# A Review of Osteoarthritis and Gouty Arthropathy SUZANNE GHARIB, MD VANDALIA HEALTH

## Learning Objectives

Learn basics of pathophysiology and management of two common arthritic conditions

- Learn importance of and how to integrate ancillary services in managing arthritic diseases
- Identify appropriate role of specialty care in two common arthritic conditions

# How common are arthritic diseases?



# How common are Rheumatic Diseases?

- Degenerative disc disease
  - ▶ 40% over the age of 40
- Knee Osteoarthritis
  - > 22.9% over the age of 40
- Gouty Arthropathy
  - ▶ 3.9%
- Rheumatoid arthritis
  - ▶ 0.5-1%
- Psoriatic arthritis
  - ▶ 1%
- Systemic lupus erythematosus
  - ▶ 0.2%

## Osteoarthritis





### Osteoarthritis—Basic concepts

Divided into two broad categories of primary and secondary

- Primary has no underlying culprit except for known risk factors
- Secondary has known underlying disease or trauma as the inciting factor

#### Risk factors

- ► Age
- Female gender
- Obesity
- Anatomical factors
- Muscle weakness

### Osteoarthritis—Pathophysiology

- Interplay of risk factors and mechanical stress leads to joint inflammation which damages the entire joint, sparing nothing
- Early—articular cartilage is damaged
- Later—synovial inflammation and hypertrophy, soft tissue structures affected (menisci, joint capsule, ligaments)

### Osteoarthritis--Patient history

Varies widely based on involved joints and severity

- Pain is typical
  - Worse with activity, improves with rest
- Stiffness
  - > Typical in the morning, lasting less than 30 minutes
  - Evening stiffness is also a common complaint
- Decrease in mobility of joint
- "Giving way" of joints—usually due to muscle weakness
- "Grinding" or crepitus of joint

### Osteoarthritis—exam

Focused musculoskeletal exam

- ► Hands
  - Heberden's and Bouchards nodes
  - Squaring of CMC joints
- Bony enlargement
- Crepitus
- Tender joint lines can be present
- Rarely—effusions





### Osteoarthritis—Work up

Diagnosis can be made clinically with confidence if:

- ► Age >45
- Pain worse with activity, improves with rest
- A.m. stiffness <30 minutes</p>
- Exam demonstrates bony enlargement or decreased ROM
- When should I consider further testing?
  - Atypical symptoms
    - ▶ I.e. prolonged a.m. stiffness, joint swelling, effusions

## Osteoarthritis--Testing

#### X-rays

- Joint space narrowing
- Marginal osteophytes
- Subchondral sclerosis
- Bone cysts
- Rarely—erosive changes
- Joint aspiration
  - ▶ Non-inflammatory fluid with WBC <2000, predominately mononuclear cells
- MRI
  - Rarely needed
  - Detects earlier disease
- Ultrasound
  - Rarely needed but can detect similar findings to X-rays

## Osteoarthritis—Testing

- But wait, what about labs???
- No need for lab testing of any kind to make or confirm diagnosis of osteoarthritis

# Osteoarthritis—Who Should Manage it and How?

- Goals of treatment
  - Improve function
  - Minimize pain
  - Target treatment to affected joints
- Requires comprehensive plan that is patient specific including educational, behavioral, psychosocial, and physical interventions
- Does not typically require intervention from specialists
  - Good use of available resources is critical

### Osteoarthritis—Patient Education

#### There are no disease modifying medications

- Available treatments can alleviate pain but do not change course of disease
- Non-pharmacologic therapies are strongly recommended and can improve quality of life and function
- Providers need to be cognizant of available programs and be proactive in referring patients accordingly

### Osteoarthritis—Role of Exercise

Exercise is strongly recommended for treatment of osteoarthritis, particularly of the hip and knee

- Yoga
- Tai Chi
- Various specific programs through Arthritis Foundation
- If patients cannot or will not engage in above activities, referral to PT for strength and balance training is a viable alternative

### Available Programs for OA Management Through Arthritis Foundation

- Walk with Ease
- Aquatics program
- Active Living Everyday
- Enhance Fitness
- Fit and Strong
- My Knee Exercise
- Chronic Disease Self Management Program

# Osteoarthritis—Other Nonpharmaceutical interventions

- Weight loss
  - Especially pertinent if weight bearing joints are involved
- Occupational therapy
  - Unload joints via bracing, cane, etc
- If non-pharmaceutical options work, avoid use of medications

## Osteoarthritis—Pharmaceutical Interventions

- General principal
  - Less is more
  - Assess co-morbidities and tailor medications to individual
- Supplements
  - Glucosamine—recommended against given absence of data
  - Chondroitin—recommended against except in hand OA where it is recommended conditionally
  - Fish oil—recommended against given absence of data
- Acetaminophen
  - Data does not show substantial pain relief over placebo but it is an option
  - Monitor for hepatotoxicity

## Osteoarthritis—Pharmaceutical Interventions

- NSAIDs—available in topical and oral formulations
- Topical—good option prior to oral NSAIDs due to less GI and systemic side effects
  - ▶ Not always practical for certain joints—i.e. Hands, Hips
- Oral—best evidence for use
  - Renal toxicity, cardiovascular, GI need to be considered
  - ▶ Tailor specific choices to patient—dosing regimens, GI sparing, etc

## Osteoarthritis—Pharmaceutical Interventions

- Duloxetine—conditionally recommended based on data
- Tramadol—conditionally recommended
  - Primarily in those with contraindication or intolerance to NSAIDs
- Opioids—not recommended unless all other options have been exhausted

### Osteoarthritis—Other interventions

- Intra-articular steroid injections
  - Strong recommendation in knee and hip OA
    - Should consider guided injection for hip OA
  - Conditionally recommended in hand OA
- Hyaluronic acid injections
  - Conditionally recommended against based on data
- Surgical interventions
  - Usually reserved for late stage osteoarthritis

# Osteoarthritis—What is the Role of the Primary Care Provider?

- Based on available therapies, can conduct the majority of care for osteoarthritis
- It is vitally important to recognize and acknowledge disease
- Referral should be reserved for very specific circumstances
  - Consider Rheumatology if suspect concomitant inflammatory disease
  - If there is a lack of experience or comfort with intraarticular glucocorticoid injections, can consider referral to a specialist including Orthopedics, Rheumatology, Pain Medicine, PMR, etc
  - Irrespective, PCP should have an ongoing role in care
- > When a referral is done, do not set unrealistic expectations
- Rarely is there a need to refer osteoarthritis to multiple specialists

# Gouty Arthropathy—The Disease of Kings

- First mention of podagra was in ancient Egypt in 2640 B.C.
- Later described by Hippocrates as the "unwalkable disease"
- Called the king's disease due to association with rich foods and alcohol consumption
- Antoni Von Leeuwenhoek first described appearance of uric acid crystals in 1679



# Gouty Arthropathy--Pathophysiology

- Very well defined pathogenesis
- Overproduction or underexcretion of uric acid leads to hyperuricemia which in turn predisposes to development of gouty arthritis



# Gouty Arthropathy—Risk Factors

#### Modifiable risk factors

- ► Hyperuricemia
- Hypertension
- Obesity
- Hyperlipidemia
- Diabetes mellitus
- Cardiovascular disease
- Alcohol
- Medications altering urate balance
- Chronic kidney disease
- Dietary factors

- Nonmodifiable risk factors
  - Age
  - Genetic variants
  - ▶ Gender
  - Ethnicity

# Gouty Arthropathy—How Much Does Uric Acid Matter?

#### ► Hyperuricemia≠Gout

- Predisposing factor that greatly increases risk of gout with its own associated risk factors
  - ► Higher BMI
  - Higher BP (both systolic and diastolic)
  - Elevated fasting glucose
  - Abnormal lipid profiles
  - Renal dysfunction
  - Male (females catch up after age of 50)

# Gouty Arthropathy—How Much Does Uric Acid Matter?

Baseline serum urate	Incidence of gout at 3 years	Incidence of gout at 5 years	Incidence of gout at 10 years	Incidence of gout at 15 years
<6.0	0.21%	0.33%	0.79%	1.12%
6.0-6.9	0.37%	0.66%	1.98%	3.70%
7.0-7.9	0.92%	1.91%	6.37%	9.00%
8.0-8.9	4.00%	6.94%	11.32%	16.28%
9.0-9.9	8.31%	14.02%	24.18%	35.21%
10.0 or greater	10.00%	26.25%	40.00%	48.47%

# Hyperuricemia: To Treat or Not to Treat?

- Some data exists that suggests hyperuricemia, not just gouty arthritis, can have a detrimental effect on health
- Clear evidence suggests development of nephrolithiasis as a result of hyperuricemia
- Uric acid deposits have been found in multiple organs including heart, eye, kidneys, etc.
  - Pathology implication is uncertain
- Currently, there are no recommendations that suggest asymptomatic hyperuricemia should be treated with urate lowering therapies

### Gouty Arthropathy--The Four Stages

Stage 1: Asymptomatic Hyperuricemia

- Essentially a "pre-gout" state—ends with first attack of gout
- > At this time, data does not suggest any intervention during this stage

## Gouty Arthropathy--The Four Stages

#### Stage 2: Acute Gout Attack

- Abrupt onset of pain and swelling
- Typical first attack is in lower extremities with first MTP (AKA Podagra) being most common
- Peak symptoms usually occur within 12-24 hours
- Symptoms typically are self limiting and resolve within 3-14 days



# Gouty Arthropathy: Deeper Dive into Acute Attacks

- Usually monoarticular early in course of disease but can rarely be polyarticular
  - Polyarticular more with lymphoproliferative or myeloprolifative disease as initial presentation
- Periarticular structures including tendons and bursa can also be affected
- More common at night and early morning while cortisol is low
- Excruciatingly painful
  - Often reports pain to light touch
- Occasional systemic symptoms—fever, fatigue, malaise
- Affected joint is red, hot, and swollen
- 60% have a second flare within a year and 80% within 3 years

## Gouty Arthropathy: The Four Stages

#### Stage 3: Intercritical gout

- Between acute attacks
- Some patients experience low grade chronic pain
- Hyperuricemia persists
- Subclinical inflammation may still be present
- Optimal stage for initiating long term treatment

## Gouty Arthropathy: The Four Stages

Stage 4: Chronic tophaecous gout

- Tophi are chronic granulomas around monosodium urate crystals
- Can develop anywhere including intraarticular, periarticular and extraarticular
- Can lead to destructive, deforming arthritis





- History and Exam
- Labs:
  - May see signs of systemic inflammation
    - Elevated ESR, CRP, Leukocystosis
  - Uric acid not helpful in acute attack—may be high, low or normal
  - Uric acid should be checked 2-4 weeks after acute attack

#### Synovial Fluid

- Gold standard: monosodium urate crystals present—needle shaped, negatively birefrigent
- Synovial fluid is inflammatory and negative gram stain



- ▶ Without MSU crystals, need to meet 6 or more of the following criteria
  - More than one attack of acute arthritis
  - Maximum inflammation developed within one day
  - > Attack of monoarthritis
  - Redness over joints
  - Painful or swollen first metatarsophalangeal joint
  - Unilateral attack on first metatarsophalangeal joint
  - Unilateral attack on tarsal joint
  - Tophus (proved or suspected)
  - Hyperuricemia
  - Asymmetric swelling within a joint on radiograph
  - Subcortical cysts without erosions on radiograph
  - Joint fluid culture negative for organisms during attack

### Gouty arthritis: Relevance of Podagra—Can Meet 6 Criteria with Good History/Exam

- More than one attack of acute arthritis
- Maximum inflammation developed within one day
- Attack of monoarthritis
- Redness over joints
- Painful or swollen first metatarsophalangeal joint
- Unilateral attack on first metatarsophalangeal joint
- Strengthen diagnosis with additional presence of hyperuricemia or tophus

#### X-rays

- Not helpful during acute attack
- In chronic disease, can see erosive changes in affected joint
  - "rat bite" erosions



- Ultrasound
  - MSU is seen as a hyperechoic enhancement
    - Double contour sign
- Dual Energy CT (DECT) scan
  - Can detect urate by beam attenuation after exposure to two X-ray spectra
  - Expensive and only available in some institutions



### Gouty Arthropathy: Treatment

Contention exists between the ACP and Rheumatology groups as to how gouty arthropathy should be approached and treated

Feature	ACR (2012) <sup>2,3</sup>	3e Initiative (2014) <sup><u>4</u></sup>	EULAR (2016) <sup>5</sup>	ACP (2016) <sup>1</sup>
Background of authors	<ul> <li>Rheumatologists (23)</li> <li>Primary care physicians (3)</li> <li>Nephrologist (1)</li> <li>Patient advocate (1)</li> <li>Medical trainees (5)</li> </ul>	Rheumatologists (474)	<ul> <li>Rheumatologists (15)</li> <li>Radiologist (1)</li> <li>Primary care physicians (2)</li> <li>Research trainee (1)</li> <li>Patient advocates (2)</li> <li>Non-physician methodologists (3)</li> </ul>	<ul> <li>Primary care physicians (3)Other decision-making committee members:</li> <li>primary care physicians (9),</li> <li>rheumatologist (1),</li> <li>pulmonologist (1)</li> </ul>
Authors' location(s)	International (USA, Europe, New Zealand)	Multinational (14 countries)	Europe (12 European nations)	USA

## Gouty Arthropathy: ACP Recommendations

- Recommendation 1: ACP recommends that clinicians choose corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), or colchicine to treat patients with acute gout. (Grade: strong recommendation, high-quality evidence)
- Recommendation 2: ACP recommends that clinicians use low-dose colchicine when using colchicine to treat acute gout. (Grade: strong recommendation, moderate-quality evidence). ACP recommends that if colchicine is used, it should be at a low dose, as lower doses of colchicine are as effective as higher doses but have fewer gastrointestinal adverse effects.
- Recommendation 3: ACP recommends against initiating long-term uratelowering therapy in most patients after a first gout attack or in patients with infrequent attacks. (Grade: strong recommendation, moderate-quality evidence)
- Recommendation 4: ACP recommends that clinicians discuss benefits, harms, costs, and individual preferences with patients before initiating urate-lowering therapy, including concomitant prophylaxis, in patients with recurrent gout attacks. (Grade: strong recommendation, moderate-quality evidence)

## Gouty Arthropathy: Rheumatology Recommendations

- Rheumatology consensus disagrees with ACP approach
  - Rooted in a differing perception of gout and its long term implications
- Rather than a treat to avoid symptoms approach, Rheumatology recommendations support a treat to target model
- At the core of recommendations is to control uric acid levels to manage symptoms
- The base principle is that uric acid <6 is soluble and can be cleared via kidney and that should be the goal of therapy

## Gouty Arthropathy: Rheumatology Recommendations



# Gouty Arthopathy: Treating an Acute Attack

- Goal is to reduce acute pain and inflammation
  - Irrespective of medication choice, consider treatment for 7 days
- Non-pharmaceutical interventions such as ice packs can be used in conjunction with other treatments

# Gouty Arthopathy: Treating an Acute Attack

#### ► NSAIDs

- Should initiate within 48 hours of flare
- No specific preference of NSAID
- Usual side effects/precautions apply—caution with GI, renal and CV disease
- Colchicine
  - Should be started within 24 hours of symptom onset
  - Can reduce pain by 50% over placebo
  - Dose should not exceed 1.8mg day one and 0.6mg once or twice a day for the next 7 days
  - Reduce dose in hepatic and renal disease
  - Side effects include GI side effects, myotoxicity and myelosuppression

# Gouty Arthopathy: Treating an Acute Attack

#### Corticosteroids

- Option if contraindications to NSAIDs or Colchicine
- Reasonable regimen is to initiate Prednisone 30 to 40mg in divided dose and taper over 7 days
  - ► Higher doses for polyarticular presentation
- Can consider intra-articular injection for a single joint
- IV or IM corticosteroids are an option if cannot tolerate oral
- Usual side effects including hyperglycemia, hypertension, fluid retention, and mood changes

#### ► ACTH

Can be efficacious but more costly

## Gouty Arthropathy: Prophylaxis

- Prevention of recurrent flares
- As concomitant therapy while initiating long term management
- Important to remember that all long term gout treatments have a side effect of acute flare of gout, especially upon initiation
- Improve adherence to medications by preventing flares

## Gouty Arthropathy: Prophylaxis

- Before intervention with medications, review medication list for medications that cause hyperuricemia
  - Diuretics—increase uric acid resorption, increase uric acid secretion
  - ASA—increase uric acid resorption, decrease uric acid secretion
  - Cytotoxic drugs—disruption of tumor cells
  - Anti-tubercular drugs
    - ▶ Pyrazinamide—increase uric acid resorption, decrease uric acid secretion
    - Ethambutol—Reduction in fractional excretion of uric acid
  - Immunosuppressants
    - Cyclosporine—increased uric acid resorption, decreased GFR
    - Tacrolimus—reduced urate excretion
  - Others
    - Fructose, Testoterone, Lactate infusions, Nicotinic acid, Xylitol

# Gouty Arthropathy: Prophylaxis

### Colchicine

Low dose daily colchicine is best choice for acute gout prophylaxis

- Low dose NSAIDs
- Low dose corticosteroids
- ► IL-1 inhibitor
  - Canakinumab
  - Anakinra

- Treat to target approach is the consensus recommendation
- Achieve lower uric acid level <6</p>
- Decrease flares and disability
- ► Why?
  - Gout is very expensive--\$1 billion a year with a lot of the cost going to ER visits and treating flares
  - May improve general health outcomes
    - Nephrolithiasis
    - ?Renal impairment improvement
    - ?Cardiac risk reduction



#### Allopurinol—Xanthine Oxidase Inhibitor

- Best strategy for tolerance and efficacy is slow introduction and gradual titration
  - Initiate at 100mg daily with incremental increase of 100mg every 2-5 weeks
    - ► Can initiate at lower dose for ≥Stage 3 renal disease
  - Can increase up to a maximum of 800 mg daily
- Goal of therapy is to achieve a serum urate concentration of <6mg/dL</p>
- Consider co-administration with medication to prevent flare—i.e. Colchicine, NSAID, or low dose Prednisone
- Consider this a life long treatment
- DO NOT discontinue during hospitalization—tends to precipitate flares
- Should consider HLA B5801 testing in patients of Southeast Asian or African American descent

- Feboxustat—Xanthine Oxidase Inhibitor
  - If intolerant or lack of efficacy with Allopurinol, reasonable to consider Feboxustat
  - Again, initiate slowly at 40mg and if target serum uric acid is not achieved, increase to 80mg
  - Special considerations
    - > New or prior cardiovascular event. Shoulder consider alternative therapies

#### Probenecid--Urocosuric

- Start at 100mg once or twice daily and can increase up to 1g twice daily
- Not very effective with sparse evidence for monitoring for uric acid reduction

#### Pegloticase—Uricase

- Uricase is an enzyme that catalyzes uric acid into 5-hydroxyisourate (5-HIU) and eventually into Allantoin which is highly soluble and can be renally excreted
  - Not present in humans and some primates
- Pegloticase is a synthetic uricase
- IV treatment every 2 weeks to rapidly reduce urate burden
- Limitations
  - ► Expensive
  - Compliance is incredibly important to maximize benefit and decrease risks
  - Infusion is complicated, often requiring co-administration of immunosuppressant medications to maximize benefit

- Should consider Allopurinol first line in majority of patients
  - Consider Feboxustat for those who cannot achieve uric acid <6</p>
  - Probenecid is an option if both fail but not a great one
  - Pegloticase is a good option if cannot achieve control with above options but with limitations as mentioned
- Exception—tophaceous gout
  - Can consider Pegloticase first line
    - Not a life long treatment—treatment for 12-18 months and then switch to other agents for maintenance

- But, wait, what about lifestyle management???
  - Diet, at best, decreases uric acid by 1 mg/dL
    - No good evidence to suggest this impacts outcomes
  - Weight loss can reduce flares
- ► My recommendations
  - Usually council weight loss if possible but rarely stress dietary changes

## Gouty Arthropathy: Role of Primary Care Provider

- Based on available data and overall consensus, should use a treat to target approach
- Initiating early and appropriate treatment with acute medications for flares and urate lowering therapies, specifically xanthine oxidase inhibitors (or probenecid for symptom control) is reasonable in a PCP office
  - Vast majority of patients can achieve good control with no further treatment needed
- If more advanced treatment is needed, consider referral, especially for more complex medications such as Pegloticase
  - Considerations—know your local Rheumatologists well. Pegloticase is a novel compound and not all Rheumatologists are comfortable using.

### SUMMARY

Osteoarthritis treatments are unfortunately limited at this time

- Majority of treatment can be done at PCP office
- Good utilization of ancillary services vital to patient care
- Appropriate specialist referral in limited cases
- Gouty arthritis—ACP guidelines are at odds with multiple other groups
  - Consensus is that treat to target approach will achieve best outcomes
  - Management of gout can generally be done at the PCP office unless control cannot be gained despite maximizing xanthine oxidase inhibitor
  - Refer to Rheumatology for refractory gout

### THANK YOU!!

Questions?