

PEDIATRICS®

Rheumatic Fever in Children Younger Than 5 Years: Is the Presentation Different?

Lloyd Y. Tani, L. George Veasy, L. LuAnn Minich and Robert E. Shaddy
Pediatrics 2003;112;1065-1068
DOI: 10.1542/peds.112.5.1065

This information is current as of January 22, 2006

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://www.pediatrics.org/cgi/content/full/112/5/1065>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2003 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



Rheumatic Fever in Children Younger Than 5 Years: Is the Presentation Different?

Lloyd Y. Tani, MD; L. George Veasy, MD; L. LuAnn Minich, MD; and Robert E. Shaddy, MD

ABSTRACT. *Objective.* To review our experience with children who presented with rheumatic fever (RF) before 5 years of age and to compare their presentation with that of older children.

Methods. The cardiology database was reviewed to identify patients who were younger than 5 years and had a diagnosis RF using the Jones criteria from January 1985 through March 2000. Patient age, sex, date and age at presentation, and the major Jones criteria fulfilled were noted. When carditis was present, its severity was judged to be moderate to severe when there was radiographic cardiomegaly and/or clinical congestive heart failure. The clinical presentation of patients who presented in the first 5 years of life were compared with the presentation of those whose RF was diagnosed after 5 years of age. Clinical findings at follow-up evaluation and echocardiographic findings both at presentation and at follow-up were noted for the children who were younger than 5 years at presentation.

Results. Of 541 cases of RF seen from January 1985 through March 2000, 27 (5%) were in children who were younger than 5 years (median: 4.0 years; range: 1.9–4.9 years). Major Jones criteria at presentation were arthritis in 17, carditis in 14, chorea in 3, and erythema marginatum in 3. The carditis was mild in 4 and moderate to severe in 10 patients. Compared with older children, younger children were more likely to present with moderate to severe carditis, arthritis without carditis or chorea, or the rash of erythema marginatum and were less likely to have chorea. The incidence of carditis was similar in the 2 groups as was the ratio of boys to girls. At follow-up (9.6 ± 5.6 years), 69% of younger children who presented with carditis have clinical rheumatic heart disease. Subclinical, echocardiographically detected valvular abnormalities were detected both at presentation (33% of all children with RF before 5 years of age) and at follow-up (55% of those who initially had carditis).

Conclusions. Approximately 5% of children with RF were younger than 5 years at diagnosis. Compared with older patients, children who presented before 5 years of age were more likely to have moderate to severe carditis and to present with arthritis or the rash of erythema marginatum and were less likely to have chorea. Chronic rheumatic heart disease was common in young children who presented with carditis. Long-term follow-up is necessary to determine the outcome for young children with subclinical echocardiographic evidence of valvular disease. *Pediatrics* 2003;112:1065–1068; *rheumatic fever*.

ABBREVIATION. RF, rheumatic fever.

Rheumatic fever (RF) is a leading cause of acquired heart disease in children and young adults in many parts of the world.^{1,2} Although less common in industrialized countries, a resurgence of RF activity occurred in the intermountain west portion of the United States in the mid-1980s³ and has persisted through the 1990s and into the 21st century. Previous series have reported that RF both is uncommon and may present differently in children who are younger than 5 years.^{4–6} The purposes of this article are to report our experience with RF in children who presented before 5 years of age and to compare the presentation of these children with that of older children.

METHODS

Patients

The Pediatric Cardiology RF database at the University of Utah was reviewed to identify children who were younger than 5 years and received a diagnosis of RF from January 1985 through March 2000 using the Jones criteria.^{7,8} Patient age at presentation, sex, and clinical presentation were compared with children who were aged 5 to 18 years and received a diagnosis of RF during the same time period. For children who were younger than 5 years at presentation, charts were reviewed for clinical follow-up data and echocardiographic findings at presentation and at follow-up evaluation.

Jones Criteria

The diagnosis of polyarthritis required clinical evidence of inflammation (typically warm, red, swollen) and limitation of motion of >1 joint. Patients with Sydenham chorea had the involuntary, spasmodic, purposeless movements characteristic of this disorder (confirmed by a pediatric neurologist). Carditis was diagnosed only when there was a new murmur of mitral and/or aortic regurgitation. The carditis was considered moderate to severe when there was radiographic cardiomegaly and/or clinical evidence of congestive heart failure. Clinical carditis without cardiomegaly or heart failure was considered mild. The diagnosis of erythema marginatum required historical or observed evidence of the characteristic evanescent macular erythematous rash with serpiginous borders and central clearing.

Echocardiography

Doppler evidence of valvular regurgitation in the absence of clinical findings was not considered carditis as stated in the Jones criteria.^{7,8} Complete 2-dimensional, M-mode, and Doppler echocardiography was performed on all but a few patients in 1985 and 1986. Since 1987, echocardiography has been performed in all cases to confirm clinical findings, evaluate chamber sizes, assess systolic ventricular function (shortening fraction and/or ejection fraction), and identify pericardial effusions. Color Doppler became a routine part of the echocardiographic evaluation in 1990. Since January 1992, strict criteria have been used to distinguish pathologic from physiologic valvular regurgitation in patients

From the Department of Pediatrics, University of Utah, and Primary Children's Medical Center, Salt Lake City, Utah.

Received for publication Dec 30, 2002; accepted Apr 14, 2003.

Reprint requests to (L.Y.T.) Primary Children's Medical Center, 100 North Medical Dr, Salt Lake City, UT 84113. E-mail: pcltani@ihc.com

PEDIATRICS (ISSN 0031 4005). Copyright © 2003 by the American Academy of Pediatrics.

without an audible murmur of mitral or aortic regurgitation.⁹ For pathologic mitral regurgitation, all of the following criteria were met: 1) a color jet seen from at least 2 imaging planes; 2) a color jet extending >1 cm into the left atrium behind the mitral valve; and 3) pulsed or continuous wave Doppler showing the regurgitant jet to be holosystolic, of high velocity, and turbulent (aliasing).⁹⁻¹² For aortic regurgitation, a diastolic color jet seen in at least 2 planes and extending >5 mm into the left ventricular outflow tract was considered pathologic. Doppler-detected aortic regurgitation rarely, if ever, occurs in normal children.^{13,14}

Clinical Follow-up

The records of children who were younger than 5 years and presented with carditis were reviewed for the most recent follow-up data, including findings on auscultation, need for surgical intervention, and echocardiographic evidence of rheumatic valvular disease.

Statistical Analysis

Patients who presented in the first 5 years of life were compared with those who presented later in life (χ^2 or Fisher exact test). For children who presented with carditis, the cardiac status at follow-up evaluation was compared with the severity of cardiac involvement at presentation. Data are presented as mean \pm standard deviation. Data were analyzed using SigmaStat software (San Rafael, CA). $P < .05$ was considered statistically significant.

RESULTS

Of 541 patients that fulfilled the Jones criteria for RF from January 1985 through March 2000, 27 (5.0%) were younger than 5 years (3.96 ± 0.87 ; median: 3.95; range: 23-59 months); 12 were between 4 and 5 years of age, 10 were between 3 and 4 years of age, 4 were between 2 and 3 years of age, and 1 was younger than 2 years. Of these 27 children, 13 were boys and 14 were girls.

The major Jones criteria at presentation are given in Table 1. Arthritis without chorea or carditis was more common in the younger group (11 of 27 [41%]) than in older patients (104 of 514 [20%]; $P = .02$). Compared with older patients, the rash of erythema marginatum was more common in the younger patients (3 of 27 [11%] vs 13 of 512 [2.5%]; $P = .04$). Any presentation with chorea (alone or with arthritis or carditis) was less common in children who were younger than 5 years at presentation (3 of 27 [11%]) than in the older children (167 of 512 [33%]; $P = .04$).

Compared with older patients, children who were younger than 5 years had a similar incidence of carditis (either alone or with arthritis or chorea). Of the 14 younger children with carditis, 12 had a murmur of mitral regurgitation alone, 1 had audible mitral and aortic regurgitation, and 1 had audible

aortic regurgitation alone. When present, the carditis was more often moderate to severe (as opposed to mild) in the younger children (10 of 14 [71%]) than in older patients (115 of 313 [37%]; $P = .02$).

Echocardiography was performed at presentation in all 27 children who presented before 5 years of age and confirmed clinical findings in all 14 cases with clinical carditis. Of the 12 patients who had a murmur of mitral regurgitation but no diastolic murmur, 3 had Doppler evidence of aortic regurgitation. The 1 child with audible aortic regurgitation but no murmur of mitral regurgitation had Doppler evidence of pathologic mitral regurgitation. Of the 13 children with no evidence of clinical carditis (ie, arthritis or chorea with no murmur), 5 (38%) had subclinical evidence of pathologic mitral and/or aortic regurgitation. Thus, 9 (33%) of 27 children who presented with RF before 5 years of age had subclinical, Doppler-detected pathologic mitral or aortic regurgitation.

Clinical follow-up data were available for 13 of 14 children who presented with clinical carditis before 5 years of age; 1 patient was lost to follow-up. At an average interval of 9.6 ± 5.6 years after presentation with RF, 9 (69%) have clinically evident rheumatic heart disease; the other 4 patients now have normal cardiac examinations. All 9 children with clinical rheumatic heart disease have audible mitral regurgitation. One patient who had audible mitral regurgitation but only Doppler-detected aortic regurgitation at presentation now has murmurs of both aortic and mitral regurgitation. No patient has a mid- to late-diastolic murmur or opening snap, findings of mitral stenosis. Follow-up echocardiography has been performed in 11 patients. Two patients have subclinical aortic regurgitation, 1 has subclinical pathologic mitral regurgitation, and 3 have subclinical mitral stenosis (thickened leaflets, restricted motion, or increased Doppler velocity). All 3 patients with subclinical mitral stenosis had moderate to severe carditis at presentation. One patient, a girl who was 3.8 years of age and had severe mitral regurgitation at presentation, has required surgery (mitral valvuloplasty almost 8 years after presentation). Initial carditis severity was not predictive of clinical chronic rheumatic heart disease at this relatively short follow-up interval. At follow-up, 7 of 9 with initially moderate to severe carditis and 2 of 4 with initially mild carditis have clinically evident chronic rheumatic heart disease.

TABLE 1. Clinical Presentation of RF

Age at presentation (y)	<5	>5
No. of patients	27	514
Sex (male:female)	13:14	267:247
Isolated carditis	30% (n = 8)	25% (n = 129)
Isolated arthritis	41% (n = 11)	20% (n = 104)
Isolated chorea	4% (n = 1)	18% (n = 95)
Carditis and arthritis	19% (n = 5)	22% (n = 113)
Carditis and chorea	4% (n = 1)	12% (n = 61)
Arthritis and chorea	4% (n = 1)	0.4% (n = 2)
Carditis and arthritis and chorea	0	2% (n = 11)
All chorea	11% (n = 3)	33% (n = 168)
Erythema marginatum	11% (n = 3)	3% (n = 13)
Subcutaneous nodules	0	2% (n = 8)

DISCUSSION

The most important finding of our study is that approximately 5% of children with RF were younger than 5 years at presentation. Therefore, RF should be considered in the differential diagnosis of young children who present with arthritis, chorea, a rash suggestive of erythema marginatum, or a murmur of mitral regurgitation. Although RF is considered to be an entity occurring mainly between the ages of 5 and 15 years,^{4,6} our numbers are similar to the 4.5% to 6.8% reported by some^{15,16} but higher than the 1% to 2% reported by others.^{4,17,18} The different incidences reported may be attributable to differences among

populations, but the method of case ascertainment also may have been important. Certainly, some cases of RF in young children may go undiagnosed, adding to the variability in the reported incidences.

The clinical presentation of children whose RF was diagnosed before 5 years of age was different from that of older children. Compared with those older than 5 years, younger children were more likely to present with arthritis without carditis or chorea but less likely to present with chorea. In addition, the rash of erythema marginatum was seen more commonly in the group of children who were younger than 5 years at diagnosis. Our data are similar to previous series that have reported arthritis to be more common in young children.^{5,19,20} Although reported by some series to be virtually nonexistent in young children,^{5,20} chorea has been reported in an 8-month-old child, and another series found a 7% incidence of chorea in young children with RF.¹⁵ Erythema marginatum is a relatively uncommon finding in patients with RF and may be easily missed because it is evanescent, occurring mainly on the trunk and proximal extremities, and is not associated with symptoms of pain or pruritus.^{21,22} Although the reasons for the higher incidence of this rash in younger children are unknown, we speculate that this may in part be because parents are more likely to participate in the bathing and dressing of younger children and thus more likely to notice a fleeting, mainly truncal rash.

When carditis was present, it was more often moderate to severe in younger than in older patients. The severity of involvement at presentation is important because the 2 main risk factors reported to influence the development of chronic rheumatic heart disease are the severity of involvement at initial presentation and RF recurrences.^{23–25} Furthermore, younger age at presentation has been reported to be associated with an increased risk of RF recurrence.²⁶ Other series have also reported greater severity of cardiac involvement in younger children.^{5,20} In contrast to some previous series reporting carditis to be more common in younger children,^{5,18,19} we found no difference in the incidence of carditis in children who were younger than 5 years of age compared with older children. The 69% of children who presented with carditis before 5 years of age and developed chronic rheumatic heart disease is similar to the overall incidence of 66% reported by Feinstein et al,²⁵ who followed 441 patients with RF of all ages. Because the natural history of rheumatic heart disease in developed countries such as the United States is one of slow progression with most adults presenting in the fourth or fifth decade,^{27,28} the follow-up interval of our study is not of sufficient duration to determine the influence of initial carditis severity on long-term outcome.

We found echocardiographic evidence of subclinical rheumatic valvular disease (mitral stenosis or regurgitation, aortic regurgitation) at the time of follow-up evaluation in several of the children who presented before 5 years of age. Doppler-detected subclinical pathologic valvular regurgitation has been reported in several other series of patients with

RF.^{10,11,29–31} There is indirect evidence supporting the existence and potentially the importance of subclinical rheumatic heart disease.²³ Many adults who present with chronic rheumatic heart disease cannot recall having an illness resembling RF.^{32,33} In addition, as many as 20% to 34% of patients with “pure” chorea have been reported to develop chronic rheumatic heart disease.^{34–36} In their classic report of 1000 patients with RF followed for 20 years, Bland and Jones²³ reported that rheumatic heart disease developed in 44% of patients who initially had no clinical evidence of carditis. Presumably, these patients had either very mild or subclinical rheumatic heart disease that progressed over time. Despite this indirect evidence, how often subclinical, echocardiographically detected rheumatic valvular changes progress to clinically significant rheumatic heart disease is unknown. In addition, Doppler may detect small amounts of valvular regurgitation in “normals.” Although criteria have been established to differentiate this physiologic mitral regurgitation from pathologic regurgitation,⁹ the existence of such valvular pathology has been disputed.^{37,38} Thus, at present, the role of echocardiography in the evaluation and management of patients with RF who have no clinical cardiac involvement remains controversial.^{8,39–41}

Our study has limitations. The study was retrospective, with a relatively small number of patients who presented before 5 years of age. As is common for a retrospective study, clinical follow-up data were incomplete. For chronic rheumatic heart disease, which usually presents in the fourth or fifth decade, the duration of follow-up in our study was relatively short.

CONCLUSION

Although uncommon, RF does occur in children who are younger than 5 years. When it occurs, presentation with arthritis is more common and chorea is less common than in older patients. In addition, the rash of erythema marginatum is noted more frequently in younger children. When present, cardiac involvement is more often moderate to severe (as opposed to mild) in these younger children. Persistent, chronic rheumatic heart disease is common in these young children who present with carditis. Subclinical, echocardiographically detected cardiac involvement is also common, but additional study will be important to determine the prognostic and clinical value of such findings.

ACKNOWLEDGMENT

We thank Paul C. Young, MD, for review of this manuscript.

REFERENCES

1. Olivier C. Rheumatic fever—is it still a problem? *J Antimicrob Chemother.* 2000;45(suppl):13–21
2. Stollerman GH. Rheumatic fever. *Lancet.* 1997;349:935–942
3. Veasy LG, Wiedmeier SE, Orsmond GS, et al. Resurgence of acute rheumatic fever in the intermountain area of the United States. *N Engl J Med.* 1987;316:421–427
4. Zaman MM, Rouf MA, Haque S, et al. Does rheumatic fever occur usually between the ages of 5 and 15 years? *Int J Cardiol.* 1998;66:17–21
5. Rosenthal A, Czoniczer G, Massell BF. Rheumatic fever under 3 years of age. A report of 10 cases. *Pediatrics.* 1968;41:612–619
6. Kumar RK, Rammohan R, Narula J, Kaplan EL. Epidemiology of strep-

- tococcal pharyngitis, rheumatic fever, and rheumatic heart disease. In: Narula J, Virmani R, Reddy KS, Tandon R, eds. *Rheumatic Fever*. Washington, DC: American Registry of Pathology; 1999:41–68
7. Jones criteria (revised) for guidance in the diagnosis of rheumatic fever. *Circulation*. 1984;69:204A–208A
 8. Guidelines for the diagnosis of rheumatic fever. Jones criteria, 1992 update. Special Writing Group of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association. *JAMA*. 1992; 268:2069–2073 (published erratum appears in *JAMA*. 1993;269:476)
 9. Minich LL, Tani LY, Pagotto LT, Shaddy RE, Veasy LG. Doppler echocardiography distinguishes between physiologic and pathologic “silent” mitral regurgitation in patients with rheumatic fever. *Clin Cardiol*. 1997;20:924–926
 10. Abernethy M, Bass N, Sharpe N, et al. Doppler echocardiography and the early diagnosis of carditis in acute rheumatic fever. *Aust N Z J Med*. 1994;24:530–535
 11. Folger GM Jr, Hajar R, Robida A, Hajar HA. Occurrence of valvar heart disease in acute rheumatic fever without evident carditis: colour-flow Doppler identification. *Br Heart J*. 1992;67:434–438
 12. Wilson NJ, Neutze JM. Echocardiographic diagnosis of subclinical carditis in acute rheumatic fever. *Int J Cardiol*. 1995;50:1–6
 13. Yoshida K, Yoshikawa J, Shakudo M, et al. Color Doppler evaluation of valvular regurgitation in normal subjects. *Circulation*. 1988;78:840–847
 14. Thomson JD, Allen J, Gibbs JL. Left sided valvar regurgitation in normal children and adolescents. *Heart*. 2000;83:185–187
 15. Abdin ZH, Eissa A. Rheumatic fever and rheumatic heart disease in children below the age of 5 years in the tropics. *Ann Rheum Dis*. 1965;24:389–391
 16. Carapetis JR, Currie BJ, Mathews JD. Cumulative incidence of rheumatic fever in an endemic region: a guide to the susceptibility of the population? *Epidemiol Infect*. 2000;124:239–244
 17. Arora R, Subramanyam G, Khalilullah M, Gupta MP. Clinical profile of rheumatic fever and rheumatic heart disease: a study of 2,500 cases. *Indian Heart J*. 1981;33:264–269
 18. Vazquez-Antona C, Calderon-Colmenero J, Attie F, et al. [Rheumatic cardiopathy in children younger than 6 years of age]. *Arch Inst Cardiol Mex*. 1991;61:143–147
 19. McIntosh R, Wood CL. Rheumatic infections occurring in the first three years of life. *Am J Dis Child*. 1935;49:835–848
 20. Majeed HA, Yousof AM, Shaltout A, Khuffash FA. Acute rheumatic fever below the age of five years: a prospective study of the clinical profile. *Ann Trop Paediatr*. 1984;4:37–40
 21. Burge DJ, DeHoratius RJ. Acute rheumatic fever. *Cardiovasc Clin*. 1993; 23:3–23
 22. Bisno AL. Noncardiac manifestations of rheumatic fever. In: Narula J, Virmani R, Reddy KS, Tandon R, eds. *Rheumatic Fever*. Washington, DC: American Registry of Pathology; 1999:245–256
 23. Bland EF, Jones TD. Rheumatic fever and rheumatic heart disease: a twenty year report on 1000 patients followed since childhood. *Circulation*. 1951;4:836–843
 24. Feinstein AR, Stern EK. Clinical effects of recurrent attacks of acute rheumatic fever: a prospective epidemiologic study of 105 episodes. *J Chron Dis*. 1967;20:13–27
 25. Feinstein AR, Stern EK, Spagnuolo M. The prognosis of acute rheumatic fever. *Am Heart J*. 1964;68:817–834
 26. Spagnuolo M, Pasternack B, Taranta A. Risk of rheumatic-fever recurrences after streptococcal infections. Prospective study of clinical and social factors. *N Engl J Med*. 1971;285:641–647
 27. Marcus RH, Sareli P, Pocock WA, Barlow JB. The spectrum of severe rheumatic mitral valve disease in a developing country. Correlations among clinical presentation, surgical pathologic findings, and hemodynamic sequelae. *Ann Intern Med*. 1994;120:177–183
 28. Carroll JD, Feldman T. Percutaneous mitral balloon valvotomy and the new demographics of mitral stenosis. *JAMA*. 1993;270:1731–1736
 29. Hilario MO, Andrade JL, Gasparian AB, Carvalho AC, Andrade CT, Len CA. The value of echocardiography in the diagnosis and followup of rheumatic carditis in children and adolescents: a 2 year prospective study. *J Rheumatol*. 2000;27:1082–1086
 30. Ozkutlu S, Ayabakan C, Saraclar M. Can subclinical valvitis detected by echocardiography be accepted as evidence of carditis in the diagnosis of acute rheumatic fever? *Cardiol Young*. 2001;11:255–260
 31. Figueroa FE, Fernandez MS, Valdes P, et al. Prospective comparison of clinical and echocardiographic diagnosis of rheumatic carditis: long term follow up of patients with subclinical disease. *Heart*. 2001;85: 407–410
 32. Feinstein AR, Spagnuolo M. The clinical patterns of acute rheumatic fever: a reappraisal. *Medicine*. 1962;41:279–305
 33. Vasan RS, Selvaraj N. Natural history of acute rheumatic fever. In: Narula J, Virmani R, Reddy KS, Tandon R, eds. *Rheumatic Fever*. Washington, DC: American Registry of Pathology; 1999:347–358
 34. Aron AM, Freeman JM, Carter S. The natural history of Sydenham’s chorea. Review of the literature and long-term evaluation with emphasis on cardiac sequelae. *Am J Med*. 1965;38:83–95
 35. Carapetis JR, Currie BJ. Rheumatic chorea in northern Australia: a clinical and epidemiological study. *Arch Dis Child*. 1999;80:353–358
 36. Bland EF. Chorea as a manifestation of rheumatic fever: a long-term perspective. *Trans Am Clin Climatol Assoc*. 1961;73:209–213
 37. Vasan RS, Shrivastava S, Vijayakumar M, Narang R, Lister BC, Narula J. Echocardiographic evaluation of patients with acute rheumatic fever and rheumatic carditis. *Circulation*. 1996;94:73–82
 38. Narula J, Chandrasekhar Y, Rahimtoola S. Diagnosis of active rheumatic carditis. The echoes of change. *Circulation*. 1999;100:1576–1581
 39. Veasy LG. Time to take soundings in acute rheumatic fever. *Lancet*. 2001;357:1994–1995
 40. Narula J, Kaplan EL. Echocardiographic diagnosis of rheumatic fever. *Lancet*. 2001;358:2000
 41. Ferrieri P. Proceedings of the Jones criteria workshop. *Circulation*. 2002; 106:2521–2523

THE INTELLIGENT MINORITY

“During one of Adlai Stevenson’s races for the presidency, a woman said, ‘Oh, Governor Stevenson, you can’t lose. You have all the intelligent people with you.’ Stevenson replied, ‘Yes, Madam, but I need a majority.’”

Strother RD. *Falling Up*. Baton Rouge: Louisiana State University Press; 2003

Submitted by Student

Rheumatic Fever in Children Younger Than 5 Years: Is the Presentation Different?

Lloyd Y. Tani, L. George Veasy, L. LuAnn Minich and Robert E. Shaddy
Pediatrics 2003;112;1065-1068
DOI: 10.1542/peds.112.5.1065

This information is current as of January 22, 2006

Updated Information & Services

including high-resolution figures, can be found at:
<http://www.pediatrics.org/cgi/content/full/112/5/1065>

References

This article cites 37 articles, 14 of which you can access for free at:
<http://www.pediatrics.org/cgi/content/full/112/5/1065#BIBL>

Citations

This article has been cited by 2 HighWire-hosted articles:
<http://www.pediatrics.org/cgi/content/full/112/5/1065#otherarticles>

Subspecialty Collections

This article, along with others on similar topics, appears in the following collection(s):
Heart & Blood Vessels
http://www.pediatrics.org/cgi/collection/heart_and_blood_vessels

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
<http://www.pediatrics.org/misc/Permissions.shtml>

Reprints

Information about ordering reprints can be found online:
<http://www.pediatrics.org/misc/reprints.shtml>

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

