Orthopedic Surgery Grand Rounds

Rheumatology Update

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No disclosures

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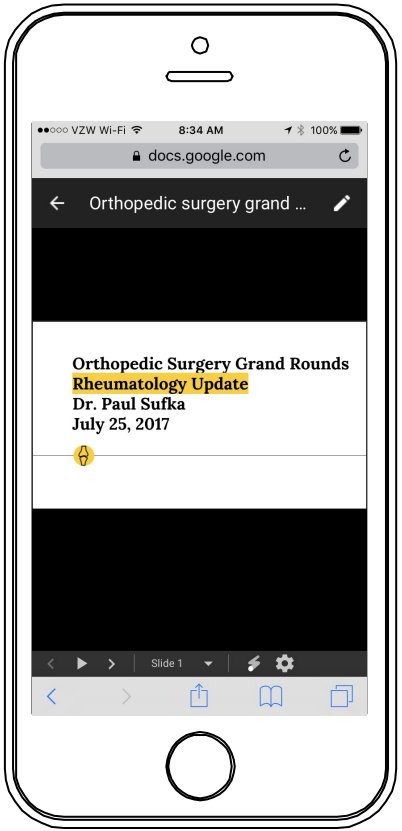

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Topics

- Quick review of inflammatory arthritis
- ACR/AAHKS Guidelines on Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty
- Risks of intraarticular steroids before surgery

I'll leave plenty of time for (unrelated) questions

Review of Inflammatory Arthritis

Review of Inflammatory Arthritis

- History: Inflammatory vs non-inflammatory pain
- Pattern?
  - Monoarticular, oligoarticular, symmetric polyarticular?
  - Neck or back? Tendons, enthesitis, or dactylitis?
- Timing?
  - Acute, subacute, chronic? Additive, migratory, episodic?
- Other clues: ROS (skin, eyes, GI, Raynaud's, etc)

Inflammatory vs non-inflammatory pain

Inflammatory

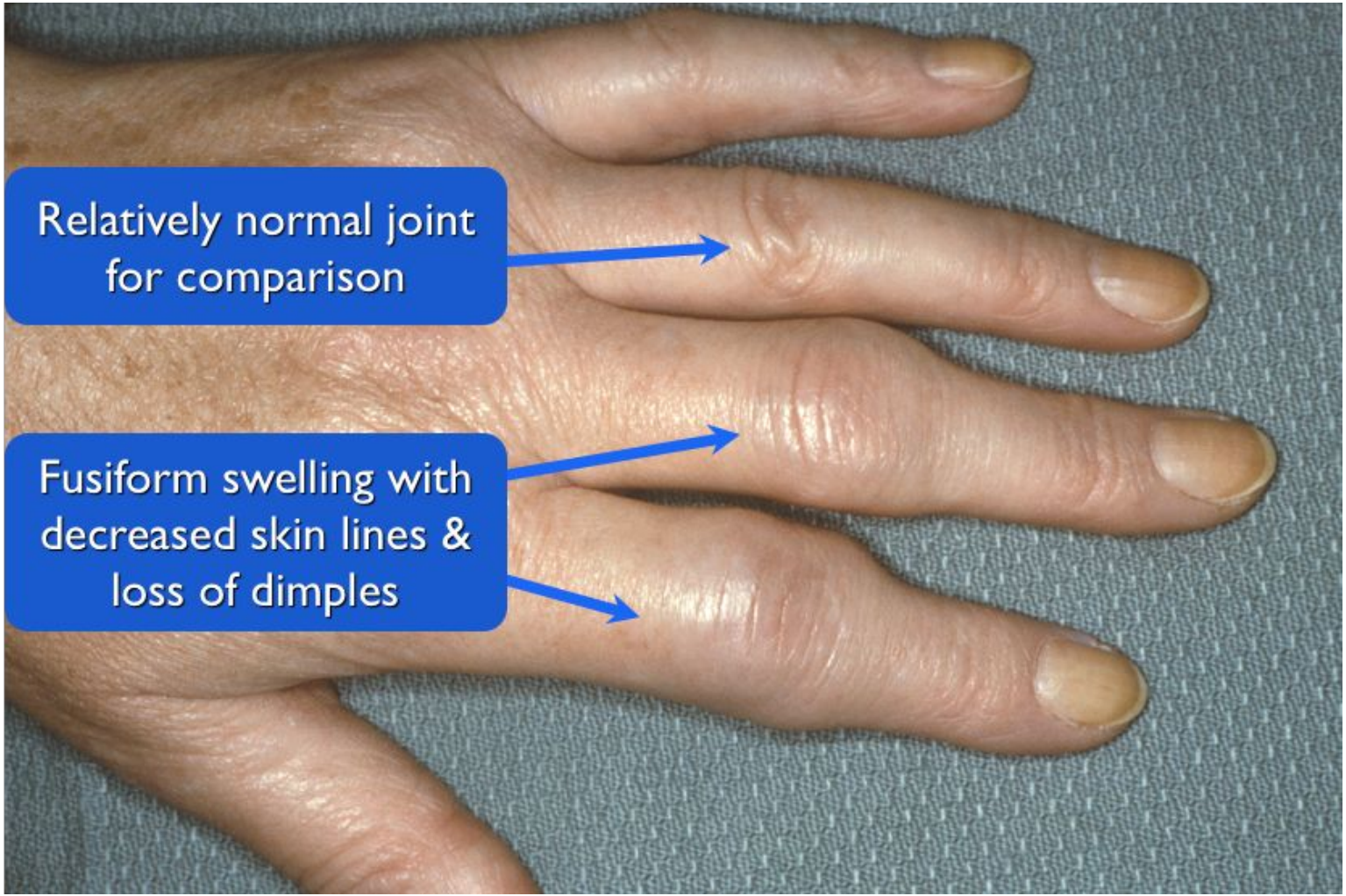
- Improves with use
- Worsens with rest
- Prolonged AM stiffness (>30-60min)
- Synovial swelling with warmth
- Inflammatory effusions

Non-inflammatory

- Worsens with use
- Improves with rest
- Minimal AM stiffness (<20min)
- Bony enlargement
- Crepitus, instability

Recognizing Inflammation on Exam

- Swelling
  - Loss of “dimples” around the joint
  - Decreased skin lines over the joint
  - Edges of the joint to feel “boggy” or less distinct (synovitis)
  - Feel effusions by pushing with one finger & sensing with the other
- Warmth: Normal joints are cooler than surrounding tissues
- Erythema, tenderness, loss of function



Update & review: Rheumatoid Arthritis

- Destructive, symmetric inflammatory polyarthritis.
- Predominantly small joints of hands/feet, also larger joints and c-spine
- Affects ~1% of the population; F:M ~2:1
- Risk factors: family history, smoking, periodontal disease
- Labs: RF, anti-CCP, 14,3,3η (eta)
- Systemic manifestations: pulmonary, rheumatoid nodules, eyes
- Increased mortality is largely due to increased cardiovascular disease

Modern Treatment of Rheumatoid Arthritis

- Start methotrexate +/- (low dose) prednisone
- Reassess in 3-6 months → If not in remission:
  - Poor prognostic markers (+RF/CCP, high dz activity, damage)→ TNFi or other biologic
  - Otherwise → add add/change DMARDs

    (leflunomide, hydroxychloroquine, sulfasalazine, etc)
- Reassess in 3-6 months → If not in remission:
  - Add/change DMARD/biologic

Expanding Treatment Options for RA

Classic Oral DMARDs

- Methotrexate
- Sulfasalazine
- Hydroxychloroquine (Plaquenil)
- Leflunomide (Arava)

TNF inhibitors

- Infliximade (Remicade/Inflectra)
- Adalimumab (Humira)
- Etanercept (Enbrel)
- Certolizumab (Cimzia)
- Golimumab (Simponi)

T cell costimulation modulator

- Abatacept (Orencia)

IL-1 inhibitor

- Anakinra (Kineret)

Anti-CD20 (B cell)

- Rituximab

IL-6 inhibitors

- Tocilizumab (Actemra)
- Siltuximab (Sylvant)

Oral JAK inhibitor

- Tofacitinib (Xeljanz)

Guidelines on Perioperative Management

Arthritis Care & Research
Vol. 00, No. 00, Month 2017, pp 00–00
DOI 10.1002/acr.23274

SPECIAL ARTICLE

2017 American College of Rheumatology/ American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty

Hypothetical Patient

Rheumatoid arthritis

Low disease activity on:

- Methotrexate 20mg weekly
- Etanercept (Enbrel) weekly
- Hydroxychloroquine (Plaquenil) 200mg BID
- Prednisone 7.5mg daily

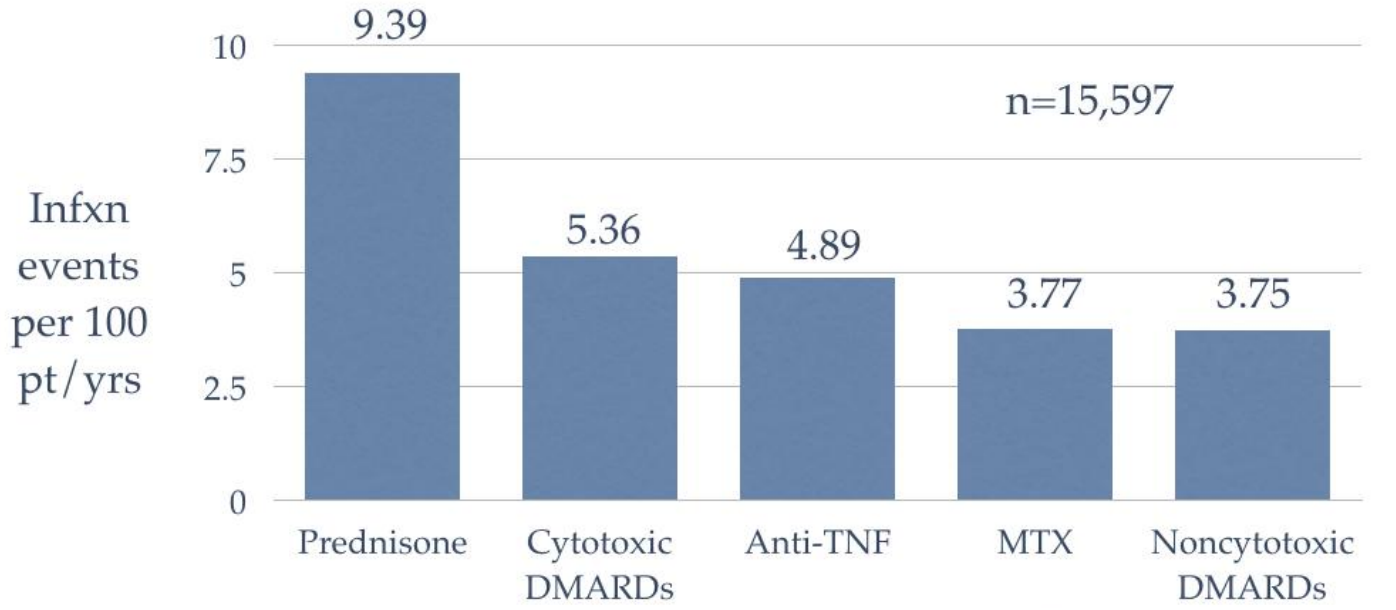
Knee osteoarthritis

Worsening mobility and pain despite:

- Weight loss (10 pounds)
- Physical therapy
- Steroid injections
- Viscosupplementation

Infectious Risks of Antirheumatics

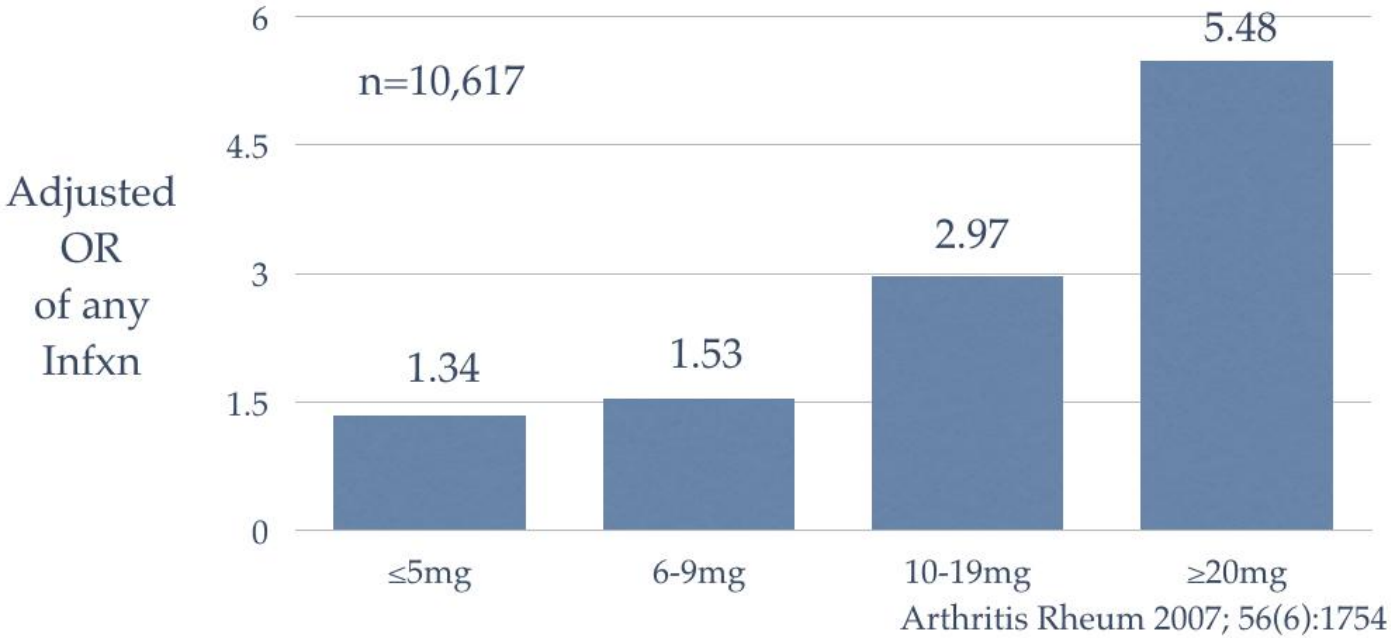
- Medicare patients in Pennsylvania, age ≥ 65 (mean 76.5)



Arthritis Rheum 2007; 56(6):1754

Infectious Risks of Prednisone

- Medicare patients in Pennsylvania, age ≥ 65 (mean 76.5)



Arthritis Rheum 2007; 56(6):1754

Determining Optimal Perioperative Strategy

- Patients may have other nonmodifiable risk factors for infection
- Management of immunosuppressants around the time of arthroplasty is an opportunity to mitigate risk
- Minimal studies, no RCTs

Goals of Perioperative Management

Applications of ACR/AAHKS Guidelines

- Adult patients with RA, spondyloarthritis, juvenile idiopathic arthritis, lupus
- Deemed appropriate candidates for THA or TKA
- Caution about extrapolating to other orthopedic surgeries

Methods of ACR/AAHKS Guidelines

- Used ACR guideline development process & GRADE methodology
- “Evidence was indirect, coming from nonsurgical studies, and all evidence was low to moderate quality.”
- Included ACR & AAHKS teams, leadership team, literature review team, expert panel, patient panel
- Patient panel attached far greater importance to infection than to flares (>10:1)

Results of ACR/AAHKS Guidelines

- All recommendations are conditional due to quality of evidence
- Conditional = “desirable effects of following the recommendation probably outweigh the undesirable effects, so the course of action would apply to the majority of the patients, but may not apply to all patients.”
- No strong recommendations

Recommendation 1

- Continue the current dose of methotrexate, leflunomide, hydroxychloroquine, and/or sulfasalazine for patients undergoing elective THA or TKA (low-moderate evidence)
  - RCTs showed that continuing DMARDs at the time of surger actually decreased risk of infection (RR 0.39 [95% CI 0.17–0.91])
  - Evidence indicates a low infection risk with these DMARDs settings other than THA and TKA
  - Disease flares after surgery occur frequently, and continuing DMARDs decreases the risk (RR 0.06 [95% CI 0.0–1.10])

Recommendation 1

DMARDs: CONTINUE these medications through surgery.	Dosing Interval	Continue/Withhold
Methotrexate	Weekly	Continue
Sulfasalazine	Once or twice daily	Continue
Hydroxychloroquine	Once or twice daily	Continue
Leflunomide (Arava)	Daily	Continue
Doxycycline	Daily	Continue

Recommendation 2

- Withhold all current biologic agents prior to surgery in patients undergoing elective THA or TKA, and plan the surgery at the end of the dosing cycle for that specific medication (low evidence)
  - RCTs (nonsurgical) demonstrated an increase in infection ris
    associated with use of all biologic agents

Recommendation 2

BIOLOGIC AGENTS: STOP these medications prior to surgery and schedule surgery at the end of the dosing cycle. RESUME medications at minimum 14 days after surgery in the absence of wound healing problems, surgical site infection, or systemic infection.	**Dosing Interval**	**Schedule Surgery (relative to last biologic agent dose administered) during**
Adalimumab (Humira)	Weekly or every 2 weeks	Week 2 or 3
Etanercept (Enbrel)	Weekly or twice weekly	Week 2
Golimumab (Simponi)	Every 4 weeks (SQ) or every 8 weeks (IV)	Week 5 Week 9
Infliximab (Remicade)	Every 4, 6, or 8 weeks	Week 5, 7, or 9
Abatacept (Orencia)	Monthly (IV) or weekly (SQ)	Week 5 Week 2
Certolizumab (Cimzia)	Every 2 or 4 weeks	Week 3 or 5
Rituximab (Rituxan)	2 doses 2 weeks apart every 4-6 months	Month 7
Tocilizumab (Actemra)	Every week (SQ) or every 4 weeks (IV)	Week 2 Week 5
Anakinra (Kineret)	Daily	Day 2
Secukinumab (Cosentyx)	Every 4 weeks	Week 5
Ustekinumab (Stelara)	Every 12 weeks	Week 13
Belimumab (Benlysta)	Every 4 weeks	Week 5
Tofacitinib (Xeljanz): STOP this medication 7 days prior to surgery.	Daily or twice daily	7 days after last dose

Recommendation 3

- Withhold tofacitinib (Xeljanz) for at least 7 days prior to surgery in patients undergoing THA or TKA (low evidence)
  - No surgical data, but increased risk of infections in other studies
  - Relatively new drug with very short half-life, so guidelines c likely to change

Recommendation 4

- Severe SLE: Continue the current dose of mycophenolate mofetil, azathioprine, cyclosporine, or tacrolimus through the surgical period in all patients undergoing THA or TKA (low evidence)
  - Very little evidence to base this on, but ideas supported by management of patients with organ transplant
  - Decisions have to be made on individual basis

Recommendation 5

- SLE (not severe): Withhold the current dose of mycophenolate mofetil, azathioprine, cyclosporine, or tacrolimus 1 week prior to surgery in all patients undergoing THA or TKA (low evidence)
  - Restart at 3–5 days after surgery in the absence of wound h
    complications or infection at the surgical site or elsewhere

Recommendations 4 & 5

SEVERE SLE-SPECIFIC MEDICATIONS: CONTINUE these medications in the perioperative period.	**Dosing Interval**	**Continue/Withhold**
Mycophenolate mofetil	Twice daily	Continue
Azathioprine	Daily or twice daily	Continue
Cyclosporine	Twice daily	Continue
Tacrolimus	Twice daily (IV and PO)	Continue
NOT-SEVERE SLE: DISCONTINUE these medications 1 week prior to surgery	**Dosing Interval**	**Continue/Withhold**
Mycophenolate mofetil	Twice daily	Withhold
Azathioprine	Daily or twice daily	Withhold
Cyclosporine	Twice daily	Withhold
Tacrolimus	Twice daily (IV and PO)	Withhold

Recommendation 6

- Restart biologic therapy in patients for whom biologic therapy was withheld prior to undergoing THA and TKA once the wound shows evidence of healing (typically ~14 days), all sutures/staples are out, there is no significant swelling, erythema, or drainage, and there is no clinical evidence of non–surgical site infections, rather than shorter or longer periods of withholding (low evidence)

Recommendation 7

- Continue the current daily dose of glucocorticoids in patients who are receiving glucocorticoids for their rheumatic condition and undergoing THA or TKA, rather than administering perioperative supra-physiologic glucocorticoid doses (so-called “stress dosing”) (low evidence)
  - Optimization for THA and TKA should include tapering the glucocorticoid dose prior to surgery to <20 mg/day when possible

Back to Our Hypothetical Patient

Perioperative plan

- Methotrexate 20mg weekly ➡ Continue
- Etanercept (Enbrel) weekly ➡ Schedule surgery 2 weeks after last dose; restart ~14 days after
- Hydroxychloroquine (Plaquenil) 200mg BID ➡ Continue
- Prednisone 7.5mg daily ➡ Continue (ween?)

Intraarticular Steroids Before Surgery

Data from 2016 AAOS Meeting: Hip Arthroplasty

- Statewide databases for FL/CA (2005-2012): 196,521 patients, tracked 1 year periprosthetic joint infection (PJI)
- 3,688 (1.9%) received a pre-THA injection
  - 1,268 patients within 12-18 weeks ➡ 0.87% (HR=1.01, p=0.985)
  - 1,562 patients within 6-12 weeks ➡ 1.34% (HR 1.58, p=0.038)
  - 858 patients within 0-6 weeks ➡ 1.52% (HR 1.76, p=0.042)
- Baseline PJI Rate (no injection) ➡ 0.87%

Schairer WW, et al. Preoperative Hip Injections Increase the Rate of Periprosthetic Infection After Total Hip Arthroplasty, Presentation/Abstract. AAOS Annual Meeting, Orlando, FL, March 2016.

Data from 2016 AAOS Meeting: Knee Arthroplasty

- 83,684 patients from Humana: knee injections within 1 year prior to TKA (2007–2014) & 90 day postoperative infection
- 29,603 (35.4%) with injection ➡ 4.4% infection, OR 1.2 (95% CI 1.15–1.3, p < 0.0001)
  - 0–1 month: OR 1.8 (1.3–2.6, p = 0.0007)
  - 1–2 months: OR 1.6 (1.2–2.0, p = 0.0003)
  - 2–3 months: OR 1.3 (1.0–1.7, p = 0.02)
- 54,081 patients (64.6%) without injection ➡ 3.6% infection

Do Injections Increase the Risk of Infection Following Total Knee Arthroplasty? Presentation/Abstract. AAOS Annual Meeting, Orlando, FL, March 2016.

Thanks!

Any questions ?

Credits

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