

REACTIVE ARTHRITIS

BOTTOM LINE

Reactive arthritis (ReA) is an inflammatory mono/oligo-articular lower-extremity predominant axial spondyloarthritis typically preceded by a mucosal infection (often gastrointestinal or genitourinary) 1-4 weeks prior. HLA-B27 positive patients tend to do worse and have extra-articular manifestations. 50% of patients have a self-limited course lasting 3-5 months, 30% have recurrent flares, and 15-20% develop a chronic seronegative spondyloarthritis.

EPIDEMIOLOGY

- Varied definitions of ReA, epidemiologic methods, population changes over time; incidence felt to declining
 - Incidence: 1-1.5% after enterogenic infection, 0.6-30% after chlamydial infection
 - Prevalence worldwide: 1/1000
- Sex: Urogenic ReA: M > F | Enterogenic ReA: F=M
- Age: 20-40 years.
- Rare in children and less common in patients of African descent.

Historically, formerly called "Reiter's Syndrome" as a triad of conjunctivitis, nongonococcal urethritis, and inflammatory arthritis following dysentery ("*Can't see, can't pee, can't climb a tree*"). Only 2/3 of ReA patients have all 3 features of this triad.

CLINICAL FEATURES

Preceding infection	Mucosal infection 1-4 weeks beforehand, usually enterogenic or urogenic - Urogenic: Chlamydia, intravesical BCG therapy for bladder cancer - Enterogenic: Salmonella, Shigella, Campylobacter, Yersinia, C. difficile - Less common: Chlamydia pneumoniae, E. coli, HIV	
Musculoskeletal	Peripheral	- Asymmetric oligoarticular lower extremity predominant arthritis often including knee - Less common mono- or polyarticular disease; sometimes upper extremity involvement - Enthesitis (ex: Achilles enthesitis, plantar fasciitis) - Dactylitis
	Axial	Inflammatory back/buttock pain
Extra-articular	Ocular	- Sterile conjunctivitis (51%) - Anterior uveitis: acute unilateral with HLA-B27 association
	Cardiac	Heart block, aortitis, aortic regurgitation, pericarditis
	Gastrointestinal	Ileitis/colitis: Sterile or infectious
	Renal	IgA nephropathy, Renal amyloid
	Genitourinary	- Circinate Balanitis (10-40%): painless erythematous ulcerating lesions on glans penis and urethral meatus; associated w/ chlamydia - Urethritis: infectious or sterile - Prostatitis - Hemorrhagic cystitis - Salpingitis, vulvovaginitis
	Cutaneous	- Painless mucosal ulcers (up to 60%) - Keratoderma Blennorrhagica (20%): hyperkeratotic skin lesions soles and palms looking like pustular psoriasis; remember to get a VDRL - Erythema nodosum - Nail changes: looks like nail psoriasis (hyperkeratotic)
	Other	Thrombophlebitis, livedo reticularis, cranial or peripheral neuropathy

HLA B27 positivity increases risk of sacroiliitis/spondylitis, ocular involvement, and other extra-articular features

INVESTIGATIONS		
Bloodwork	CBC	Leukocytosis, thrombocytosis
	ESR or CRP	Elevated usually
	RF, ANA	Negative
	HLA-B27	30-50% positive
Fluids, Culture	Synovial Fluid	- Inflammatory, i.e.: 2000-50,000 WBC/mm³ predominantly neutrophils - Culture negative
	Urine	Pyuria, microhematuria, bacteriuria
	Infectious	- Stool culture: diarrhea usually resolved before onset of arthritis Can do culture or immunoassay for Salmonella, Shigella, Campylobacter, Yersina - Urine/genital swab: chlamydial trachomatous Serologic testing for past infection not normally performed
Imaging	X-rays	- Acutely: Not specific, may see soft tissue swelling - Chronically: Bulky syndesmophytosis, ankylosis, bony proliferation, peri-osteitis, enthesitis, erosions, spondylitis, sacroiliitis
Other	- ECG: can see heart block chronically - Colonoscopy: ileitis/colitis	
DIAGNOSIS		
Diagnosis can be made in a patient with history of preceding gastrointestinal/genitourinary infection 1-4 weeks before onset of lower-limb predominant oligoarticular inflammatory spondyloarthritis with possible extra-articular manifestations like iritis/conjunctivitis, urethritis, mucosal ulcers, and hyperkeratotic skin/nail. Elevated and inflammatory markers, inflammatory synovial fluid, and HLA-B27 positivity may be supportive.		
TREATMENT		
Antibiotics	- Long-term antibiotics are not used treat inflammatory arthritis - Enteric infection: antibiotics not indicated for uncomplicated infections; some may require treatment depending on organism (ex: C. diff) or if patient has many co-morbidities - Genitourinary infection: Chlamydial infections should be given standard treatment (ex: azithromycin 1g POx1 or doxycycline 100mg BID x 7 days for patient and partner)	
Arthritis	Acute	NSAIDs and intra-articular or systemic corticosteroids
	Chronic	- Consider if >4-6 months of persistent inflammatory arthritis despite NSAIDs and prednisone >5-7.5mg/day - csDMARDs: Sulfasalazine, methotrexate, leflunomide - bDMARDs: TNF-inhibitors (case series evidence)
Extra-articular	Ocular	Ophthalmology referral for ?uveitis if redness, photophobia, vision change
	Skin	Topical steroids
PROGNOSIS		
- Most remit in 6-12 months 15-20% may have chronic inflammatory arthritis - HLA-B27 positivity may be poor prognostic indicator		

FURTHER READING

Bentaleb, I., *et al.* (2020). Reactive Arthritis: Update. *Current clinical microbiology reports*, 7(4), 124–132. <https://doi.org/10.1007/s40588-020-00152-6>

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