Vitamin D Deficiency and Rickets

Jeremy Allgrove
Consultant Paediatric Endocrinologist,
Royal London Children’s Hospital
Barts Health NHS Trust
Rickets – what is it?

- Condition principally affecting the growth plate
- Disruption of the growth plate with:
  - distortion of the normal chondrocyte development
  - failure of normal apoptosis of chondrocytes
  - widening of growth plate
  - failure of vascularisation of cartilage
- Can’t occur in adults
- Doesn’t affect intramembranous bone (e.g. skull vault)
Osteomalacia – what is it?

- Failure of normal mineralisation of the osteoid surfaces during remodelling of bone
- Matrix unaffected
- Dependent upon supply of calcium and phosphate as mineral substrate
- Not clear the effect on bone strength
Osteoporosis – what is it?

- Primary defect in matrix formation resulting in secondary reduction in mineral deposition
- Leads to weakened bones and increased fracture tendency
- May be
  - primary e.g. OI or
  - secondary e.g. chronic steroid use
Proliferative
Prehypertrophic
Hypertrophic
Apoptotic
Calcified
Proliferating

Prehypertrophic

Hypertrophic

Apoptotic

Sox9

Ihh ↔ PTHrP

Runx2

Phosphate
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<tr>
<th>Condition</th>
<th>Biochemistry</th>
<th>Gene</th>
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## Classification of Rickets

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<td>Calciopaenic (inc Vitamin D related)</td>
<td>↑PTH mediated</td>
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<td>Phosphopaenic</td>
<td>↑FGF23 mediated</td>
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*Tiosano D & Hochberg Z J Bone Miner Metab 2009; 27:392-401*
7-Dehydrocholesterol

sunlight

Previtamin D

body heat

Cholecalciferol/Ergocalciferol (Vitamin D)

Vitamin D 25-hydroxylase

25-OH vitamin D

25-hydroxyvitamin D 1α-hydroxylase

1α-hydroxycholecalciferol (alfacalcidol)

PTH ↓PO₄

+ 

Vitamin D 25-hydroxylase

1,25(OH)₂ vitamin D

Vitamin D receptor

Peripheral action

24,25-dihydroxyvitamin D

1,24,25-trihydroxyvitamin D

Diet

Vitamin D 24-hydroxylase

Vitamin D 25-hydroxylase
Classification of Calciopaenic, PTH dependent rickets

- Vitamin D deficiency
  - true deficiency (poor sunlight exposure)
  - malabsorption etc
- 25-hydroxylase deficiency
- 1α-hydroxylase deficiency (VDDR1)
- HVD receptor defect (VDDR2)
  - with alopecia (receptor defect)
  - without alopecia (nuclear defect)
  - unknown cause
- Calcium deficiency
Definition of Deficiency (25OHD)

- Toxic: >200 nmol/L
- Fully replete: 75-200 nmol/L
- Replete: 51-75 nmol/L
- Insufficient: 26-50 nmol/L
- Deficient: 15-25 nmol/L
- Seriously deficient: <15 nmol/L
Clinical Syndromes

- Congenital rickets
- Dilated cardiomyopathy
- Classical rickets (+/- convulsions)
- Hypocalcaemic convulsions
- Generalised aches and pains, muscle weakness etc
Conclusions

- Vitamin D receptor mutations result in:
  - severe rickets with poor development
  - Poor growth
- Treatment with intravenous calcium (and magnesium and phosphate) corrects the biochemical abnormalities and heals the rickets
- Oral treatment may be sufficient thereafter if adequate supplements are given
Allgrove’s Adage 1

THE TREATMENT OF VITAMIN D DEFICIENCY IS VITAMIN D
Allgrove’s Adage 2

YOU CAN’T MAKE A DIAGNOSIS RELATED TO RICKETS OR HYPOCALCAEMIA UNTIL VITAMIN D DEFICIENCY HAS BEEN EXCLUDED OR CORRECTED
VITAMIN D SUPPLEMENTATION IS THE MOST COST-EFFECTIVE MEASURE THAT WOULD IMPROVE THE HEALTH OF THE POPULATION OF THE EAST END OF LONDON
Thank you