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## JUVENILE SPONDYLOARTHROPATHIES

### **What is it?**

The juvenile spondyloarthropathies constitute a group of chronic inflammatory diseases of the joints (arthritis) and tendon attachments to certain bones (enthesitis) affecting, predominantly, the lower limbs and, in some cases, the pelvic and spinal joints (sacroiliitis - buttock pain and spondylitis - lower back pain).

In some cases, the onset of symptoms is triggered by enteric (gastro-intestinal) or urogenital bacterial infections (reactive arthritis). Juvenile spondyloarthropathies are significantly more common in people carrying HLA-B27, a genetic marker, which predispose individuals to this disease, although why this is the case is not fully understood, as yet.

The prevalence of some clinical features at onset and severity throughout the course of the disease, differ in the childhood form to those of adults, but may still resemble adult onset spondyloarthropathies.

Patients with juvenile idiopathic arthritis, classified into the enthesitis related arthritis group (see JIA information), are included in the group of juvenile spondyloarthropathies.

### **What diseases are called juvenile spondyloarthropathies?**

Despite some controversy, juvenile spondyloarthropathies include the same diseases belonging to the group of adult spondyloarthropathies, including ankylosing spondylitis, reactive arthritis (and Reiter's syndrome), psoriatic arthritis (of the spondyloarthropathy type), and arthritis associated with inflammatory bowel disease (of the spondyloarthropathy type). Some children, not fulfilling diagnostic criteria for the disease enlisted above, may have the so-called undifferentiated spondyloarthropathy.

Other conditions, specifically the seronegative enthesopathy and arthropathy (SEA) syndrome and enthesitis related arthritis refer to juvenile spondyloarthropathies.

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

Spondyloarthropathies are one of the most frequent forms of chronic arthritis in childhood and account for about 30 % of children with chronic arthritis.

Spondyloarthropathies are seen more often in boys, with the disease starting mainly between 10 and 15 years of age. Since a great part of the patients carry a genetic predisposing factor (**HLA-B27**) the frequency of juvenile and adult spondyloarthropathies in the general population and even in certain families (familial history), depends on the frequency of this marker in the normal population.

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

The cause and precise mechanisms that cause juvenile spondyloarthropathies are unknown. It is thought that the mechanisms that might be responsible for the disease include several components of the immune system. Spondyloarthropathies are associated with other kinds of chronic inflammation for example of the bowel, the genito-urinary

tract, or the skin. Infections by some micro-organisms (i.e. Salmonella, Shigella, Yersinia, Campylobacter and Chlamydia) may play a role in triggering the arthritis in some children (i.e. reactive arthritis).

### **Is it inherited?**

Large numbers of patients with a juvenile spondyloarthropathy carry the genetic marker **HLA-B27**. This does not mean that every individual carrying this genetic factor will have spondyloarthropathy. For example, if the frequency of HLA-B27 in the population is 10 %, only 1 % of this population will develop the disease. If someone else in the close family is affected with spondyloarthropathy, the presence of HLA-B27 increases the risk to about 25 % for an individual of that family to develop a spondyloarthropathy. Spondyloarthropathies are present with a higher frequency in members of the family of an affected child when compared to families of non-affected children.

Genetic factors, and in particular HLA-B27, refer to disease susceptibility. They are not sufficient for disease development. The agreement in the scientific community is that these diseases are multifactorial, which means that they are the result of a combination of genetic predisposition and exposure to environmental factors (probably infections) that are still unknown.

### **Can it be prevented?**

Prevention is not possible since the causes of the disease are unknown. It is not useful to test other siblings for the HLA-B27 if they do not have any symptoms that can be linked to a spondyloarthropathy

### **Is it contagious?**

Spondyloarthropathies are not contagious diseases.

### **What are the main symptoms?**

Juvenile spondyloarthropathies have common clinical characteristics:

#### **Arthritis**

1) Most common symptoms include joint pain and swelling, and limited mobility of the joints.

2) Many children have oligoarthritis of the lower limbs. Oligoarthritis means that the disease involves four or less joints. Those developing chronic disease may have polyarthritis. Polyarthritis means that the articular involvement is more extensive and affects five or more joints.

3) Arthritis mainly involves the joints of the lower limbs: the knee, the ankle, the mid-foot, and the hips. Less frequently, arthritis involves the small joints of the foot.

4) Some children may have arthritis of any joint of the upper limbs, particularly the shoulders.

#### **Enthesitis**

Enthesitis, the inflammation of the enthesis (the site where a tendon or ligament attaches to the bone) is very frequent in children with spondyloarthropathies. Commonly affected entheses are located at the heel, in the mid-foot and around the kneecap. Most common symptoms include heel pain, mid-foot pain and swelling, and kneecap pain.

Chronic inflammation of the enthesis may lead to bony spurs (bony overgrowth). These spurs occur particular in the heel causing heel pain.

#### **Sacroiliitis**

It is the inflammation of the sacroiliac joint, located in the rear of the pelvis. It is rare at onset and most frequently occurs five to 10 years after the onset of arthritis.

The most common symptom is alternating buttock pain.

#### **Lumbar pain; spondylitis**

Involvement of the spine is very rare at onset, but may occur later in the disease course. The most common symptoms include low back pain, morning stiffness, and reduced mobility. Low back pain is frequently accompanied by neck and chest pain.

In the spine, long-term disease may cause the formation of bridges between the spinal bones ("bamboo spine"). This occurs in only few patients and after a long disease duration. It is, therefore, almost never observed in children.

#### **Eye involvement**

Acute anterior uveitis is an inflammation of the iris of the eye. It is not frequent. The eye is acutely red and painful. Immediate control by the ophthalmologist (the eye doctor) is necessary.

#### **Skin involvement**

A small subset of children with spondyloarthropathy may have psoriasis. Psoriasis is a chronic skin disease with patches of scaling skin mainly located on the elbows and the knees. The skin disease may precede arthritis by years. In other patients the arthritis can already exist several years before a first psoriasis spot occurs.

#### **Bowel involvement**

Some children with intestinal inflammatory disorders may develop a spondyloarthropathy.

Inflammatory bowel disease (IBD) is used to designate chronic bowel inflammation of unknown origin. These diseases are called Crohn's disease or ulcerative colitis.

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

The spectrum is wide. While some children have mild and short-term disease, others have severe, long-term and disabling disease.

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

Juvenile spondyloarthropathies differ from adult spondyloarthropathies in some aspects.

- 1) Peripheral (limbs) joints are much more frequently affected in the beginning of the disease in contrast to the more frequent axial (spine) involvement in adults.
- 2) In children, the hip is more frequently affected.

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

Doctors say it is a juvenile spondyloarthropathy if the onset of the disease is before the age of 16, the arthritis lasts for more than six weeks and the characteristics fit into the clinical pattern described above (see definition and symptoms). The diagnosis of specific spondyloarthropathies (i.e. ankylosing spondylitis, reactive arthritis, etc.) is based on specific clinical and radiographic features.

It is clear that these patients should be treated and followed by a paediatric rheumatologist.

### **What is the importance of tests?**

The HLA-B27, a cellular marker that is positive in up to 80-85 % of patients with juvenile spondyloarthropathies, is useful in orientating the diagnosis. Its frequency in the general healthy population is much lower (5–12 % depending on the region). Therefore, it is not the presence of HLA-B27 by itself, but its association with the characteristic signs and symptoms of spondyloarthropathies, which has relevance.

Exams, such as erythrocyte sedimentation rate (ESR), or C-reactive protein (CRP), give information about general inflammation and, indirectly, about disease activity. They are useful in disease management, although this is based much more on clinical manifestations than on laboratory examinations. Laboratory tests are also used to monitor possible side effect of the treatment (blood cell count, liver and kidney function). X-ray examinations are useful to follow disease evolution and assess joint damage caused by the disease.

Computer tomography (CT scan) and magnetic resonance imaging (MRI) may be useful, especially in children, to evaluate the involvement of sacroiliac joints.

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

There is no curative treatment since the cause of spondyloarthropathies is unknown. However, therapy can be very useful to control disease and prevent damage.

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

Treatment is based mainly on the use of drugs in combination with physiotherapy and rehabilitation procedures that preserve joint function and contribute to prevent deformities.

**1) Non-steroidal anti-inflammatory drugs (NSAIDs).** They are symptomatic anti-inflammatory and antipyretic (fever reducing) medications. Symptomatic means that they serve to control symptoms due to inflammation. The most widely used in children are naproxen and ibuprofen. Aspirin, although effective and cheap, is much less used nowadays due to its risk of toxicity. They are usually well tolerated and gastric discomfort, the most common side effect, is uncommon. NSAIDs are not prescribed in conjunction with one another, but one NSAID may be effective were another has failed.

**2) Joint injections** are used when one or very few joints are involved and when joint deformity is a real possibility. The drug injected is a long-acting steroid preparation.

**3) Sulphasalazine** is indicated in children that have a chronic course of disease, despite adequate therapy with NSAIDs and steroid injections. It is added to previous NSAID therapy (which has to be continued) and its effect becomes fully evident only after several weeks or months of treatment.

Experience with other drugs, including methotrexate, is limited.

New perspectives have been introduced in the last few years with anti-TNF drugs (called biological agents). They selectively block tumor necrosis factor (TNF), an essential mediator in the inflammatory process. Yet there are no studies known about the effect or risks of this kind of treatment in patients with juvenile spondyloarthropathies.

**4) Corticosteroids** have a role in the short-term management of patients that are more severely ill. Topical steroids (eye drops) are used in the treatment of acute anterior

uveitis. In more severe cases, peribulbar steroid injections or systemic steroid administration may be required.

**5) Orthopaedic surgery** is usually needed for prosthetic joint replacement, in the case of severe joint damage, particularly in the hip.

**6) Physiotherapy** is an essential component of treatment. It must be started early and should be performed routinely to maintain range of motion, muscle trophism and strength and to prevent, limit or correct articular deformities. Moreover, if axial involvement is prominent, the spine has to be mobilised and respiratory exercises performed.

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

The drugs used in the treatment of juvenile spondyloarthropathies are usually well tolerated. Gastric intolerance, the most frequent side effect of NSAIDs, is less common in children than in adults. NSAIDs can cause increase in the blood levels of some liver enzymes, but this is a rare event with drugs other than aspirin.

Sulphasalazine is reasonably well tolerated; the most frequent side effects are stomach problems, elevated liver enzymes, low white blood cells count and skin rash. Periodic laboratory examinations are needed to monitor toxicity.

Methotrexate is also well tolerated. Gastroenteric side effects, such as nausea and vomiting, are not uncommon. The administration of folinic or folic acid is effective in reducing the frequency of liver problems. Hypersensitivity reactions to methotrexate can occur, but are rare. Periodic laboratory examinations are needed to monitor toxicity.

The long-term use of steroids in significant dosage is associated with several important side effects. These include stunting growth and osteoporosis. Steroids at high doses cause a marked increase in appetite, which can in turn lead to obesity. It is, therefore, important to instruct children to eat foods that can satisfy the appetite without increasing caloric intake.

### **How long should the treatment last for?**

It should last as long as symptoms and disease activity persist. Disease duration is unpredictable. In some patients, arthritis responds very well to NSAIDs. In these patients the treatment can be stopped rapidly, within months. In other patients, with a more prolonged or aggressive course of disease, sulphasalazine and other medications are needed for years. Complete treatment withdrawal is then considered only after prolonged and complete disease remission.

### **What about unconventional and complementary therapies?**

There is no proof that any unconventional therapy has an effect in the juvenile spondyloarthropathies.

### **How long will the disease last for? What is the prognosis (predicted outcome) of the disease?**

The disease course can be different from one patient to another. In some patients the arthritis disappears quickly, with little treatment, within a period of months. In others the disease will have periods of remission and recurrence. In other patients, arthritis may follow an unremitting course.

At the beginning of disease symptoms are confined to peripheral joints and the entheses (tendons) in the vast majority of patients. With disease progression, some of them may develop involvement of the sacroiliac joints and the spine. These patients and those with persistent peripheral arthritis, carry the higher risk of developing joint damage in adulthood.

At the beginning of the disease it is impossible to predict the long-term outcome.

### **How could the disease affect the child and family's daily life?**

During the periods of active arthritis, almost every child will experience limitations to some extent in daily life. Since mainly the lower limbs are affected, walking and sports are the domains where the limitations are felt the most.

Major attention should be paid to the psychological impact of the disease on the child and family. A chronic disease is a difficult challenge for the whole family and, of course, the more serious the disease, the harder it is to cope. It will be difficult for the child to cope properly with his disease if the parents don't. The parents often develop an abnormal attachment towards their sick child and, in order to prevent possible problems, become overprotective. This can cause the child to feel inadequate, which can damage personality development with worse long-term damage than the disease itself. A positive attitude from parents who support and encourage the child to be independent as much as possible, despite the disease, will be extremely valuable to help the child to overcome difficulties. If the family cannot endure the burden of the disease, psychological support is needed.

### **What about school?**

It is extremely important for the child to attend school regularly. There are a few factors that may cause problems for school attendance, including difficulty in walking, minor resistance to fatigue, pain and stiffness. It is, therefore, important to explain to teachers possible needs, such as proper desks and regular movements during school hours to avoid articular stiffness. Patients should take part, whenever possible, in gym lessons and the considerations discussed below in the issue of sports, have to be taken into account.

School is a place where a child learns how to become an autonomous person, productive and independent. Parents and teachers have to do whatever they can to make the sick child participate to school activities in a normal way, in order to have academic success. A normal school life is also vital to ensure the child develops a good capacity for communication with peers and adults.

### **What about sports?**

Playing sports is an essential aspect of the everyday life of a normal child. Therefore, the general tendency is to leave patients to play the sports they want and to trust that they will stop if a joint hurts. Although mechanical stress is not beneficial in an inflamed joint, it is assumed that the little damage that could ensue is much smaller than the psychological damage of being prevented from playing sports with friends because of the disease. This choice is part of a more general attitude to encourage the child to be autonomous and to cope with the limits imposed by the disease.

Apart from these considerations, it is better to favour sports in which mechanical stress to the joints is absent or minimal, such as swimming and riding a bike.

**What about diet?**

There is no evidence that diet can influence the disease. In general the child has to take a balanced, normal diet for his age. Overeating has to be avoided in patients taking steroids since steroids increase the appetite.

**Can climate influence the course of the disease?**

There is no evidence that climate can affect the disease.

**Can the child be vaccinated?**

Since most of the patients are treated with either NSAIDs or sulphasalazine, a normal vaccination scheme can be advised. If a patient is being treated with an immunosuppressive therapy (steroids, methotrexate, anti-TNF etc.) vaccination with live attenuated viruses (such as anti-rubella, anti-measles, anti-parotitis, anti-polio Sabin) have to be postponed because of the increased risk of infections. Vaccines that do not contain living viruses (anti tetanus, anti diphtheria, anti polio Salk, anti hepatitis B, anti pertussis, pneumococcus, haemophilus, meningococcus) can be administered, the only theoretical risk being vaccination failure due to the condition.

**What about sexual life, pregnancy, birth control?**

There are no restrictions for having a normal sexual life or pregnancy due to the disease. Yet, in patients taking medications, one should always be very careful about the possible toxic effects of these drugs on the foetus.

There is no reason for not having children, despite of the genetic aspects of the disease. The disease is not lethal and even if the predisposing genetic factor should be inherited, the siblings have a much greater chance of not developing a spondyloarthropathy than of develop one.

**Will the child have a normal adult life?**

This is one of the main goals of the therapy and it can be reached in the majority of cases. Therapies for these kinds of diseases in childhood have improved dramatically in the last ten years. The combined use of pharmacological treatments and rehabilitation is now able to prevent joint damage in the majority of patients. Yet in patients with chronic disease, joint damage may be important and can limit the patient's daily life and professional ambitions.