

Rheumatic Fever in Pernambuco, Brasil

Lurildo R. Saraiva*

Titular Professor University Federal of Pernambuco Hospital das Clínicas UFPE Cidade Universitária, BRASIL.

***Corresponding Author:** Lurildo R. Saraiva, Titular Professor University Federal of Pernambuco Hospital das Clínicas UFPE Cidade Universitária, Brasil.

Received Date: February 10, 2023; **Accepted Date:** February 17, 2023; **Published Date:** February 24, 2023

Citation: Lurildo R. Saraiva, (2023), Rheumatic Fever in Pernambuco, Brasil. *Biomedical Research and Clinical Reviews*. 8(1); DOI:10.31579/2692-9406/148

Copyright: © 2023, Lurildo R. Saraiva. this is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

The State of Pernambuco, located in the Northeast of Brazil, is a region with a high level of pauperism in the working class, especially for those who live in slums, and for the peasants, who live in the hinterland (“SERTÃO”) Rheumatic Fever in this population tends to present in its severe form. The present review shows peculiar clinical aspects of this disease, which is still very present in our country.

Key words: salivary gland neoplasm; pleomorphic adenoma; submandibular gland; benign

Introduction

Rheumatic Fever (RF), better known amongst us with the term Rheumatic Disease (RD), due to the influence of the great master of Brazilian Cardiology, Luiz V. Décourt, who published a classic book on the subject in 1969 [1] - for him, the word “disease” says more about a illness, which can appear even without fever, especially in its typical recurrences – since its appearance amongst us, in the 1940s, it persists as the major cause of cardiac surgeries in Brazil, reaching the percentage of 40% of all of them. As our country has a profoundly unfair and very unequal distribution of income, in the big cities it is seen, above all, in slums and popular neighborhoods, with an accentuated degree of pauperism, and in very poor, isolated communities in rural areas.

The disease is distributed in our patients from five to fifteen years of life in the acute form, silences in youth and again has an important presentation in the third and fourth decades of life, now, in its chronic form, characterized by the presence of mitral or mitral-aortic valve disease symptomatic, in patients seeking valve correction in Cardiac Surgery Services, found throughout the country. There is no exact number of the incidence of RD in the country, but it is assumed that the prevalence is around 5% [2].

The preponderant symptoms, in the different stages of life, are dyspnea, palpitations, wet cough and edema of the lower limbs. Fever that is not very high may appear in younger children, but it does not have the character of a prominent symptom [3]. Abdominal pain is not uncommon, often suggesting acute appendicitis.

Etiopathogenesis

Since the classic description of RD in France, in the 19th century, by Jean Baptiste BOUILLAUD [4] - *the author showed that there was more*

agreement between arthritis of large joints and valve lesions than disagreement, - joining the descriptions of other researchers over the centuries In the 19th and 20th centuries, it is accepted that the disease results from an autoimmune reaction due to infection of the pharynx by group A beta-hemolytic Streptococcus by Rebecca LANCEFIELD, beyond nine days, in a genetically predisposed individual.

Thus, not every patient who has strep throat has RD: only 3% of patients with streptococcal pharyngotonsillitis develop RD, in the presence of epidemic outbreaks, and only 0.3%, in an endemic situation. Amongst us streptococcal skin infection does not seem to be relevant.

What would lead a patient to develop RD? What characteristics would he have? A curious note was made by the London clinician Walter CHEADLE [5] at the end of the 19th century, when he found that his only son had mitral stenosis and his wife had RD – for him, then, there would be a “*family predisposition*” to the onset of RD. As at that time the so-called “connective tissue diseases” were unknown, most likely, cases of RD would result from these diseases.

The work of great importance on this fact was that of Manoel PATARROYO et al [6], carried out in the city of Bogotá, Colombia, in 1979. The contact of the blood of 41 rheumatic patients with the blood of a multiparous woman allowed the group to identify rheumatic patients “883 +” and others “883-”. As the patient's blood ran out, in New York, ZABRISKIE et al [7], injecting blood samples from Colombian rheumatic patients studied in monkeys, obtained two monoclonal antibodies, **883S19.23** and **256S.10**, which, when used with precision, recognized the candidates to have DR in 92% of the

time. Later, the same authors identified the **D8/17** monoclonal antibody capable of identifying in almost 100% of choreic patients.

As a disease resulting from altered immunity, its symptoms and signs were grouped by Duchet JONES, in 1944, in what the medical literature has always called “**Jones' Criteria**”, which are periodically changeable, with the last change taking place recently, in 2015 [8]

How is the disease produced? In rheumatic patients, an initial phase is described by alteration in humoral immunity, with the production of autoantibodies by B lymphocytes, which are directed against aggressor antigens, resulting in tissue necrosis in the skin, subcutaneous tissue, joint synovium, in the nuclei of the cerebral base in Sydenham's chorea [9] and in the heart tissue, especially in the valve endocardium of the mitral and aortic valves.

The action of B lymphocytes is carried out through glycoproteins found on the surface of macrophages or antigen-presenting cells, which, like “cups”, having two layers α and β , allow the insertion of an antigenic fragment (epitope) [10].

It is current knowledge that the amino acids that make up the M protein, - which, crossing the entire cytoplasm and cell wall of bacteria, hatch in the external environment as “**fimbriae**”, - and the fibrillar proteins of the human heart are similar in 45% of the times. On the other hand, the M protein, myosin, actin and tropomyosin of the human heart are shaped like an *alpha-helix*, thus, whether due to structural homology or the shape of the protein, the possibility of a similar cross-reaction produced against them is evident.

The participation of altered cellular immunity also takes place simultaneously, or at a later stage, by the HLA-DR system, through activated DR4 T helper lymphocytes, in the intimacy of the valve tissue, with a marked inflammatory alteration and production of lymphokines and other inflammatory factors, which tends to perpetuity, explaining what McCARTY [11] said back in the 1940s: “**in some way, the streptococcus inserts itself into the human heart and remains there for a lifetime**”, thus, theoretically, RD is incurable.

The participation of the HLA-DR system allowed the authors to identify rheumatic patients by typing activated DR4 T lymphocytes. Luisa GUILHERME et al [12] recognized in Brazil the predominant loci DR7 and DR53 in individuals with rheumatic valvular heart disease, and thus, in the same way, loci DR3 were recognized in India [13], DR2 and DR4 in the United States – DR2 in blacks and DR4 in whites [14] -, DR4 in Saudi Arabia [15], although in Turkey, even in the same city and in the same racial group, disparate results have emerged, as in Ankara, with DR4 [16] and DR11 [17] being identified. Faced with this multiplicity of loci, CARLQUIST and ANDERSON [18] raised doubts about this argument

The most curious aspect of the disease - *something that fascinates us* - is that *there is production of cross-reactive antibodies against bacterial*

proteins, which have structural homology with the contractile proteins of the human heart, such as myosin, actin, tropomyosin and vimentin, located on the edge of the valves, and of course, against the human heart.

In 1962, and in subsequent years, KAPLAN et al [19], by injecting bacterial macerates into guinea pigs, found antibodies in their blood that were directed against the bacterial M protein and, at the same time, against structures of the human heart and the ocular cornea. of the human being. In 1967, GOLDSTEIN et al [20] working with the carbohydrate layer of the streptococcus, containing N-acetyl-glucosamine, verified an antigen-antibody cross-reaction against the mitral and aortic valves, which structurally contain the same N-acetyl-glucosamine – such antibodies, which turn against cardiac valve proteins, disappear with the debatable “cure” of the disease, but remain perennial, in case it is a real rheumatic heart disease, or, on the other hand, *there is permanent production of antibodies against the valve system of the heart of the man with rheumatic stigmata*, a fact consistent with McCARTY's statement in 1946. which *is to say, again, RD is incurable* [1], [11]

Jones Criteria, 2015

Proposed by the author in 1944, it received successive modifications with the evolution of knowledge, and in 2015, after a suggestion by RD researchers in Australia, Latin America and Asia, regions with a high incidence of RD, a new update of these criteria was carried out, with emphasis on Doppler echocardiography, which had already recognized long before, **the existence of subclinical carditis** [21], revealing valve lesions not perceived with the stethoscope and which tend to reproduce the real valve lesion.

In this context [22], “**major signs or manifestations**” are considered – arthritis, carditis, chorea, erythema marginatum and subcutaneous nodules – and “**minor signs or manifestations**” – fever, increased erythrocyte sedimentation, elevated C-reactive protein and first-degree AV block in the ECG. Classically, two major signs or one major and two minor signs allow the diagnosis of initial acute RD and, at recurrences, two major signs or one major and two minor signs or three minor signs make the diagnosis of disease recurrence: they all require that there be at least one patient evidence or history of pharyngeal streptococcus.

In the changes just made, the authors started to consider “**low risk populations**” in developing RD compared to others of “**moderate and high risk**”.

Low-risk populations are those with an incidence of acute RD ≤ 2 per 100,000 school-aged children and, for any age, with a prevalence of rheumatic heart disease ≤ 1 per 1000 per year.

Major criteria:

Low risk populations populations	Moderate and high-risk populations
Clinical and/or subclinical carditis	Clinical and/or subclinical carditis
Arthritis/polyarthritis only	Arthritis: monoarthritis/polyarthritis/polyarthralgia
Chorea	Chorea
Erythema marginatum	Erythema marginatum
Subcutaneous Nodules	Subcutaneous Nodules

Minor criteria:

Low risk populations populations	Moderate and high-risk populations
Polyarthralgia	Monoarthralgia
Fever (≥ 38.0 C)	Fever (≥ 38.0 C)
ESV ≥ 60 mm 1st hour and/or CRP ≥ 3.0 mg/dl	ESV ≥ 30 mm/h and/or CRP ≥ 3.0 mg/dl
Age-corrected prolonged PR interval	Age-corrected prolonged PR interval

ESR: erythrocyte sedimentation rate; **CRP:** C-reactive protein; **Pernambuco, Brazil:** there is a population at high risk for the development of RD.

Arthritis – It is the most frequent clinical manifestation of RD, reaching the percentage of 80 to 90%, affecting even small children, as we have shown in a two-year-old girl, decades ago, today a working lady and without complaints linked to the joint system or the heart [23]
Classically, it affects large joints, especially in the lower limbs (knees and ankles), but also in the upper limbs (wrists and elbows), which, in a peculiar way, migrates from joint to joint, without leaving sequelae.

A particularity of rheumatic arthritis is that it responds promptly to the use of acetylsalicylic acid, within 48 hours at most. If this response does not occur, the diagnosis of RD is called into question.

In recent years, we have observed participation in the inflammatory process of the small joints of the hands, above all, also, the complaint of pain involving lower joints of the lumbar spine is not uncommon.

Carditis – found in 65 to 70% of the cases, it is the most worrisome sign of JONES CRITERIA, as it can result in perennial involvement of the heart, characterizing chronic rheumatic heart disease. In RD, there is a predilection for mitral valves producing, in the acute phase, mitral insufficiency (MI) and, later, double mitral lesion or isolated mitral stenosis (MS), including **the malignant type**, described by ROY et al [24], in India, in 1963, which It mainly affects adolescents under 20 years of age.
Probably, the richness of N-acetyl-glucosamine in the mitral valve or the pressure factor in the left ventricle, justify this tropism for the mitral valve.

In our midst, a child hospitalized with fever, arthralgia and the presence of a gallop rhythm by B3, with a holosystolic murmur detected in the mitral area, will have active rheumatic carditis, until further notice.

Thus, we can even see older children with acute pulmonary edema, a very rare phenomenon in rich countries.
In clinical practice, MI is mild, moderate or severe, but regardless of this classification, choreic movements may be associated with it in the victimized child, i.e., by the presence in brain neurons of the same N-acetyl-glucosamine, with antibody genesis directed against it
In a serious situation, on the ECG we can detect signs of left ventricular overload, with an inverted U wave, an aspect seen only in chronic oro-valvar lesions, noting significant cardiomegaly in the chest radiological study.

Sydenham Chorea – named after the English physician who recognized it as part of acute RD. It is found in Pernambuco about 12% of the time, a much lower percentage than that found in rich countries such as the USA, where it is described in up to 30% of the cases. appear late, weeks after the pharyngeal infection.
Currently, it is accepted that Chorea is the extreme of a syndrome, which ranges from anxious behavior, or even slightly obsessive-compulsive behavior, or restlessness of the lower limbs, going to TOURETTE's disease and, finally, to Chorea [25]. Famous characters like the American painter Andy Warhol had DR, who presented himself in this way.

Historically, it was called **“Saint Vitus Dance”** because it was confused with

a manic attitude of dancing, present in communities in Central Europe, the Czech Republic and Italy, in the Middle Ages, where bystanders danced nonstop, even with lethal success. Authorities of these small communities thought that the dancers were “**possessed by the devil**”, and the only way to curb this mania was to have them exorcised by the Italian priest Vito, considered a saint and active in northern Italy.

Despite these historical data, we know that in the serious capitalist economic crisis of the 1930s, there were similar dance contests, also endless, as seen in New York and Boston, also with records of deaths in couples, who lived in a situation of deprivation.

Chorea sufferers are hypersensitive, and any physical or psychic damage produced against them, in a tumultuous environment, there is a clear accentuation of uncoordinated and aimless muscular movements. On the contrary, in a calm, soberly lit environment, in psychic stillness, these movements disappear.

Choreic syndrome predominates in females, but regardless of gender, patients easily fall to the ground, breaking plates, cutlery and glasses during meals. Individuals with Chorea have a characteristic handwriting and sometimes suffer from a change in the timbre of the voice. Physical signs of Chorea are restlessness, inability to stick out the tongue, and the so-called “**milkmaid's grip**”.

Considered as benign, this impression goes against what DÉCOURT [1] has

always warned about, as the choreic syndrome can recur, take months, and be accompanied by mitral valve insufficiency. In our midst, despite being accepted as a late sign of RD, *it is by no means unusual for us to come across in our wards with girls admitted with the “arthritis, carditis and chorea conjunction”*.

Subcutaneous Nodules and Erythema Marginatum – are the least expressive manifestations of RD, being found around 8% - **nodules** – and 4% - **erythema**. Similar to the other manifestations, they result from antibodies that act against the carbohydrate layer of the streptococcus, cross-reacting against the keratin of the skin - **erythema marginatum** - and the subcutaneous nodules result from granulomatous lesions, which develop in the cutaneous dermis, as a result of the same delayed hypersensitivity against streptococcal antigens - **Meynert's nodules**. A similar mechanism produces the so-called “Aschoff bodies” in the heart valves and in the intimacy of the myocardium.

With regard to nodules, it has long been accepted that their presence indicates the occurrence of **severe valve damage**, however, in the LAPA's Master thesis [26], who studied subclinical rheumatic carditis, the occurrence of these nodules was verified in two cases. From this assumption, we began to admit subclinical carditis as a “**micro-expression**” of RD, occurring in the same way as RD itself, which would be the “**macro-expression**”



Figure 1: A poor peasant 12-year-old boy, in the first rheumatic attack, he reveals signs of protein-calorie malnutrition, with the presence of subcutaneous nodules over the thoracic spine. On the echoDopplercardiogram, the presence of moderate rheumatic mitral-aortic insufficiency.

Laboratory Findings 1 -

1. **Complete blood count** – in acute RD, there is mild hypochromic anemia, and, in the leukocyte formula, the alteration is consistent with a mild bacterial infection, with mild leukocytosis with a shift to the left, drop in eosinophils and monocytosis. *In rare serious situations, leukocytosis can reach values above 17,000 /mm³, with a marked shift to the left.*

2. **The measurement of anti-streptolysin O levels** remains very useful, being the most used anti-enzyme in the clinic. Titers increase at the end of the first seven days of illness, reaching above 250 units, this increase being seen more in adolescents than in children. In about 3% of patients, titers can remain high, without finding a cause for this: curiously, there is a “certain rigidity” of the measured value.

In case of normal antistreptolysin O values, the measurement of anti-

deoxyribonuclease B levels is very useful in the diagnosis of active RD. On the other hand, in 40% of choreic individuals, we can find an increase in antideoxyribonuclease B.

3. **Serum acute phase reactions** – we are particularly interested in erythrocyte sedimentation (ESR), C-reactive protein (CRP) and mucoprotein dosage.

a) Amongst us, **erythrocyte sedimentation (ESV)** reaches values around 50 mm/h, which are contemporaneous with the onset of the disease, with higher values in more severe cases, however they may be less expressive in milder cases and be modified to very high levels to low due to complications of the disease, such as congestive heart failure (CHF)

b) **C-reactive protein**, an anomalous protein that does not exist in normal

blood, which precipitates with carbohydrate C from pneumococcus, is found in almost all rheumatic patients before the end of the second week of evolution of the acute condition, so that two negative determinations speak for themselves absence of RD - however, may disappear from serum prematurely with RD still present.

c) **The measurement of mucoproteins** can reveal high values in 95% of rheumatic patients and is parallel to the evolution of the condition in a similar way to α 2-globulins, not being modified by the influence of medication and disappearing with the presumed cure of the disease. Maximum normal values are 4 mg% (tyrosine content) and 14.5 mg% (polysaccharide content)

3. Alterations found in serum protein electrophoresis – a slight decrease in albumin, elevation of α 1-globulins and α 2-globulins, in the initial and intermediate phases of RD, and of γ -globulins, in a later phase, when it occurs more intense tissue alteration. *Among us, this aspect is often found in RD, which makes it characteristic of the disease (Figure 2)*

The modification that best suits the follow-up of a rheumatic patient is that of **α 2-globulins**, since it is constant, seen from the beginning of the disease, changes according to the treatment and normalizes with the cure of RD. The elevation of α 1-globulins is very inconstant and transient.

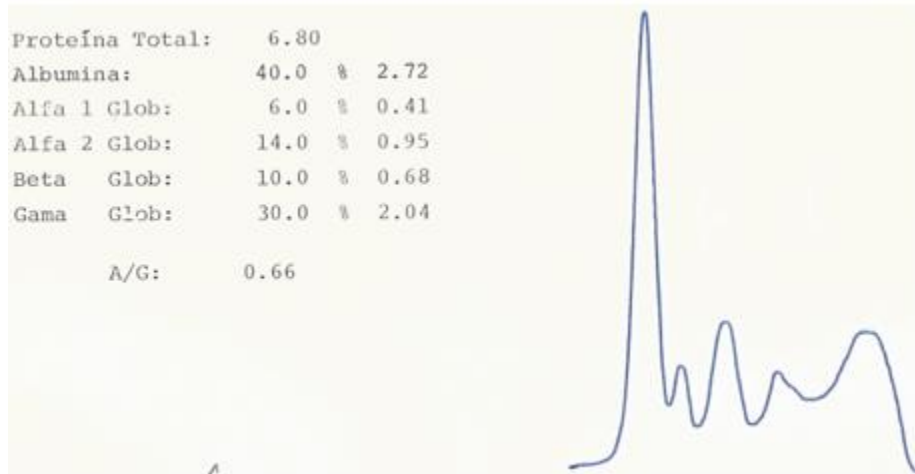


Figure 2 - Serum protein electrophoresis of a 12-year-old adolescent in the second rheumatic attack. Observe the increase in α 2-globulins.

4. Electrocardiographic modifications –

Cardiac chamber overload are found, according to the severity and type of existing valve lesions. Regardless of the predominant type of injury, in acute RD we can register extrasystoles and, sometimes, decrease in QRS voltage in the frontal plane and its alternation exposing “pericardial effusion”, which is frequent in the disease.

Changes in the ST segment and T wave are not uncommon, as is also seen in other situations that produce peri-myocardial inflammation.

Indicators that have a certain specificity with rheumatic carditis are AV blocks, ranging from the first to the third degree, and QTc elongation.

First-degree AV block is found in 11% of patients, while QTc elongation is diagnosed in 28% of our acute rheumatic patients.

A relevant aspect amongst us is the “conjunction AV block and elongated QTc”, which is not rare (Figure 3)

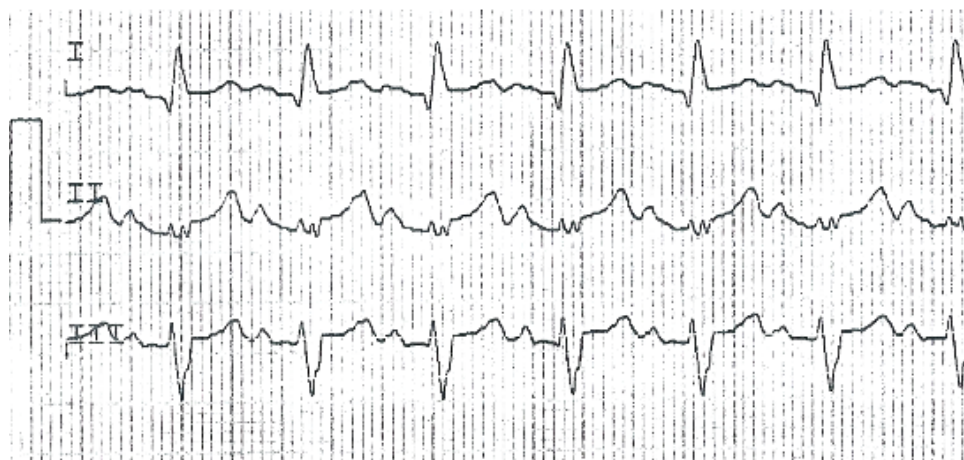


Figure 3 - A 19-year-old male patient with his third rheumatic attack, the first having occurred at the age of 4-year-old. Note the prolonged PR interval (190 msec) and the also lengthened QTc (430) with the signs of overloading both atria.

The arrhythmias that are useful for diagnosing RD, especially in recurrences, are atrial fibrillation and isorhythmic AV dissociation (**Figure 4**)



Figure 4: Isorhythm AV dissociation in a 12-year-old boy in the first rheumatic attack, with mild damage to the mitral valve.

Treatment and prevention

treatment

1. **Rest**-it is essential, especially when severe carditis with CHF is present. Bed rest with an elevated headboard can, *per se*, reduce the intensity of the damage that the disease may produce in heart valves.

2. **Extirpation of the streptococcus**-assuming that the patient harbors bacterial cells in the pharynx, if the patient is hospitalized at an adult or weighing more than 20 kg, **1,200,000 IU of benzathine penicillin are applied intramuscularly**, preferably on the buttocks, where the musculature is deeper; for patients weighing less than 20 kg, **600,000 units are used**.

While the patient is hospitalized, the antibiotic will be given every 8 days, starting the prevention of the disease.

3. **Arthritis** - due to the excellent response of the joint inflammatory process, acetyl salicylic acid is used, at a dose of 80 to 100 mg per kg of weight, a maximum of 4 g per day, which is divided into four intakes. The attack lasts for about four or five days, when the drug is gradually reduced. Another very useful drug is ibuprofen.

4. **Carditis** - despite the controversies about the reduction or not of valve damage by hormonal anti-inflammatory drugs, for a long time, we use prednisone, for all forms of carditis, with an attack of 1 to 2 mg/kg, with a

maximum dose of 80 mg, maintained for ten days, when the drug is gradually reduced by around 10 to 20% per week - in this way, there is coverage of the entire “**rheumatic cycle**”, which can reach 90 to 120 days.

It is not uncommon for the patient to develop a “**Cushingoid aspect**”, however, usually, this is a transitory finding, which gradually disappears, with real benefit from its use. The observation accepted by GHATI et al [27] in India, that *the steroid reduces inflammation, resolves the toxic state, prevents the appearance of new murmurs and acts in the resolution of pericardial effusion*, justifies its use.

By the way, **the picture of a six-year-old patient**, hospitalized with a great variety of symptoms and signs of severe RD, illustrates this fact. With complaints of uncoordinated movements in the left hemibody, arthritis of the right knee and exertional dyspnea, EAF she was admitted to the Pediatrics Unit of the Barão de Lucena hospital, with edema in the lower limbs, hepatomegaly with pain, jugular stasis at 45o and uncoordinated and aimless movements, making “*grimaces*”, *with the mother fearful that the girl “would fall apart”*.

On cardiac auscultation, with a heart rate of 130 beats/min, a protodiastolic gallop rhythm was perceptible, with a very intense holosystolic murmur in the mitral area, radiating to the back, indicating severe IM. She was medicated with prednisone (60 mg/day), diuretics (furosemide, 2md/day), oral digoxin, and haloperidol (0,5 mg/day, in increasing dose), in addition to weekly injectable penicillin.

The attached Doppler echocardiogram was recorded during admission:

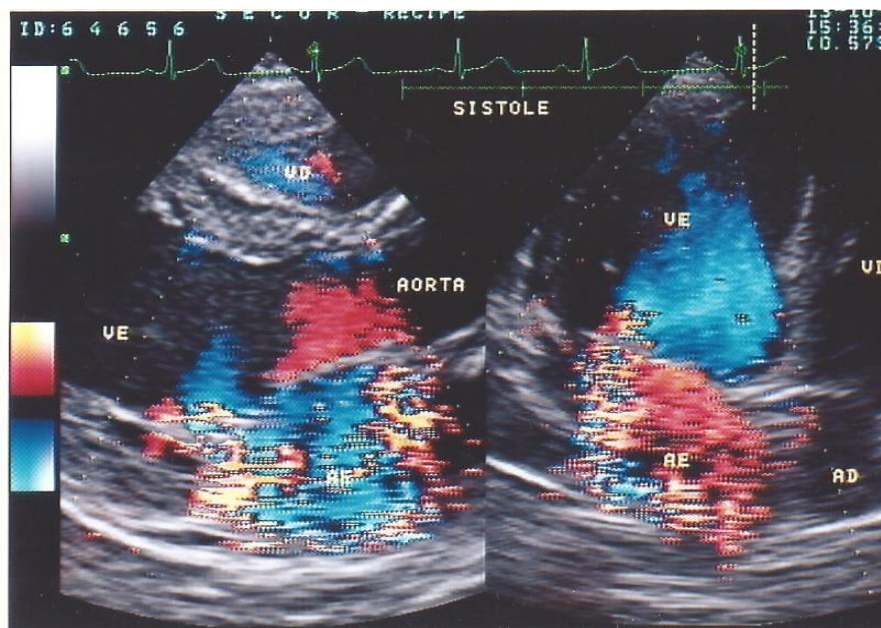


Figure 5: EchoDopplercardiogram of EAF, a 6 -years- old female Severe mitral regurgitation in an acute rheumatic condition, rich in symptoms and signs.

During follow-up, the mother religiously obeyed our instructions, including making the patient sleep in an isolated room, using benzathine penicillin every 15 days. After a long period of seven years, the mitral systolic murmur practically disappeared, being replaced by a clear mid-systolic click (Figure 6)

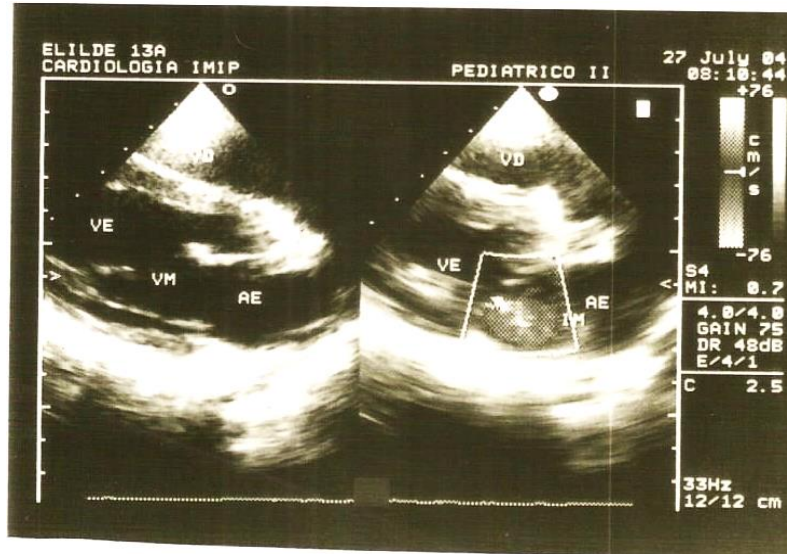


Figure 6: EAF, echoDopplercardiogram at age 13 - years-old. Note the marked reduction in mitral regurgitation, now considered mild, in the presence of thickened anterior leaflet prolapse.

Altogether, this case of EAF was the most beautiful we have seen, with almost complete resolution of the valve damage, which was so severe at the beginning.

Currently, the patient is a married woman and mother of two children!

5. Complications

a) **Cardiac arrhythmias** are not life threatening. Even the infrequent third-degree AV block tends to disappear with the use of anti-inflammatory drugs.

b) The rare "**rheumatic pneumonia**" [1], [23], controversial but accepted by the Décourt's School, is closely related to severe carditis. It usually appears in the lower third of the right lung and is revealed clinically by coughing with hemoptoics, tachypnea and drowsiness, concomitantly with severe congestive conditions, hence being confused with mere pulmonary congestion. It has a poor prognosis and is treated with corticosteroids.

c) The **surgical treatment** of the valve disease is based on the initial observations [28], showing an excellent response in cases of severe carditis, unresponsive to conventional therapy, to surgical treatment of mitral regurgitation, this technique started to be used in the presence of refractory CHF.

Prevention -

In the triad that produces acute RD – *the host, the bacteria and the environment* – it is clear that the only way to curb the disease is to change the environment in which the patients live. Caravetis et al [2] recently instituted what they call "**primordial prevention**", which fundamentally concerns changing homes that are incompatible with life, with the patient always having to sleep alone in a single bedroom.

In the absence of a vaccine to prevent new streptococcal pharyngeal infections, the only way to curb these infections is through "**secondary prevention**", which begins with the patient still hospitalized, as we have seen. The antibiotic of choice is benzathine penicillin, since after its discovery 70 years ago, until today, there is no streptococcal strain resistant

to it; only in the presence of allergy to penicillin, we use other antibiotics or sulpha drugs, thus, oral penicillin itself – penicillin V 250 mg every 12 hours – or sulfadiazine, at a dose of 1 g/day orally for adults and 0.5 g/ PO day in children weighing less than 20 kg.

The ideal is the use of benzathine penicillin, thus, in patients weighing less than 20 kg, 600,000 IU are given every 15 days in the first two years, then, every 21 days; in patients weighing more than 20 kg, 1,200,000 IU of depot penicillin is used every 15 days in the first two years, then every 21 days.

Surgical correction of rheumatic valve disease constitutes the **tertiary prevention** [2] of the disease, maintaining the use of injectable benzathine penicillin throughout life.

How long is secondary prevention maintained?

- *in the operated valve disease patient, for life;*

- *in patients with residual valve damage, up to the age of 40, or for life;*

- *RD with previous carditis, residual IM or resolution of the valve disease, up to 25 years or 10 years after the last attack, whichever covers the longer period;*

- *RD without previous carditis, up to 21 years or 5 years after the last outbreak, whichever covers the longer period.*

The Current Scenario In The Poorest Countries

In the mid-twentieth century, with countries with greater economic support drastically reducing the incidence of RD and obtaining effective control of the disease, with great scientific data on the causative bacteria, better understanding of how the disease occurs and better living conditions and housing for victims of RD. At the same time, publications on RD have faded, especially in the United States.

Several years later, the discovery of subclinical carditis through Doppler echocardiography and the finding of a latent form of rheumatic heart disease,

as well as the perennial search for an effective vaccine against the disease, which was so limiting, led once again to the production of excellent clinical research, coming mainly from Asia and Africa.

Subclinical valvitis was discovered by echoDoppercardiography. surprisingly, since it was recorded in children with normal cardiac auscultation. As we saw in LAPA's work, subclinical valvitis appears in silent subclinical cases as if it were a “**micro-expression**” of rheumatic fever, which is the most discreet and least aggressive form of rheumatic heart disease. We must keep in mind, however, that this form also results from the same immune reaction already discussed, therefore, the same assumptions accepted for the usual form, of “**macro-expression**”, should guide the clinician's conduct.

So, faced with a form that is also cardiologically silent, which is the latent form of rheumatic heart disease, what should we do? What is our conduct? In 2014, the cohort study by BEATON et al [29], using Doppler echocardiography, initially showed the occurrence of rheumatic heart disease in asymptomatic patients, **which they called latent**, corresponding to children of school age, with no previous history of rheumatic outbreak and without symptoms, but with Doppler ultrasound revealing clear signs of rheumatic heart disease.

The follow-up of the 63 patients studied for two years revealed clinical stability in 91% of the cases, but in 10% there was a morphological alteration of the mitral valve with present MI, progressing to definitive rheumatic heart disease. In established rheumatic heart disease, improvement is difficult. According to BEATON et al [29], younger children, those with multiple abnormalities in the mitral valve apparatus and those who show higher titers of antistreptolysin O are the least likely to obtain improvement, even in the face of well-conducted secondary prophylaxis

On other hand, in populations at high risk for rheumatic heart disease, these subclinical changes are reasonably interpreted as signs of latent RHD.

The observations made by three great researchers of this serious disease - YUSUF, NARULA and GAMRA [30] - recognize that, in compliance with WHO recommendations implemented in poor countries, such as Cuba, Tunisia and Costa Rica, there was a significant drop in acute DR and rheumatic heart disease. In Tunisia, for example, which even doubled its population in a period of ten years, saw the reduction in the incidence of RD fall from 900 cases per year to nine cases per year.

The measures taken by the Central Government were:

1. Compulsory notification to the Ministry of Health;
2. Preferential use of benzathine penicillin to prevent disease recurrences;
3. Forwarding of surgical cases to centers specialized in cardiac surgery;
4. Nursing participation;
5. Promotion of decent housing of habitation with rheumatic patients sleeping in an isolated room.

References

1. DÉCOURT L V. Doença Reumática. 2 ed. SARVIER EDITORA. São Paulo, 1972.
2. CARAPETIS JR, BEATON A, CUNNINGHAM M et al. Acute rheumatic fever and rheumatic heart disease. *Nature Reviews*, 2016 (2):1-24.
3. DÉCOURT LV. Personal communication. 1996.
4. BOUILLAUD JB. Nouvelles recherches sur le rhumatisme articulaire aigu en général. Thesis. Paris, 1836. Chez J. -
5. Baillière B. 148 p.
5. CHEADLE WB. Harveian lecture on the various manifestations of the rheumatic state as exemplified in childhood and early life. *Lancet* 1889; 1: 821 - 827; 871-877; 921-927.
6. PATARROYO ME, WINCHESTER R, VERANO A. Association of B-cell alloantigen with susceptibility of Rheumatic Fever. *Nature* 1979; 278: 173-174.
7. ZABRISKIE JB. Rheumatic fever: the interplay between host, genetics and microbe. *Circulation*, 1985; 71: 1077-1086.
8. GEWITZ MH, BALTIMORE RS, TANI L Y et al. Revision of the Jones Criteria for the Diagnosis of Acute Rheumatic Fever in the Era of Doppler Echocardiography. A Scientific Statement From the American Heart Association. *Circulation*, 2015; 131: 1806-1818.
9. NARULA J, CHANDRASEKHAR Y, RAHIMTOOLA S. Diagnosis of active rheumatic carditis. The echoes of change. *Circulation* 1999; 100: 1576 – 1581.
10. AUALA T, ZAVALA BEN LAURO GONÇALVES, MBAKWE A C, MOCUMBI A O. Acute Rheumatic Fever and Rheumatic Heart Disease: Highlighting the Role of Group A Streptococcus in the Global. *Pathogens*, 2022; 11: 496.
11. McCARTY M. An adventure in the pathogenetic maze of rheumatic fever. *J Infect Dis* 1981; 143: 375 - 385.
12. GUILHERME L, WEIDEBACH W, KISS MH, SNITCOVSKY R, KALIL J. Association of human leukocyte class II antigens with rheumatic fever or rheumatic heart disease in a Brazilian population. *Circulation* 1991; 83: 1995-1998.
13. JHINGHAN N K, MEHRA NK, REDDY KS, TANEJA V, VAIDYA MC, BHATIA ML. HLA, blood groups and secretor status in patients with established rheumatic fever and rheumatic heart disease. *Tissue Antigens* 1986; 27: 172-178.
14. AYOUB EM, BARRETT DJ, MacLAREN NK, KRISCHER JP. Association of class II human histocompatibility leukocyte antigens with rheumatic fever. *J Clin Invest* 1986; 77(6): 2019-2026.
15. RAJAPAKSE CNA, HALIM K, AL-ORAINY I, AL-NOZHA M, AL-ASKA AK. A genetic marker for rheumatic heart disease. *Br Heart J* 1987; 58: 659-662.
16. KHOSROSHAHI HE, KAHRAMANYOL O, DOGANCI L. HLA and rheumatic fever in Turkish Children. *Pediatr Cardiol* 1992; 13(4): 204-207.
17. ERTUG MH. HLA antigens in Rheumatic Fever and Rheumatic Heart Disease (Letter) *Rheumatology*, 1993; 32(4): 347-348.
18. CARLQUIST JF, ANDERSON JL. HLA, autoimmunity, and rheumatic heart disease. Apparent or real associations? (Editorial). *Circulation* 1993; 87: 2060-2062.
19. KAPLAN MH, MEYESERIAN M. An immunological cross-reaction between group-A streptococcal cells and human heart tissue. *LANCET* 1 (7232): 706-710.
20. GOLDSTEIN L, HALPERN B, ROBERT L. Immunological relationship between streptococcus polysaccharide and the structural glycoprotein of heart valve. *Nature* 1967; 213: 44-47.
21. TUBRIDY-CLARK M, CARAPETIS JR. Subclinical carditis in rheumatic fever. A systematic review. *Int J Cardiol* 2007; 119: 54-58.
22. GEWITZ M H, BALTIMORE RS, TANI LY et al. Revision of the Jones Criteria for the Diagnosis of Acute Rheumatic Fever in the Era of Doppler Echocardiography. *Circulation*

- 2015; 131: 1806 - 1818.
23. SARAIVA LR, CARNEIRO, RW, WILLCOX, G. Rheumatic pneumonia with carditis and arthritis in a three-year-old girl. *Cardiol Young* 1995; 5: 197-198.
 24. ROY SB. BHATIA ML, LAZARO EJ, RAMALINGASWAMI V. Juvenile mitral stenosis in India. *Lancet* 1963; 2 (7319): 1193 - 1195.
 25. MELL LK, DAVIS RL, OWENS D. Association between streptococcal infection and obsessive-compulsive disorder, Tourette`s syndrome, and tic disorder. 2005; 116: 56-60.
 26. LAPA, CCS. Aspectos clínicos e ecoDopplercardiográficos de uma série de crianças em primeiro surto de febre reumática sem sinais clínicos de cardite. Master`s Thesis. Federal University of Pernambuco. 2006. 58 p.
 27. GHATI N. A case of rheumatic heart disease with a history of complicated pregnancy. *J Pract Cardiovasc Sci* 2018; 4: 41-48.
 28. 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.
 29. BEATON A, OKELLO E, ALIKU T et al. Latent Rheumatic Heart outcomes 2 years after echocardiographic detection. *Pediatric Cardiol* 2014; 35(7): 1259-1267
 30. YUSUF S, NARULA J, GAMRA H. Can we eliminate rheumatic fever and premature deaths from RHD ? *Global Heart* 2017; 12(1): 3-4.



This work is licensed under Creative Commons Attribution 4.0 License

To Submit Your Article Click Here:

Submit Manuscript

DOI: [10.31579/2692-9406/148](https://doi.org/10.31579/2692-9406/148)

Ready to submit your research? Choose Auctores and benefit from:

- fast, convenient online submission
- rigorous peer review by experienced research in your field
- rapid publication on acceptance
- authors retain copyrights
- unique DOI for all articles
- immediate, unrestricted online access

At Auctores, research is always in progress.

Learn more <https://www.auctoresonline.org/journals/biomedical-research-and-clinical-reviews->