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# Juvenile Spondyloarthritis / Enthesitis Related Arthritis (SpA-ERA)

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## 2. DIAGNOSIS AND THERAPY

### 2.1 How is it diagnosed?

Doctors diagnose juvenile SpA-ERA if the onset of the disease is before the age of 16 years, the arthritis lasts for more than 6 weeks and the characteristics fit into the clinical pattern described above (see definition and symptoms). The diagnosis of a specific SpA-ERA (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, or an adult rheumatologist with experience in children´s rheumatic diseases.

### 2.2 What is the importance of tests?

A positive HLA-B27 test is useful in the diagnosis of juvenile SpA-ERA, particularly in mono-symptomatic children. It is very important to know that less than 1% of people with this marker develop spondyloarthritis and that the prevalence of HLA-B27 in the general population might be as high as 12%, depending on the region of the world. It is also important to note that most children and adolescents practice some kind of sport and that these activities might result in injuries somewhat similar to the initial symptoms of juvenile SpA-ERA. Therefore, it is not the presence of HLA-B27 by itself but rather its association with the characteristic signs and symptoms of SpA-ERA that has relevance. Laboratory tests such as erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) provide information about general inflammation

and therefore, indirectly, about inflammatory disease activity; they are useful in disease management, although this should be based much more on clinical manifestations. Laboratory tests are also used to monitor possible adverse events related to treatment (blood cell count, liver and kidney function).
X-ray examinations can be useful to follow disease evolution and assess any joint damage caused by the disease. However, the value of X-ray examinations is limited in children with SpA-ERA. Since X–ray results may be normal, ultrasonography and/or magnetic resonance imaging (MRI) of the joints and entheses is required to reveal the early inflammatory signs of the disease. With MRI, inflammation of the sacroiliac joints and/or the spine can be detected without the use of irradiation. Ultrasonography of the joints, including power Doppler signal, can provide a better idea of the occurrence and severity of a peripheral arthritis and enthesitis (limbs).

## 2.3 Can it be treated/cured?

Unfortunately, there is still no curative treatment for SpA-ERA since we do not know its cause. However, current therapy can be very useful to control disease activity and probably to prevent structural damage.

## 2.4 What are the treatments?

Treatment is based mainly on the use of drugs and physiotherapy/rehabilitation procedures that preserve joint function and contribute to preventing deformities. It is important that the use of medications depends on approval by local regulatory agencies.

### Non-steroidal anti-inflammatory drugs (NSAIDs)

These drugs are symptomatic anti-inflammatory and antipyretic medications. Symptomatic means that they serve to control symptoms due to inflammation. The most widely used in children are naproxen, diclofenac and ibuprofen. They are usually well-tolerated and the most frequent adverse event, gastric discomfort, is in fact rare in children. A combination of NSAIDs is not recommended, although it may be necessary to switch from one NSAID to another in case of inefficacy or adverse events.

## Corticosteroids

These drugs have a role in the short-term management of patients with more severe symptoms. Topical (eye drops) corticosteroids are used in the treatment of acute anterior uveitis. In more severe cases, periocular (around the eyeball) injections or systemic corticosteroid administration may be required. In prescribing corticosteroids for arthritis and enthesitis, it is important to bear in mind that there are no adequate studies about efficacy and safety in children with SpA-ERA; in some cases, expert opinion supports their use.

## Other treatments (Disease Modifying Drugs)

### Sulfasalazine

This drug is indicated in children with peripheral disease manifestations that persist despite adequate therapy with NSAIDs and/or intralesional corticosteroid injections. Sulfasalazine is added to previous NSAID therapy (which must be continued) and its effect might be evident only after several weeks or months of treatment. Nevertheless, there is only limited evidence of sulfasalazine efficacy in these children. At the same time, despite their widespread use, there is no clear evidence that methotrexate, leflunomide or anti-malarial drugs would be effective in juvenile SpA-ERA.

### Biologics

Anti-tumour necrosis factor (TNF) agents are recommended in early stages of the disease because of their significant efficacy in treating inflammatory symptoms. There are studies on the efficacy and safety of these drugs that support their use in patients with severe juvenile SpA-ERA. These studies have been submitted to health authorities and are waiting for approval to start their use in SpA-ERA. In some European countries, anti-TNF agents are already approved for children.

## Joint injections

Joint injections are used when one or very few joints are involved and when persistence of joint contracture may cause deformity. In general, long-acting corticosteroid preparations are injected. It is recommended that children are admitted to the ward and sedated to perform this procedure under the best conditions.

## Orthopaedic surgery

The main indication for surgery is prosthetic joint replacement in the case of severe joint damage, particularly in the hip. Thanks to better drug treatment, the need for orthopaedic surgery is decreasing.

### Physiotherapy

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

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

The drugs used in the treatment of juvenile SpA-ERA are usually well-tolerated.

Gastric intolerance, the most frequent side effect of NSAIDs (which should therefore be taken with food), is less common in children than in adults. NSAIDs may cause an increase in the blood levels of some liver enzymes, but this is a rare event with drugs other than aspirin.

Sulfasalazine is reasonably well-tolerated; the most frequent side effects are stomach problems, elevated liver enzymes, low white blood cell counts and skin reactions. Repeated laboratory examinations are needed to monitor its possible toxicity.

The long-term use of high dose corticosteroids is associated with moderate to severe adverse events, including stunted growth and osteoporosis. Corticosteroids at high doses cause a marked increase in appetite, which can in turn lead to marked obesity. It is therefore important to instruct children to eat foods that can satisfy their appetite without increasing caloric intake.

Treatment with biologic agents (TNF blocking agents) may be associated with a higher frequency of infections. Preventive screening for (latent) tuberculosis is mandatory. To date, there is no evidence of a higher frequency of malignancies (except for some forms of skin cancer in adults).

## 2.6 How long should the treatment last?

Symptomatic treatment 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, treatment can be stopped early on, within months. In other patients with a more prolonged or aggressive course of disease, sulfasalazine and other types of medications are needed for years. Total drug withdrawal may be considered after prolonged and complete disease remission on drugs.

### 2.7 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 both in terms of time, burden to the child and money. If you want to explore complementary and alternative therapies, please discuss these options with your paediatric rheumatologist. Some therapies can interact with conventional medications. Most doctors will not be opposed, provided you follow medical advice. It is very important not to stop taking your prescribed medications. When medications 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.

### 2.8 How long will the disease last? What is the long-term evolution (prognosis) of the disease?

The disease course can be different from one patient to another. In some patients, arthritis disappears quickly with treatment. In others, it is characterised by periodic remissions and recurrences. Finally, in other patients, arthritis may follow an unremitting course. In the vast majority of patients, symptoms are confined to peripheral joints and enthesis at the beginning of disease. As the disease progresses, some children and adolescents may develop sacroiliac and spinal joint involvement. Patients with persistent peripheral arthritis and axial symptoms have a higher risk of developing joint damage in adulthood. Nevertheless, at the beginning of the disease it is impossible to predict the long-term outcome. In contrast, adequate treatment can influence the course and prognosis of the disease.