Crystal Diseases

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Arthritis in the Elderly

- Crystal diseases
  - Gout
  - CPPD
  - Hydroxyapatite disease (Milwaukee Shoulder)
- Treatment
  - Special considerations in the elderly
Assessment of Arthritis

- History
- Physical examination
- Radiographs
  - Weight bearing films
- Laboratory – CBC, ESR, CRP, chemistry, uric acid level, serologies
- Joint fluid – crystal, cell count, culture
Gout

- Epidemiology
  - Prevalence increases with age and serum uric acid concentration: 2.24% 45-64 y.o., 3.17% 65-74 y.o., 8% 75-84 y.o.
  - Increased in men than women with advancing age
  - Current estimate of 5.1 million people in the US have gout
Gout

- Incidence: 4.9% > uric acid 9mg/dl, 0.5% 7mg/dl to 8.9mg/dl and 0.1% < 7mg/dl.
  Peak age of onset: 50 y.o. in men, 60-70 y.o. in females
  M:F ratio: 5th -6th decade 7-9:1 and 1:1 7th to 8th decade
  Women develop gout 10 to 20 years following menopause
Risk Factors

- Medications ie: low dose ASA, thiazide diuretics, cyclosporine
- HTN, HL, CAD, insulin resistance, CKD, obesity (metabolic syndrome)
- Diet: red meat (liver, brain, sweetbread), seafood (shellfish, tuna, dark fish, sardines, anchovies, cod, haddock), beer, sodas sweetened with fructose, veal, turkey, venison
- High purine vegetables not associated with gout: spinach, cauliflower, asparagus, mushrooms, peas
- “Dairy has a protective effect”
<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted RR</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>Male</td>
<td>7.64</td>
<td>7.46-7.81</td>
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<tr>
<td>CKD</td>
<td>4.95</td>
<td>4.28-5.72</td>
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<tr>
<td>HTN</td>
<td>3.93</td>
<td>1.60-9.70</td>
</tr>
<tr>
<td>Obesity</td>
<td>3.81</td>
<td>1.22-11.84</td>
</tr>
<tr>
<td>CAD</td>
<td>1.75</td>
<td>1.70-1.79</td>
</tr>
<tr>
<td>Diuretics</td>
<td>1.72</td>
<td>1.67-1.76</td>
</tr>
<tr>
<td>Seafood/Etoh (beer/liquor)</td>
<td>1.51/1.17</td>
<td>1.07-1.86/1.11-1.2</td>
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</tbody>
</table>
Risk Factors

- Hypertension
- Obesity
- Insulin resistance
- Renal Insufficiency
- Metabolic syndrome
  - Current debate whether hyperuricemia is an independent RF for cardiovascular disease and hypertension
  - Is high uric acid level directly toxic to microvasculature?
Stages of Gout

- Hyperuricemia: serum uric acid > 6.8mg/dl (decreased renal excretion or over production-less common)

Asymptomatic period followed by followed by acute attack due to crystallization and inflammation

Intercritical period: period between acute attacks, usually have ongoing inflammation

Advanced gouty arthritis: persistent hyperuricemia with tophaceous deposits, polyarthritis, urate nephropathy
Features of Gout

- Classic:
  - Monoarticular
  - Acute painful attack of 1\textsuperscript{st} MTP, can also affect: ankle, tarsal bones, knee, small joints
  - May resemble septic arthritis or cellulitis
Features of Gout (cont.)

- Tophaceous gout-occurs over years (5y)
- Elderly: 60% new cases found in postmenopausal females (rare premenopausal):
  - Polyarticular in distribution of OA
  - May resemble RA
  - Consider in patient using diuretic, low dose ASA
Gout

- Diagnosis
  - Clinical history and synovial fluid analysis
  - ACR Criteria
    - Radiographs- erosions with overhanging edges/cysts
    - Ultrasound reveals erosions, crystals deposited on cartilage, tophi
### American College of Rheumatology Criteria for Gout

| Gout may be diagnosed if either of these are present | Monosodium urate crystals in synovial fluid  
Tophi confirmed with crystal exam |
|--------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|
| Diagnosed if at least 6 are present | More than one attack of acute arthritis  
Maximal inflammation in a day  
Monoarthritis  
Erythema  
First MTP painful/swollen  
Unilateral MTP involvement  
Unilateral tarsal joint  
Tophi  
Hyperuricemia, xray + cysts  
Xray with swelling  
Synovial fluid culture negative |
Treatment Considerations in the Elderly

- Multiple morbidities - CHF, CKD, CVA, PUD
- Physiologic alterations in organ systems: renal, hepatic function
- Altered drug distribution, metabolism and elimination
- Altered end organ sensitivity to certain drugs
- Drug-drug interactions
- Increased incidence of adverse effects
### Physiologic Changes with Aging that Affect Drug Distribution

<table>
<thead>
<tr>
<th>Category</th>
<th>Changes</th>
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<tbody>
<tr>
<td>Absorption</td>
<td>Altered physiology&lt;br&gt;increased gastric pH&lt;br&gt;Decreased gastrointestinal blood flow&lt;br&gt;Reduced cell mass in gastrointestinal mucosa</td>
</tr>
<tr>
<td>Distribution</td>
<td>Reduced total body water&lt;br&gt;Decreased lean body mass&lt;br&gt;Increased body fat&lt;br&gt;Reduced serum albumin</td>
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<tr>
<td>Elimination</td>
<td></td>
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<tr>
<td>Hepatic metabolism</td>
<td>Decreased hepatic blood flow&lt;br&gt;Decreased hepatic mass&lt;br&gt;Reduced enzyme activity</td>
</tr>
<tr>
<td>Renal excretion</td>
<td>Decreased renal plasma flow&lt;br&gt;Decreased glomerular filtration rate&lt;br&gt;Decreased tubular function</td>
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Gout

Treatment--Nonpharmacologic

Rest joint, ice packs, eliminate contributing factors (diuretics/ASA)

Behavioral modification: weight loss, eliminate alcohol intake, decrease intake meats, seafood, decrease carbohydrate, increase dairy intake
Pharmacologic Management

- Acute Flare
  - Nonsteroidal Anti-inflammatory drugs
    - Caution in elderly, patients with risk factors of PUD, CRI, hypersensitivity, hepatic disease, CHF
  - Gastroprotective agents in elderly: misoprostol, omeprazole
  - Colchicine (Colcrys): two tablets of (0.6mg) followed by 0.6 mg one hour later (avoid with ESRD)
    - Use within 48 hours of flare
    - Side effects: GI, neuromyopathy, rhabdomyolysis, myelosuppression, IV formulation taken off market
Pharmacologic Management

- **Systemic corticosteroids**
  - Prednisone 20-40mg taper over 10 days
  - Methylprednisolone 100-150mg x 2d
  - Triamcinolone acetonide 60mg IM x1 dose
- **Corticotropin**
  - 25 units to 40 units subcutaneously, IM or IV
- **Intraarticular steroids**
  - Useful if one or two joints affected
    - Triamcinolone acetonide 20-40mg
    - Methylprednisolone
Investigational Agents

• Interleukin-1 Inhibitors
  ➢ IL-1: Mediator of inflammation and target in acute gout
    ■ Anakinra (Kineret): IL-1 receptor antagonist
      ▪ 100mg sq daily for 3 days
    ■ Canakinumab: humanized monoclonal Ab blocks IL-1B signal
      ▪ 150mg sq
Suppressive and Antihyperuricemic Therapy

- Lifestyle modification and risk reduction
- Prophylactic or suppressive therapy during urate lowering therapy
  - Colchicine 0.6 mg po daily (GFR 35-50 cc/min), every 2-3 days (GFR 10-34 cc/min), do not use if GFR <10cc/min
  - NSAIDs: monitor closely for ADR
  - Low dose steroids
Uric Acid Lowering Agents

• Agents Inhibiting Uric Acid Production
  ➢ Allopurinol: adjust to renal function and uric acid, CrCl nl: 300mg daily, CrCl < 60cc/min 200mg daily, CrCl < 30cc/min 100mg, ESRD qod, monitor for dermatitis, hypersensitivity reaction
  ➢ Nonpurine selective xanthine oxidase inhibitors: febuxostat 40-80 mg daily

• Agents Increasing Uric Acid Excretion
  ➢ Probenicid: 250mg-1000mg bid, monitor for gouty flares, urolithiasis, ineffective for GFR,<80 cc/min
  ➢ Sulfinpyrazone: 50mg bid, slow titration to 200mg bid, ineffective with CRI
  ➢ Benzbromazone (not available in U.S.)
  ➢ Losartan, fenofibrate, Vit C
Novel Agents

- Rasburicase: recombinant Aspergillus Flavus uricase: for tumor lysis syndrome--approved for short course
- Uricase: enzymatically degrades uric acid
- Pegloticase: porcine uricase linked to polyethylene glycol
  - Treatment resistant gout
Calcium Pyrophosphate Dihydrate Disease (Pseudogout)

- Epidemiology
  - Prevalence: 15% (65 – 74 years old), 30% – 60% (over 84 years)
  - M = F
  - Classified as idiopathic, familial
Features of CPPD

- Acute or chronic monoarticular or polyarticular flare
- Affects shoulders, wrists, elbows, fibrocartilage and hyaline cartilage of knees, hips and symphysis pubis
- Joint pain either acute, subacute, or chronic
- Asymptomatic with evidence of chondrocalcinosis found on radiographs
- Due to elevated microlevels of calcium and pyrophosphate in the joint
Metabolic Disorders Associated with CPPD

- Hemachromatosis
- Hypothyroidism
- Hyperparathyroidism
- Hypophosphatemia
- Hypomagnesemia
- Wilson’s Disease
Diagnosis and Treatment of CPPD

- **Diagnosis:**
  - Synovial fluid
  - X-ray evidence of chondrocalcinosis

- **Treatment:**
  - NSAID’s
  - Colchicine – caution in elderly
  - Oral or intra-articular steroids
Hydroxyapatite Disease

- Acute arthritis or periarthritis in elderly
- “Milwaukee Shoulder” – destructive arthritis found in 65-76 year old females
- Periarthritis – calcification of joints, tendons and bursa which can occur at any age and present as severe pain at the affected site
- Spinal deposition within intervertebral discs resulting in pain (along with CPPD)
Treatment of Hydroxyapatite Disease

- NSAID’s
- Intra-articular or oral corticosteroids
- Colchicine
- ? Hydroxychloroquine