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Review article

Rheumatic fever: update on the Jones criteria according to the American Heart Association review – 2015

Breno Álvares de Faria Pereira[a,*], *Alinne Rodrigues Belo*[a], *Nilzio Antônio da Silva*[b]

[a] *Universidade Federal de Goiás (UFG), Faculdade de Medicina, Departamento de Pediatria, Goiânia, GO, Brazil*
[b] *Universidade Federal de Goiás (UFG), Faculdade de Medicina, Goiânia, GO, Brazil*

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ABSTRACT

Rheumatic fever is still currently a prevalent disease, especially in developing countries. Triggered by a Group A β-hemolytic *Streptococcus* infection, the disease may affect genetically predisposed patients. Rheumatic carditis is the most important of its clinical manifestations, which can generate incapacitating sequelae of great impact for the individual and for society. Currently, its diagnosis is made based on the Jones criteria, established in 1992 by the American Heart Association. In 2015, the AHA carried out a significant review of these criteria, with new diagnostic parameters and recommendations. In the present study, the authors perform a critical analysis of this new review, emphasizing the most relevant points for clinical practice.

Febre reumática: atualização dos critérios de Jones à luz da revisão da *American Heart Association* – 2015

Palavras-chave:
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RESUMO

A febre reumática ainda é uma doença prevalente nos tempos atuais, sobretudo nos países em desenvolvimento. Deflagrada por uma infecção pelo Streptococcus β-hemolítico do grupo A, pode afetar pacientes geneticamente predispostos. A cardite reumática é a mais importante das manifestações clínicas, podendo gerar sequelas incapacitantes e de grande impacto para o indivíduo e para a sociedade. Atualmente, seu diagnóstico é feito baseado nos Critérios de Jones, estabelecidos em 1992 pela American Heart Association (AHA). Em 2015, a AHA procedeu uma significativa revisão destes critérios, com novos parâmetros e recomendações diagnósticas. No presente estudo, os autores realizam uma análise crítica desta nova revisão, enfatizando os pontos de maior relevância para a prática clínica.

* *Corresponding author.*
E-mail: faria.breno@hotmail.com (B.Á. Pereira).
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Introduction

Rheumatic fever (RF) is an inflammatory, systemic disease, triggered by the group A β-hemolytic *Streptococcus* infectious agent, which occurs in genetically predisposed individuals. The most relevant clinical manifestation of the disease consists of heart disorders and is characterized, in most part, by valvulitis, especially in the mitral and aortic valves, which can be chronic and cause disabling sequelae.

Note: the levels of evidence indicated throughout the text are those endorsed by the Guidelines of the Federal Medical Council (CFM) with the Brazilian Medical Association (AMB) and are listed in Table 1.

Diagnosis

Currently, the diagnosis of rheumatic fever is still based on a set of criteria, i.e., the Jones criteria, which have been reviewed at irregular intervals by the American medical associations – currently, by the American Heart Association (AHA). According to the latest review, published in 2015,[1] 2 major changes have been made in relation to the criteria established in 1992.[2]

The first one consisted in the stratification of susceptible individuals into 2 groups, based on epidemiological considerations regarding the risk to acquire the disease. A low-risk group is one in which the incidence of RF is less than 2/100,000 schoolchildren (aged 5–14 years) per year or that has a prevalence of chronic rheumatic carditis in any age group lower than or equal to 1/1000 per year. Children from communities that exhibit levels above these would have moderate-to-high risk for acquiring the disease.

The second important change was to include the possibility of using the Jones criteria to diagnose rheumatic fever relapses (until then its purpose was only to diagnose early episodes of the disease).

- At the diagnosis of initial RF outbreaks:

For low-risk individuals, the interpretation of the diagnostic criteria remains the same as for the 1992 review.[2] In these cases, an initial outbreak (1st episode) of rheumatic fever will be highly likely when, in the presence of evidence of a previous infection by group A β-hemolytic *Streptococcus*, 2 major criteria are met, or 1 major and 2 minor.

Moreover, regardless of the risk classification, the Echocardiography with Doppler findings suggestive of carditis – even if they are not accompanied by heart murmur or other clinical signs ("subclinical carditis"), are considered enough to contemplate 1 major sign of the criteria.

Concerning joint involvement, for individuals with moderate to high risk, polyarthralgia and monoarthritis (and not only polyarthritis, as in the past) also started to be considered as major signs of the criteria. Additionally, monoarthralgia was also considered as a minor sign for this risk group.

In both risk groups, there were no changes in the other minor signs of the criteria. Isolated Chorea, with an undefined etiology, remains sufficient for the diagnosis to be attained, even in the absence of other manifestations[1] (D).

- At the diagnosis of disease relapse (recurrent RF):

For patients that have already had the initial RF outbreak, the criteria remain the same as those listed above for low-risk and moderate-to-high risk populations – what changes is the minimum number of criteria to be met. For these individuals, in addition to meeting 2 major criteria or 1 major and 2 minor ones (as in the initial outbreak), one can also consider the possibility of meeting three minor criteria as a disease recurrence diagnosis, regardless of the risk group to which the patient belongs (Table 2).

There are some characteristics that are specific to the clinical manifestations of rheumatic fever, which, when identified, increase the positive predictive value of that finding. Although it cannot be said that there is a typical clinical picture of rheumatic fever, the most common forms of involvement are:

- Arthritis – Large joints such as knees, elbows, wrists, and ankles are the most affected ones. The pattern of involvement is migratory and can be fully resolved, most often leaving no sequelae. The response to nonsteroidal inflammatory drugs is excellent, with symptom remission within 48–72 h[1,3] (D)[4] (B).
- Carditis – the affected leaflet is the endocardium in more than 90% of the cases, which is expressed as mitral regurgitation, manifesting as an apical systolic murmur. In approximately 50% of the cases, it may be accompanied by basal diastolic murmur, due to aortic regurgitation. The concomitance of mitral and aortic regurgitation in a previously healthy patient is highly suggestive of rheumatic fever. Occasionally, myocarditis and pericarditis may be present. In the absence of valvulitis, these manifestations are rare in rheumatic fever[1] (D)[4] (B)[5] (D)[6] (B).
- Chorea – disordered, involuntary, abrupt movements of skeletal striated muscle groups. Complaints include stumbling during ambulation, slurred speech, dropping or throwing objects such as dishes, cups, notebooks, and bad calligraphy. It affects more females than males, in the adolescent age group. There is considerable emotional lability, easily alternating between crying and laughter. The differential diagnosis with systemic lupus erythematosus is necessary, especially in cases of difficult therapeutic control[1,3] (D).

Table 1 – Level of Scientific Evidence by Type of Study – "Oxford Centre for Evidence-Based Medicine" – last updated in May 2001.[19]

Level of recommendation	Strength of scientific evidence
A	Experimental or observational studies of better consistency
B	Experimental or observational studies of lesser consistency
C	Case reports, uncontrolled studies
D	Opinion without critical evaluation, based on consensuses, physiological studies or animal models

Table 2 – Jones criteria – 2015 review.

1st rheumatic fever outbreak:	Rheumatic fever relapse (recurrent RF):
- 2 major criteria; or - 1 major + 2 minor	- 2 major criteria; or - 1 major + 2 minor; or - 3 minor
Criteria	
Low-risk populations	Moderate-to-high risk populations
Major criteria: - Carditis (clinical or sub-clinical); - Arthritis (polyarthritis only); - Chorea; - Erythema marginatum; - Subcutaneous nodule	*Major criteria:* - Carditis (clinical or sub-clinical); - Arthritis (polyarthritis, polyarthralgia and/or monoarthritis); - Chorea; - Erythema marginatum; - Subcutaneous nodule
Minor criteria: - Polyarthralgia - Fever (≥38.5 °C) - Elevation of ESR (≥60 mm in the 1st hour) and/or CRP ≥3 mg/dL (or > as indicated by the reference value) - Prolonged PR interval, corrected for age (only when there is no carditis)	*Minor criteria:* - Monoarthralgia - Fever (≥38 °C) - Elevation of ESR (≥60 mm in the 1st hour) and/or CRP ≥3 mg/dL (or > as the indicated reference value) - Prolonged PR interval, corrected for age (only when there is no carditis)
Proven evidence of prior infection with A-group B-hemolytic *Streptococcus* (positive oropharyngeal culture, positivity in rapid tests for the detection of streptococcal antigens, high titers of anti-streptococcal antibodies).	

- Erythema marginatum and subcutaneous nodules – are rare but highly specific to rheumatic fever. Erythema marginatum is a pink macular lesion with a rounded margin and pale center. It is usually not pruriginous and spares the face. The subcutaneous nodules are painless and are usually located on the extensor surfaces of the joints and along the tendons. They are associated with the presence of carditis[1,3,7–9] (D).
- Complementary examinations:
  - o There is an increase in the concentration of serum proteins that are referred to as acute phase reactants, erythrocyte sedimentation rate and C-reactive protein, being minor manifestations of the disease. Leukocytosis and mild anemia are frequent nonspecific findings[1,3,7–9] (D).
  - o Anti-streptolysin O – the most commonly used method in our country to demonstrate a previous infection by group A β-hemolytic *Streptococcus*. Ideally, each community should promote studies that could establish which levels or cutoff points of this antibody should be considered as high. As this is not our current reality, for children, levels above 320 U Todd are considered high. Other methods of documentation of previous infection by Group A β-hemolytic *Streptococcus* are listed in Table 2 [1] (D).
  - o Antidesoxyribonuclease B – like anti-streptolysin O, is another antibody against streptococcal product, but persists at higher levels for longer periods in the serum of patients with rheumatic fever. As Chorea frequently occurs months after infection with Group A β-hemolytic *Streptococcus*, it has a higher positivity percentage when compared to other methods of documentation for this infection in patients with this clinical manifestation[8,9] (D).
  - o Doppler Echocardiogram – is considerably more sensitive than auscultation to detect valvular heart lesions in the acute phase of the disease. When available, it should be requested in all suspected rheumatic fever cases to detect "silent" valvular lesions[10] (D)[11] (A)[12–14] (B).

Treatment

The first therapeutic measure is the eradication of the causative infectious agent, the group A β-hemolytic *Streptococcus*[15] (D): penicillin G benzathine, IM, 1,200,000 U, for children weighing more than 20 kg; 600,000 U for children weighing up to 20 kg.

Alternatives

- For patients with hemorrhagic disorders (that cannot receive medication through IM route) penicillin-V, orally (50 mg/kg/day, 4 times daily) or amoxicillin (50 mg/kg/day, taken three times daily), both for 10 days.
- For atopic patients, allergic to penicillin and derivatives: erythromycin (40 mg/kg/day, four times daily for 10 days) or azithromycin (20 mg/kg/day, once daily for 3 days). Tetracyclines (high prevalence of resistance), sulfonamides (do not eradicate the agent), chloramphenicol (high toxicity) should not be used[15] (D).

Treatment of the different clinical manifestations:

- Arthritis[3,8] (D): nonsteroidal anti-inflammatory drugs for about 7–10 days, preferably orally:
  - o Acetyl-salicylic acid (80–100 mg/kg/day);
  - o Naproxen (10–20 mg/kg/day);
  - o Ibuprofen (30–40 mg/kg/day);
  - o Ketoprofen (1,5 mg/kg/day)
- Carditis[3] (D): prednisone (1–2 mg/kg/day), orally, maximum of 60 mg/day. Use full dose, fractionated into 2 or 3 daily doses for 15 days; then reduce 20–25% of the dose per week.

Note: in case of concomitant arthritis and carditis, there is no need to use nonsteroidal anti-inflammatory drugs; when promoting the gradual reduction of prednisone, it is not necessary to introduce nonsteroidal anti-inflammatory drugs, providing that a weekly reduction higher than 25% is not intended.

- Chorea: haloperidol, orally, at a dose of 1 mg/day (and not per kg) twice daily. Increase 0.5 mg every 3 days until a good response is attained (more than 75% remission of the movements) or up to a maximum dose of 5 mg/day. Treatment duration of three months[3] (D)[16] (B).
  Note: Doses close to the maximum dose may cause impregnation or extrapyramidal syndrome. Valproic acid (30 mg/kg/day, orally, starting with 10 mg/kg/day and increasing 10 mg/kg, weekly) is indicated as an alternative[3] (D)[17] (B).

Prophylaxis

Primary prophylaxis – appropriate identification and treatment of upper airway infections, such as pharyngotonsillitis, caused by Group A β-hemolytic *Streptococcus*. The antibiotics recommendation is the same as that used for the agent eradication during treatment, as described above[15] (D).

Secondary prophylaxis – sporadic and long-term use of antibiotics that maintain minimum inhibitory concentrations for Group A β-hemolytic *Streptococcus*, aiming to prevent rheumatic fever recurrence in patients who have already had a first outbreak of the disease. The most commonly used and most effective drug is:

- Penicillin G benzathine, IM, every 21 days, 1,200,000 U, for children weighing more than 20 kg and 600,000 U for children weighing up to 20 kg.

As an alternative, the following is indicated:

- Patients with hemorrhagic diseases (which cannot receive IM medications): oral V-penicillin (250 mg, twice a day, every day).
- Atopic patients allergic to penicillin and derivatives: erythromycin (250 mg twice daily) or sulfadiazine (500 mg for patients up to 30 kg, 1 g for those weighing more than 30 kg), both daily[15] (D).

Duration of secondary prophylaxis:

- Patients that did not have carditis – the prophylaxis should last until the age of 21 years or up to five years after the last episode, in cases of recurrence, whichever lasts longer.
- Patients who had previous carditis with moderate to severe valve damage – prophylaxis should last until the age of 40 years or until 10 years after the last episode, in case of recurrence (whichever lasts longer); and in cases where the risk of re-infection persists (high risk of exposure to Group A β-hemolytic *Streptococcus*), prophylaxis should last for a lifetime.
- Patients who had previous carditis with mild residual mitral regurgitation or valve lesion resolution – prophylaxis should last until the age of 25 years or up to 10 years after the last outbreak, whichever covers the longest period[15] (D).

Note: The antibiotics and/or doses listed herein are not effective in the prophylaxis of infective endocarditis. Patients with orovalvular lesions should undergo specific prophylactic regimens[18] (D).

Conclusion

The review of the Jones criteria incorporated changes that had long been requested by the medical community. Three of them were the main pillars of this review. First, the possibility of diagnosing rheumatic fever relapses was included in the Jones criteria – previously, the purpose of the criteria was to diagnose only the first episode. Disease recurrence can now be diagnosed with the presence of three minor criteria.

The second change was the separation of individuals susceptible to rheumatic fever into two major groups based on disease prevalence (one with low risk and another with moderate to high risk). For individuals with moderate to high risk, "atypical" joint manifestations were included, both in the major criteria (polyarthritis, polyarthralgia and/or monoarthritis), and in the minor ones (monoarthralgia).

Finally, considering the several publications in the last few years on the subject, we started to consider subclinical carditis, diagnosed through echocardiographic alterations, as a major criterion for the diagnosis of rheumatic fever – and not only clinical carditis (presence of murmur) as before.

Thus, considering the high prevalence of the disease, especially in the developing countries, the review of the Jones criteria was an important measure to increase diagnostic sensitivity, resulting in earlier disease identification, better clinical outcome for the individual and, consequently, a reduction in the social impact of this disease.

Conflicts of interest

The authors declare no conflicts of interest.

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