Current Practice

Diagnosis and treatment of rheumatic fever

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Diagnostic criteria

In 1944, Dr Duckett Jones published a set of guidelines for diagnosis of rheumatic fever (RF), which became known as Jones criteria[1]. This was based on combinations of clinical and laboratory findings, none of which alone was specific for RF. He organized the salient features of RF into major and minor categories. Clinical features that were most useful diagnostically were designated major manifestations and included carditis, joint symptoms, subcutaneous nodules and chorea. Historical evidence of RF or rheumatic heart disease (RHD) also constituted a major manifestation. Other less characteristic findings were listed as minor manifestations and included fever, erythema marginatum and laboratory markers of inflammation. Presence of 2 major or 1 major and 2 minor manifestations indicated a high probability of RF.

To improve specificity, these guidelines have been periodically revised by the American Heart Association. In the first revision of 1956[2], objectively identifiable arthritis replaced joint symptoms as a major manifestation and arthralgia was assigned to the minor category. History of previous RF or RHD was downgraded to the minor category and erythema marginatum made a major criterion[2]. Evidence of preceding group A ß-haemolytic streptococcal pharyngitis was added to the list of minor manifestations[2]. In the 1965 revision[3], evidence of a prior streptococcal infection was made mandatory for diagnosis of RF. Each revision increased specificity but decreased sensitivity of the criteria and 20-25% of RF cases diagnosed by 1956 criteria[2] could not be diagnosed by 1965 criteria[3]. Chorea and indolent carditis usually presented in the relatively late phase of the disease when antistreptococcal antibody titres suggestive of preceding streptococcal infection had already normalized. Therefore, in a 1984 revision[4], chorea and indolent carditis were exempted from the requirement of elevated antistreptococcal antibody titres.

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Diagnosis of rheumatic carditis by Jones criteria becomes difficult when carditis is the isolated manifestation of RF. This is true especially when carditis is subclinical, when it is apparent but supportive noncarditic criteria for diagnosis of RF are not fulfilled, or when the previous cardiac findings are not known for documentation of interval change in cardiac findings during the recurrence of disease[5]. These difficulties led to the 1992 update[6] of Jones criteria where the previous history of RF or RHD was excluded from the list of minor manifestations, limiting applicability of Jones criteria only to first episodes of RF (Table 1). The 2002-03 criteria from the World Health Organization (WHO)[7] allow for the diagnosis of recurrent RF in patients with established RHD to be based only on minor manifestations (Table2).

Table 1 - Jones criteria (1992 update)[6]

- Two major or one major and two minor manifestations must be present, plus evidence of antecedent group A streptococcus infection.
- Chorea and indolent carditis do not require evidence of antecedent group A streptococcus infection.
- Recurrent episode requires only one major or several minor manifestations, plus evidence of antecedent group A streptococcus infection.
- *Major manifestations*
  Carditis
  Polyarthritis
  Chorea
  Erythema marginatum
  Subcutaneous nodules
- *Minor manifestations*
  Arthralgia
  Fever
  Raised erythrocyte sedimentation rate or C-reactive protein concentrations
  Prolonged PR interval on electrocardiogram

- *Evidence of antecedent group A streptococcus infection*
  Positive throat culture or rapid antigen test for group A streptococcus
  Raised or rising streptococcal antibody titre

Table 2
WHO criteria (2002–03)[7]

- Chorea and indolent carditis do not require evidence of antecedent group A streptococcus infection

- *First episode*
  As per Jones criteria

- *Recurrent episode*
  In a patient without established RHD: as per first episode
  In a patient with established RHD: requires two minor manifestations, plus evidence of antecedent group A streptococcus infection. (Evidence of antecedent group A streptococcus infection as per Jones criteria, but with addition of recent scarlet fever)

Echocardiography

Echo-Doppler examination identifies valvular regurgitation not detectable with clinical examination, allows visualization of valve structure and allows detection of unrelated causes of valve dysfunction, such as mitral valve prolapse. It is important to note that the incremental utility of echo-Doppler would be inversely proportional to the clinical skills. In the Utah outbreak of RF, whereas carditis was confirmed by auscultation in 53 of the 74 patients (72%) with RF, Doppler evidence of MR was demonstrated in an additional 14 patients (19%) who were clinically considered to have isolated arthritis or pure chorea[8]. In another report from the same group, asymptomatic cardiac involvement was detected in 47% of RF patients presenting with polyarthritis[9]. Folger et al. also demonstrated significant valvular involvement with colour flow Doppler examination in the patients with RF, polyarthritis and no clinical evidence of carditis[10]. On the other hand, a large prospective study of RF from India did not find evidence of Doppler regurgitation in the patients without clinical evidence of carditis[11]. Echo-Doppler evidence of trivial-to-mild valvular regurgitation is also commonly observed in the normal population[12] and this may be exaggerated on colour-Doppler examination. Likelihood of transient valvular regurgitation may further increase in the clinical setting of patients with polyarthralgia, who may be febrile and thus have hyperdynamic circulation. Thus, although echo-Doppler is a powerful tool for diagnosing pathologic valvular regurgitation. in RF, a fair amount of overlap with regurgitation in normal people (physiological) cannot be avoided. Use of serial echocardiographic studies has been proposed to facilitate identification of organic valvular involvement.[10]. Although this may improve the specificity of abnormal echocardiographic findings, it may cause a delay in diagnosis. At present, echocardiography during the acute attack cannot be recommended as a routine modality for investigating RF in developing countries.

Treatment

Not all treatments for RF are based on randomised controlled trials. Some are based on anecdotal evidence, common sense and proven safety.

1. Antibiotics

Penicillin (or erythromycin) in adequate doses given for 10 days is considered mandatory to eradicate persistent group A streptococci from the pharynx though this treatment has not been shown in controlled studies to alter the cardiac outcome after one year[13].

2. ***Rest in bed***[14]

All patients with RF should be hospitalized and kept in bed for the first three weeks of illness because carditis, if not already present, may appear during this period.

- Patients with *polyarthritis only*, are usually asymptomatic by the 2nd or 3rd week of salicylate therapy and may then be gradually ambulated while continuing on salicylates.

- Patients with *significant murmurs* (or echocardiographic evidence of carditis), but no definite cardiomegaly or heart failure (with or without polyarthritis), should be kept in bed for four weeks. This bed rest need not be strict and in the last week may be broken by periods of supervised ambulation of a few hours per day.

- Patients with *carditis* and *cardiomegaly*, but no heart failure (with or without polyarthritis), should be kept on bed rest for six weeks, the first two weeks of which should be strict.

- Patients with *carditis* and *heart failure* (with or without polyarthritis), should be kept on strict bed rest until failure is controlled. It is wise to maintain a modified bed rest until four weeks after anti-inflammatory treatment is stopped (if no rebound occurs) or two weeks after the spontaneous subsidence of a rebound.

- No randomized studies have been done on the value of bed rest in RF.

3. ***Salicylates and/or steroids***[14]

- In patients with *arthralgia* or *mild arthritis only*, salicylates should be given in analgesic dosage. This is particularly wise when the diagnosis is not definite.

- Patients with *moderate or severe arthritis* but no carditis or with *carditis* but no cardiomegaly or failure, should be treated with salicylates 90-120 mg/kg/day for the first two weeks and then two-thirds of the dose for the next 4-6 weeks.

- Patients with *carditis* and *cardiomegaly* but no heart failure (± polyarthritis), should be treated with salicylates as above. However, in patients with marked cardiomegaly, salicylates are often insufficient to control fever, discomfort and tachycardia or do so only at toxic or near toxic doses. These patients may then be switched to steroids.

- Patients with *carditis* and *heart failure* (± polyarthritis), should receive prednisolone in a dose of 2mg/kg/day to be increased if control of heart failure is not achieved. In severe cases, therapy may be initiated with intravenous methylprednisolone[14,15]. After 2 or 3 weeks, prednisolone may be slowly withdrawn, decreasing the daily dose at the rate of every 2 or 3 days and adding salicylates at standard doses. Salicylates should be continued for 3 or 4 weeks after prednisolone is stopped. This "overlap" therapy reduces the incidence of post-therapeutic clinical rebounds.

- Findings of meta-analyses indicate no benefit of salicylates over corticosteroids or vice-versa in reducing the subsequent development of RHD[16].

4. ***Other therapies***

- Naproxen has been used successfully as an alternative to salicylates in one small randomized trial[17].

- The heart failure of rheumatic carditis is often controlled with bed rest and steroids only. If it is not, diuretics may be added first followed by digitalis, if needed. Diuretics and vasodilators may be used in patients with more severe haemodynamic decompensation. Digoxin should be used with caution because of the risk of toxicity in the presence of active myocarditis[14,18]. Surgical treatment in the acute stage should be considered when clinical therapy is ineffective to control cardic failure. Valve repair, although technically more difficult, is the first choice for younger patients[19].

- Most cases of mild Sydenham chorea need no treatment. The condition is usually benign and self-limited and many of the drugs are potentially toxic. Treatment should be reserved for individuals with moderate to severe chorea refractory to conservative management (reassurance and moving of patient to a quiet and calm environment) or if movements are distressing to patient or family. Findings of a small study[20] concluded that valproic acid was more effective than carbamazepine or haloperidol.

- Intravenous immunoglobulin does not seem to alter the extent and severity of carditis or decrease chronic morbitidy[21].

5. ***Treatment of rebounds***[14]

- The termination of anti-inflammatory treatment may be followed in all RF patients by the re-appearance within 2 or 3 weeks of lab abnormalities (lab rebounds) or clinical abnormalities as well (clinical rebounds).

- All the lab rebounds and most of the clinical rebounds are best left untreated or should be treated symptomatically with analgesic doses of salicylates lest the full treatment be followed by another rebound and the duration of the attack be lengthened. Only the most severe clinical rebounds necessitate re-institution of the full original treatment.

- Once rheumatic fever has subsided and more than 2 months have elapsed after stopping treatment with anti-inflammatory drugs, RF does not re-appear unless a new streptococcal infection occurs.

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