

Juvenile rheumatoid arthritis

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Musculoskeletal problems account for the majority of initial complaints attended to by primary care physicians. It is likely that a child who eventually has juvenile rheumatoid arthritis diagnosed will initially be evaluated by a family physician or a pediatrician. Primary care physicians will play an increasingly important role in management of juvenile rheumatoid arthritis, as the availability of specialists in many communities is limited, and access to them may be further limited by managed care initiatives. This article offers a brief review of the definition and classification of juvenile rheumatoid arthritis and introduces a diagnostic algorithm to provide a simplified approach toward evaluating children with arthritis. Treatment and outcomes are summarized in text and graphic formats.

(Key words: Juvenile rheumatoid arthritis, treatment outcomes)

It is likely that a child who eventually has a rheumatic disorder diagnosed will initially consult a primary care physician with a musculoskeletal complaint. Juvenile rheumatoid arthritis (JRA) is the most common childhood rheumatic disorder. It affects approximately 32,000 US children, with an incidence of approximately 16 in 100,000 children per year.¹ Although uniform nomenclature and diagnostic criteria are lacking, the term *juvenile rheumatoid arthritis* and the American Rheumatism Association (ARA) classification criteria² are widely accepted, and will be considered for this review. This review includes a discussion of the definition and classification of JRA and introduces a diag-

nostic algorithm. We describe treatment and outcomes according to the classification.

Definition and classification

Juvenile rheumatoid arthritis is defined as arthritis lasting 6 weeks or more in a child younger than 16 years. The upper age limit of 16 years and the duration of 6 weeks or more have been arbitrarily set for classification purposes and may not apply clinically. Classification schemes designed for research protocols are often used clinically as diagnostic guides. Infectious, neoplastic, endocrine, and other rheumatic disorders must be excluded before making the diagnosis of JRA in a child. Classification *subtypes* (Table 1) of JRA include polyarticular (40%), pauciarticular (40%), and systemic onset (20%). Polyarticular JRA involves five or more joints; involvement of less than five joints is considered pauciarticular. Systemic onset may be pauciarticular or polyarticular, but is characterized by significant systemic features. Subtypes are split into *subsets* according to laboratory profiles.

Polyarticular onset juvenile rheumatoid arthritis

Classification into polyarticular subtype requires involvement of five or more joints. Symmetric involvement of the wrists, upper cervical spine, and the temporomandibular joints commonly occur. Systemic features are mild, consisting primarily of fatigue and low-grade fever, and are more likely to occur in those who are rheumatoid factor (RF)-positive. The disease in this subset resembles rheumatoid arthritis seen in adults; it has female predominance, onset in the teenage years, periarticular erosions, rheumatoid nodules, with progression into adulthood. The RF-negative polyarticular subset occurs primarily in preschoolers. Joint and systemic features are milder, and progression into adulthood is rare.

Pauciarticular onset juvenile rheumatoid arthritis

Classification into the pauciarticular subtype requires

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Table 1 Classification of Juvenile Rheumatoid Arthritis	
Subtype	Subset
☐ Polyarticular onset	Rheumatoid factor–positive Rheumatoid factor–negative
☐ Pauciarticular onset	Antinuclear antibody–positive HLA B-27*–positive
☐ Systemic onset	None

*HLA B-27 = histocompatibility locus antigen B-27.

involvement of less than five joints, usually asymmetrically. It is best understood in terms of two subsets, antinuclear antibody (ANA)–positive and histocompatibility locus antigen B-27 (HLA B-27)–positive. The ANA-positive subset occurs in female preschoolers and indicates a higher incidence of iridocyclitis. The HLA B-27–positive subset occurring in teenage boys often presents with unilateral hip involvement, and subsequently, other large joint involvement. Axial disease primarily involves the sacroiliac joints and may progress into adulthood as ankylosing spondylitis or psoriatic arthritis.

Systemic onset juvenile rheumatoid arthritis

Systemic features readily distinguish this subtype from its pauciarticular and polyarticular counterparts. Joint involvement is often overshadowed by a quotidian or diquotidian spiking fever of two or more weeks' duration. A centripetal salmon-colored macular rash is characteristic, but evanescent. Reticuloendothelial system involvement results in tender lymphadenopathy and splenomegaly. Chest pain and abdominal pain result from polyserositis. There is neither age nor gender bias, and attacks may recur into adulthood. Laboratory studies are not specific, but reflect the systemic nature of this subtype. Leukocytosis, thrombocytosis, anemia, and elevated acute-phase reactants are common. Rheumatoid factor, ANA, and HLA B-27 are negative.

Diagnosis

The evaluation of patients with JRA is directed toward classifi-

cation into subtypes and subsets. Therapeutic intervention and prognosis can be defined on this basis. A patient who is 16 years old or younger with arthritis that has lasted for 6 weeks or more can be entered into a diagnostic algorithm (*Figure 1*) if diagnostic exclusions (that is, infectious, neoplastic, endocrine, or other rheumatic disorders) have been met. If a daily fever spike to a temperature of 103°F has occurred for 2 weeks, the most probable diagnosis is systemic onset JRA. In the absence of spiking fevers, if five or more joints are involved, the polyarticular subtype is most likely and a test for an RF is necessary to determine the subset. If less than five joints are involved, the pauciarticular subtype is most probable, and an HLA B-27 and ANA test will determine the subset.

All patients with JRA require an ANA test to assess risk of iridocyclitis and to determine frequency of required ophthalmologic examinations.³ Patients with pauciarticular disease in whom tests for ANA, RF, and HLA B-27 were initially negative should be reevaluated for the presence of ANA or RF if new signs or symptoms suggest reclassification is probable. Seronegative (RF-negative) patients with polyarticular JRA that becomes aggressive may require a second test for the presence of RF. The test for HLA B-27 may be repeated if sample cell viability is low and a spondyloarthritis is suspected. Otherwise, a false-negative HLA B-27 test is unlikely. Reclassification may suggest alterations in therapeutic approach and outcome projections.

Treatment

Regardless of subtype and subset, nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, occupational therapy, and counseling are generally necessary. Surgical correction of deformities is usually delayed until epiphyseal closure. Bian-

Table 2
Nonsteroidal Anti-inflammatory Drugs (NSAIDs) Commonly Used in Treatment of Juvenile Rheumatoid Arthritis

NSAID*	Dose,† mg/kg per day	Frequency per day	Liquid form available
Aspirin	75 to 100	4 times	No
Choline magnesium trisalicylate	50	2 times	Yes
Ibuprofen	30 to 40	4 times	Yes
Tolmetin sodium	15 to 30	3 times	No
Naproxen	10 to 15	2 times	Yes

*Administered orally with meals.
†Total daily dose should not exceed recommendations for adults.

Table 3
Slow-acting Antirheumatic Drugs (SAARD) Used in Treatment of Juvenile Rheumatoid Arthritis

SAARD*	Dose†	Frequency	Liquid form available	Tests required‡
Gold (IM)	1 mg/kg	Monthly§	...	CBC and UA before each dose
Hydroxychloroquine	5 to 7 mg/kg per day	Twice daily	No	Retinal examination quarterly CBC periodically
Sulfasalazine	30 to 40 mg/kg per day¶	Twice daily	Yes	CBC and LFTs periodically
Methotrexate	10 to 20 mg/m ²	Weekly	No	CBC and LFTs monthly

*Administered orally unless otherwise noted.

†Should not exceed adult doses.

‡Baseline measurements and other periodic clinical monitoring required.

§Maintenance dose; initially given more frequently; test dose required.

||200-mg tablet only, may administer less frequently

¶Maintenance dose; initially lower.

Key: IM = intramuscular; CBC = complete blood cell count; UA = urinalysis; LFT = liver function test.

nual or quarterly ophthalmologic examinations are required for ANA-negative or positive patients, respectively. Patients with systemic onset JRA require annual ophthalmologic examinations.

Several NSAIDs are effective and safe for use in the pediatric population (*Table 2*). They include salicylates, naproxen, tolmetin sodium, and ibuprofen.⁴ The greatest experience has been with salicylates. They are particularly useful in the systemic onset subtype and the polyarticular, RF-positive subset. Tolmetin may be preferred for the pauciarticular, HLA B-27-positive subset. Common adverse effects of NSAIDs in children include gastropathy and central nervous system alterations. A rash resembling porphyria has been reported with use of naproxen. Reye's syndrome, although rare, must be considered during intercurrent viral illnesses. Periodic monitoring of all patients with JRA on NSAID therapy is prudent.

Slow-acting antirheumatic drugs (SAARDs) are considered in patients with progressive joint disease (*Table 3*). Parenteral gold therapy has been the most extensively studied and is the only SAARD approved by the Food and Drug Administration for JRA. Other SAARDs are currently under investigation. Among them, methotrexate appears to have a reasonable efficacy and toxicity profile, and is increasingly being used for the polyarticular, RF-positive subset.⁵ Sulfasalazine, an agent abandoned for years and then recently exonerated, shows promising results, particularly in the pauciarticular, HLA B-27-positive subset.⁶ Bone marrow,

renal, liver, or retinal toxicities may occur with specific SAARDs. Periodic monitoring is required (*Table 3*).

Systemic corticosteroids may be required for severe systemic disease, or the iridocyclitis seen principally in the pauciarticular, ANA-positive subset, but are generally avoided. Topical applications of corticosteroids are less likely to result in complications such as osteoporosis, early epiphyseal closure, and leg length abnormalities.

Clinicians should be thoroughly knowledgeable in the administration of these pharmacologic agents. Consultation with a specialist is advised.

Osteopathic manipulative treatment is directed toward reducing swelling and increasing range of motion in affected joints. Attention to juxta-articular structures, such as tendons and ligaments, is important. High-velocity techniques should be avoided when treating inflamed or unstable joints; soft tissue and muscle energy techniques are preferred. Joint pump techniques are designed to reduce swelling in inflamed joints. They may potentiate clearance of immune complexes and inflammatory mediators through lymphatics.

Tendons surrounding inflamed joints are often stretched. Pain emanating from the joints and tendons results in guarding of the affected joints. Although protective to the affected joint when in motion, prolonged guarding can result in myalgias and altered biomechanics, which may have extended ramifications. Inflamed joints should be rested several times during the day. Self-learned lym-

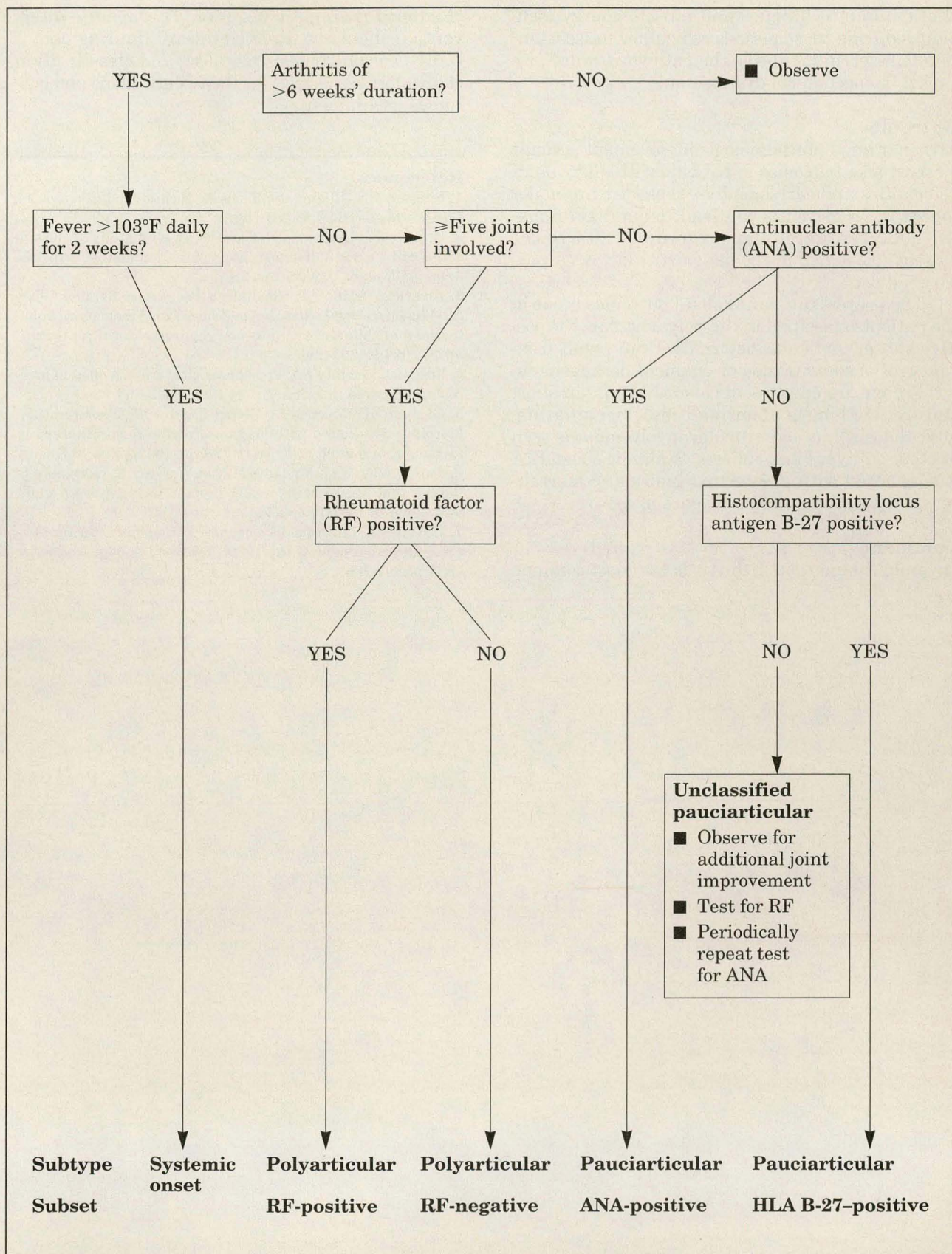


Figure. Diagnostic algorithm for juvenile rheumatoid arthritis.

phatic pump techniques and muscle energy techniques during these periods may allow muscle tension to reset, interrupting the pathway toward prolonged biomechanical dysfunction.

Outcomes

Articular and ophthalmologic involvement account for most poor outcomes in patients with JRA.⁷ Joint deformities and early epiphyseal closure are major concerns. Iridocyclitis can lead to band keratopathy and eventual blindness in up to 20% of the patients classified in the pauciarticular, ANA-positive subset.

The poorest musculoskeletal outcomes occur in the patients classified in the polyarticular, RF-positive subset. Articular deformities can result from joint erosions and tendon or ligament derangement.

Premature epiphyseal closure results in short stature, leg length abnormalities, micrognathia, and scoliosis. Limited articular involvement is seen in other subtypes and subsets. Systemic onset JRA is associated with greater morbidity and mortality when occurring before 5 years of age.

Comment

Juvenile rheumatoid arthritis is the most common

childhood rheumatic disorder. Therapeutic intervention should be directed toward limiting potentially poor outcomes. Diagnosis and classification of JRA forms the basis for therapeutic plans and outcomes assessment.

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