Bone Health and DMD

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Bones – Not a steel building frame

Bones – The house that first expands then keeps remodeling
What do builders and remodelers need?

**Home**
- Building materials
- Workers
- Foremen
- Quality control
- Supply chain

**Bone**
- Calcium and Phosphorus
- Osteoblasts and Osteoclasts
- Hormones (PTH, Vitamin D)
- QC: Muscle (bone muscle unit)
- Diet (Vitamin D, Calcium in diet)
Osteoclasts and Osteoblasts

Bricks made of Calcium and Phosphorus
Muscles – for Quality Control

Bone- Muscle Unit

Skeletal muscle pulls against the bone, causing it to rebuild and become denser.
Factors affecting Bone Building/remodeling process

- Mechanical factors
- Diet
- Familiar genetic background
- Glucocorticoid
- Thyroid hormone
- PTH 25(OH)D
- GH/IGF-1
- Testosterone
- Estrogen
- Genetic diseases
- Chronic diseases
- Insulin
- Leptin
- Diponectin
Side effects of corticosteroids

- Increased appetite
- Centripetal distribution of body fat
- Depression
- Emotional disturbances
- Peptic ulcer
- Decreased growth in children
- Osteoporosis
- Negative calcium balance
How do glucocorticoids affect bones?

• Weaken/Disable Osteoblasts
What can I do to help Bob the (weakened) osteoblast?

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Bone Muscle Unit

• When ambulatory, boys should “participate in regular submaximum (gentle) functional strengthening/activity, including a combination of swimming-pool exercises and recreation-based exercises in the community”.

• “Additional benefits might be provided by low-resistance strength training and optimization of upper body function”
The Calcium and Vitamin D supply chain...aka Recommendations for Daily Calcium and Vitamin D intake (at minimum)

Often, boys need 2000-3000 IU daily to maintain desired Vit D levels.
A word about supplements

• Calcium carbonate (Tums and friends)
  – Want the ‘elemental’ calcium dose to be 1200-1500 mg per day, so read labels
  – Take with Food!!!
  – Is not absorbed if taking heartburn meds

• Calcium Citrate (Citracal and friends)
  – Want the ‘elemental’ calcium dose to be 1200-1500 mg per day, so read labels
  – Do not have to take with food
  – Theoretically better for persons on corticosteroids, to mitigate any kidney stone producing effects of corticosteroids+ bicarbonate (alkaline) urine
Where do bone breaks occur?

• Long Bones
  – 20-60% of boys

• Vertebrae
  – 30-50 % of boys
2017 CDC Guidelines on Treatment of Bone Disease in Children with DMD on Corticosteroids (Preview)
CDC Guidelines on Monitoring Bone Health in Children with DMD on Corticosteroids

• Yearly:
  Diet history
  Vitamin D level (> 30 ng/dL)
  DXA Scan to assess bone density (BMD)

• Every 1-2 years:
  X-ray of Spine \textit{regardless of back pain}
Measuring Bone Density/Strength
DXA: Dual Energy x-Ray Absorptiometry

- Less radiation than a airplane trip
- Must be positioned flat on back
- Lie still for short periods of time X 30 minutes
- No zippers/snaps on clothes
- Need to have done in specialized centers with software specific to children
- A Score is assigned for the whole body, spine, hip, head of femur
2017 CDC Guidelines

• If pathologic long bone fracture occurs:
  – Get DXA and treat with bisphosphonate intravenously until “clinically stable” then continue on ‘maintenance’ dose
    • Pamidronate infusion once every 3 month X 2 years
    • then twice a year
2017 CDC Guidelines

- If back pain + vertebral fracture(s) OR high grade fracture without pain:
  - Get DXA and treat with bisphosphonate intravenously until back pain improved and reshaping of vertebrae have occurred
    - Pamidronate infusion once every 3 month X 2 years
    - then twice a year
Guideline considerations

- No data on ability of bisphosphonates to prevent first fracture (primary prevention) in children with steroid induced osteoporosis
- Vertebral fractures often occur and progress before a long bone fracture, hence the recommendation to treat severe/symptomatic vertebral fractures with bisphosphonates (secondary prevention)
Guideline considerations

• If low bone density on DXA without vertebral or long bone fracture → no bisphosphonate treatment

• →”Spine radiographs should be prioritized over BMD/DXA”

• Bone Density/DXA used as an adjunct during therapy to monitor treatment efficacy and need after the 2 year treatment.
Bisphosphonates

• Intravenous bisphosphonates
  – Pamidronate dosed every 1 mg/kg every 2-3 months (max dose per year 9 mg/year). First dose use 0.5 mg/kg
  – Zolendronate dosed every 6 mos 0.0125 mg/kg first dose, 0.025-0.05 mg/kg subsequent doses. Max dose 0.1 mg/kg/year
  – Greatest body of literature/experience is that IV bisphosphononates improve BMD in children and prevent additional fractures in children with Osteogenesis imperfecta. No data on fractures in children with chronic illness.
Bisphosphonates

• Oral bisphosphonates
  – Alendronate
  – Poor absorption from the gut (< 1%)
  – Conflicting reports on whether BMD is improved in treated children
  – When used in children with Osteogenesis imperfecta (randomized control trial) did not decrease fracture frequency

• Oral bisphosphonates not endorsed
Bisphosphonates side effects

- Acute phase reactions – flu like symptoms, fever, myalgia, respiratory difficulty
  - First infusion, less so with subsequent infusions
  - Pre-treat with acetaminophin and benadryl
- Post treatment ↓Ca and ↓PO4
  - Pre-treat with calcium supplementation +/- calcitriol starting day before infusion up to 4 days after infusion
- Osteonecrosis of the Jaw
  - No major dental work prior to first infusion and ideally during treatment
- Aberrant heart rhythms
  - EKG prior to first infusion
Bisphosphonates – Long term

With both the important players in bone remodeling disabled, what about the health of the bone long term (in decades)???

Answer: ???
Questions?