



## CLINICAL REPORT

Guidance for the Clinician in Rendering  
Pediatric Care

# Ophthalmologic Examinations in Children With Juvenile Rheumatoid Arthritis

James Cassidy, MD, Jane Kivlin, MD, Carol Lindsley, MD, James Nocton, MD, the Section on Rheumatology, and the Section on Ophthalmology

## ABSTRACT

Unlike the joints, ocular involvement with juvenile rheumatoid arthritis is most often asymptomatic; yet, the inflammation can cause serious morbidity with loss of vision. Scheduled slit-lamp examinations by an ophthalmologist at specific intervals can detect ocular disease early, and prompt treatment can prevent vision loss.

## INTRODUCTION

Chronic uveitis is an important and sometimes devastating complication of juvenile rheumatoid arthritis (JRA).<sup>1-3</sup> The intraocular inflammation primarily affects the iris and ciliary body (iritidocyclitis), but the choroid may also be involved.<sup>4</sup> Overall, the frequency varies from 2% to 34% in children with JRA.<sup>5-8</sup> Diagnosis of early involvement is not possible by direct ophthalmoscopy, but slit-lamp examination will reveal the presence or absence of inflammatory cells and increased protein within the anterior chamber of the eye.

Morbidity includes cataracts, glaucoma, band keratopathy, phthisis bulbi, and loss of vision.<sup>7,9</sup> Visual outcome has improved in the past 20 years; most children have a relatively good prognosis if the disorder is detected and treated early.<sup>9,10</sup> However, uveitis in children with JRA remains a leading cause of loss of vision and blindness in the United States.

## RISK FACTORS FOR CHRONIC UVEITIS

### Articular Features

The classification of JRA describes a heterogeneous group of disorders of predominantly peripheral arthritis with onset of disease before 16 years of age. The 3 major onset types defined by clinical manifestations in the first 6 months of the disease are oligoarticular (pauciarticular), polyarticular, and systemic.<sup>11</sup> The onset type is determined by the systemic features of the illness and the number of joints with arthritis at diagnosis. Oligoarticular JRA is defined by involvement of 4 or fewer joints; polyarticular JRA is defined by involvement of >4 joints (usually 10–20); and systemic-onset JRA is defined by quotidian fevers during the first 6 weeks of the illness, almost always associated with a characteristic rash. Less than 1% of children with systemic-onset JRA develop chronic uveitis.<sup>5,7</sup> Most children with uveitis have an oligoarticular onset.<sup>1,2,7</sup>

[www.pediatrics.org/cgi/doi/10.1542/peds.2006-0421](http://www.pediatrics.org/cgi/doi/10.1542/peds.2006-0421)

doi:10.1542/peds.2006-0421

All clinical reports from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

### Key Words

juvenile rheumatoid arthritis,  
ophthalmologic examination

### Abbreviation

JRA—juvenile rheumatoid arthritis  
PEDIATRICS (ISSN Numbers: Print, 0031-4005;  
Online, 1098-4275). Copyright © 2006 by the  
American Academy of Pediatrics

**TABLE 1 Frequency of Ophthalmologic Examination in Patients With JRA**

Type	ANA	Age at Onset, y	Duration of Disease, y	Risk Category	Eye Examination Frequency, mo
Oligoarthritis or polyarthritis	+	≤6	≤4	High	3
	+	≤6	>4	Moderate	6
	+	≤6	>7	Low	12
	+	>6	≤4	Moderate	6
	+	>6	>4	Low	12
	−	≤6	≤4	Moderate	6
	−	≤6	>4	Low	12
Systemic disease (fever, rash)	−	>6	NA	Low	12
	NA	NA	NA	Low	12

ANA indicates antinuclear antibodies; NA, not applicable.

Recommendations for follow-up continue through childhood and adolescence.

Chronic uveitis may be detected at the time of initial diagnosis of arthritis; however, if not present at onset, it most often presents during the next 4 to 7 years.<sup>7,12</sup> The period of highest risk is within 4 years of onset of arthritis, although the risk is never entirely absent.<sup>7,12</sup> Eye involvement precedes involvement of the joints in approximately 5% of cases.

Children with JRA remain at risk of developing uveitis into adulthood. There are reports of uveitis diagnosed initially more than 20 years after onset of arthritis.<sup>13</sup> The activity of the uveal inflammation does not parallel that of the joint disease.<sup>14,15</sup>

### Age

Children at greatest risk of developing uveitis are those with oligoarticular-onset JRA.<sup>1,2,13</sup> The peak age of onset of arthritis in oligoarthritis is 1 to 5 years.<sup>12</sup>

### Immunogenetic and Serologic Markers

The serologic marker most strongly associated with chronic uveitis is the presence of antinuclear antibodies.<sup>1,2,16</sup> Antinuclear antibodies are present in 65% to 90% of children with chronic uveitis and are a major risk factor for its development.<sup>7,17</sup> They are usually detected in low to moderate titers on HEp-2 cells and are of unknown antigenic specificity. Rheumatoid factor is not usually present in children with JRA, including those with uveitis. Immunogenetic factors may predispose to the development of chronic uveitis. The associated alleles are located predominantly in the major histocompatibility complex (MHC) region on chromosome 6 and involve specificities in the HLA-DR, DP, and DQ regions.<sup>18</sup>

### Clinical Characteristics

The onset of ocular inflammation is insidious and asymptomatic in most young children.<sup>1,2,17</sup> Because of the lack of symptoms or the cognitive recognition by the child, the exact time of onset of ocular involvement is frequently difficult to determine. This observation em-

phasizes the requirement for slit-lamp examination by an ophthalmologist at diagnosis of JRA and periodically thereafter.

Signs or symptoms in older children, rare as they are, may include a red eye, decreased vision, unequal pupils, ocular pain, and headaches and should prompt an urgent eye examination. Most cases of uveitis are bilateral (70% to 80%); unilateral disease may progress to bilateral involvement.

Data compiled before widespread therapy with methotrexate and tumor necrosis factor blockers indicated that the prognosis was good in 25% of cases, and 25% of children responded poorly to treatment and/or might require surgery for cataracts or glaucoma.<sup>3</sup> Approximately 50% of patients required prolonged treatment for moderate to severe chronic inflammation; the visual prognosis in these patients remained guarded. Early and aggressive treatment of intraocular inflammation has helped to reduce the morbidity of the ocular disease.<sup>19</sup>

## FREQUENCY OF OPHTHALMOLOGIC EXAMINATIONS IN CHILDREN WITH JRA

The suggested frequency of ophthalmologic visits for children with JRA without known uveitis at diagnosis and during follow-up is presented in Table 1. Once uveitis is diagnosed, the pediatric ophthalmologist will determine the frequency of examinations on the basis of response to therapy and complications. Because a substantial number of patients may have the eye disease before or shortly after their arthritis is diagnosed, they should have their initial eye examination within 1 month of the diagnosis of arthritis rather than waiting for the first available appointment.

### SECTION ON OPHTHALMOLOGY, 2004–2005

Edward Buckley, MD, Chairperson  
 James Ruben, MD  
 Jane Kivlin, MD  
 Stephen Glaser, MD  
 Gregg Lueder, MD  
 David Granet, MD

Steven Lichtenstein, MD, Immediate Past Chairperson

### STAFF

S. Niccole Alexander, MPP

### SECTION ON RHEUMATOLOGY, 2004–2005

Michael Henrickson, MD, Chairperson  
 John Bohnsack, MD  
 Harry Gewanter, MD  
 Kathleen Haines, MD  
 Mary Moore, MD  
 James Nocton, MD  
 Carlos Rosé, MD

Charles Spencer, MD, Immediate Past Chairperson

## STAFF

Laura Laskosz, MPH

## REFERENCES

1. Rosenberg AM. Uveitis associated with childhood rheumatic diseases. *Curr Opin Rheumatol.* 2002;14:542-547
2. Petty RE. Current knowledge of the etiology and pathogenesis of chronic uveitis accompanying juvenile rheumatoid arthritis. *Rheum Dis Clin North Am.* 1987;13:19-36
3. Kanski JJ. Juvenile arthritis and uveitis. *Surv Ophthalmol.* 1990;34:253-267
4. Chadwick AJ, Rosen ES. Papillitis and Still's disease. *Am J Ophthalmol.* 1968;65:784-787
5. Chylack LT Jr, Beinfang DC, Bellows AR, Stillman JS. Ocular manifestations of juvenile rheumatoid arthritis. *Am J Ophthalmol.* 1975;79:1026-1033
6. McGill NW, Gow PJ. Juvenile rheumatoid arthritis in Auckland: a long term follow-up study with particular reference to uveitis. *Aust N Z J Med.* 1987;17:305-308
7. Chalom EC, Goldsmith DP, Koehler MA, et al. Prevalence and outcome of uveitis in a regional cohort of patients with juvenile rheumatoid arthritis. *J Rheumatol.* 1997;24:2031-2034
8. Kotaniemi K, Kaipainen-Seppanen O, Savolainen A, Karma A. A population-based study on uveitis in juvenile rheumatoid arthritis. *Clin Exp Rheumatol.* 1999;17:119-122
9. Cabral DA, Petty RE, Malleon PN, Ensworth S, McCormick AQ, Shroeder ML. Visual prognosis in children with chronic uveitis and arthritis. *J Rheumatol.* 1994;21:2370-2375
10. Wolf MD, Lichter PR, Ragsdale CG. Prognostic factors in the uveitis of juvenile rheumatoid arthritis. *Ophthalmology.* 1987;94:1242-1248
11. Cassidy JT, Levinson JE, Bass JC, et al. A study of classification criteria for a diagnosis of juvenile rheumatoid arthritis. *Arthritis Rheum.* 1986;29:274-281
12. Guillaume S, Prieur A, Coste J, Job-Deslandre C. Long-term outcome and prognosis in oligoarticular-onset juvenile idiopathic arthritis. *Arthritis Rheum.* 2000;43:1858-1865
13. Cassidy JT, Sullivan DB, Petty RE. Clinical patterns of chronic iridocyclitis in children with juvenile rheumatoid arthritis. *Arthritis Rheum.* 1977;20(2 suppl):224-227.
14. Rosenberg AM, Oen KG. The relationship between ocular and articular disease activity in children with juvenile rheumatoid arthritis and associated uveitis. *Arthritis Rheum.* 1986;29:797-800
15. Cimaz RG, Fink CW. The articular prognosis of pauciarticular onset juvenile arthritis is not influenced by the presence of uveitis. *J Rheumatol.* 1996;23:357-359
16. Dana MR, Merayo-Llodes J, Schaumberg DA, Foster CS. Visual outcomes prognosticators in juvenile rheumatoid arthritis-associated uveitis. *Ophthalmology.* 1997;104:236-244
17. Kotaniemi K, Kautiainen BA, Karma A, Aho K. Occurrence of uveitis in recently diagnosed juvenile chronic arthritis: a prospective study. *Ophthalmology.* 2001;108:2071-2075
18. Melin-Aldana H, Giannini EH, Taylor J, et al. Human leukocyte antigen-DRB1\*1104 in the chronic iridocyclitis of pauciarticular juvenile rheumatoid arthritis. *J Pediatr.* 1992;121:56-60
19. Kotaniemi K, Savolainen A, Karma A, Aho K. Recent advances in uveitis of juvenile idiopathic arthritis. *Surv Ophthalmol.* 2003;48:489-502