# Treatment of Rheumatic Carditis

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**Abstract.** Rheumatic fever and rheumatic heart disease continue unabated in most of the developing nations, affecting young individuals. Focal outbreaks of smaller magnitude have also been reported since mid 1980s from industralized western nations, where this disease had almost disappeared. Introduction of penicillin in mid 1940s had markedly changed the natural history of rheumatic fever, although the incidence of rheumatic fever declined in developed nations before that, due to better living conditions. Treatment of rheumatic fever chiefly involves use of antibiotics (penicillin) to eradicater strepcocci, and anti-inflammatory drugs like salicylates or corticosteriods. Patients with severe carditis, congestive heart failure and/or pericarditis are best treated with corticosteriods as these are more potent anti-inflammatroy agents than salicylates. Salicylates may be sufficient for cases with mild or no carditis. The treatmnet must be continued for 12 weeks. Several studies have shown that valvular regurgitation, and not myocarditis, is the cause of congestive heart failure in active rheumatic carditis. Therefore surgery with mitral valve replacement or repair is indicated in cases with intractable hemodynamics due to mitral regurgitation. Development of chronic valvular lesion after an episode of rheumatic fever is dependent upon presence or absence of carditis in the previous attack and compliance with secondary prophylaxis. Recurrences due to inadequate penicillin prophylaxis are responsible for hemodynamically significant chronic valvular lesions requiring surgery.
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Rheumatic fever and rheumatic carditis continue to have a high prevalence in India, particularly among school children and young adults. The disease is a major public health problem resulting in significant cardiovascular morbidity and mortality in some of the developing nations. The prevalence rate for rheumatic heart disease were reported to vary between 1.8 to 11 per 1000 of school children between 1940 and 1983. The rate between 1984 and 1995 have varied from 1 to 5.4 per 1000.[1] The prevalence of rheumatic fever is also high in school children, being 0.32 to 0.54 per 1000. In contrast, the prevalence of rheumatic heart disease in children aged between 5 to 15 years is below 0.05 per 1000 in western countries. Also the attack rate has fallen 20 to 100 fold in the last 50 years in most of the developed countries, the reasons for this fall are not very clear.[2] In developing countries including India, the attack rates appear to have remained unchanged.

## RHEUMATIC CARDITIS : ETHNIC VARIATIONS

The incidence of carditis in patients with rheumatic fever has varied from 40% to 99%, however the highest figures for cardiac involvement are from the developing countries. The diagnosis of carditis is mostly based on clinical examination in these studies.[3-6] Not only carditis is more common, it often affects younger age group and the frequency of recurrences is greater when compared to data from western countries. All these factors result in progressive deterioration with severe valve involvement and congestive heart failure, commonly encountered in young children. It is not clear if these ethnic differences are solely due to socio- economic factor or genetic susceptibility also plays a role.

### Treatment of Rheumatic Carditis

A variety of therapeutic regimens for acute rheumatic carditis have been used. Unfortunately, all types of treatment cause suppression of the inflammatory disease without entirely preventing its sequelae. The mainstays of therapy are use of salicylates in high doses and/or corticosteroids. Although there are numerous studies using different regimens, the treatment of rheumatic carditis remains controversial and different studies have attempted to demonstrate the superiority of salicylates or hormones in suppressing the activity of the lesion and in decreasing the chronic valvular sequel of carditis. There is general consensus on eradication of streptococci from the throat by using penicillin or other antibiotics in those sensitive to penicillin. One also needs to give prophylaxis with penicillin or other antibiotics against future attacks of rheumatic fever, to which these children are more prone.

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## ANTI-INFLAMMATORY DRUGS

Corticosteroids are more potent anti-inflammatory agents than salicylates and hence many experts like to use steroids for patients who are very ill with pericarditis or congestive heart failure. However others do not agree with this protocol of therapy. This controversy has been discussed in an article by Dr.Albert and colleagues, published recently.[7] These authors have done a literature review and of the 119 non-randomized studies, 117 favoured the use of corticosteroids for treatment of rheumatic carditis. Further they performed analysis of 11 controlled randomized trials. The treatment effect was expressed as the estimated relative odds of having a pathologic murmur at one year follow-up. Of the 11 controlled, randomized studies, only five could be used for meta-analysis since only these studies presented data on the outcome measured i.e. apical systolic murmur at one year after entry. The results of these five trials are given in the table. As can be seen, the Rheumatic Fever Working Party (RFWP) and Rheumatic Fever Study Group (RFSG) revealed no benefit of corticosteroids over aspirin. Since RFWP study enrolled more patients than the other studies combined, the results of meta-analysis are dominated by their findings. The overall estimated odds ratio were also not in favour of either steroids or aspirin for patients with rheumatic carditis.

There were several limitations of this meta-analysis. There were instances of cross over of severely ill patients from salicylates to corticosteroids group, the reverse did not occur in any case. Also, influence of treatment on end points such as pericarditis, congestive heart failure and mortality was not analysed due to the small number of such cases. Finally, different studies used different types of steroids and dosage schedule, and thus lack of uniformity could also affect the results.

It seems that the question of superiority of steroids over salicylates will remain unanswered. Many pediatricians chose to use steroids for treatment of a child with severe carditis as steroids are more potent anti-inflammatory agents and hence result in early symptomatic relief of acute manifestation of rheumatic carditis. There is no conclusive proof, that corticosteroids lessen the long term complications of carditis, however they do result in rapid resolution of acute manifestations of carditis like fever, tachycardia, pericardial rub and subcutaneous nodules. The normalization of erythrocyte sedimentation rate is also faster. It has also been observed by various workers that new murmur, pericardial rub do not appear in a patient of rheumatic carditis being treated with corticosteroids, on the other hand new murmur do arise during salicylate therapy.[8]

Prolonged corticosteroids therapy over 12 weeks, as for treating rheumatic carditis uniformly results in Cushingoid appearance. There may be other complications in a minority of patients, including flaring up of tuberculosis or other infections, hypertension, hypokalemia, depression or psychosis. Most textbooks currently recommend using corticosteroids for patients with severe carditis, congestive heart failure or pericarditis. Such type of cases are common in clinical practice in our country. On the other hand salicylates may be enough for mild carditis cases although it is advisable to keep these cases under close observation as risk of progression of carditis is reported to be 1-4%. One should shift from salicylates to corticosteroids if there is any evidence of carditis progression.

### Dosage Schedule

**Salicylates :** Aspirin 50-80 mg/kg/day in four divided doses for 10 weeks, then taper over next two weeks.
**Corticosteroids :** Prednisolone 1-2mg/kg/day (upto 60 mg/day) for three to four weeks, gradually taper over next 8-9 weeks.

**Table 1. Randomized Trials of Treatment of ARF In Patients with Carditis at Entry**

| Reference (year) | No. of patients | Agent and dose | % with apical murmur at 1year | | P value |
|---|---|---|---|---|---|
| | | | Steroid | ASA | |
| RFSG (1960) | 57 | Prednisone 60 mg/d × 21 d then taper vs ASA 50 mg/lb/d × 9 wks then taper | 57.1% | 37% | 0.14 |
| RFSG (1965) | 93 | Prednisone 3 mg/lb/d × 7d then taper vs ASA 50 mg/lb/d × 6 wks | 41.3% | 55% | 0.18 |
| Dorfman *et al* (1961) | 42 | Hydrocortisone 250 mg and/or ASA level 20-30 mg% | 17.4% | 53% | 0.014* |
| REWP (1955) | 373 | ACTH 80–120 U and taper vs cortisone 300 mg and taper vs ASA 60 mg/lb/d and taper | 60.4% | 55% | 0.35 |
| Stolzer *et al* (1955) | 50 | ASA 30-60 mg/lb/d × 6 wks vs cortisone 50-300 mg/d vs ACTH 20-120mg/d | 36.7% | 50% | 0.35 |

Stronger immunosuppression with COX-2 inhibiting nonsteroidal anti-inflammatory drugs may be useful for these cases, further trails are warranted. There are also reports of using immunomodulators like intravenous gamma globulin in high dose for treatment of rheumatic carditis. The results, however, are not encouraging.[9]

### Valve Surgery During Active Rheumatic Carditis

The study by Essop *et al* revealed that mitral regurgitation and not myocarditis is the cause of cardiac enlargement and congestive heart failure in patients with active rheumatic carditis.[10] These authors used echocardiography to demonstrate an increased left ventricular dimension with supernormal fractional shortening in these children, normalizing after surgical repair of the valve. Similar findings are also reported by Barlow *et al*[11] and Gentles *et al.*[12] Hence surgery is recommended during the acute stage of carditis in patients with intractable hemodynamic deterioration and the results are encouraging.[13,14] Essop *et al*[10] have reported 32 cases of mitral or mitral and aortic valve replacements during the active stage. Postoperatively, there was marked improvement in clinical condition and left ventricular dilatation. The mortality of operating in the active stage of carditis is reported to be 0-5%. Mitral valve repair is not recommended during active carditis, as chances of reoperation are more likely.[15] In conclusion, valve replacement surgery should be performed in life threatening cases, not responding adequately to medical means.

### Treatment of Heart Failure

The general guidelines for treatment of heart failure due to rheumatic carditis are the same. However, these patients are sensitive to digoxin, hence lower doses should be used and initial digitalization is not recommended. Diuretics should be used as needed. Vasodilator therapy is of immense use in those with valvar regurgitation. In acute cases with severe mitral regurgitation with evidence of pulmonary edema, intravenous infusion of sodium nitroprusside may be life saving. A close monitoring of arterial pressure, preferably with an intraarterial pressure monitoring line, is mandatory when using intravenous sodium nitroprusside as precipitous fall in blood pressure may occur in these sick children. In refractory cases, valve surgery should be performed as a last resort.

### General Measures and Role of Bed Rest

Rest is important in the recovery of rheumatic carditis, however the duration and extent of bed rest is still controversial and the data is anecdotal in the literature. It seems logical that the duration of rest should be proportional to the severity of carditis. A bed rest for four weeks and gradual ambulation in the next four weeks may suffice for an episode of mild carditis. For more severe forms, but without congestive failure, the period of rest should be extended to six weeks. For cases of rheumatic carditis with congestive heart failure, bed rest should be prescribed for 12 weeks or longer if heart failure persists and the ambulation should also be gradual over a period of 12 weeks or so.

A nutritious diet should be prescribed, however in more severe forms of carditis, salt restriction is advisable.

### Replase and Rebound

Relapse is worsening of rheumatic fever on therapy and is seen in 2-4% of children who are treated with salicylates. It rarely occurs in those on corticosteroids.[16] The symptoms worsen and there is progression of cardiac findings or a new murmur appears. If a relapse is suspected, one should quickly switch over to corticosteroids.

Rebound is defined as reappearance of manifestations of rheumatic fever when the drug like salicylates or corticosteroids is being tapered off. Unlike relapse, rebound is more likely to occur in children who are treated with corticosteroids rather than salicylates and when the total duration of treatment is inadequate. Some experts advocate adding salicylates to corticosteroids tapering if rebound is suspected.

### Assessment of Therapy

As the active rheumatic carditis resolves there is improvement in symptoms, appetite and resting heart rate. Features of congestive heart failure, if present, subside. Certain laboratory parameters also show trend towards normalization.

Antistreptolysin O (ASO) titer is raised in about 80% of patients with rheumatic carditis, however the titers remained elevated on therapy and hence should not be used to assess the efficacy of treatment. On the other hand, the erythrocytic sedimentation rate (ESR) and the C-reactive protein levels vary with the activity of the disease and hence can be used to assess the improvement in the disease process. A normocytic normochronic anemia unresponsive to iron therapy improves as the activity resolves.

### Outcome of Rheumatic Carditis

The outcome of patients with rheumatic carditis depends on the severity and frequency of attacks. Although the mortality in acute stage has decreased markedly, but still some of the episodes can be fatal. The carditis is generally more severe in young children with inadequate nutrition and from a poor socio-economic background. Understandably, these children often have inadequate secondary prophylaxis with penicillin and hence more

recurrences and more severe forms of chronic valvular heart disease. In our country rheumatic carditis and chronic rheumatic heart disease are the single largest cause of acquired heart disease and death in children.

## CONCLUSION

Rheumatic carditis is primarily a valvulitis resulting in valvar regurgitation, mostly of the mitral valve. The cause of heart failure in carditis is severe valvular disease resulting from inflammation, prolapse of the valve, annular dilatation and chordal elongation. There is strong evidence that the congestive heart failure is not due to primary myocardial involvement as seen in other forms of myocarditis. An episode of rheumatic carditis lasts for less than 12 weeks duration in >95% of cases and hence support with symptomatic therapy is very important during this time. In addition to adequate treatment with penicillin for streptococcal pharyngitis, anti-inflammatory therapy should be instituted. Corticosteroids are clearly more effective; however these are associated with frequent side effects and rebound. Inspite of this, children with severe carditis must receive steroids, those with milder forms may be managed with salicylates. There is no convincing evidence that either steroids or salicylates modify the course or natural history of the disease.

Other general measures include decreased physical activity and bed rest and nutritious low sodium diet (for those with severe form of carditis). Surgery in the form of mitral valve repair or replacement can be done at low risk, however it should be only considered in fulminant cases, refractory to medical therapy.

## REFERENCES


1. Padmavati S. Rheumatic heart disease: prevalence and preventive measures in the Indian subcontinent. *Heart* 2001; 86 : 127.
2. Mortimer EA Jr. Control of rheumatic fever. How are we doing (editorial). *JAMA* 1977; 237 : 1720.
3. Mabilangan LM, Mojica BA Jr. A study on rheumatic fever and rheumatic heart disease among 208 Filipino Children. *Philippine J Cardiol* 1974; 2 : 4-12.
4. Robinson RD Jr, Sultana S, Abbasi AS *et al.* Acute rheumatic fever in Karachi, Pakistan. *Am J Cardiol* 1966; 18 : 548-551.
5. Sueblinvong V. Clinical pattern of rheumatic heart disease and rheumatic fever in Bangkok. Proceedings of Second World Congress of Cardiology. New York: Springer-Verlag, 1986; 1004.
6. Vaishnava S, Webb JK, Cherian J. Juvenile rheumatism in south India. A clinical study of 166 cases. *Indian J Child Health* 1960; 9 : 290-299.
7. Albert DA, Harel L, Karrison T. The treatment of rheumatic carditis: A review and meta-analysis. *Medicine* 1995; 74 : 1-12.
8. Rothman PE. Treatment of rheumatic carditis. A critical review. *Clin Pediatr* 1965; 4 : 619-625.
9. Voss LM, Wilson NJ, Neutze JM *et al.* Intravenous immunoglobulin in acute rheumatic fever. A randomized controlled trial. *Circulation* 2001, 103 : 401-406.
10. Essop MR, Wisenbaugh T, Sareli P. Evidence against a myocardial factor as the cause of left ventricular dilatation in active rheumatic carditis. *J Am Coll Cardiol* 1993; 22 : 826-829.
11. Barlow JB, Marcus RH, Pocock WA, Barlow CW, Essop R, Sareli P. Mechanisms and management of heart failure in active rheumatic carditis. *South Afr Med J* 1998; 78 : 181-186.
12. Gentles TL, Colan SD, Wilson NJ, Biosa R, Neutze JM. Left ventricular mechanics during and after acute rheumatic fever: contractile dysfunction is closely related to valve regurgitation. *J Am Coll Cardiol* 2001; 37 : 201-207.
13. Al kasab S, Al Fagih MR, Shahid M, Habbab M, Al Zaibag M. Valve surgery in acute rheumatic heart disease. One to four year follow up. *Chest* 1988; 94 : 830-833.
14. Veasy LG, Wiedmeier SE, Ormand GS *et al.* Resurgence of acute rheumatic fever in the intermountain area of the United States. *N Engl J Med* 1987; 316 : 421-427.
15. Skoularigis J, Sinovich V, Joubert G, Sareli P. Evaluation of the long term results of mitral valve repair in 254 young patients with rheumatic mitral regurgitation. *Circulation* 1994, 90 (Part II) : 167-174.
16. Massel BF, Jhaveri S, Czoniczer G, Beernet R. Treatment of rheumatic fever and rheumatic carditis: Observations providing a basis for selection of aspirin or adrenocortical steroids. *Med Clin North Am* 1961; 45(5) : 1349-1368.