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## **RHEUMATIC FEVER AND POST-STREPTOCOCCAL REACTIVE ARTHRITIS**

### **What is it?**

Rheumatic fever has been defined as a disease triggered by infection caused by streptococcus. The disease may cause permanent damage to the heart, and presents itself by transient arthritis, carditis, or a movement disorder called chorea, in addition to skin rashes or skin nodules.

### **How common is it?**

In the past, epidemics of rheumatic fever and localized outbreaks in communities have provided the background to suggest it is triggered by infection, before antibiotics became available. A dramatic incidence decline was seen worldwide after the widespread use of penicillin for treatment of pharyngitis. It most commonly occurs between the ages of 5-15, with peak incidence around eight. In developing countries, it remains a challenge as the leading cause of heart disease disability amongst young people, with recurrent attacks more likely to increase heart damage.

During the eighties however, a resurgence in outbreaks was reported in areas, in what would otherwise be considered low-risk populations.

It is included among the many rheumatic diseases of children and adolescents, because of its joint manifestations.

### **What are the causes of the disease?**

The disease is the consequence of an abnormal immune response to throat infection with streptococcus in genetically predisposed individuals. This means that the immune system attacks, not only the streptococcus, but also normal body tissue. The time lapse between the infection and disease onset is very variable.

This unique relation to infection provides the basis for treatment and prevention. Streptococcal throat infection is common in the general population, although only a small minority of patients will develop the disease. The risk increases in patients with a previous flare, mostly three years after the onset of disease.

### **Is it inherited?**

Rheumatic fever is not a hereditary disease, since it cannot be transmitted directly from parents to their children. Genetic factors may still influence susceptibility to the disease.

### **Why has my child got this disease? Can it be prevented?**

The environment and streptococcus are important factors for the development of the disease, but in practice it is difficult to predict who will get it. The disease is caused by an abnormal reaction, which means that the immune response directed against streptococcus components also attacks human tissues. Some streptococcus types are more likely to lead to rheumatic fever. Crowding is an important environmental factor, since it favors transmission of the causal infection.

Prevention of rheumatic fevers relies on prompt identification and antibiotic treatment of streptococcal throat infection.

**Is it contagious?**

Rheumatic fever by itself is not contagious. What is contagious is streptococcal pharyngitis. Streptococci are spread from person to person and is, therefore, associated with crowding in the home, school or military installation, etc.

**What are the main symptoms?**

Rheumatic fever usually presents by a combination of features that may be unique in each patient. It follows untreated or not properly treated streptococcal pharyngitis, or tonsillitis.

Pharyngitis, or tonsillitis, can be recognized by fever, sore throat, headache, red palate and tonsils with purulent secretions and enlarged, painful neck lymph nodes. However, these symptoms can be very mild or completely absent in school age children and adolescents.

After an asymptomatic period, the child may present with fever and major signs of the disease that are:

Arthritis, mainly a “Flitting” arthritis, can affect many joints (knees, elbows, ankles, or shoulders). The inflammation goes from one joint to another, involving the hands and cervical spine less frequently. Joint pain may be severe, although swelling may not be so evident. It should be mentioned that pain usually subsides promptly with Aspirin or non-steroidal anti-inflammatory drugs (NSAIDs).

Carditis means heart inflammation and is the most serious manifestation. An accelerated heartbeat during rest or sleep can elicit the suspicion of rheumatic carditis. A heart examination should be performed to check for heart murmurs. It varies from a subtle to a loud murmur that may indicate inflammation of the heart valves, which is called endocarditis. If there is an inflammation located in the heart sac, called Pericarditis, some fluid may collect around the heart, but this is usually asymptomatic and clears of its own accord. In the most severe cases of myocarditis, the pumping of the heart may become inflamed and weak. It can be recognized by a cough, chest pain, accelerated pulse and breathing. A cardiologist referral and tests may be indicated.

Chorea is a movement disorder due to inflammation of parts of the brain controlling the coordination of movements. It is seen in about 10-30% of the patients. Unlike arthritis and carditis, chorea appears later on the disease course, mostly from one to six months, after the throat infection. Early signs are poor handwriting, difficulties with dressing and self-care, or even walking and feeding, due to purposeless involuntary movements. Movements may be suppressed voluntarily for short periods and can disappear during sleep, or can be exacerbated by stress, or fatigue. In scholars, it reflects on academic achievements due to poor concentration and anxiety. If subtle, it might be overlooked as a behaviour disturbance. Usually it will clear up on its own between two to six months, but supporting treatment and follow up are needed.

Less common manifestations of rheumatic fever are the skin signs. Erythema marginatum is a transient rash over the trunk with expanded spots, clear centre and red margins resembling a snake-like appearance. Subcutaneous nodules are painless mobile grain nodules with normal overlying skin colour, usually seen over joints. These signs are

present in less than 5% of cases and may be overlooked, because of their subtle and transient appearance.

There are signs that may be first noticed by parents such as fever, fatigue, functional distress, loss of appetite, pallor, abdominal pain and nosebleeds. These may occur in the early stages of disease.

### **Is the disease the same in every child?**

The most common presentation is the appearance of a murmur in older children, or adolescent, with arthritis and fever. Younger patients tend to present carditis and less severe joint complaints.

Chorea may present itself isolated, or in combination with carditis, but close follow up looking for carditis is recommended for all cases.

The disease onset and disease course are also quite variable, regardless of treatment.

### **Is the disease in children different from the disease in adults?**

Rheumatic fever is a disease of school children and young people under 25 years of age. It is rare before the age of three and more than 80% of the patients are between 5-19 year old. However, flares may occur later in life, if permanent antibiotic protection is not followed.

### **How is it diagnosed?**

Careful analysis of overall clinical signs and tests are important, because there is no specific test for diagnosis. The clinical criteria guidelines, followed for diagnosis, are named after a physician as Jones's criteria.

Paediatric Rheumatologists worldwide are aware of the disease in all its forms. A child under suspicion of rheumatic fever must be put under close supervision.

Referral to other specialists, such as a Cardiologist, may be necessary where carditis is present.

### **Which diseases are like rheumatic fever?**

There is an illness usually called post-streptococcal reactive arthritis, meaning only arthritis is present following streptococcal infection. This may be part of the many clinical features of rheumatic fever.

### **What are the importance tests?**

Some tests are essential for diagnosis and follow up.

Blood tests are useful during flares to support the diagnosis.

As in many others rheumatic diseases, signs of systemic inflammation are seen in nearly all patients, unless chorea is the only presenting sign.

Evidence of previous streptococcus infection is very important for diagnosis. However, streptococcal culture by throat swab is not the ideal test, as most patients have already cleared the streptococcus by disease onset. There are some blood tests to detect streptococcal antibodies, even if the parents and patient are not able to recall the infection. Rising levels of these antibodies, detected by blood tests done two to four weeks apart, may indicate recent infection. However, these tests are often normal in those presenting with isolated chorea, making this diagnosis tricky. Isolated, abnormal values

of antistreptolysin O (ASO) titre means that prior exposure to the bacteria has stimulated the immune system to produce antibodies, so, by itself, does not mean that rheumatic fever is present.

### **How to detect Carditis?**

A new murmur, resulting from heart inflammation, is the most common feature of Carditis and is usually detected by the physician listening to the heart. An electrocardiogram is the assessment of the heart's electrical activity registered in a paper strip. It is useful to ensure the extent of heart involvement, as is a Chest X-ray.

Doppler echocardiogram, or heart ultrasound, is a very sensitive test for Carditis. However, it cannot be used for diagnosis in the absence of clinical signs.

All these procedures are absolutely painless and the only discomfort is that the child has to keep still for a while during the performance of tests.

### **Can it be treated or cured?**

This condition is an important health problem in certain areas of the world.

Treating streptococcal pharyngitis as soon as it is recognized can prevent the disease. There is research going on to produce a vaccine that can protect against the streptococcus without eliciting the abnormal reaction observed in rheumatic fever. This approach might become the prevention in the future.

### **What are the treatments?**

During the first flare, after the diagnosis is confirmed, a full course of antibiotics is recommended. Treating throat infections is necessary, because the streptococcus may still exist within the tonsils and stimulate the immune system.

One shot of 1,200,000 units of benzathine penicillin eradicates the bacteria and gives protection for three to four weeks. In patients who already had rheumatic fever, long-term use of benzathine penicillin every three weeks is mandatory to prevent further flares.

Salicylates, or other NSAIDs, are recommended for Arthritis during six to eight weeks, or until it disappears. For severe Carditis, bed rest and high dose oral steroids (prednisone) are recommended for two to three weeks, tapering it off gradually.

For chorea, parental support for personal care and school tasks may be required. Drug treatment for chorea movement control with Haloperidol, or Valproic acid, may be prescribed under close follow-up to check for side effects. Common side effects are sleepiness and trembling, which can be easily controlled by dose adjustment. In a few cases, chorea may last for several months despite adequate treatment.

### **What are the side effects of drug therapy?**

Considering the short-term symptomatic treatment, Salicylates and other NSAIDs are usually well tolerated. The most visible side effects of steroids are, an increase in weight, facial swelling, acne, striae (stretch marks) and an increase in body hair (hirsutism).

The risk of penicillin allergy is quite low, but must be watched out for.

### **How long should secondary prevention last for?**

The natural history of the disease in the past has shown that the risk of flares is higher during the first three to five years. The risk for developing carditis damage increases with each new flare.

For these reasons, secondary prevention of streptococcal infection is recommended for all patients who have had rheumatic fever, regardless of the severity at presentation, as mild forms may flare as well.

Most physician agree that antibiotic prevention, for those without heart damage, should last for at least five years, or until the child is 18 years old, whichever is longer. In cases where the patient has developed heart damage, it is recommended until the age of 40.

Prevention for bacterial endocarditis with antibiotics is recommended to all patients with heart valve damage undergoing dental work and surgery. It is necessary, because bacteria can move from other sites of the body, especially from the mouth, and cause heart valve infection.

### **What kind of periodic check-ups are necessary?**

Regular check ups and periodic tests may be required more often during flare ups. Closer follow up is recommended in cases of carditis and chorea. After remission of the symptoms, a supervised schedule for preventive treatment and long term follow up, looking for late heart damage, is recommended.

### **How long will the disease last for?**

The main symptoms of the disease are self-limiting, however, the risk of new flares remains, being higher during the first five years after onset.

Continuing with preventive treatment is mandatory, in order to decrease the chance of a new flare.

### **What is the prognosis (predicted outcome and course) of the disease?**

Flares tend to be unpredictable as far as how long they will last and their severity. Having carditis in the first attack is potentially a higher risk for heart damage, however, complete healing may follows carditis in some cases. The most severe heart damage may require heart surgery for valve replacement.

### **Is it possible to recover completely?**

Complete recovery is possible, unless Carditis has resulted in severe heart valve damage.

### **How is every day life?**

Family support during flares is recommended for patients with carditis and chorea. Arthritis is usually self-limiting and responds well to NSAIDs. When the main symptoms subside, if there is no residual heart damage during regular check ups, there is no special recommendation for daily activities and routine life, schooling, sports, or vaccines.

As the major symptoms are self-limiting, the main concern is the long-term compliance with antibiotics. For this reason, the community primary care services must be fully involved.

Education is needed to improve compliance with treatment, especially for adolescents. In dealing with adolescents battling for emerging independence, if the decision affects the health of the patient, the parents have to know when to step in to take control.

## **POST-STREPTOCOCCAL ARTHRITIS**

### **What is it?**

In adults and youngsters, cases of streptococcal associated arthritis are described that do not fulfill the criteria of acute rheumatic fever. Arthritis develops in the earlier phase of the disease and may involve joints of the hands. It responds poorly to anti-inflammatory treatment and, usually, lasts for months. These features resemble other forms of arthritis. The diagnosis relies on clinical findings, in association with evidence of recent streptococcal infection.

Some of these patients have been shown to develop carditis later on. Most doctors agree that post-streptococcal arthritis is a variant of rheumatic fever, therefore, antibiotic prevention is recommended, as well as heart evaluation checking for carditis.