What To Do After A Patient With IBD Develops A Spondyloarthropathy?

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Conflict of Interest Disclosure

(over the past 24 months)

Commercial or Non-Profit Interest	**Relationship**
• Spondyloarthritis Research Consortium of Canada • International Psoriasis and Arthritis Research Team • Group for Assessment and Assessment of Psoriasis and Psoriatic Arthritis • Spondyloarthritis Research and Treatment Network	• Executive Committee Member • Member • Member • Member
Abbvie, Amgen, BioJAMP, BMS, Celgene, Celltrion, Eli-Lilly, Fresenius Kabi, Gilead, Janssen, Merck, Novartis, Organon, Pfizer, Roche, Sandoz, UCB, Viatris	Advisory boards, consultant
Abbvie, Celltrion, Eli-Lilly, Fresnius Kabi, Janssen, Novardis, Pfizer, Sandoz, UCB	Speaker
UCB	Research support

CanMEDS Roles Covered

X	**Medical Expert** (as *Medical Experts*, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. *Medical Expert* is the central physician Role in the CanMEDS Framework and defines the physician's clinical scope of practice.)
X	**Communicator** (as *Communicators*, physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)
X	**Collaborator** (as *Collaborators*, physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)
X	**Leader** (as *Leaders*, physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)
X	**Health Advocate** (as *Health Advocates*, physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)
X	**Scholar** (as *Scholars*, physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)
X	**Professional** (as *Professionals,* physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)

Objectives

Recognize	Recognize the rheumatological manifestations of IBD
Know	Know when a referral to rheumatology is needed (and what you need to tell us!)
Review	Review treatment options

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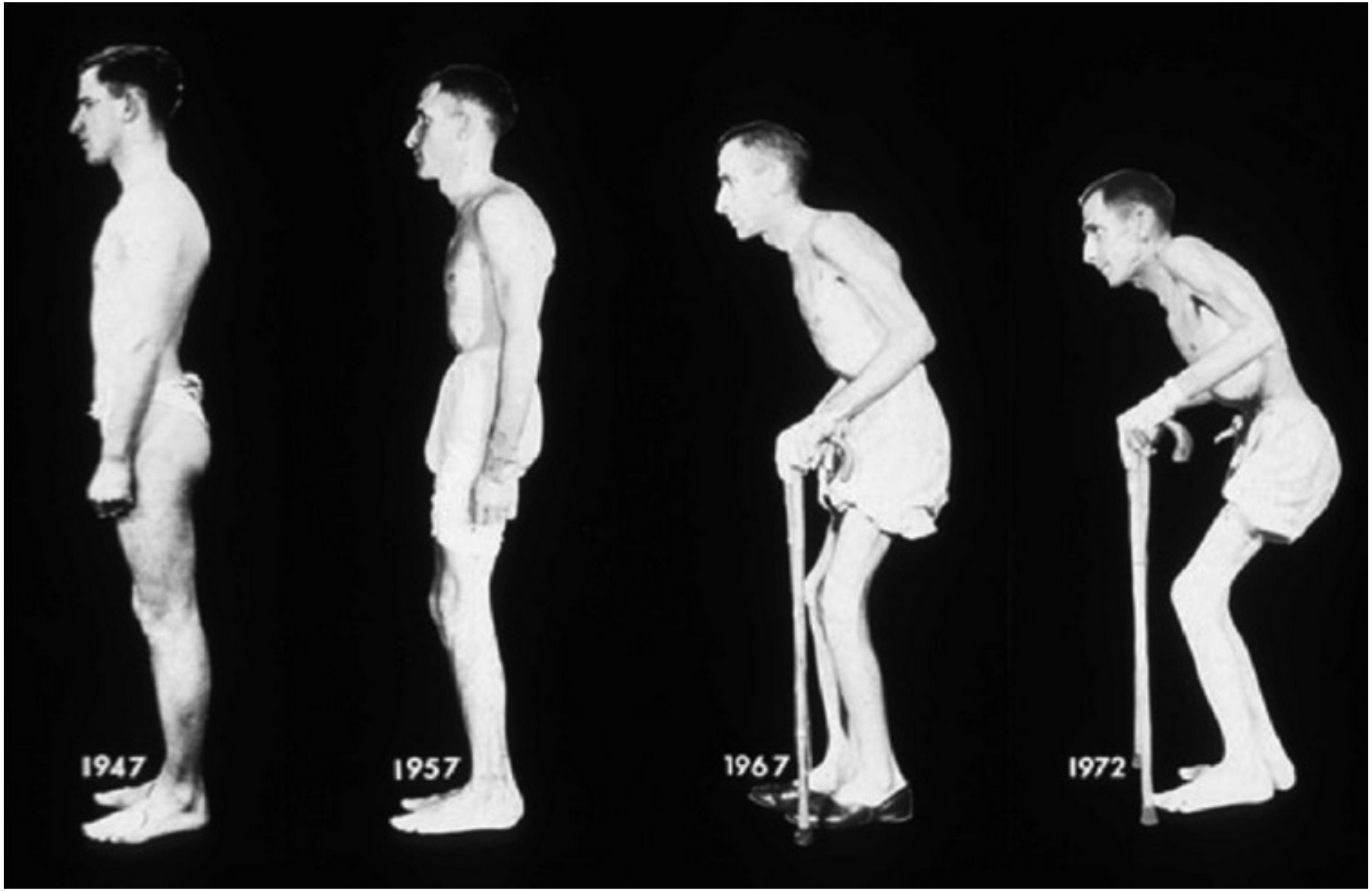
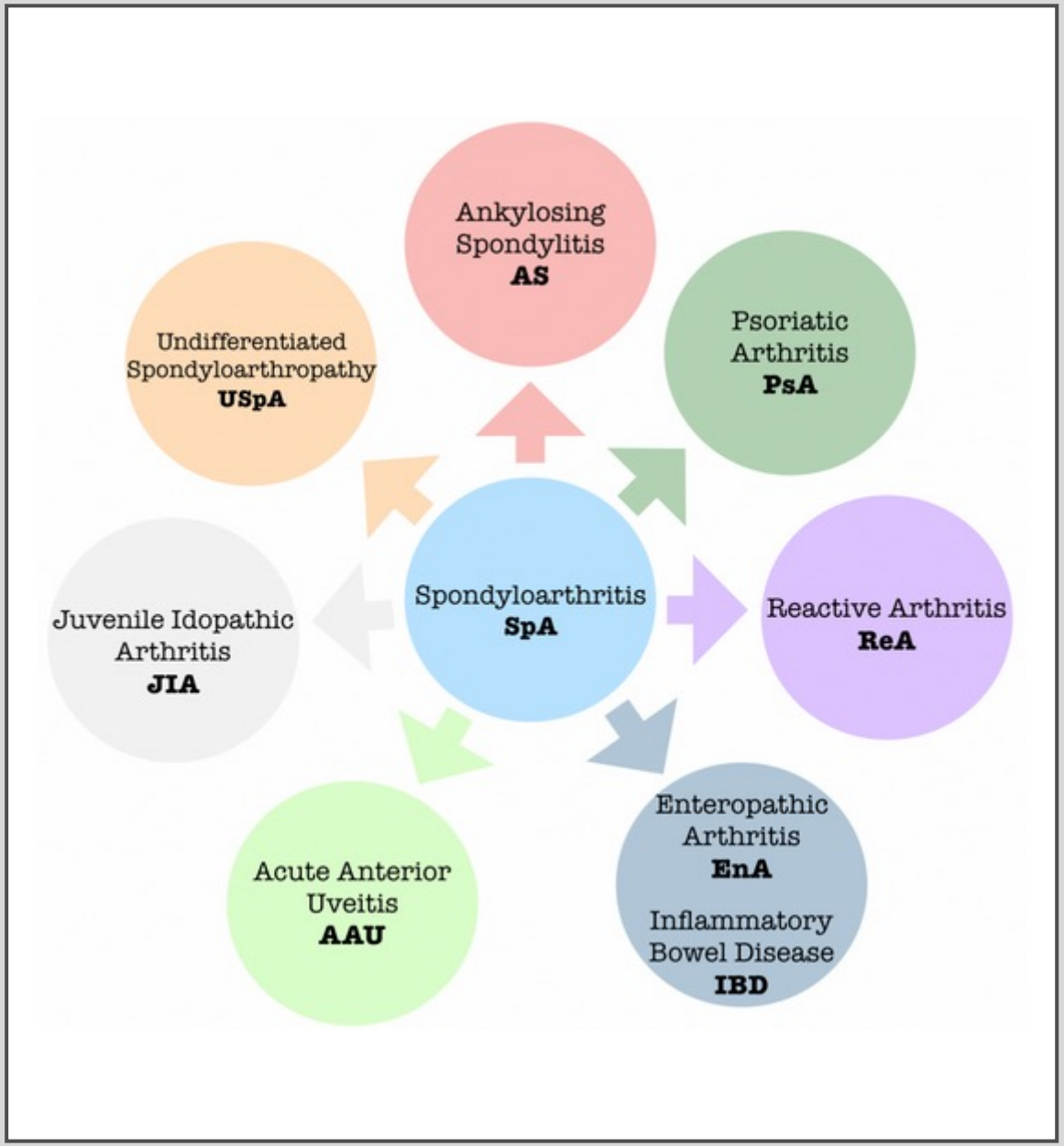
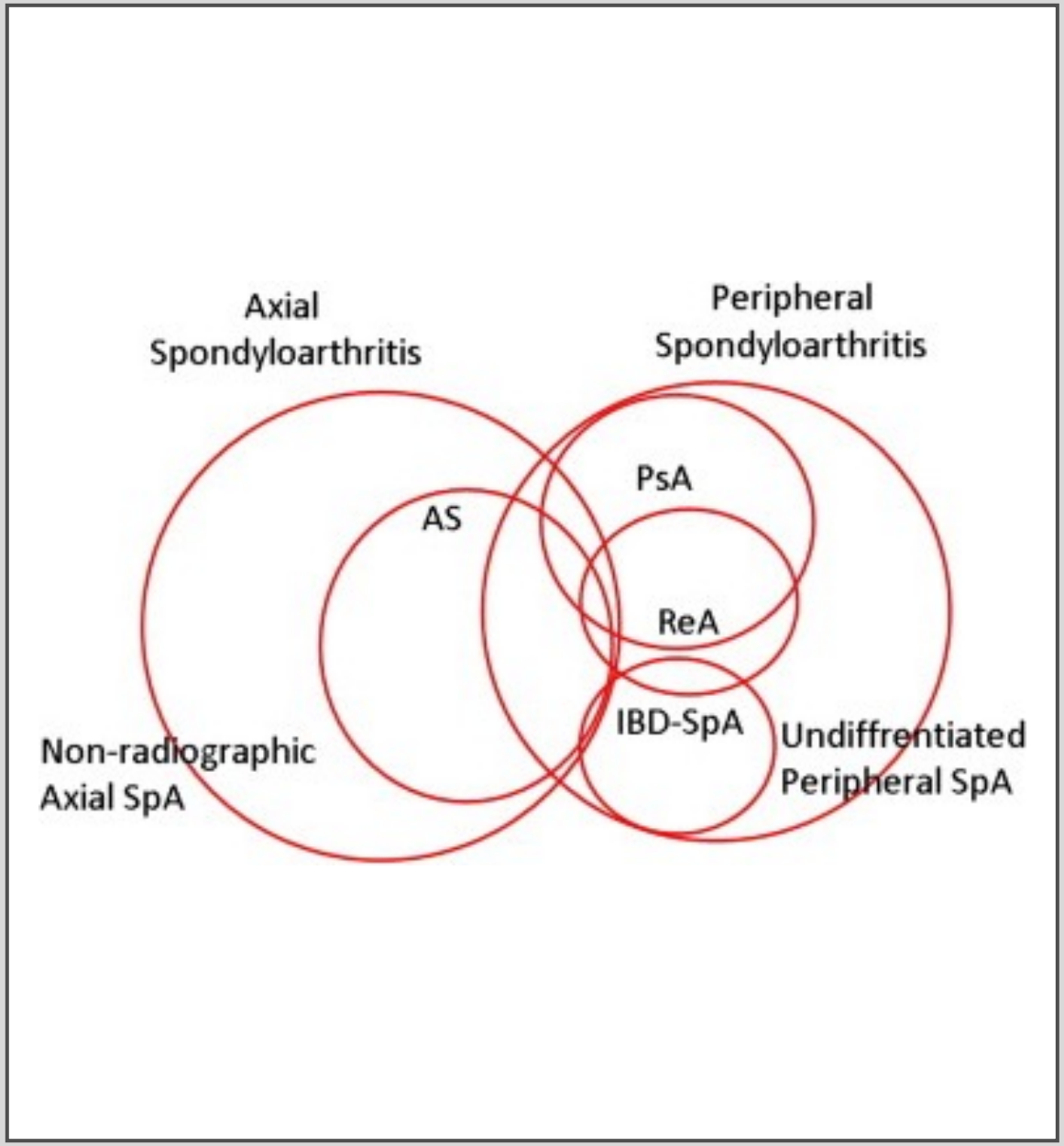
Spondyloarthritis (SpA)

- Refers to inflammatory changes involving the spine and the spinal joints
- May also present with predominantly peripheral arthritis symptoms with no spinal symptoms!
- Often called “seronegative spondyloarthritis” due to absence of rheumatoid factor


1947
1957
1967
1972


Ankylosing Spondylitis
AS
Undifferentiated Spondyloarthropathy
USpA
Psoriatic Arthritis
PsA
Juvenile Idopathic Arthritis
JIA
Spondyloarthritis
SpA
Reactive Arthritis
ReA
Acute Anterior Uveitis
AAU
Enteropathic Arthritis
EnA
Inflammatory Bowel Disease
IBD


Axial Spondyloarthritis
Peripheral Spondyloarthritis
AS
PsA
ReA
IBD-SpA
Non-radiographic Axial SpA
Undiffrentiated Peripheral SpA

Concept of Spondyloarthritis (SpA)

Predominantly axial SpA

Non-radiographic axial SpA

Ankylosing spondylitis

Predominantly peripheral SpA

Psoriatic arthritis

Reactive arthritis

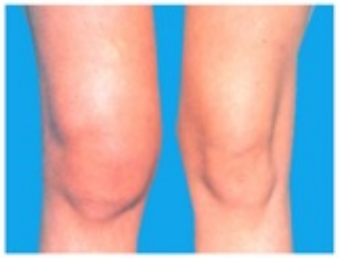
Enteropathic arthritis

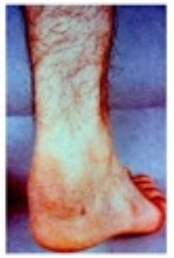
Undifferentiated SpA

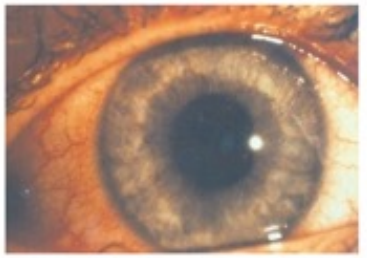
Clinical Characteristics Used For Diagnosis

Symptoms

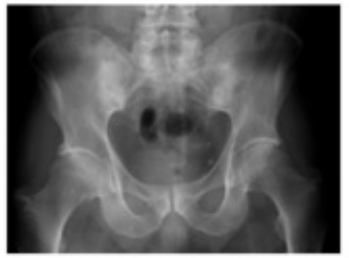
Inflammatory back pain

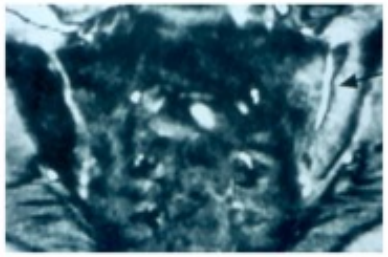






Imaging





Lab

ESR/CRP

Patient's history

Good response to NSAIDs

ASAS

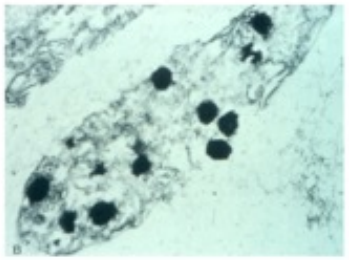
Clinical Characteristics Used For Diagnosis

Genetics

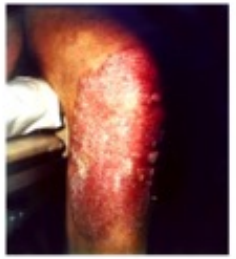
HLA-B27 positive

family history

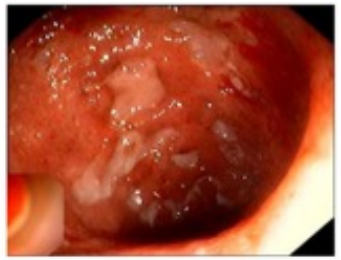
Predisposing/ concomitant diseases



Infection*



psoriasis



Crohn‘s

*positive staining for Chlamydia in synovial membrane[1]

1. Schumacher HR et al. Arthritis Rheum 1988;31:937-946

You Don’t Need Sacroiliitis On X-Rays

Non-radiographic axial SpA (nr-axSpA)

Axial SpA lacking diagnostic SI joint changes on x-ray but having diagnostic MRI findings

More women have nr-axSpA vs. AS

Less abnormal CRP in nr-axSpA vs. AS

Same pain and functional disabilities in both groups

Rudwaleit M et al. Arthritis Rheum 2009
Kiltz U et al. Arthritis Care Res 2012

ASAS Inflammatory Back Pain Criteria

- Age at onset < 40 years
- Insidious onset
- Improvement with exercise
- No improvement with rest
- Pain at night (with improvement upon getting up)

Inflammatory back pain if ≥ 4/5 parameters fulfilled

Sensitivity 79.6%
Specificity 72.4%

Sieper J et al. Ann Rheum Dis 2009

Epidemiology

Rheumatic manifestations are the most frequent extraintestinal manifestation in IBD

Prevalence 17-39%

Can occur before, simultaneously or after the diagnosis of IBD

Risk factors for enteropathic arthritis:

Active bowel disease

Family history of IBD

Appendectomy

Smoking

Presence of other EIMs such as erythema nodosum or pyoderma gangrenosum

Peluso R et al. Clin Dev Immunol 2013

Presentation

Axial

Prevalence 2-16% of IBD patients

Crohn’s Disease > Ulcerative Colitis

Male > Female

Sacroiliitis

HLA-B27 +

Peripheral

Prevalence 0.4-34.6% IBD patients

Crohn’s Disease > Ulcerative Colitis

Female > Male

Usually affects the lower extremities

Peluso R et al. Clin Dev Immunol 2013

Presentation

Type 1

Pauciarticular

Asymmetric

Acute attacks

Coincides with relapse of IBD

Strongly associated with other extra-intestinal manifestations

Type 2

Polyarticular

Persistent symptoms

Erosive

Course is independent of IBD

Affects both large and small joints

Strongly associated with uveitis

Spondylitis

Usually precedes onset of IBD

Course is independent of IBD

Clinically similar to idiopathic AS

Associated with uveitis

Strongly associated with HLA-B27

Peluso R et al. Clin Dev Immunol 2013

SPaCE Study: Prevalence of Crohn's Disease in Patients with SpA

Design

- Prospective cross-sectional study of patients with established SpA
- Exclusion: treatment with TNFi, NSAIDs in past month
- All patients had video capsule endoscopy (VCE), followed by standard ileo-colonoscopy (IC) with biopsies
- 63 patients (54% female, mean age 42±13 years) were recruited; 2 patients refused IC and were disqualified.

Kopylov U, et al. *Arthritis Rheumatol.* 2015; 67 (suppl 10)

How many patients with AS had subclinical bowel inflammation on VCE?

a. <10%

b. 20%

c. 30%

d. >40%

OAG GAMIFICATION

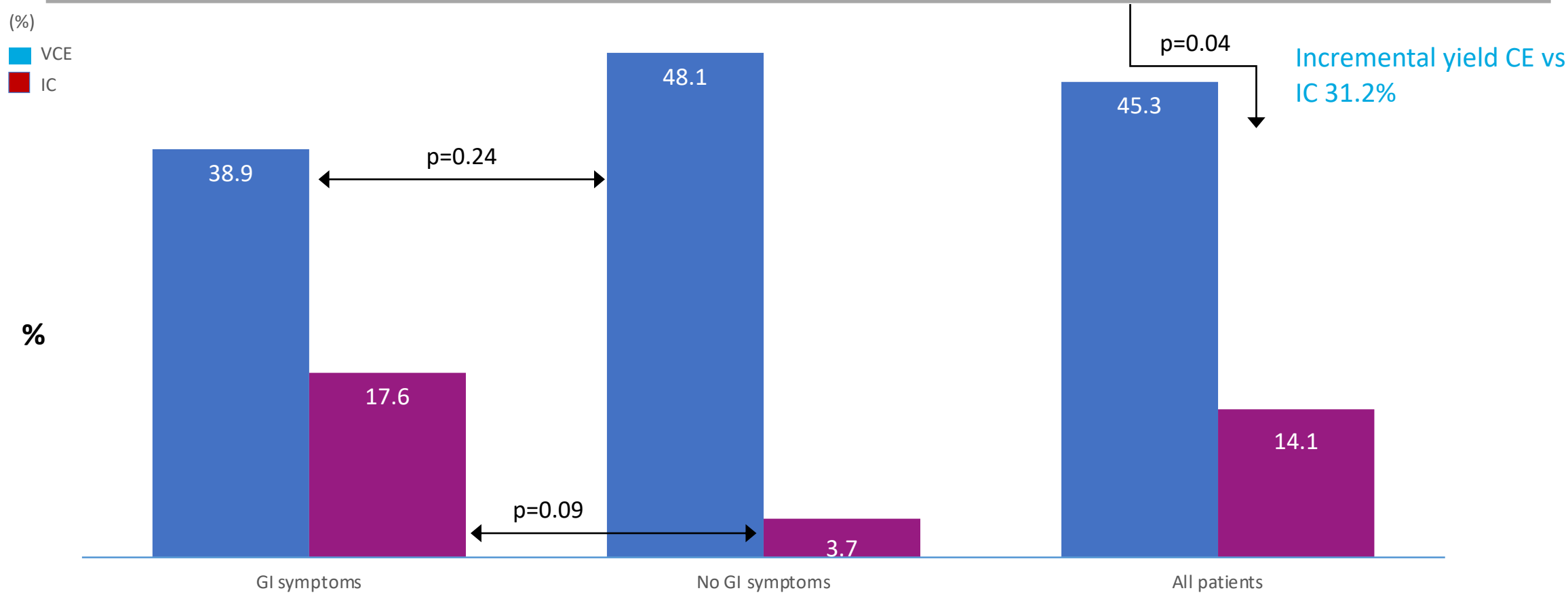
Rohekar - Game Code:

SNOWCAT

How many patients with AS had subclinical bowel inflammation on VCE?

d. >40%

SPaCE Study: Inflammatory Lesions on VCE vs Ileo-Colonoscopy in SpA



No correlation between GI symptoms and inflammatory bowel lesions

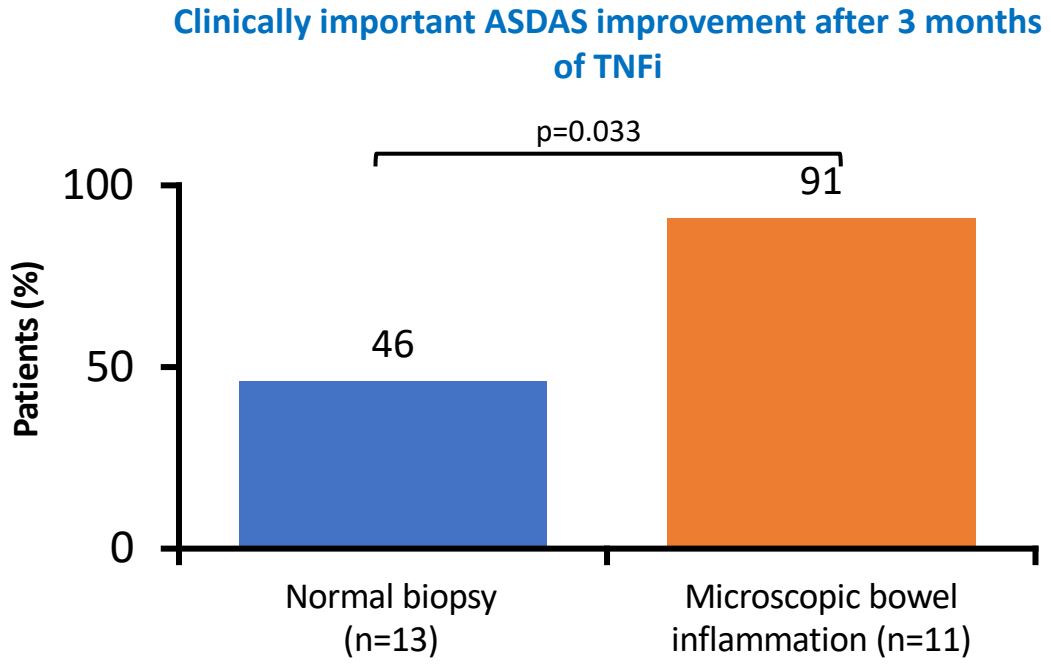
Overall, inflammatory bowel lesions present in 45% of SpA patients

Kopylov-SPaCE study Gastroenterol 2013: 144, 5: S-416

OTHER STUDIES: up to 68% of patients have microscopic gut inflammation

Microscopic Bowel Inflammation in AS Predicts Response to TNFi

- GIANT cohort
- Presence of gut inflammation positively correlated to TNFi use ($p<0.01$)
- Presence of microscopic bowel inflammation associated with increased ASDAS response



Patients with axSpA who had microscopic bowel inflammation at baseline responded better to TNFi therapy than those with normal bowel histology

ASDAS, Ankylosing Spondylitis Disease Activity Score

Cypers H, et al. Arthritis Rheumatol 2015;67(Suppl. 10): Abstract 2060

Theories Regarding the Relationship Between the Gut and the Synovium

Spreading of infectious micro-organisms

Transportation of antigenic determinants

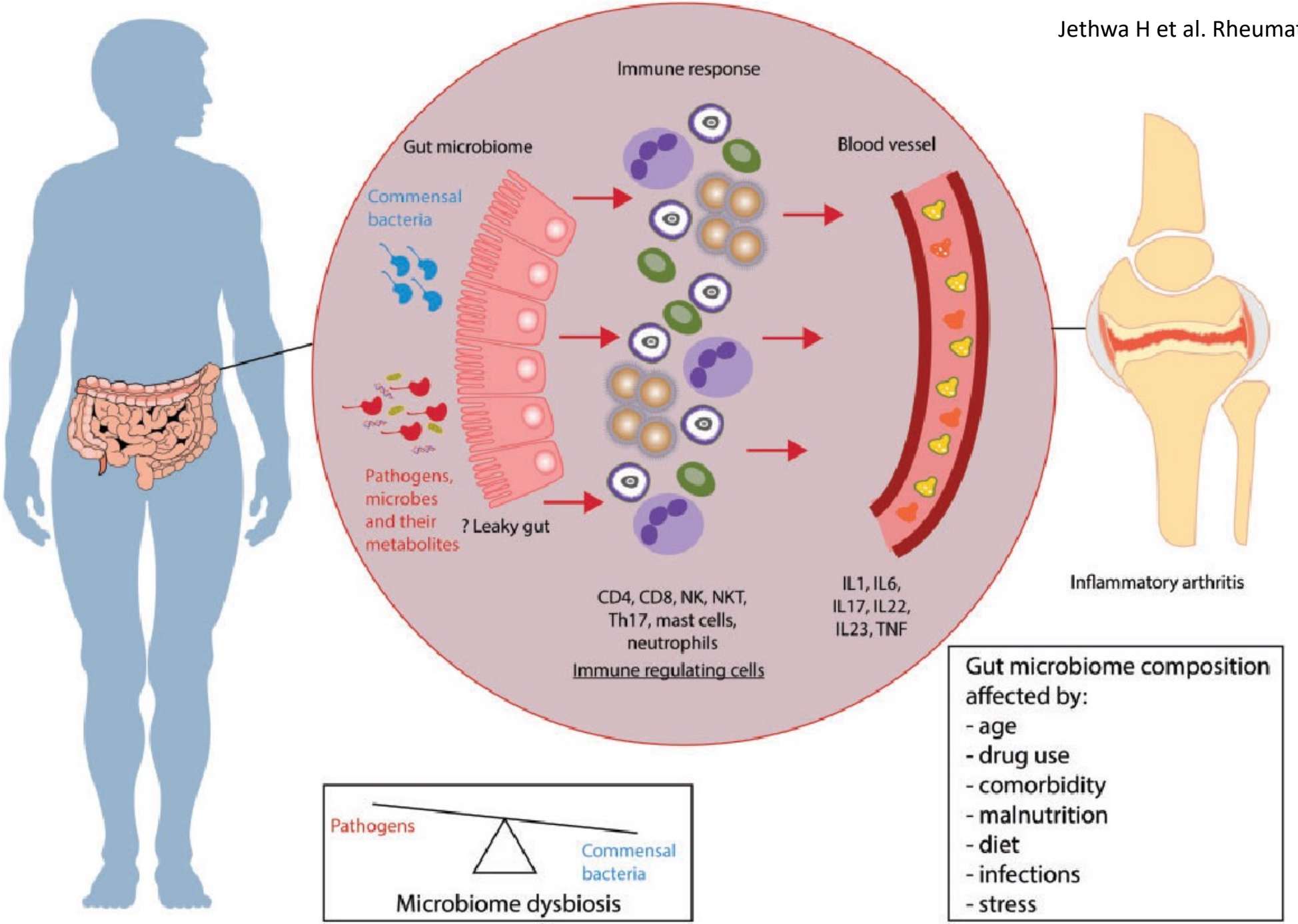
Antigenic crossreactivity

Trafficking of monocytes and lymphocytes in the gut

Hemodynamic aspects of circulation

Peluso R et al. Clin Dev Immunol 2013

Jethwa H et al. Rheumatology 2017



Objectives

Recognize	Recognize the rheumatological manifestations of IBD
Know	Know when a referral to rheumatology is needed (and what you need to tell us!)
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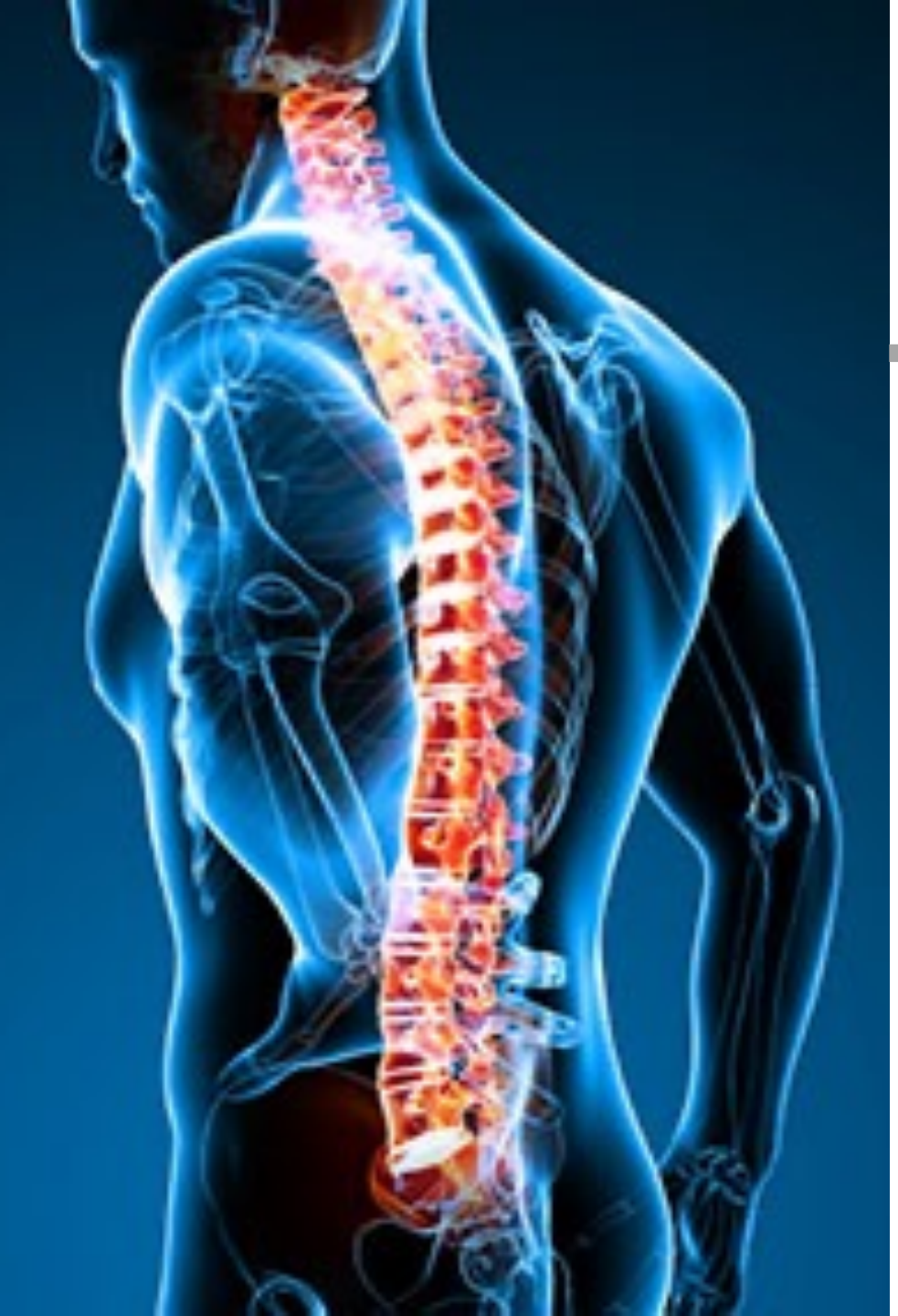


Who To Refer

- **Chronic back pain, duration ≥ 3 months, back pain onset before 45 years of age** and at least one of:
  - Inflammatory back pain
  - HLA-B27 +
  - Sacroiliitis on imaging
  - Peripheral manifestations (arthritis, enthesitis, dactylitis)
  - Extramusculoskeletal manifestations (psoriasis, IBD, uveitis)
  - Positive family history of SpA
  - Good response to NSAIDs
  - Elevated acute phase reactants

Poddubnyy D et al. Ann Rheum Dis 2015

Referrals: What Rheumatologists Want to Know

Does the patient have inflammatory back pain?

Are there any swollen joints? Where? Dactylitis? Enthesitis?

Are the inflammatory markers up?

Greater response to biologics

Does the patient have psoriasis (including nail changes only)?

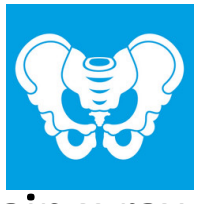
Scalp and nail involvement → greater incidence of axial SpA

Does the patient have uveitis?

What treatment are you using?

Can the treatment be modified? Can NSAIDs be used?

Referrals: What Rheumatologists Would Appreciate You Ordered



Plain x-ray of pelvis and hips in all

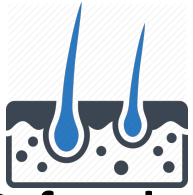
No need for specific SI joint views

If symptoms of axial arthritis, x-rays C-, T-, and L-spine

If symptoms of peripheral arthritis, x-rays hands/wrists and feet/ankles

HLA-B27

Referral to ophthalmology as needed



Referral to dermatology as needed

Psoriasis

Hidradenitis suppurativa

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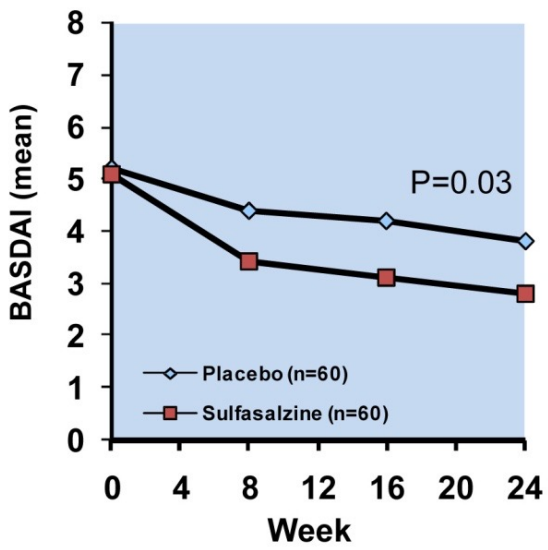
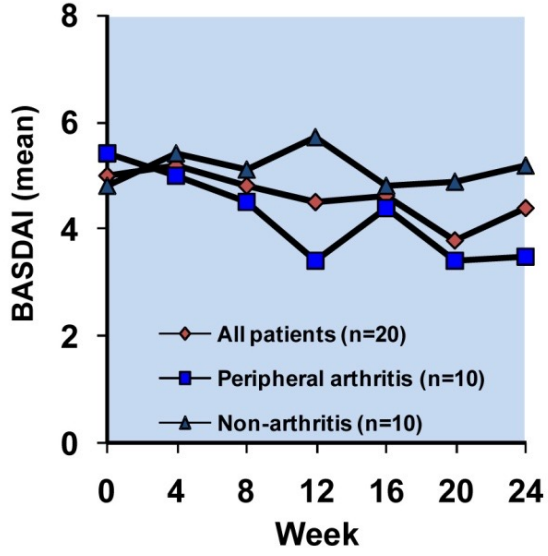
Conventional DMARDs Are Largely Not Effective for the Treatment of Patients with AS

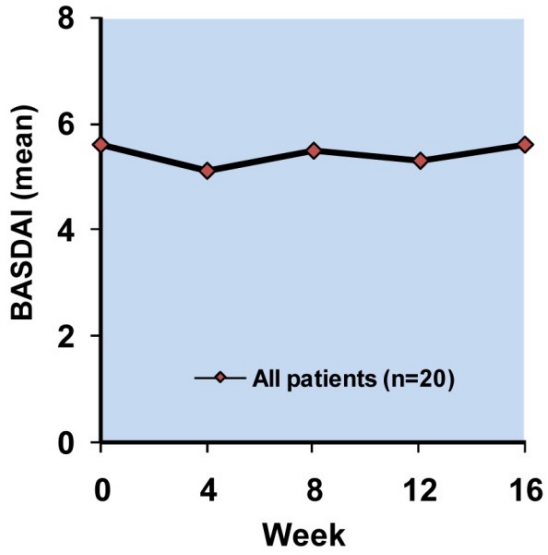
Sulfasalazine[1]
2 g/day



Leflunomide[2]
20 mg/day



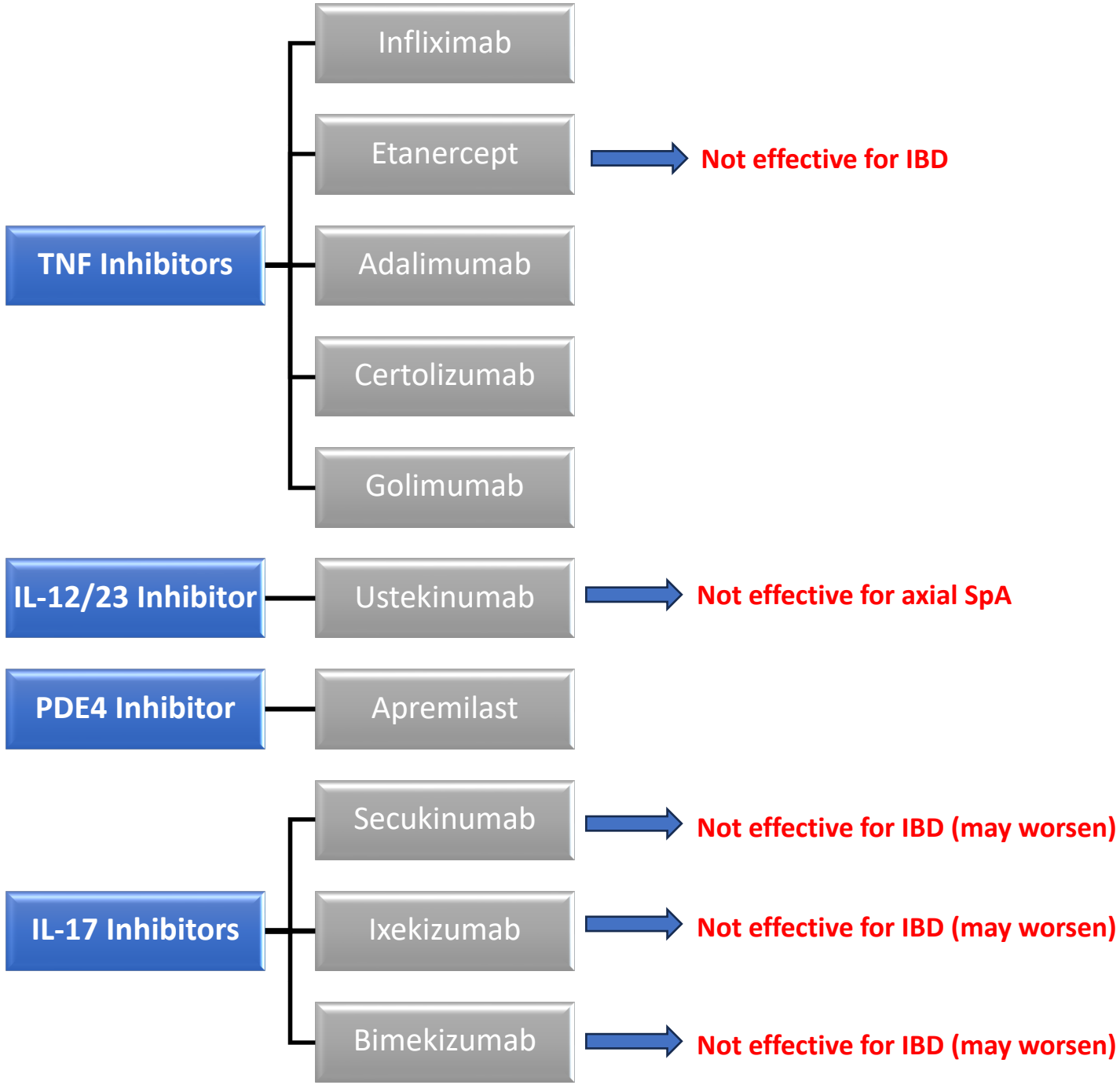
Methotrexate[3]
20 mg/week sc

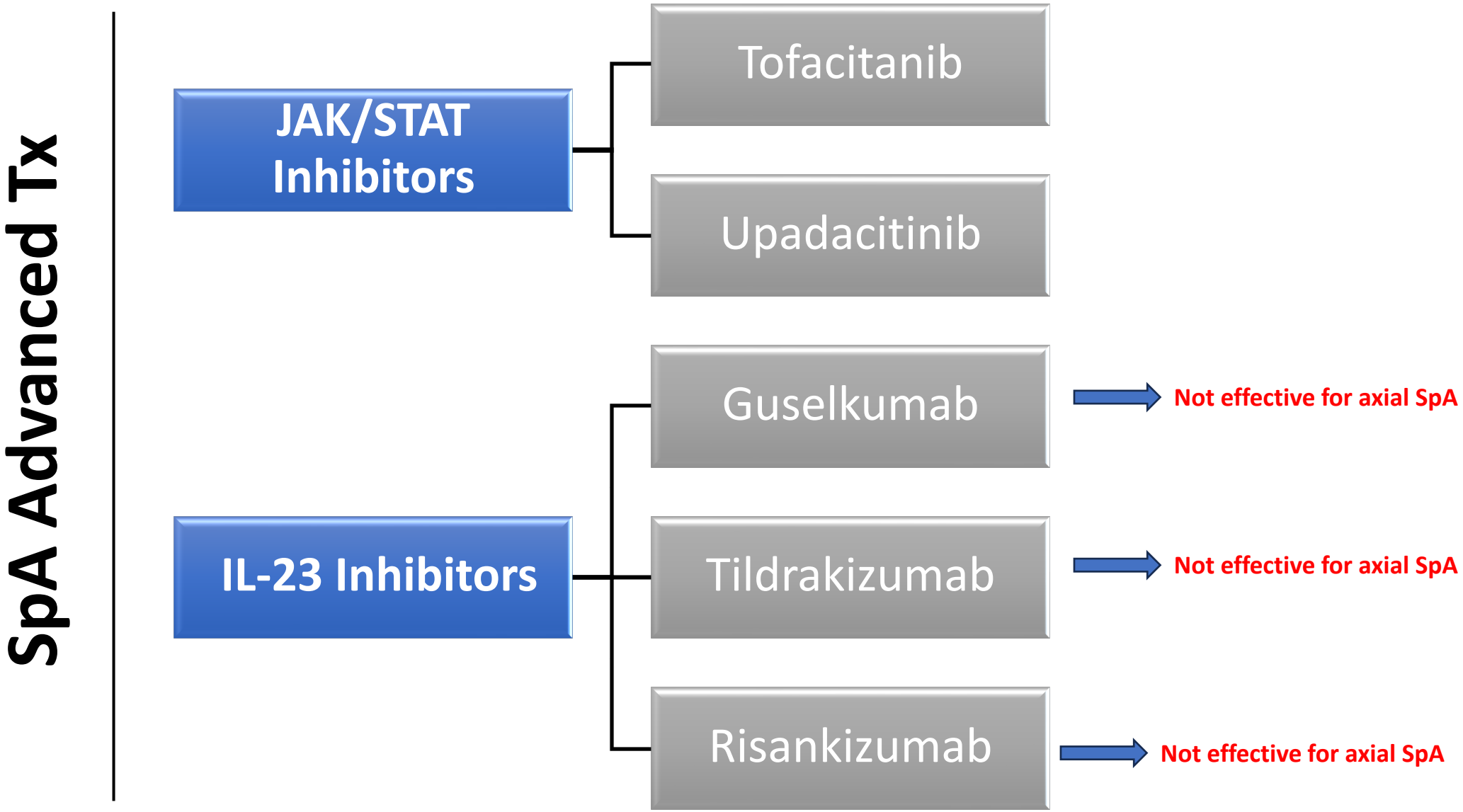


1. Braun J et al. Ann Rheum Dis 2006;65:1147-53
2. Haibel H et al. Ann Rheum Dis 2005;64:296-8
3. Haibel H et al. Arthritis Rheum 2006;54:678-81

ASAS

SpA Advanced Tx




SpA Advanced Tx
JAK/STAT Inhibitors
Tofacitanib
Upadacitinib
IL-23 Inhibitors
Guselkumab
Not effective for axial SpA
Tildrakizumab
Not effective for axial SpA
Risankizumab
Not effective for axial SpA

Treatment Notes

Patients with axial disease are often the hardest to treat due to limited options

Combining vedolizumab with another biologic

Beware of paradoxical psoriasis

Increased use of IL-17 inhibitors in rheumatology; may worsen or unmask IBD

Combining systemically immunosuppressive biologics?

Partnering with a rheumatologist is key!

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Thank you.

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