Rheumatological Manifestations in IBD

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Nov 15, 2019

Disclosures

None

Objectives

- Differentiate between IBD arthritis, drug-induced arthritis, comorbid immune mediated inflammatory disorders (IMID) and non-inflammatory disorders (mechanical back pain, fibromyalgia)
- Discuss axial and peripheral spondyloarthritis? How can GI assess the patient with joint pain?
- How can gastroenterology and rheumatology best work together to choose the best biologic? Can you combine biologics?
- Focus on common clinical scenarios
- Review the importance of collaboration between the specialties

Joint pain in an IBD patient

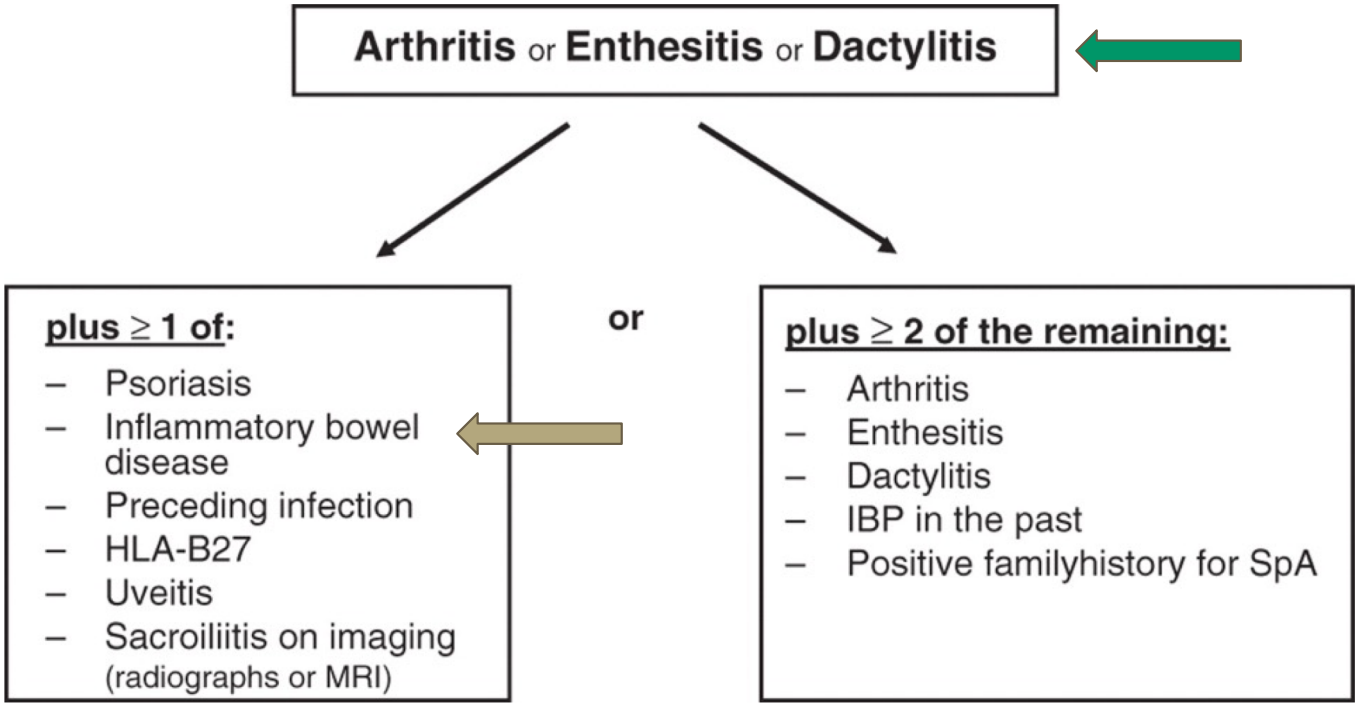
Is this an inflammatory arthritis?

Spondyloarthritis

In the peripheral joints → Is there joint swelling (synovitis)?

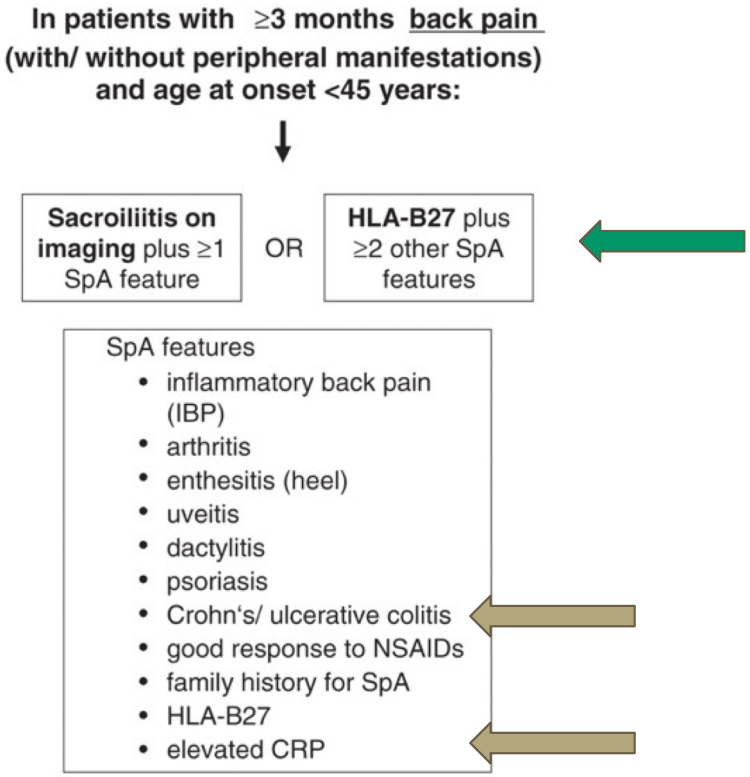
In the axial skeleton → Is the back pain inflammatory?

Peripheral Spondyloarthritis: ASAS Classification criteria



Rudwaleit M et al. The Assessment of SpondyloArthritis international Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis. 2011 Jan;70(1):25-31. doi: 10.1136/ard.2010.133645. Epub 2010 Nov 24.

Axial Spondyloarthritis: ASAS Classification criteria



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Peripheral spondyloarthritis: History

- Swelling!
  - “Does/did the joint look swollen to you?” (many patients will report a joint feels swollen, even when its not)
- Morning stiffness (swelling trumps this!)
- The time course of the symptoms:
  - Insidious, widespread (fibromyalgia) versus more focal, defined onset (inflammatory)
- IBD activity, other extra-articular manifestations

Inflammatory back pain (IBP) - ASAS criteria

Have you suffered from back pain for >= 3 months?

If yes:

1. Age of onset <= 40 years?
2. Insidious onset?
3. Improvement with exercise?
4. No improvement with rest?
5. Pain at night (with improvement throughout the day)?

Criteria for IBP: 4 out of 5

New criteria for inflammatory back pain in patients with chronic back pain: a real patient exercise by experts from the Assessment of SpondyloArthritis international Society (ASAS). Ann Rheum Dis. 2009 Jun;68(6):784-8. doi: 10.1136/ard.2008.101501. Epub 2009 Jan 15.

Morning stiffness

- Quantified: “How long does it take from when you wake up until you’re as good as you’re going to be?” (> 30 minutes)

Remember the buttocks!

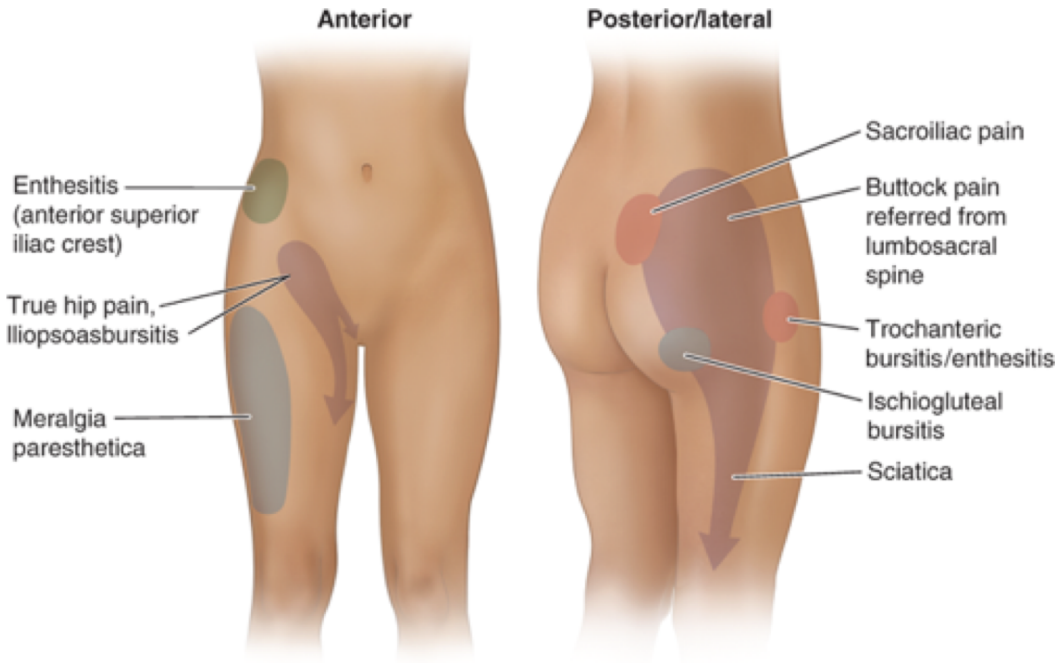
Alternating buttock pain

Patients often call this ‘hip’ pain

If someone says their back/hip hurts, ask them where exactly

Image from: Vanelderen, Pascal et al. In: Evidence-based Interventional Pain Medicine according to clinical diagnoses, Chapter 13 Sacroiliac joint pain.

‘Hip’ and ‘back’ pain mean many things...



Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition
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Citation: Approach to Articular and Musculoskeletal Disorders, Jameson J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. *Harrison's Principles of Internal Medicine, 20e;* 2018. Available at: https://accessmedicine.mhmedical.com/ViewLarge.aspx?figid=192286019&gbosContainerID=0&gbosid=0&groupID=0 Accessed: November 06, 2019

Enthesitis

Many sites, but typically will ask about heel pain (achilles, plantar fascia)

Can be imaged using x-ray (not sensitive) or ultrasound (but requires experienced tech)

Dactylitis

Have you ever had a finger or toe that's been swollen? If yes, was the whole toe swollen? Like a sausage?

Physical exam: peripheral joints (without actually touching the joint)

- Ask the patient if it looks swollen to them
- Look at the joint(s) and compare to the other side (inspection)
- Can the patient move it fully (active range of motion)?
    - Able to move fully → unlikely to be swollen
    - Pain-free → suggests referred pain

Physical exam: peripheral joints (touching the joint)

- Palpation: Key is to find where the pain is coming from
  - Focal (and where) versus generalized
  - Helpful when you don't already know its an inflammatory arthritis

Physical exam: peripheral joints (touching the joint)

Range of motion:

- Active (they move it)
- Passive (you move it)
- Provocative maneuvers - resisted static motion (they try to move it, you stop them)

The problem is...	Active ROM	Passive ROM	Provocative maneuvers
In the joint	Pain	Pain	-
Outside the joint	Pain	-	Pain

Physical exam: axial skeleton

- Main point of exam is to try to localize symptoms, identify other causes of back pain
  - Press on the SI joints, lateral hip
  - Move the hips: is the pain in the groin (*hip*), or in the back?
- Spinal mobility measurements generally not helpful: too much variability

Axial SpA: Investigations

- Plain radiographs not very sensitive, but should be ordered: An AP pelvis x-ray often sufficient; dedicated SI views can be added if high index of suspicion
- MRI is the gold standard: Order MRI SI joints and L-spine, spondylitis protocol (entire spine can be done)
- Consider a bone scan, if unable to access MRI
    - Somewhat helpful if positive: Positive likelihood ratio (LR+) 2.3 in patients with suspected sacroiliitis (Song IH et al. Ann Rheum Dis 2008;67:1535–1540)

What about an HLA-B27?

- In suspected inflammatory back pain (all comers), a high positive likelihood ratio (LR+ 9): one of the best predictive tests
- In IBD-patients with suspected inflammatory back pain, still helpful[1]
  - 50-70% of IBD patients with spondyloarthritis are B27 positive
  - 10% of IBD patients without spondyloarthritis are B27 positive
  - LR+: 5-7

[1]Ossum AM et al. Journal of Crohn's and Colitis, 2018, 96–104

Acute monoarthritis (aside)

Aspirate the joint (send the pt to ER)

Patients on biologics, prior arthritis, increased risk of septic arthritis

Fibromyalgia: AAPT diagnostic criteria[1]

- Multisite pain
- Moderate to severe sleep problems OR fatigue
- Symptoms have been present for at least three months

[1]Arnold LM et al. The Journal of Pain, Vol 20, No 6 (June), 2019: pp 611–628

Fibromyalgia pearls

- Widespread pain (hurts all over)
- Fatigue: “What happens if you ‘over-do’ it?” (post exertional fatigue)
- Waking unrefreshed: “Are you tired in the morning even if you get a good number of hours of sleep?”

And…

- Pain or cramps in lower abdomen
- Depression
- Cognitive symptoms
- Headache…

TNF-induced SLE

- Quite rare: ~1/1000 prevalence
- Associated with development of dsDNA antibodies
- Not typically associated with anti-histone antibodies (as with classic drug-induced lupus), although they can be seen
- Rash, joint symptoms (symmetric, small +/- large joint polyarthritis, NOT axial disease), serositis (less common)
- The really bad things with SLE probably not associated

TNF-induced SLE: when to think about it

- Arthritis + rash (get dermatology opinion)
- Peripheral arthritis in a patient whose bowel disease is controlled on TNFi (note: joint pain in this situation is +++ more likely to be fibromyalgia/ mechanical cause)
- dsDNA - helpful if normal; if abnormal, not as helpful, as many patients on TNFi get dsDNA antibodies

Check: ANA, ENA, dsDNA, complements (C3, C4), CBC, Liver enzymes, Cr, U/A

Other types of immune mediated inflammatory diseases

- Inflammatory arthritis
  - Rheumatoid arthritis: Check RF, CCP, radiographs (erosions); if none of these, cannot make the diagnosis
- Vasculitis: can be drug (TNF)-induced; extremely rare
- IBD myositis
  - Painless weakness, elevated CK

Back to the case...

You wonder whether she is exhibiting back stiffness (but as a gastroenterologist, you are not quite sure how to examine a back). Other joints don’t demonstrate obvious ‘swelling’

In other words...

The patient has alternating buttock pain and low back pain with 60 minutes of morning stiffness (*suggestive of sacroiliitis*). Full, pain-free internal rotation of hip (*the hip is not the issue*), pain in the buttock on external rotation and tender over the SI joint (*supportive of sacroiliac origin*). No entheseal tender points (*I pushed on the achilles and plantar fascia and it didn't hurt*). CRP normal (*not too unsurprising*) and an AP radiograph of the pelvis was normal (*expected, as this is acute*). Bone scan shows intense uptake in the right SI joint (*in this context, highly suggestive of sacroiliitis*).

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Pearls for the gastroenterologist

If the IBD is controlled, and chronic widespread peripheral joint symptoms are present, it is usually fibromyalgia

Drug-induced SLE is quite rare, typically requires derm opinion. Don't stop the biologic right away, get input from rheum/derm

The only way to really know if someone has axial spondyloarthritis is with an MRI → very important, particularly if considering switching biologics solely based on back symptoms.

What the rheumatologist will do

Confirm an inflammatory arthritis

Help with treatment:

- Non-pharmacologic treatment
- Adjunctive drug treatment: intra-articular steroids, NSAIDs
- Add in a conventional DMARD (immunomodulator)
- Add/switch the biologic

Non-pharmacologic treatment

Axial spondyloarthritis[1]

> "Exercise probably slightly improves function (moderate-quality evidence), slightly reduces patient-reported disease activity (moderate-quality evidence), and may reduce pain (low-quality evidence). We are uncertain of the effect on spinal mobility and fatigue (very low-quality evidence)"

Still strongly recommended for axial spondyloarthritis[2]

[1]Regnaux J et al. Cochrane Database of Systematic Reviews 2019, Issue 10
[2]Ward MM et al. Arthritis Rheumatol. 2019 Oct;71(10):1599-1613

Adjunctive treatment

Topical NSAIDs: Enthesitis (weak evidence)

Local steroids:

- Effective for peripheral arthritis, sacroiliitis
- Hips/SI joint need to be done through diagnostic imaging
  - Should document activity first
- Can be used for enthesitis in some situations: Peritendon injections of Achilles, patellar, and quadriceps tendons should be avoided

Systemic steroids

Useful short-term treatment for peripheral arthritis:

- 80-100 mg intra-muscular kenalog (gluteal, split between right/left)
- Typically lasts ~ 6 weeks
- Excellent for bridging therapy, while DMARD taking effect
- Depo-medrol can be used as an alternative (same dose): shorter effect, less chance of atrophy (good for small-medium joint intra-articular injections, tendons)

No role in axial disease:

- One recent RCT showed modest benefits at high doses (50 mg/day), not at 20 mg/day[1]

[1]Haibel H et al. Ann Rheum Dis. 2014 Jan;73(1):243-6.

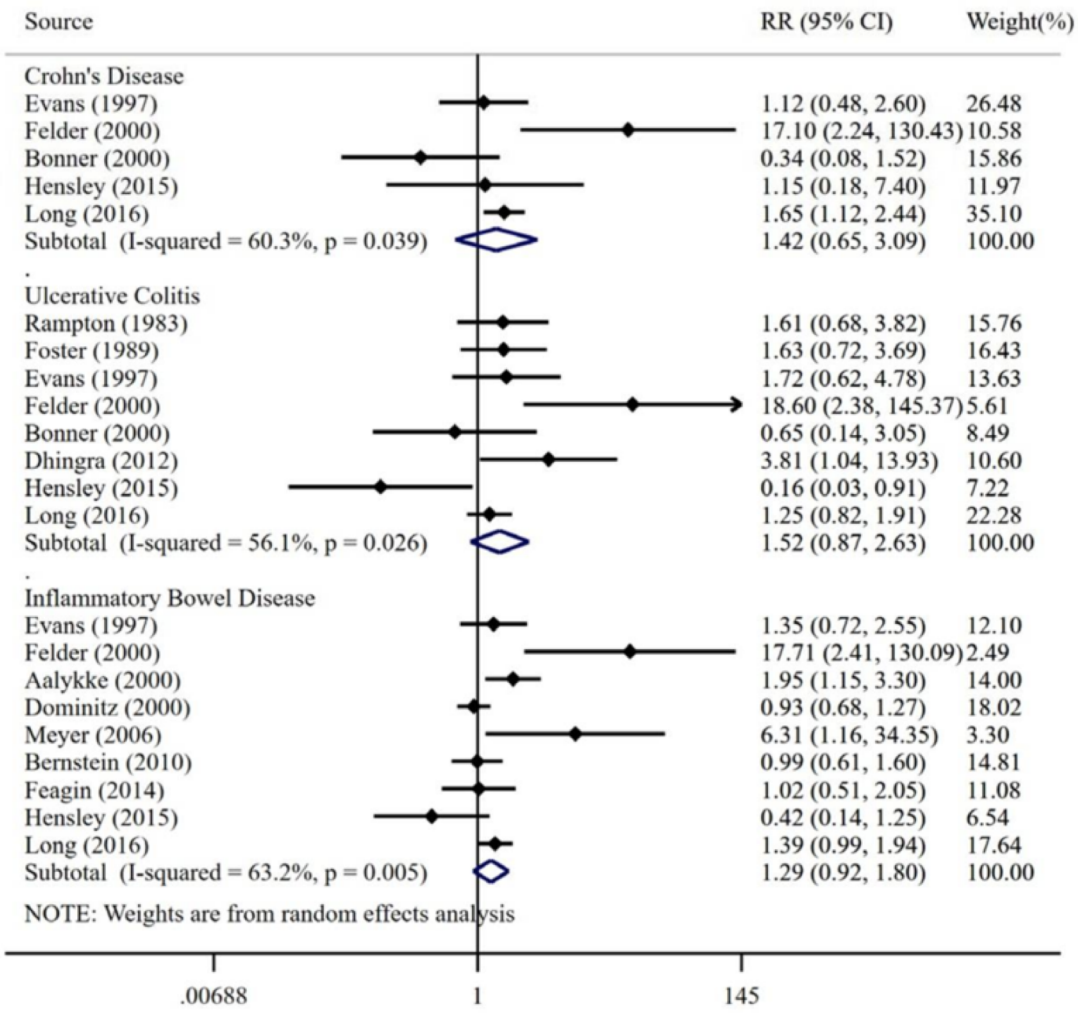
NSAIDs

Can be very beneficial for axial disease, less so for peripheral arthritis (although can be used as adjunctive therapy)

Some options:

- Celecoxib
- Naproxen

Shift away from continuous use, even for ankylosing spondylitis without IBD



Risk of IBD exacerbation

Long MD, et al. Aliment Pharmacol Ther. 2018 Jun; 47(11): 1428–1439.

RCTs of NSAIDS in IBD

2 studies, both with COX-2 inhibitors:

- Sandborn, 2006[1]: Multicenter RCT in 222 patients with Crohn's disease:
  - Celecoxib 200mg BID x 14 days
  - No significant difference in rate of UC exacerbation between treatment and placebo groups. RR=0.73 (0.17,3.18)
- El Miedany, 2006[2]: Multicenter RCT in 146 patients with UC & CD
  - Etoricoxib 60–120 mg/day x 3 months
  - No difference between treatment and control groups in disease activity index of IBD. RR=0.92 (0.37, 2.32)

[1]Sandborn WJ, et al. Clin Gastroenterol Hepatol. 2006; 4(2):203–11
[2]El Miedany Y, et al. Am J Gastroenterol. 2006; 101(2):311–7.

Conventional DMARDs (immunomodulators)

Axial spondyloarthritis: No role, other than maybe preserving life of biologic

Peripheral spondyloarthritis:

- Most evidence comes from outcomes for peripheral arthritis in ankylosing spondylitis and psoriatic arthritis studies:
  - Sulphasalazine: Low-Moderate quality evidence
  - Methotrexate: Low quality evidence

[1]Singh JA et al. Arthritis & Rheumatology. Vol. 71, No. 1, January 2019, pp 5–32
[2]Ward MM, et al. Arthritis & Rheumatology. Vol. 71, No. 10, October 2019, pp 1599–1613

Biologic therapy

Biologic Agent	UC	CD	Ank Spon	PsA
Adalimumab	Yes	Yes	Yes	Yes
Infliximab	Yes	Yes	Yes	Yes
Golimumab	Yes	No	Yes	Yes
Ustekinumab	No	Yes	No	Yes
Tofacitinib	Yes	No	Phase III ongoing	Yes
Vedolizumab	Yes	Yes	No	No

What to do in the patient on TNFi with active SpA?

- Confirm that the SpA is active
  - For axial symptoms: consider MRI if it will change management
  - For peripheral symptoms: Clinical diagnosis
- IBD controlled: (preserve the biologic)
  - Axial only: Physio; Add an NSAID; local steroid (if sacroiliitis)
  - Peripheral only: Add/change/optimize DMARD (MTX/SSZ); local treatment
  - Both Axial and peripheral: Combination of the above
  - If above insufficient, can try changing to another TNFi

What to do in the patient on TNFi with active SpA?

- IBD not controlled:
  - Would avoid NSAIDs
  - Peripheral SpA: Could add MTX or SSZ, switch to a second TNFi or another mechanism of action
  - Axial SpA: Switch biologic to a second TNFi +/- MTX/SSZ

Combining biologics

- Combining 2 systemic agents been tried in rheumatoid arthritis (RCTs)[1]:
  - Rituximab + anti-TNF: Higher serious AEs, no additional benefit
  - Abatacept + anti-TNF: Higher serious AEs, no additional benefit
  - Anakinra + anti-TNF: Higher serious AEs, no additional benefit
  - Rituximab + anti-TNF: Similar AEs, not powered for benefit (n=51)
  - Rituximab + atacicept: Higher withdrawals due to AEs; no benefit
  - Abatacept + biologic (mostly TNFi): Higher withdrawals due to AEs; no benefit

[1]Hirton RP et al. Clinical Gastroenterology and Hepatology 2018;16:1374–1384

Combining biologics

- Psoriasis/psoriatic arthritis
  - Case reports for Etanercept + ustekinumab

- IBD
  - Most data for vedolizumab + TNFi, case reports/series; Case reports for vedolizumab + ustekinumab and vedolizumab + tofacitinib
    - Experience to date: efficacy seen, no major safety signals

Summary

- With history and physical exam, keys are to classify as inflammatory/non-inflammatory, and to localize the pain; joint exams don’t need to be complicated
- Lots of adjunctive things can be done to avoid needing to switch a biologic
- Collaboration is key!