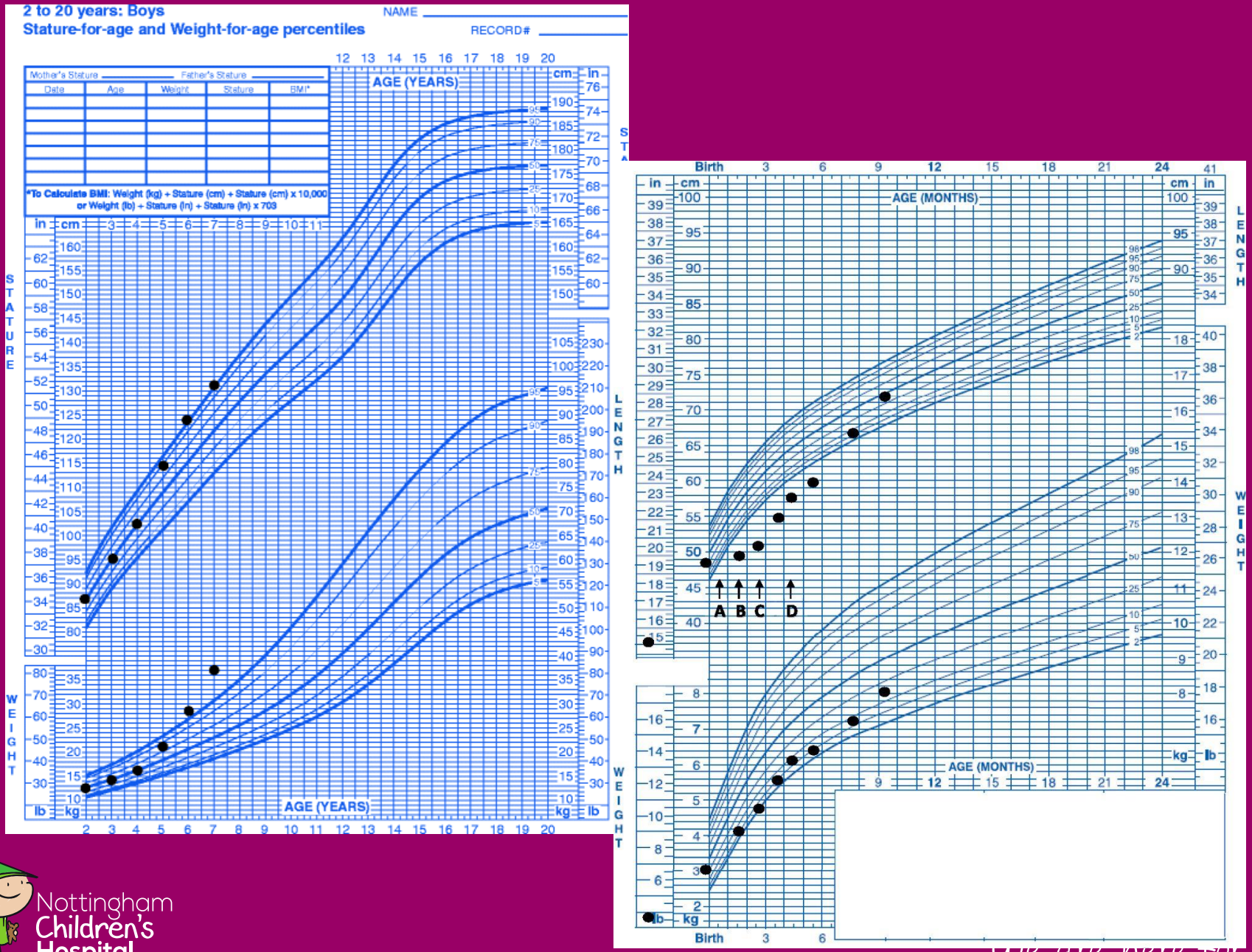
- Are all steroids the same?
- Growth
- Adrenals
- Bone
- What to do?

Steroid dose equivalents – potency c/w Hydrocortisone

Steroid	Anti-inflammatory effect	Adrenal suppressive effect
Prednisolone	4	10
Methylprednisolone	5	10
Dexamethasone	25	100

Growth and exogenous steroids

- Normal cortisol levels needed for normal function of growth hormone (GH) axis
- Excess cortisol suppresses GH
- Also causes insulin-like growth factor 1 (IGF1) resistance



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Adrenals and exogenous steroids

- Suppression of the hypothalamic-pituitary-adrenal axis
- Glucocorticoids only affected
- Detectable biochemically in majority of children
- Unpredictable

Adrenals and exogenous steroids

Cochrane review of steroids & ALL

- All children had adrenal suppression in days after stopping steroids
- Most recover in a few weeks
- Some take months
- Worse if have Fluconazole

Cochrane review, Rensen 2017

Adrenals and exogenous steroids

Adrenal suppression and nephrotic syndrome

- Adrenal suppression common
- Relapse appears more common in those with adrenal suppression (Abeyagunawardena, ADC 2007)

Adrenals and exogenous steroids

How do you assess adrenal function?

- Low dose synacthen test (1 μg)
- High dose synacthen test (250 μg)
- Early morning cortisol

How often have you seen an adrenal crisis?

Adrenals and exogenous steroids

Adrenal crisis signs/symptoms

- Nausea and vomiting
- Sodium and potassium levels generally normal if secondary adrenal failure

Adrenals and exogenous steroids

Adrenal crisis signs/symptoms

- Hypoglycaemia (BG < 2.6)
- Hypotension
- Confusion/ coma
- Extreme weakness

Adrenals and exogenous steroids

Hydrocortisone replacement therapy:

- 6-8 mg/m^2/day in 3 divided doses
- Biggest dose in the morning
- Stress dose – 50mg/m^2/day 6 hourly
- IM hydrocortisone for emergencies (25mg <1yr, 50mg 1-5 yrs, 100mg >5 yrs)

Surface area calculation

$$\sqrt{\left\{\frac{\text{Height (cm) x weight (kg)}}{3600}\right\}}$$

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Adrenals and exogenous steroids

Need IM/IV hydrocortisone if:

- Not able to tolerate oral medication
- Accident or illness severe enough to need urgent hospitalisation
- At induction of anaesthesia

Adrenals and exogenous steroids

- GIVING HYDROCORTISONE IM WHEN IT'S NOT NEEDED WILL DO NO HARM
- NOT GIVING IT CAN LEAD TO SEVERE BRAIN INJURY OR DEATH

Bones and exogenous steroids

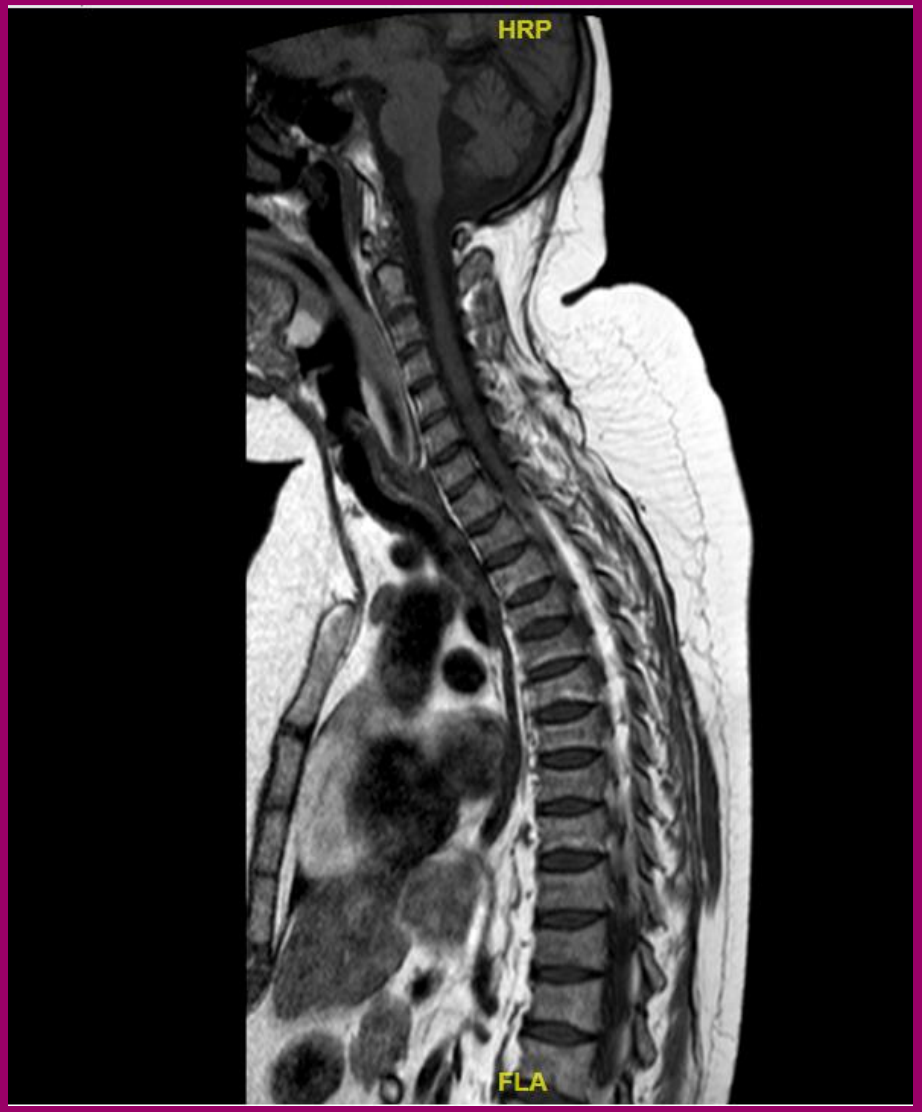
- Reduce numbers of osteoblasts
- Block normal osteoblast function
- Increase bone resorption
- Block calcium absorption
- Increase urine calcium excretion
- Reduce GnRH so sex steroid levels drop

Bones and exogenous steroids

Result = osteoporosis

(Ishikura et al 2015)

NB OSTEOPOROSIS IS NOT CAUSED BY BISPHOSPHONATE DEFICIENCY



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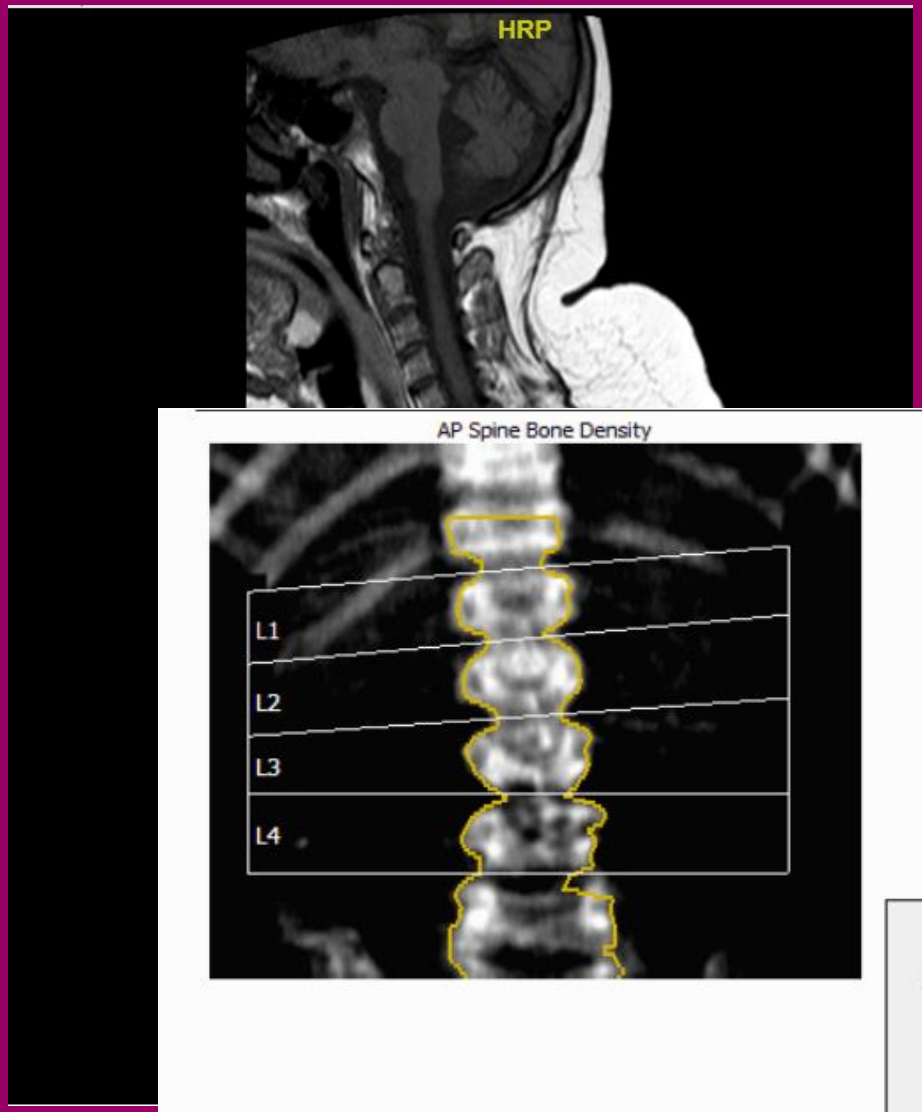
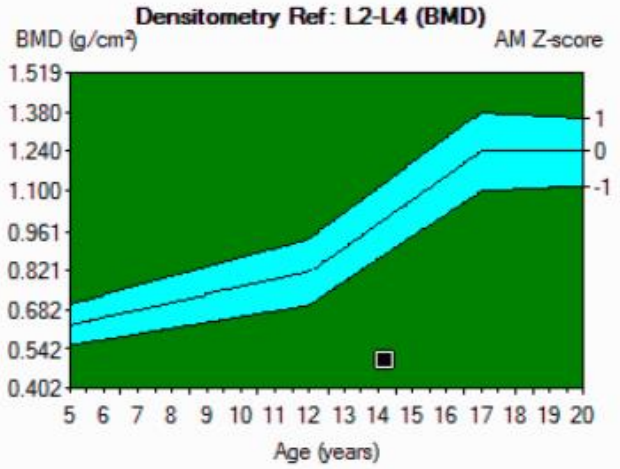


AP Spine Bone Density



Region	BMD[1] (g/cm²)	Age-Matched[2,3] Z-score
L1	0.477	-3.4
L2	0.505	-3.7
L3	0.494	-3.8
L4	0.498	-3.8
L2-L4	0.499	-3.8

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Bones and exogenous steroids

How to avoid osteoporosis

- Adequate Vitamin D intake
- Adequate Calcium intake
- Puberty at the appropriate time

Bones and exogenous steroids

- DXA scans ***must*** be done on specifically calibrated equipment
- Height and weight and pubertal status all will impact on interpretation

Bones and exogenous steroids

- No indication for prophylactic bisphosphonates
- Would only consider if clinically proven fracture
- Discuss with metabolic bone team first

Avoiding adverse effects of exogenous steroids

- Use lowest possible dose for shortest possible time
- Consider formal assessment of adrenal function after long-term treatment
- Sick day rules if on long-term steroids

Avoiding adverse effects of exogenous steroids

- Vitamin D supplements 400 – 1000 Units/day (10-25μg/day)
- Ensure adequate calcium intake
- Check puberty and ensure is progressing appropriately
- DXA scan if fracture

Questions?

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