

# BONE PROTECTION IN CORTICOSTEROID TREATED DUCHENNE MUSCULAR DYSTROPHY

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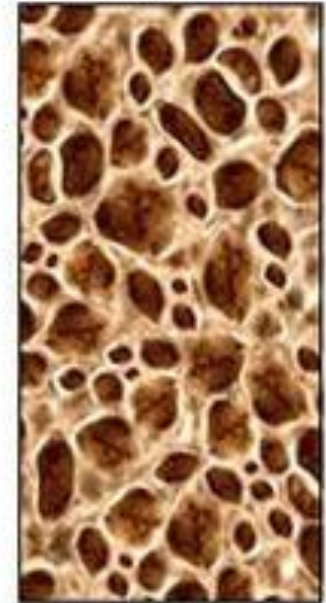
# Why is bone protection important?

- Bones are constantly remodelled
- Osteoporosis occurs when bone loss exceeds bone gain
- Corticosteroid treatment increases bone loss and decreases bone gain leading to osteoporosis

Normal bone



Bone with Osteoporosis



# Why do weak bones matter?

- Weak bones break more easily especially in the vertebrae
- Fractures reduce height and can eventually cause a stooped kyphotic posture



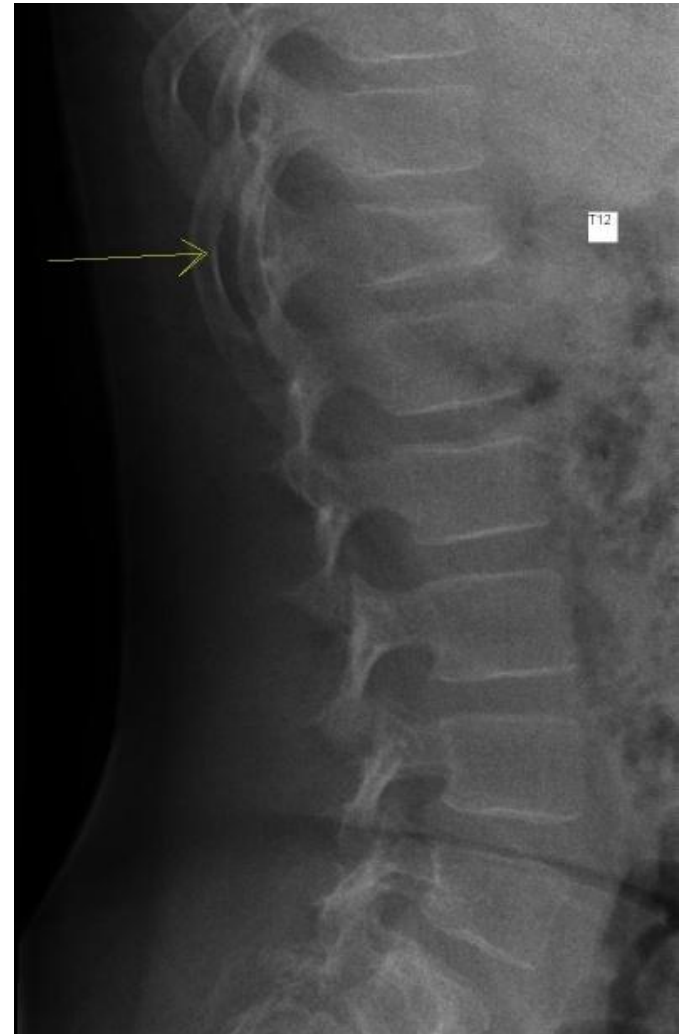
# Houde 2008: Daily deflazacort for DMD

## Mean 66 months

	steroid n=37	non steroid n=42
loss ambulation	11.5y	9.6y
scoliosis°	14°	36°
limb fracture	24%	26%
Vertebral fracture	20%	0

# Vertebral fractures

- 80% acute back pain
- 20% asymptomatic
- May follow a fall onto the coccyx
- Assessment is made by spinal X Ray
- But radiation dose is relatively high



# Assessing weak bones

- Dual-energy x-ray absorptiometry
- DXA



# What does DXA measure?

- Whole body, spine and hip
- Bone mineral content (BMC)
- Bone area (BA)
- Bone mineral density (BMD)
- Results are expressed as
  - t-Score
  - z-Score

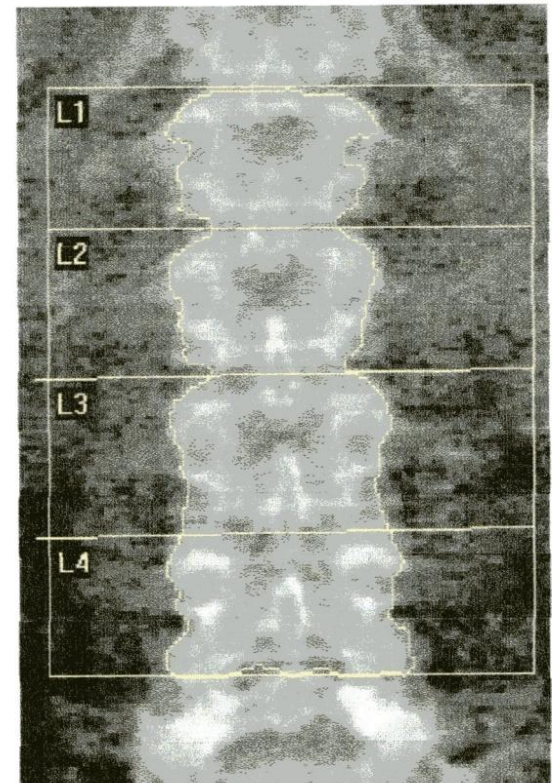
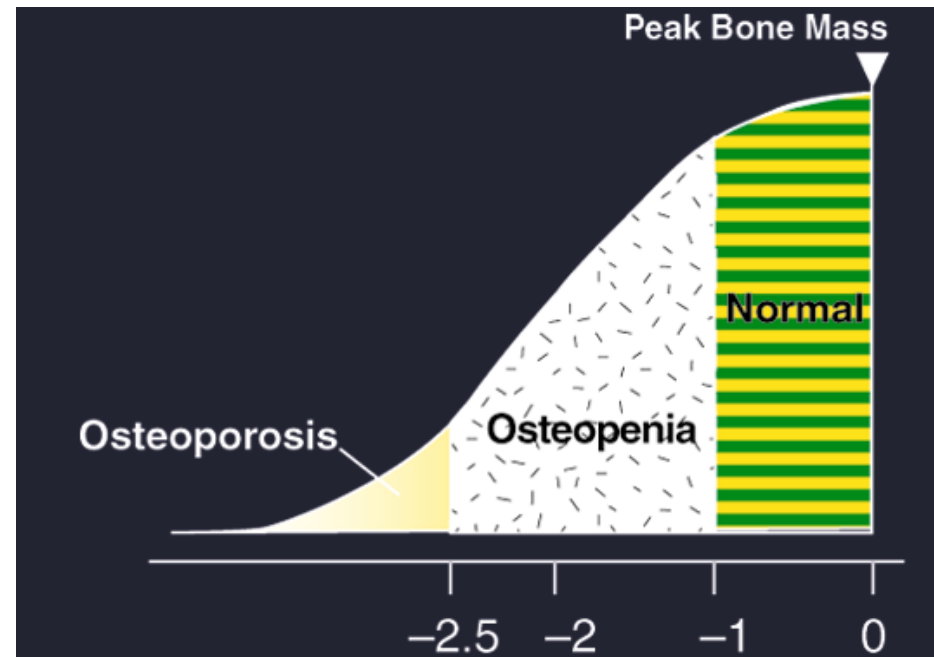


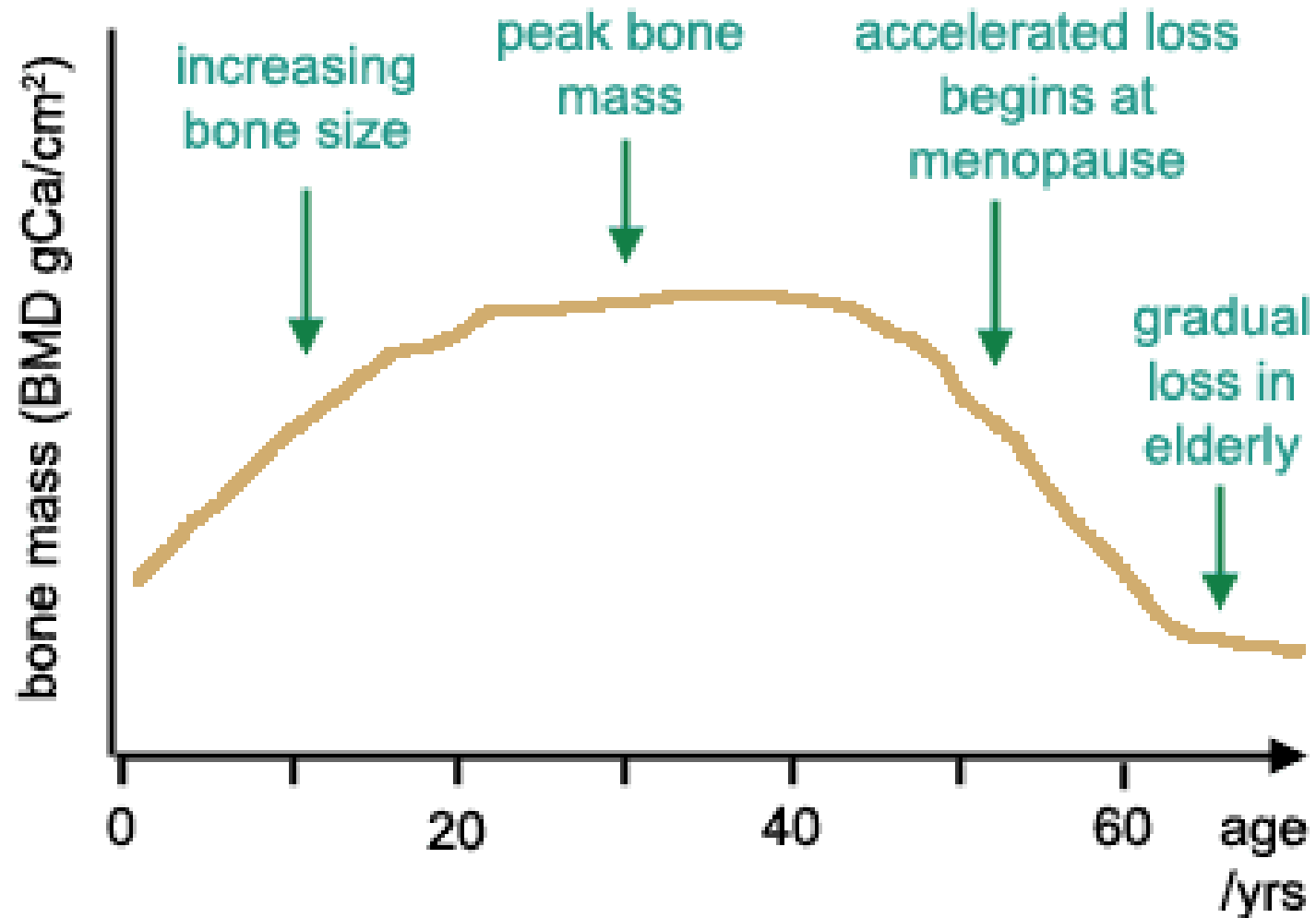
Image not for diagnostic use  
k = 1.131, d0 = 47.5  
116 x 142

# What is a T-score?

- Result is compared with data from average 30 year old
- Unit is standard deviation (SD)
- The lower the value below zero, the lower the BMD and the higher the risk of fracture

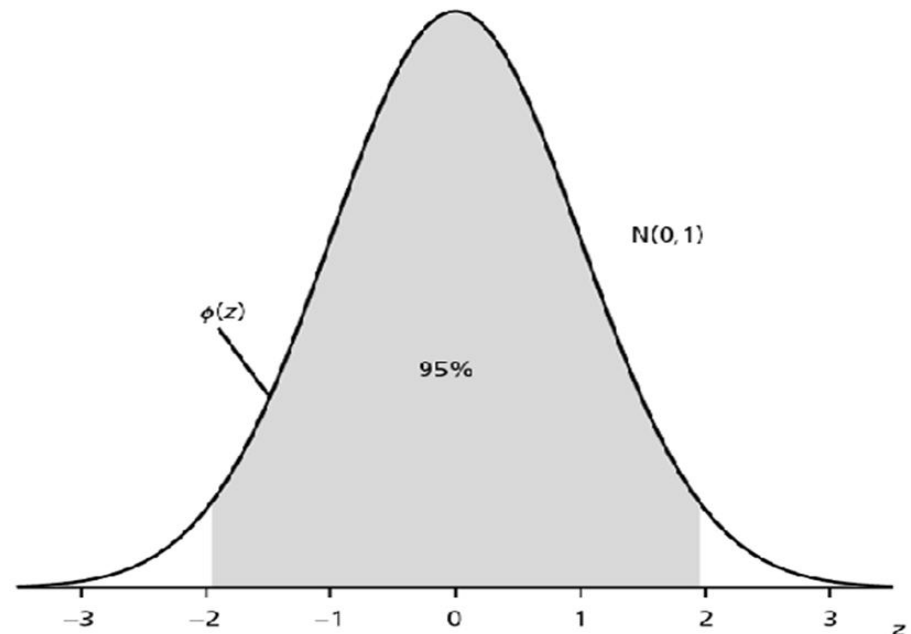


# Effect of age on peak bone mass



# What is a Z score?

- Z score is an average BMD corrected for age and size



# Factors affecting bone gain

- Genetics (60%)
  - Hormones (13%)
  - Nutrition (13%)
  - Physical activity (13%)
- 
- Increasing peak bone mass may reduce fracture risk



# Nutrition: Calcium

- 149 girls aged 7yrs
- Calcium containing food vs placebo for 1 year
- BMD was greater in the calcium treated group
- Follow-up of 116 girls showed sustained effect 3-5 years later

Bonjour et al 1997



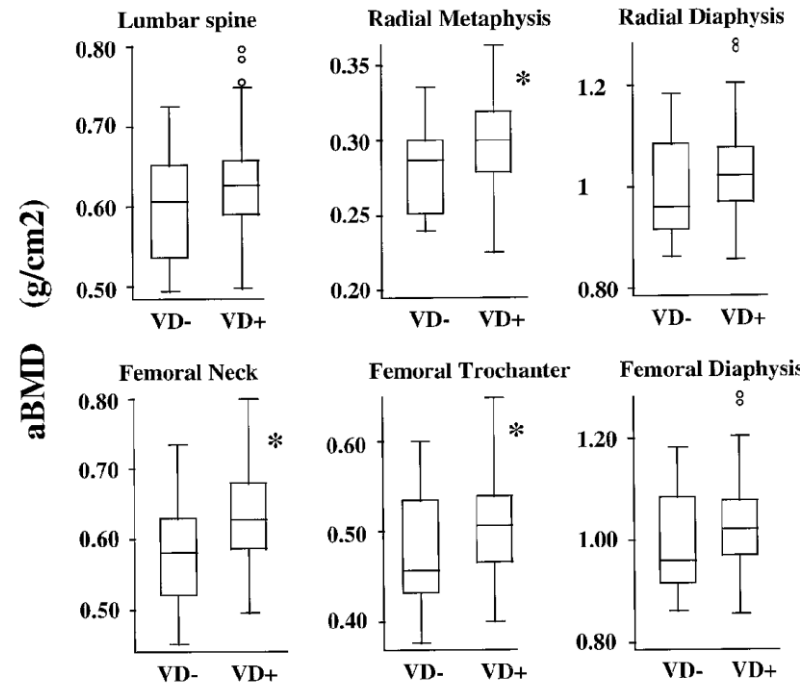
# Foods that contain calcium

- Dairy products
  - Milk
  - Yogurt
  - Cheese
  - Ice cream
- Almonds
- Broccoli
- Juices with added calcium
- Tofu with added calcium
- Breads and cereals with added calcium
- Dark-green, leafy vegetables

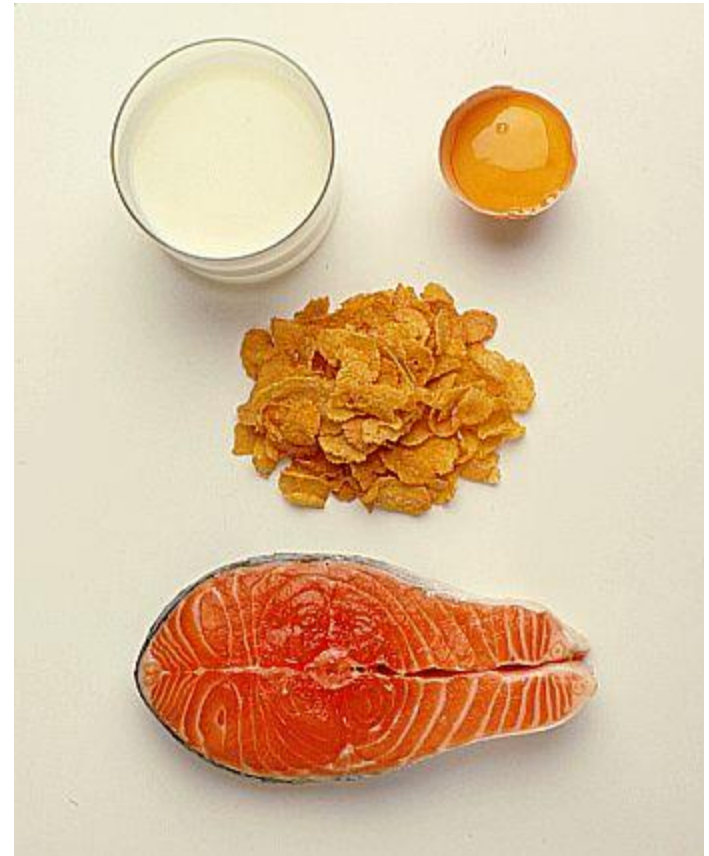


# Nutrition: Vitamin D

- 116 newborns given Vitamin D for 1 year vs placebo
- BMD significantly greater at age 7-9 years in treated group
- Zamora et al 1999



# Sources of Vitamin D



# North Star Audit data (Manzur 2009)

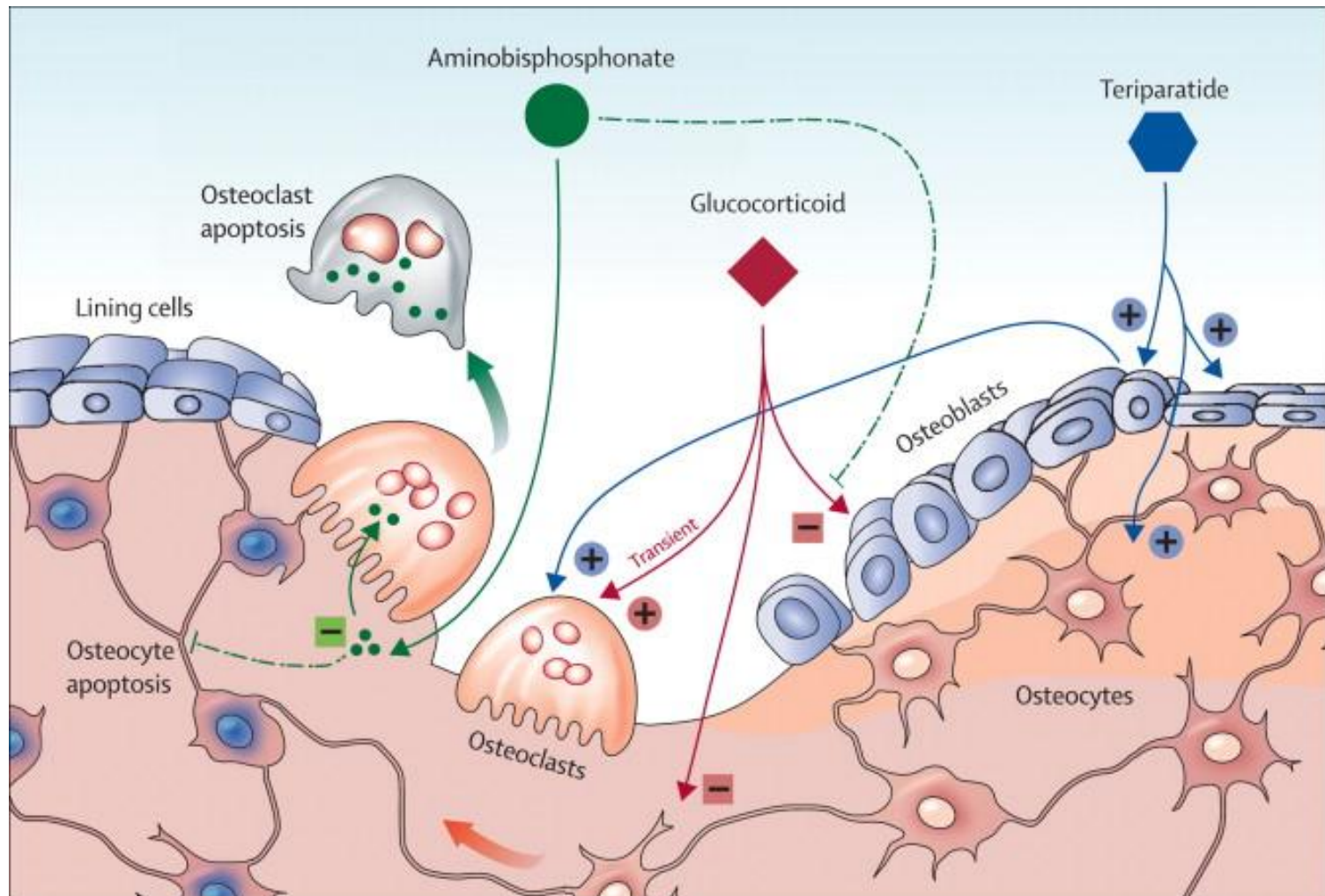
- Vitamin D levels from 152 DMD patients taken before starting steroids
  - Median level 35.8nmol/l (range 4-155)
  - 15% severe vitamin D deficiency (<17.5 nmol/l)
  - 43% Vitamin D deficient (17.5-37.5 nmol/l)
  - 22% Vitamin D 'sufficient'
- 
- Aim to keep Vitamin D levels 50-100 nmol/l

# Factors that increase bone loss

- Non-weight bearing
- Delayed puberty
- Cumulative corticosteroid dose
  - ▣ Duration of treatment
  - ▣ Frequency of treatment
  - ▣ Dose



# Bone loss vs Bone gain



# Bisphosphonate bone protection in adults on steroids

- Meta-analysis 45 randomised controlled trials
- Bisphosphonates better than calcitonin or vitamin D alone
- Vitamin D and Bisphosphonate better than Bisphosphonate alone

Amin S et al. J Bone Miner Res 2002; 17: 1521-26

# Bisphosphonates in corticosteroid treated children

- Intravenous Pamidronate increases bone mineral density, reduces pain and reshapes vertebral bodies after fracture
  - ▣ Steelman et al 2003
  - ▣ Shaw et al 2000
  - ▣ Acott et al 2005
- Oral Alendronate vs placebo increased bone mineral density after one year in 22 children aged 4-17 years
  - ▣ Rudge et al Rheumatology 2005

# Oral Alendronate in DMD

## (Hawker et al 2005)

- Two year open study of 16 boys on daily deflazacort (0.25-7 yrs duration)
  - ▣ Alendronate 0.08mg/kg
  - ▣ Calcium 750 mg daily
  - ▣ Vitamin D 1000 units daily
- Side effects
- Headache, dizziness, GI upset, muscle, bone pain

# Results

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- BMD Z scores remained stable
- In younger patients BMD improved
- Reasonably well tolerated
- Effect on reducing fractures not known

# Audit of Oral Risedronate (Bushby, Sarcozy ENMC 2009)

- Oral Risedronate plus calcichew
- Some discontinued because of side-effects
- No new fractures following trauma
- Overall there was a significant increase in BMD
- The effect of Risedronate was less in patients who had been on steroids for more than 6 years, and in some cases it worsened

# Oral Risedronate (Davie, ENMC 2009)

- 19 patients aged 6.3-21.3
- 6 vertebral deformity (30%)
- Mean duration of steroids to deformity 3.46 years (0.6-4.9 years)
- Mean spinal Z score without steroids -1.8
- Oral Risedronate 35 mg every two weeks
- Mean Spinal BMD
  - Before Risedronate -2.04
  - After two years on Risedronate -1.32
- Well tolerated

# Oral Bisphosphonates

- Reasonably well tolerated
- Comparison with intravenous bisphosphonates unknown
- Effect of all Bisphosphonates on growing skeleton over time is unknown
- Side-effects
  - ▣ Indigestion
  - ▣ Headache
  - ▣ Mandibular necrosis



# Summary

- Exercise (standing), sunshine, calcium and Vitamin D very important for bone health
- Vitamin D supplement
- Vertebral deformity/ fracture common
- Frequency of vertebral deformity relates to duration of steroid treatment and regimen
- I.V. Bisphosphonate for painful acute fractures
- Role for oral/ i.v. bisphosphonates for prevention of fractures is still not clear



## SUMMARY

1. Children with DMD treated with corticosteroids are at risk for osteoporosis and vertebral fractures. This effect of corticosteroids can be delayed by ensuring the child is physically active and has a diet rich in calcium and vitamin D. All children with DMD should have sun exposure to obtain sufficient amounts of vitamin D.
2. All children with DMD on corticosteroids should have vitamin D levels monitored and a daily vitamin D supplement should be given routinely. A DXA scan should be undertaken every 12-24 months to monitor bone mineral density. If the bone mineral density is very low or if there is acute back pain an X ray of the spine should be undertaken.
3. If there is a vertebral fragility fracture treatment with a bisphosphonate should be given.
4. Using a bisphosphonate to prevent fragility fractures is still controversial and should be considered on an individual basis by a specialist in children's metabolic bone health.



## BONE PROTECTION FOR DMD CHILDREN TREATED WITH STEROIDS

**IT'S TIME TO STOP WASTING!**

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# Acknowledgements

- European Neuromuscular Centre
- 170<sup>th</sup> ENMC Bone protection workshop participants

Nick Shaw

Katie Bushby

Doug Biggar

Ann-Charlotte Soderpalm

Mar Tulinius

Corado Angelini

David Rawlings

Anna Mieke Boot

Nicola Crabtree

Adnan Manzur

Mike Haddaway

Mike Davie

Maria Luisa Bianchi

Helen Roper

Anna Sarcozy

Brenda Wong