Fracturing Points: Bone Disease in CF

Camille Washowich, MSN, ACNP
Understanding Bone Disease

Bone Physiology
Pathophysiology
Prevalence in US
Diagnosis & Treatment
Manifestations of Cystic Fibrosis

General
- Growth failure (malabsorption)
- Vitamin deficiency states (vitamins A, D, E, K)

Nose and sinuses
- Nasal polyps
- Sinusitis

Liver
- Hepatic steatosis
- Portal hypertension

Gallbladder
- Biliary cirrhosis
- Neonatal obstructive jaundice
- Cholelithiasis

Bone
- Hypertrophic osteoarthropathy
- Clubbing
- Arthritis
- Osteoporosis

Intestines
- Meconium ileus
- Meconium peritonitis
- Rectal prolapse
- Intussusception
- Volvulus
- Fibrosing colonopathy (strictures)

Lungs
- Bronchiectasis
- Bronchitis
- Bronchiolitis
- Pneumonia
- Atelectasis
- Hemoptysis
- Pneumothorax
- Reactive airway disease
- Cor pulmonale
- Respiratory failure
- Mucoid impaction of the bronchi
- Allergic bronchopulmonary aspergillosis

Heart
- Right ventricular hypertrophy
- Pulmonary artery dilation

Spleen
- Hypersplenism

Stomach
- GERD

Pancreas
- Pancreatitis
- Insulin deficiency
- Symptomatic hyperglycemia
- Diabetes

Reproductive
- Infertility (aspermia, Absence of vas deferens)
- Amenorrhea
- Delayed puberty
Bone Physiology

Bone Formation: Osteoblasts

Bone Remodeling: Osteoclasts

Bone Types:
- Cortical: 80% bone mass; mineralized collagen; major component of tubular (long bones)

- Travascular: sponge, providing strength/elasticity to axial skeleton
Normal Bone Development

- **Attainment of peak bone mass**
- **Consolidation**
- **Age-related bone loss**
- **Males**
- **Females**
- **Menopause**

Adapted from:
Ref: Compston JE. Clin Endocrinol 1990
Normal vs Osteoporotic Bone
Pathophysiology of Bone Disease

Bone disease first seen in CF 1979
Noted low BMD (bone mineral density) on DXA
Abnormal bone turnover markers

CFTR protein dysfunction 2004
Decreased production of osteoprotegerin and prostaglandin E2, regulators of bone formation/resorption process
Pathophysiology of Bone Disease in CF

Chronic infection/inflammation cycles:
  Increased release of cytokines (IL 1/6) and TNF increases bone reabsorption and decrease bone formation

ABPA: following IgE levels

Colonized Organisms:
  Bacterial: PA, MSSA/MRSA, B Cepecia, Achromobacter, Steno
  Mycobacterium: MAC, M Abscessus
Pathophysiology of Bone Disease in CF

- Malnutrition with low BMI
- Malabsorption: low vitamin D/K levels
- Pancreatic Insufficiency
- Delayed puberty/hypgonadism
- Decreased peak bone mass
- Steroid Therapy (pulse/chronic)
- Decreased/Inactivity
- Chronic Pain
Prevalence of Fractures Non-CF

- **Men**
  - Incidence per 100,000 person-years
  - Age (years): 35-39, ≥85
  - Trends for Hip, Vertebrae, Colles'

- **Women**
  - Incidence per 100,000 person-years
  - Age (years): 35-39, ≥85
  - Trends for Hip, Vertebrae, Colles'
### Secondary Osteoporosis Development

<table>
<thead>
<tr>
<th>Risk of secondary osteoporosis:</th>
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<tr>
<td>Diagnosis+</td>
<td>5</td>
<td>6.0%</td>
<td>78</td>
<td>7.2%</td>
<td>83</td>
<td>7.1%</td>
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<tr>
<td>Chronic glucocorticoid use*</td>
<td>20</td>
<td>24.1%</td>
<td>42</td>
<td>3.9%</td>
<td>62</td>
<td>5.3%</td>
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<tr>
<td>Anti-convulsant use</td>
<td>4</td>
<td>4.8%</td>
<td>41</td>
<td>3.8%</td>
<td>45</td>
<td>3.8%</td>
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<tr>
<td>Any secondary osteoporosis risk* (see note)</td>
<td>29</td>
<td>34.9%</td>
<td>149</td>
<td>13.7%</td>
<td>178</td>
<td>15.2%</td>
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</table>

<table>
<thead>
<tr>
<th>Risk from falls:</th>
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<tbody>
<tr>
<td>Falls-risk diagnosis++</td>
<td>34</td>
<td>41.0%</td>
<td>425</td>
<td>39.1%</td>
<td>459</td>
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<tr>
<td>Tertiary tricyclic anti-depressant at index</td>
<td>5</td>
<td>6.0%</td>
<td>27</td>
<td>2.5%</td>
<td>32</td>
<td>2.7%</td>
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<tr>
<td>Long-acting benzodiazepine at index</td>
<td>0</td>
<td>0.0%</td>
<td>14</td>
<td>1.3%</td>
<td>14</td>
<td>1.2%</td>
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<tr>
<td>Any risk from falls (see note)</td>
<td>38</td>
<td>45.8%</td>
<td>445</td>
<td>40.9%</td>
<td>483</td>
<td>41.3%</td>
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<table>
<thead>
<tr>
<th>Chronic medical conditions:</th>
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<tr>
<td>Diabetes mellitus</td>
<td>11</td>
<td>13.3%</td>
<td>195</td>
<td>17.9%</td>
<td>206</td>
<td>17.6%</td>
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<tr>
<td>Heart disease</td>
<td>26</td>
<td>31.3%</td>
<td>354</td>
<td>32.5%</td>
<td>380</td>
<td>32.5%</td>
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<tr>
<td>Hypertension</td>
<td>29</td>
<td>34.9%</td>
<td>423</td>
<td>38.9%</td>
<td>452</td>
<td>38.6%</td>
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<tr>
<td>Hyperlipidemia</td>
<td>15</td>
<td>21.4%</td>
<td>233</td>
<td>18.1%</td>
<td>248</td>
<td>21.2%</td>
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<tr>
<td>Malignant neoplasms**</td>
<td>30</td>
<td>36.1%</td>
<td>246</td>
<td>22.6%</td>
<td>276</td>
<td>23.6%</td>
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<tr>
<td>COPD/asthma**</td>
<td>33</td>
<td>39.8%</td>
<td>294</td>
<td>27.0%</td>
<td>327</td>
<td>27.9%</td>
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<tr>
<td>Arthropathies</td>
<td>33</td>
<td>39.8%</td>
<td>341</td>
<td>31.3%</td>
<td>374</td>
<td>31.9%</td>
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<tr>
<td>Osteoarthritis</td>
<td>17</td>
<td>20.5%</td>
<td>195</td>
<td>17.9%</td>
<td>212</td>
<td>18.1%</td>
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<tr>
<td>Depressive disorders</td>
<td>5</td>
<td>6.0%</td>
<td>113</td>
<td>10.4%</td>
<td>118</td>
<td>10.1%</td>
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</tbody>
</table>
Diagnosing Bone Disease

Diagnostics:
DXA
CXR: fracture
CT Chest/MRI

Labs:
Calcium
Vitamin D3
Albumin
DXA: Dual Energy X-ray Absorptiometry

Measures BMD in femor/lumbar/wrist
Painless
Outpatient
T/Z Score are similar in adults
Results:
  Normal > -1
  Osteopenia -1 to -2.5
  Osteoporosis < -2.5
Normal CXR
CXR: Left Thoracic Fracture
MRI Findings: Lumbar Fracture
Treatment Options for Osteopenia/porosis

Life Style Modifications
Medications
Nutritional Needs
Exercise
Surgery
## Oral and Intravenous Bisphosphonates

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<tr>
<th>Brand Name</th>
<th>Manufacturer</th>
<th>Generic Name</th>
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<tr>
<td><strong>Oral Formulations</strong></td>
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<tr>
<td>Actonel</td>
<td>Procter &amp; Gamble Pharmaceuticals</td>
<td>risedronate</td>
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<tr>
<td>Bonefos</td>
<td>Micromedex</td>
<td>clodronate (not commercially available in the U.S.)</td>
</tr>
<tr>
<td>Boniva</td>
<td>Roche/GlaxoSmithKline Pharmaceuticals</td>
<td>ibandronate</td>
</tr>
<tr>
<td>Didronel</td>
<td>Procter &amp; Gamble Pharmaceuticals</td>
<td>etidronate</td>
</tr>
<tr>
<td>Fosamax</td>
<td>Merck &amp; Co.</td>
<td>alendronate</td>
</tr>
<tr>
<td>Fosamax Plus D</td>
<td>Merck &amp; Co.</td>
<td>alendronate</td>
</tr>
<tr>
<td>Skelid</td>
<td>Sanofi-aventis</td>
<td>tiludronate</td>
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<tr>
<td><strong>Intravenous Formulations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aredia (cancer therapy)</td>
<td>Novartis</td>
<td>pamidronate</td>
</tr>
<tr>
<td>Bonefos (cancer therapy)</td>
<td>Schering AG</td>
<td>clodronate</td>
</tr>
<tr>
<td>Boniva IV (quarterly infusion for osteoporosis)</td>
<td>Roche/GlaxoSmithKline</td>
<td>ibandronate</td>
</tr>
<tr>
<td>Reclast (yearly infusion for osteoporosis)</td>
<td>Novartis</td>
<td>zoledronic acid</td>
</tr>
<tr>
<td>Zometa (cancer therapy)</td>
<td>Novartis</td>
<td>zoledronic acid</td>
</tr>
</tbody>
</table>
Nutritional Needs
Exercise Options

Weight Bearing:
Running, Dancing, Sports

Non-Weight Bearing:
Swimming

Safe, Fun, Affordable
Surgery Options
Decreasing Fracture Risk

Take Calcium with Vitamin D twice daily

Regular bone density testing
  Normal: every 2yrs
  Osteoporosis/Osteopenia: every year

Regular weight bearing exercise daily
  Minimum of 30min daily

Avoid smoking/excessive alcohol (>1 beer/day)
Thank You!