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Rheumatic Fever And Post-streptococcal Reactive Arthritis

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1. WHAT IS RHEUMATIC FEVER

1.1 What is it?

Rheumatic fever is a disease caused by throat infection by a bacterium called streptococcus. There are several groups of streptococci but only group A causes rheumatic fever. Although streptococcal infection is a very common cause of pharyngitis (throat infection) in school-age children, not all children with pharyngitis will develop rheumatic fever. The disease may cause inflammation and damage to the heart; it presents first with short-lived joint pains and swelling, and later with carditis (inflammation of the heart) or an abnormal involuntary movement disorder (chorea) due to brain inflammation. Skin rashes or skin nodules may also occur.

1.2 How common is it?

Before antibiotic treatment became available, the number of cases was high in countries with warm climates. After antibiotic treatment became a common practice for treating pharyngitis, the frequency of this disease decreased, but it still affects many children from 5-15 years of age all over the world, leading to heart disease in a small proportion of cases. Because of its joint manifestations, it is included among the many rheumatic diseases of children and adolescents. The burden of rheumatic fever is unequally distributed around the world.
The occurrence of rheumatic fever varies from country to country: there are countries where no case is registered and countries with medium or

high rates (more than 40 cases per 100,000 persons per year). It is estimated that there are over 15 million cases of rheumatic heart disease worldwide, with 282,000 new cases and 233,000 deaths annually.

1.3 What are the causes of the disease?

The disease is the result of an abnormal immune response to throat infection with Streptococcus pyogenes, or Group A β haemolytic Streptococcus. Sore throat precedes the disease onset by an asymptomatic period of variable length.
Antibiotic treatment is needed to treat the throat infection, stop stimulation of the immune system and prevent new infections, because new infections can cause a new disease attack. The risk of a repeated attack is higher in the first 3 years after disease onset.

1.4 Is it inherited?

Rheumatic fever is not a hereditary disease, since it cannot be transmitted directly from parents to their children. However, there are families with several members who developed rheumatic fever. This may be due to genetic factors associated with the possibility of transmission of streptococcus infections from person to person. Streptococcal infection is transmissible through respiratory airways and saliva.

1.5 Why does my child have this disease? Can it be prevented?

The environment and the streptococcus strain are important factors for the development of the disease, but in practice it is difficult to predict who will get it. Arthritis and heart inflammation are caused by abnormal immune response against streptococcus proteins. The chances of getting the disease are higher if certain types of streptococcus infect a susceptible person. Crowding is an important environmental factor, since it favours the transmission of infections. Prevention of rheumatic fever relies on prompt diagnosis and antibiotic treatment (the recommended antibiotic is penicillin) of streptococcal throat infection in healthy children.

1.6 Is it infectious?

Rheumatic fever by itself is not infectious, but streptococcal pharyngitis is. Streptococci are spread from person to person and therefore infection is associated with crowding at home, in schools or at the gym. Careful hand washing and avoidance of close contact with individuals with streptococcal throat infections is important to stop the spread of the disease.

1.7 What are the main symptoms?

Rheumatic fever usually presents a combination of symptoms that may be unique in each patient. It follows streptococcal pharyngitis or tonsillitis not treated with antibiotics.
Pharyngitis or tonsillitis can be recognized by fever, sore throat, headache, red palate and tonsils with purulent secretions and enlarged and painful neck lymph nodes. However, these symptoms can be very mild or completely absent in school-age children and adolescents. After the acute infection has resolved, there is an asymptomatic period of 2-3 weeks. Then the child may present with fever and the signs of the disease described below.

Arthritis

Arthritis most commonly affects several large joints at the same time or may move from one joint to another affecting one or two at a time (knees, elbows, ankles or shoulders). It is called "migratory and transient arthritis". Arthritis affecting hands and cervical spine is less common. Joint pain may be severe even when swelling is absent. Note that pain usually subsides promptly after administration of anti-inflammatory drugs. Aspirin is the most used anti-inflammatory drug.

Carditis

Carditis (heart inflammation) is the most serious manifestation. Accelerated heartbeat during rest or sleep can elicit the suspicion of rheumatic carditis. Abnormal heart examination, with the presence of heart murmurs, is the main sign of heart involvement. It varies from a subtle to a loud murmur that may indicate inflammation of the heart valves, known as "endocarditis". If inflammation is located in the heart sac, known as "pericarditis", some fluid may collect around the heart

but this usually causes no symptoms and clears on its own. In the most severe cases of myocarditis, the heart may become inflamed and pumping may be weakened. It can be recognized by cough, chest pain and accelerated pulse and breathing. Referral to a cardiologist and tests may be indicated. Rheumatic valvular heart disease may be a result of the first attack of rheumatic fever, but it is usually a consequence of repeated episodes and might become a problem later in adult life, so prevention is crucial.

Chorea

The term chorea is derived from a Greek word meaning dance. Chorea is a movement disorder resulting from inflammation of parts of the brain controlling the coordination of movements. It affects 10-30% of patients with rheumatic fever. Unlike arthritis and carditis, chorea appears later during disease course, from 1 to 6 months after the throat infection. Early signs are poor handwriting in school age patients, difficulties with dressing and self-care, or even with walking and feeding, due to trembling involuntary movements. Movements may be suppressed voluntarily for short periods, may disappear during sleep or be exacerbated by stress or fatigue. In students, it reflects on academic achievements due to poor concentration, anxiety and mood instability with easy crying. If subtle, it might be overlooked as a behavioural disturbance. It is self-limited, although supporting treatment and follow-up is needed.

Skin rashes

Less common manifestations of rheumatic fever are the skin rashes called "erythema marginatum", which look like red rings, and "subcutaneous nodules" that are painless mobile grain nodules with normal overlying skin colour, usually seen over the joints. These signs are present in less than 5% of cases and may be overlooked because of their subtle and transient appearance. These signs are not isolated, but they occur together with myocarditis (inflammation of the heart muscle). There are other complaints that may be first noticed by parents such as fever, fatigue, loss of appetite, pallor, abdominal pain and nosebleeds, which may occur in early stages of the disease.

1.8 Is the disease the same in every child?

The most common presentation is the heart murmur in older children or adolescents with arthritis and fever. Younger patients tend to present with carditis and less severe joint complaints.
Chorea may present itself as the only manifestation or may be combined with carditis, but close follow-up and examination by a cardiologist are recommended.

1.9 Is the disease in children different from the disease in adults?

Rheumatic fever is a disease of school children and young people up to 25 years of age. It is rare before the age of 3 and more than 80% of patients are between 5 and 19 years old. However, it may occur later in life if there is non-compliance with permanent antibiotic prevention.

2. DIAGNOSIS AND THERAPY

2.1 How is it diagnosed?

Clinical signs and investigations have special importance, because there is no specific test or sign for the diagnosis. Clinical symptoms of arthritis, carditis, chorea, skin changes, fever, abnormal laboratory tests for streptococcal infection and changes in the conduction of the heartbeat, as seen on an electrocardiogram, can help establish the diagnosis (so called Jones criteria). Evidence of a preceding streptococcal infection is generally needed to make the diagnosis.

2.2 Which diseases are like rheumatic fever?

There is a disease called "post-streptococcal reactive arthritis" that also occurs after streptococcal pharyngitis, but which features arthritis of longer duration and which has a lower risk of carditis; antibiotic prophylaxis may be indicated. Juvenile idiopathic arthritis is another disease resembling rheumatic fever, but the duration of arthritis is longer than 6 weeks. Lyme disease, leukaemia, reactive arthritis caused by other bacteria or viruses may also present with arthritis. Innocent murmurs (common heart murmurs with no heart disease), congenital or other acquired heart diseases can be misdiagnosed as rheumatic fever.

2.3 What is the importance of tests?

Some tests are essential for the diagnosis and follow-up. Blood tests are useful during attacks to confirm the diagnosis.
As in many other rheumatic diseases, signs of systemic inflammation are seen in nearly all patients, except those with chorea. In most patients, there is no sign of throat infection and the streptococcus bacteria in the throat are cleared by the immune system by the time of disease onset. There are blood tests to detect streptococcal antibodies, even if the parents and/or the patient are not able to recall the signs of throat infection. Rising titres (levels) of these antibodies, known as anti-streptolysin O (ASO) or DNAse B, can be detected by blood tests carried out 2-4 weeks apart. High titres indicate a recent infection, but there is no proven relationship with disease severity. However, these tests yield normal results in patients with only chorea, making this diagnosis tricky. Abnormal ASO or DNAse B test results mean prior exposure to the bacteria stimulating the immune system to produce antibodies, and by itself, does not make the diagnosis of rheumatic fever in patients without symptoms. Antibiotic treatment is therefore generally not necessary.

2.4 How to detect carditis?

A new murmur, resulting from heart valve inflammation, is the most common feature of carditis and is usually detected when a physician auscultates (listens to) the heart sounds. An electrocardiogram (an assessment of heart’s electrical activity registered on a paper strip) is useful to ensure the extent of heart involvement. Chest X-rays are also important to check for enlargement of the heart.
Doppler echocardiogram or heart ultrasound is a very sensitive test for carditis. All these procedures are absolutely painless and the only discomfort is that the child must keep still for a while during the test.

2.5 Can it be treated/cured?

Rheumatic fever is an important health problem in certain areas of the world, but it can be prevented by treating streptococcal pharyngitis as soon as it is recognized (i.e. primary prevention). Antibiotic therapy started within 9 days of onset of pharyngitis is effective in preventing

acute rheumatic fever. Symptoms of rheumatic fever are treated with non-steroidal anti-inflammatory medications.
Research is currently being carried out to produce a vaccine that can protect against streptococcus: prevention of the initial infection would provide protection against the abnormal immune reaction. This approach might prevent rheumatic fever in the future.

2.6 What are the treatments?

During the past several years, there have been no new treatment recommendations. While aspirin has remained the mainstay of therapy, the exact action of effect is unclear; it appears to be related to the anti-inflammatory properties. Other non-steroidal anti-inflammatory drugs (NSAIDs) are recommended for arthritis for 6-8 weeks or until it disappears.
For severe carditis, bed rest and, in some cases, oral corticosteroids(prednisone) are recommended for 2-3 weeks, tapering the drug off gradually after the inflammation is controlled by observing the symptoms and by blood tests.
In the event of chorea, parental support for personal care and school tasks may be required. Drug treatment for chorea movement control with steroids, haloperidol or valproic acid may be prescribed with close monitoring for side-effects. Common side effects are sleepiness and trembling that can be easily controlled by dose adjustment. In a few cases, chorea may last for several months despite adequate treatment. After the diagnosis is confirmed, long-term protection with antibiotics is recommended to avoid recurrence of acute rheumatic fever.

2.7 What are the side effects of drug therapy?

In terms of short-term symptomatic treatment, salicylates and other NSAIDs are usually well tolerated. The risk of a penicillin allergy is quite low, but its use must be monitored during the first injections. The main considerations are the painful injections and possible refusal by patients who fear pain; therefore, education about the disease, topical anaesthetics and relaxation before injections are recommended.

2.8 How long should secondary prevention last?

The risk of relapse is higher during the 3-5 years after onset and the risk of developing carditis damage increases with new flares. During this time, regular antibiotics treatment for preventing new streptococcal infections is recommended for all patients who have had rheumatic fever, regardless of the severity, as mild forms may flare as well.
Most physicians agree that antibiotic prevention should continue for at least 5 years after the last attack or until the child is 21 years old. In the event of carditis without heart damage, secondary prophylaxis is recommended for 10 years or until the patient is 21 years old (whichever is longer). If heart damage is present, 10 years of prophylaxis are recommended, or until the age of 40 - or later in life if the disease is complicated by valve replacement.
Prevention of bacterial endocarditis with antibiotics is recommended for all patients with heart valve damage undergoing dental work or surgery. This measure is necessary because bacteria can move from other sites of the body, especially from the mouth, and cause heart valve infection.

2.9 What about unconventional/complementary therapies?

There are many complementary and alternative therapies available and this can be confusing for patients and their families. Think carefully about the risks and benefits of trying these therapies as there is little proven benefit and they can be costly in terms of time, burden to the child and money. If you want to explore complementary and alternative therapies, it is wise to discuss these options with your paediatric rheumatologist. Some therapies can interact with conventional medications. Most doctors will not be opposed to complementary therapies, provided you follow medical advice. It is very important not to stop taking your prescribed medications. When medications, such as corticosteroids, are needed to keep the disease under control, it can be very dangerous to stop taking them if the disease is still active. Please discuss medication concerns with your child’s doctor.

2.10 What kind of periodic check-ups are necessary?

Regular check-ups and periodic tests may be required during long-term disease course. Closer follow-up is recommended in cases where there is carditis and chorea. After remission of the symptoms, a supervised

schedule for preventive treatment and long-term follow-up under supervision of a cardiologist looking for late heart damage is recommended.

2.11 How long will the disease last?

Acute symptoms of the disease recede over several days to weeks. However, the risk of recurrent attacks of acute rheumatic fever persists and heart involvement can cause life-long symptoms. Ongoing antibiotic treatment to prevent recurrence of streptococcal pharyngitis is necessary for many years.

2.12 What is the long-term evolution (prognosis) of the disease?

Relapses of symptoms tend to be unpredictable in time and severity. Carditis in the first attack increases damage risk, although complete healing may follow carditis in some cases. Most severe heart damage requires heart surgery for valve replacement.

2.13 Is it possible to recover completely?

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

3. EVERYDAY LIFE

3.1 How might the disease affect the child and the family’s daily life?

With proper care and regular check-ups, most children with rheumatic fever lead a normal life. However, family support during flare-ups is recommended for patients with carditis and chorea.
The main concern is long-term compliance with antibiotics prevention. Primary care services must be involved and education is needed to improve compliance with treatment, especially for adolescents.

3.2 What about school?

If there is no residual heart damage detected during regular check-ups, there is no special recommendation for daily activities and routine school life; children can proceed with all activities. Parents and teachers should do whatever they can to allow the child to participate in school activities in a normal way, in order not only for the child to be successful academically but also to be accepted and appreciated by both peers and adults. During acute phases of chorea, some limitations during school tasks are expected, and families and teachers may have to cope with this for 1 to 6 months.

3.3 What about sports?

Playing sports is an essential aspect of the everyday life of any child. One of the aims of therapy is to allow children to conduct a normal life as much as possible and to consider themselves not different from their peers. All activities can therefore be performed as tolerated. Nevertheless, restricted physical activity or bed rest may be necessary during the acute phase.

3.4 What about diet?

There is no evidence that diet can influence the disease. In general, the child should enjoy a balanced, normal diet for his/her age. A healthy, well-balanced diet with sufficient protein, calcium and vitamins is recommended for a growing child. Overeating should be avoided in patients taking corticosteroids because these drugs may increase appetite.

3.5 Can climate influence the course of the disease?

There is no evidence that climate can affect the disease manifestations.

3.6 Can the child be vaccinated?

The physician should decide which vaccines the child can receive, considering case by case. Overall, vaccinations do not appear to increase the disease activity and do not cause severe adverse events in patients. However, live-attenuated vaccines are generally avoided because of the hypothetical risk of inducing infection in patients

receiving high dose immunosuppressive drugs or biologic agents. Non-live composite vaccines appear to be safe in patients, even those receiving immunosuppressive drugs, although most studies cannot fully assess rare vaccination-induced harm.
A patient on high dose immunosuppressive drugs should be advised by their physician to measure pathogen-specific antibody concentrations after vaccination.

3.7 What about sexual life, pregnancy, birth control?

There are no restrictions on sexual activity or pregnancy due to the disease. Nevertheless, all patients taking medications should be very careful about the possible effects of these drugs on a foetus. Patients are advised to consult their physician about birth control and pregnancy.

4. POST-STREPTOCOCCAL REACTIVE ARTHRITIS

4.1 What is it?

Cases of streptococcal-associated arthritis have been described both in children and young adults. It is usually called "reactive arthritis" or "post-streptococcal reactive arthritis" (PSRA).
PSRA commonly affects children between 8 to 14 years of age and young adults between 21 to 27 years. It usually develops within 10 days after a throat infection. If differs from arthritis of acute rheumatic fever (ARF), which mainly involves large joints. In PSRA, large and small joints and the axial skeleton are involved. It usually lasts longer than ARF — about 2 months, sometimes longer.
Low grade fever might be present, with abnormal laboratory tests indicating inflammation (C reactive protein and/or erythrocyte sedimentation rate). The inflammatory markers are lower than in ARF.
The diagnosis of PSRA relies on arthritis with evidence of recent streptococcal infection, abnormal streptococcal antibody tests (ASO, DNAse B) and the absence of the signs and symptoms in a diagnosis of ARF according to "Jones criteria".
PSRA is a different entity to ARF. PSRA patients will probably not develop carditis. Currently, the American Heart Association recommends prophylactic antibiotics for one year after symptoms

onset. In addition, these patients should be carefully observed for clinical and echocardiographic evidence of carditis. If heart disease appears, the patient should be treated as in ARF; otherwise prophylaxis can be discontinued. Follow-up with a cardiologist is recommended.