The Initial Attack of Acute Rheumatic Fever During Childhood in North India
A Prospective Study of the Clinical Profile

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SUMMARY
A prospective study was done to determine the clinical profile of first attacks of acute rheumatic fever in children in North India. Unlike other reports, the clinical profile described here closely resembles the spectrum prevalent in the West. Arthritis, the most common manifestation, was seen in 66.6% of the 102 patients, chorea in 20.7%, and carditis in 33.7%. Carditis was considered mild in 22 patients and severe in 12; a persistent elevation of sleeping pulse rate and mitral regurgitation was noted in each case. Patients with severe carditis also had significant cardiomegaly and apical mid-diastolic murmur. Two patients with severe carditis developed congestive heart failure; one of them had pericarditis as well. Murmur of aortic origin was not noted in this series. One patient with severe carditis died from the disease. Erythema marginatum was noted in two, both of whom had severe carditis. There were two instances of subcutaneous nodules, one with and one without carditis. The close similarity of these results with those in the West is attributed to the prospective design of the study, analysis of first attacks only and survey of a general pediatric population for all manifestations suggestive of the disease.

Additional Indexing Words:
Acute rheumatic fever Carditis Arthritis Chorea Streptococcus
Subcutaneous nodules Erythema marginatum

In recent years widely conflicting views have been expressed regarding the nature of acute rheumatic fever in children in India and neighboring countries. According to DeSilva,1 the disease occurred in a mild form in Ceylon; acute manifestations such as chorea, subcutaneous nodules, erythema marginatum, and carditis were rare. In Pakistan, however, Robinson et al.2 observed carditis in 75% of their rheumatic fever patients, cardiomegaly in 45%, and gross congestive heart failure in 29%. A similar severe profile has been reported from Iran3,4 and Egypt.5 Observations from India are also in marked variance. Padmavati, in a study from North India,6 could document only 38 cases of acute rheumatic fever in the pediatric age group over a period of four years and emphasized the absence of acute manifestations of the disease during childhood. In marked contrast, Vaishnava et al.7 from South India described cardiac involvement in 90% and gross congestive heart failure in 45% of their patients. According to Roy et al.,8,9 the clinical features of acute rheumatic fever in India differ from those in Boston, with a higher incidence of carditis and congestive heart failure.

All but one of these studies,2 however, are retrospective in nature and no attempt has been made in any of the studies to analyze the clinical profile of acute rheumatic fever in children with first attacks separately from those with recurrent episodes. This makes reappraisal of acute rheumatic fever in children desirable. A prospective study was therefore begun to ascertain the clinical profile of acute rheumatic fever in children with first attack in North India and then to compare it with that.
reported from the West and from neighboring countries.

Material and Method

This prospective study includes 102 children with a first attack of acute rheumatic fever seen over a period of four years (July, 1967, to June, 1971). There were 55 boys and 47 girls. Two of the patients were below five years, one above 12 years, and the rest between five and 12 years of age. These patients were first seen in the general pediatric outpatient clinic of Safdar Jung Hospital, New Delhi, which serves a large section of the pediatric population of Delhi and neighboring states. From the general pediatric clinic, children suspected of having acute rheumatic fever were admitted to the Pediatric Service for further evaluation. Only those children whose symptoms fulfilled the modified Jones criteria\textsuperscript{10} for diagnosis of acute rheumatic fever and additional qualifications as suggested by Feinstein and Spagnuolo,\textsuperscript{11} and had no previous history of acute rheumatic fever or evidence of rheumatic heart disease, were included in this report.

A detailed history was obtained for each patient to determine the exact mode of onset of illness, its chronological development, the presenting complaints, treatment received, if any, and other pertinent clinical features. The presence and severity of cardiac involvement was ascertained on the basis of physical findings, roentgenologic and electrocardiographic data. Two independent observers examined each patient and the findings recorded represented the consensus of both. Chest X-rays were interpreted independently without initial regard to clinical or laboratory data.

The diagnosis of carditis was made on the basis of the following features:

1. **The presence of a significant heart murmur:** apical systolic, apical mid-diastolic, basal diastolic. An apical systolic murmur was considered to be significant only if it met the following criteria: i) The murmur started with the first heart sound and lasted either throughout or at least during two-thirds of the systole. ii) Its intensity was at least grade 2 on a scale of 6. iii) It had a high-pitched and blowing quality. iv) Its maximum intensity was at or just to the left of the apex, transmitting to the axilla. v) The intensity of the murmur did not change with deep inspiration or with change in position of the patient.

2. **Pericarditis:** This was diagnosed only in the presence of an unequivocal pericardial friction rub and/or pericardial effusion.

3. **Cardiomegaly:** This was defined as the presence of at least 2+ enlargement (on a scale of 0 to 4+) or of at least moderate enlargement of one or more cardiac chambers as evidenced by four position X-rays (postero-anterior, left anterior oblique, right anterior oblique, left lateral) with barium.\textsuperscript{12}

4. **Congestive heart failure:** The diagnosis of congestive heart failure was made on the basis of currently acceptable criteria of heart failure, namely, tachycardia (heart rate exceeding 100 to 110 beats per minute, depending on the age of the patient), tachypnea (respiratory rate above 40 per minute), cardiomegaly (clinical and radiologic evidence) and hepatomegaly (liver edge palpable at least 3 cm below the right costal margin).

5. **Persistent elevation of sleeping pulse rate:** Heart rate was recorded every 3 hours during the night while the patient was asleep and the sleeping pulse rate was considered to be elevated when the average rate exceeded 70 to 90 beats per minute, depending on the age of the patient.

Carditis was termed mild if a persistent elevation of the sleeping pulse rate and mild degree of cardiomegaly with or without significant murmur were the only findings. It was considered severe in patients who developed gross cardiomegaly with or without congestive heart failure and pericarditis. Such patients invariably had a significant heart murmur, apical systolic and mid-diastolic, as well as a persistent elevation of sleeping pulse rate. A prolonged P-R interval was not considered an indication of carditis.

Sedimentation rate, C-reactive protein and antistreptolysin O titers were determined in each patient by standard methods.\textsuperscript{13} Throat cultures were planted directly and immediately upon 5% blood agar, and the presence of beta-hemolytic streptococci was identified by colony count and microscopic morphology. Patients with the triad of polyarthritis, fever, and elevated sedimentation rate were tested routinely for collagen disease, rheumatoid arthritis, and lupus erythematosus with uniformly negative results. Of the patients presenting with arthralgia, fever, and elevated sedimentation rate, only those who met the Jones criteria by having carditis simultaneously or by subsequently developing chorea, carditis, or arthritis were included in this study.

The patients were examined on admission and then every day during the entire hospital stay. Following their discharge from the hospital, the patients were seen at regular intervals while antibiotic prophylaxis was being maintained.

**Results**

A reliable history of sore throat was obtainable in 35 patients. A positive family history of acute rheumatic fever was noted in only one instance.

**Presenting Complaints**

Painful, red, hot swelling of the joint(s) was the presenting complaint in 60 patients (58.8%). Twenty children (19.6%) presented with joint pain without swelling or tenderness. However, later in the course of the illness, carditis developed in seven, carditis and chorea in four, chorea in one, and arthritis in eight to fulfill the modified Jones criteria for diagnosis of acute rheumatic fever.\textsuperscript{10,11} Involu-
tary movement was the chief complaint in 15 patients (14.6%) (fig. 1). Of seven patients initially presenting without joint symptoms or chorea, two complained of shortness of breath, two of exertional dyspnea, and three of palpitation. All of these patients subsequently developed carditis. Fever was the presenting complaint in 85 children, abdominal pain in six, and skin rash in one patient. None of the patients had epistaxis.

Clinical Profile

Arthritis. Sixty-eight patients (66.6%) developed painful, red, hot swelling of one or several joints (fig. 2). Arthritis was isolated in 53 cases and was associated with carditis in 15. In none of the patients did arthritis occur simultaneously with chorea. Joint involvement was polyarticular in 87% and monoarticular in 13%. The joints involved in order of frequency were: knee (86%), ankle (64.9%), wrist (28%), hip (15%), elbow (11%), and shoulder (8%). Metacarpophalangeal joint involvement was noted in three patients. There was one instance each where arthritis affected the spine, temporomandibular or metatarsal joint.

Chorea. Twenty-one children (20.5%), 14 girls and seven boys, showed evidence of chorea. Chorea manifested as involuntary movements in 76%, clumsiness in 70%, change in behavior in 59%, change in speech in 30%, and muscular weakness in 11.8%. Chorea occurred as an isolated phenomenon in 15 patients and was associated with carditis in one, carditis and arthralgia in four and arthralgia in one.

Carditis. Cardiac involvement was noted in 34 (33.3%) patients. Two patients with carditis were below five years of age; none of these children developed congestive heart failure. Carditis occurred as an isolated lesion in seven patients but was associated with arthritis in 15, arthralgia in seven, arthralgia and chorea in four, and chorea in one. Each child in this group of 34 had a significant apical systolic murmur indicative of mitral insufficiency; an additional apical mid-diastolic murmur was noted in 12 children. We did not detect a murmur of aortic origin or a classical rumbling presystolic murmur of mitral stenosis in any patient with carditis. Carditis was considered mild in 22 patients and severe in 12. A persistent elevation of the sleeping pulse rate was noted in each child. All patients with severe carditis had, in addition, significant cardiomegaly and apical systolic and mid-diastolic murmur. Two patients with severe carditis developed congestive heart failure, one had pericarditis as well.

Severity of joint and cardiac involvement. It is of interest to note that carditis developed in 14 of 68

Figure 2

This shows the clinical profile of first attack of acute rheumatic fever. Sixty-eight patients developed arthritis, isolated in 53 cases and associated with carditis in 15. Twenty-one children showed evidence of chorea which occurred as an isolated phenomenon in 15 patients and was associated with carditis in one, carditis and arthralgia in four, and arthralgia in one. Cardiac involvement was noted in 34 patients. Carditis developed as an isolated lesion in seven patients but was associated with arthritis in 15, arthralgia in seven, arthralgia and chorea in four, and with chorea in one. Of 20 children who presented with arthralgia, carditis developed in seven, carditis and chorea in four, chorea in one, and arthritis in eight. Note that in none of the patients did arthritis occur simultaneously with chorea.
patients (22%) with red, hot, tender, swelling of the joints, in 11 out of 20 patients (55%) with arthralgia, and in seven out of seven patients (100%) who initially did not present with joint symptoms or chorea (table 1). The carditis was severe in 71.4% of the patients belonging to the last group.

Erythema marginatum. Two patients (1.9%) developed erythema marginatum. Both had severe carditis.

Subcutaneous nodules. Nodules developed in two patients. Mild carditis was observed in one. The other patient who had recurrent crops of nodules subsequently developed chorea, with no evidence of arthritis or carditis at any stages of the illness.

Mortality. One patient died during the acute stage of illness giving a mortality rate of 0.98%.

Discussion

In recent years reports from several developing countries have reflected important differences in the clinical course of acute rheumatic fever in children. The spectrum ranges from rare occurrence of the disease with a marked paucity of acute manifestations to a very severe form characterized by a high incidence of carditis, congestive heart failure, and mortality (table 2). Observations of the present study (fig. 3), however, suggest that the clinical profile of the initial episode of acute rheumatic fever in children from North India does not differ significantly from that found in the Western countries.

In a previous study from North India, Roy observed arthritis in only 32% of his patients, but found arthralgia in 90%. On the basis of these findings, he suggested that a syndrome of joint pain, elevated sedimentation rate, positive C-reactive protein, and high antistreptolysin O titer should be regarded as major criteria in India for the diagnosis of acute rheumatic fever. Our observations do not support this contention. Objective arthritis, the most common finding in the present study, was seen in 66.6% of our cases, an incidence very similar to the one reported by Feinstein et al and others. In none of our patients did arthritis and chorea occur concurrently.

During the past decade the frequency of chorea has declined significantly in the Western countries. Among patients admitted to the House of Good Samaritan at Boston, the annual incidence of chorea dropped from 43 to 18.6% between 1921 and 1940, remained stationary at a level of 19 to 22% over the next 15 years, and showed a further decrease to 15% from 1956 to 1960. A similar downward trend has been reported by Mayer et al. Twenty-one patients (20.7%) in the present

<table>
<thead>
<tr>
<th>Clinical profile</th>
<th>DeSilva (Ceylon) 1969</th>
<th>Padmavati (New Delhi, North India) 1962</th>
<th>Robinson et al. (Karachi, Pakistan) 1966</th>
<th>Ghari (Shiraz, Iran) 1969</th>
<th>Roy (New Delhi, North India) 1969</th>
<th>Tahernia et al. (Shiraz, Iran) 1971</th>
<th>This study (New Delhi, India)</th>
</tr>
</thead>
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<tr>
<td>Arthritis</td>
<td>NI</td>
<td>20.55</td>
<td>75.0</td>
<td>30.0</td>
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<td>56</td>
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<tr>
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<td>1.52</td>
<td>7.0</td>
<td>2.8</td>
<td>5</td>
<td>4</td>
<td>20.0</td>
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<tr>
<td>Carditis</td>
<td>35</td>
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<td>75.0</td>
<td>64.5</td>
<td>46</td>
<td>83</td>
<td>33.3</td>
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<tr>
<td>Sub. Cut. N.</td>
<td>Rare</td>
<td>0.63</td>
<td>3.5</td>
<td>1.4</td>
<td>3</td>
<td>1</td>
<td>1.9</td>
</tr>
<tr>
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<td>Rare</td>
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<tr>
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<td>NI</td>
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<td>1.9</td>
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<tr>
<td>Mortality</td>
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<td>NI</td>
<td>14.0</td>
<td>14.5</td>
<td>NI</td>
<td>4</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Abbreviations: Sub. Cut. N. = subcutaneous nodules; Ery. Marg. = erythema marginatum; CHF = congestive heart failure; NI = no information.

*Numbers in table express percent of rheumatic fever patients who develop complications during the initial attack.
study developed chorea. The disease was more common in girls than in boys, confirming its well-known affinity for females. Although the incidence of chorea in our series is similar to that reported by Massel et al.,14 it is higher than that reported in previous studies from North India and other developing countries.1-8 Whether this reflects a cyclic variation merits further prospective analysis of the disease.

Of the major manifestations of acute rheumatic fever, carditis is the most important since it is the only one that can cause death or result in permanent cardiac damage. In contrast to the United States, a very high incidence of carditis ranging from 64 to 83% has been reported recently from various developing countries.2-4 In our study carditis was noted in only 33.7% of the subjects, although in another study from the same area, Roy reported a 46% incidence of the disease. As pointed out by the author, this higher incidence may be due to the fact that all cases probably did not represent the first attack. In this respect, it is of interest that other studies reporting a very high incidence of carditis also do not differentiate between children with first attack of acute rheumatic fever from those with recurrent ones. That failure to do so may give a falsely high incidence of cardiac involvement has been well emphasized by Feinstein and Spagnuolo.11 Another factor that may have contributed to the diversity of the results is the retrospective nature of the studies.

An inverse relationship between the severity of cardiac involvement and severity of joint symptoms has been emphasized by several investigators. Feinstein and Spagnuolo11 observed carditis in 26% of the patients with overt objective arthritis and in 95 to 100% of the patients with no joint symptoms or chorea. These authors postulated that when acute rheumatic fever "bites" the joints, it usually "licks" or spares the heart. Our observations are in accord with these investigators.

Recently, Rosenthal et al.20 reported ten episodes of acute rheumatic fever in children under three years of age and were impressed with the apparent high prevalence of rheumatic carditis and congestive heart failure. According to the authors, these findings suggest a strong predisposition to cardiac involvement in the very young children afflicted with rheumatic fever. In another study of acute rheumatic fever and rheumatic heart disease in children below the age of five years in the tropics, Abdin and Eissa5 observed congestive heart failure in nine out of 24 patients. The youngest patient, a boy of 11 months, had arthritis without cardiac involvement. Thus, these authors concluded that the incidence of severe carditis with gross cardiac enlargement and heart failure was only slightly higher in this age group than that in the older children. Two patients in the present study were below five years of age. Both had carditis but in neither was the disease severe enough to cause congestive heart failure.

Roy et al.8 reported that the clinical features of acute rheumatic fever were different in North India in that erythema marginatum was not seen and subcutaneous nodules were uncommon. In our series, two patients developed erythema marginatum; the cutaneous manifestation was associated with severe carditis in each case. It is generally believed that subcutaneous nodules are invariably associated with severe carditis and that patients with nodules have poor prognosis. Baldwin et al.22 reported a higher mortality rate in patients with nodules than in children who had carditis without nodules. Of the two patients with subcutaneous nodules in our study, one had mild carditis. The other patient21 developed recurrent crops of subcutaneous nodules without evidence of arthritis or carditis. It seems, therefore, that in some patients with acute rheumatic fever subcutaneous nodules may occur without evidence of either joint or heart disease as has been suggested by Taranta23 and Burrington.24 Thus, observations of the present study suggest that the true spectrum of acute rheumatic fever is most likely to be defined in a prospective survey of a general pediatric population for all manifestations suggestive of the disease.
Rheumatic fever ended fatally in only one patient. The low mortality rate in children with initial attack of acute rheumatic fever in this series is similar to the incidence reported in the Western countries and adds further support to the concept that most fatal terminations from rheumatic fever are due to either recurrence of the disease with consequent increase in severity of carditis, or to advanced rheumatic heart disease with mechanically insufficient valves resulting in a severe compromise of myocardial function.

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