

## Juvenile Rheumatoid Arthritis (JRA)

### Introduction:

JRA is not simply rheumatoid arthritis (RA) in children. It is also not a single disease. It is a group of arthritis conditions with a wide variety of manifestations occurring in about 1 in 1,000 children. Although less common than the adult form of RA, JRA is as common in this age group as juvenile diabetes and more common than cystic fibrosis.

There are 3 major forms of JRA: pauciarticular (meaning “few joints”) onset, polyarticular (meaning “many joints”) onset, and systemic onset. These subsets of JRA will be further described below, but each displays a distinctly different pattern. This variability and lack of similarity between most forms of JRA and adult RA have led some to prefer the term “juvenile chronic arthritis.”

While the long-term outlook of JRA varies with different forms of the disease, over 1/3 of children in general will have active disease that persists into their adult lives, while the remainder experience a remission by the time they reach adulthood. Moreover, 30-50% of patients experience significant limitations in daily functioning 10 years after the onset of their disease. For these reasons, prompt recognition of and proper therapy for JRA are crucial and can have a lasting impact on the quality of the child's life.

### Features of JRA:

Before discussing the different forms of JRA, it is important to remember a few issues important when dealing with arthritis in children. First of all, JRA is often diagnosed late due to the fact that children may communicate symptoms differently or that symptoms may be misinterpreted as “growing pains.” In younger children, the only sign that joint disease is present may be a limp or a reduction in playtime activities without any complaints on the part of the child.

Secondly, JRA, as well as some of the therapies, affect growth. This may be manifest as general growth impairment or as unequal growth of a limb. Depending on the stage of growth, inflammation of a joint may either speed up or shut down the rate of growth, leaving the child with one leg or arm that is longer than the other.

Pauciarticular onset (PaO) is the most common form of JRA and is also the form with the best long-term outcomes. Children with this type of JRA typically experience pain and/or swelling of one or a few joints in the lower limbs, such as the hip, knee, or ankle. Even within this group of patients, there are 2 subsets, one with an average onset around the age of 2 where girls predominate, and one with an average onset around the age of 10 that is seen more commonly in boys. In the latter group of patients, lower back and heel pain are more common, and some of these children evolve into a condition known as ankylosing spondylitis (AS) when they become adults (see related section).

Polyarticular onset (PoO) JRA most closely resembles adult RA. These children experience pain and swelling in small and large joints, typically in a symmetrical pattern. The hands, wrists, elbows, knees, ankles, and feet are the most common joints involved. Like PaO disease, patients with PoO JRA can be divided into two groups, one beginning at an average age of 3 and one beginning at an average age of 12. Girls outnumber boys in both of these subsets of patients. Deforming changes and joint damage are more common in PoO disease than in any other form of JRA.

Systemic onset (SO) disease is characterized by fever, often occurring once per day, elevated white blood cell count, a transient rash, and less commonly inflammation of the lining of the heart or lungs or enlargement of the lymph nodes, liver, or spleen. Joint disease in SO JRA may either resemble the PaO or PoO forms of the disease, but in some children the joint disease may be minimal or absent (somewhat of a misnomer in a disease classified as “arthritis”). The average age of onset is 5 years, and boys and girls are equally affected. While it is the least common form of JRA, both growth impairment and life-threatening complications occur more commonly in SO JRA than in the other two forms.

To some extent or another, iritis or uveitis (inflammation of the eyes) may occur in all forms of JRA. This complication occurs more commonly in patients with PaO JRA than in other forms, affecting up to 25-30% of these children, versus 5% or less of those with PoO or SO disease. While the eye may become red, painful, or blurry when iritis is present, this process is often silent and slowly progressive. For this reason, screening for eye disease through an ophthalmologist is recommended routinely, anywhere between one to four times per year depending on the child's age and type of JRA. Your doctors will make individual recommendations to patients and families depending on these factors.

## **Diagnosis:**

To diagnose any form of JRA, one or more swollen joints must be observed for at least 6 weeks, and other causes of bone or joint disease (tumors, infections, injuries, etc.) must be excluded. To classify a patient as “juvenile,” symptoms should be present before the age of 16. The most important factors in making a diagnosis of JRA are the history of the symptoms and the findings on examination of the joints.

Classifying the form of JRA present depends on the number of swollen joints present during the first 6 months of the disease. If 4 or fewer joints are involved, the child has PaO disease; if there are 5 or more joints involved, the child has PoO disease. SO JRA can be diagnosed if a daily intermittent fever is present along with the arthritis or the skin and internal organ involvement. When arthritis is absent, the diagnosis is more difficult to confirm.

Laboratory testing is less helpful in JRA than in adult RA or lupus. While many abnormalities may be present in certain children and may help classify their disease, it is not unusual for children with active arthritis to have entirely normal laboratory studies. Markers of inflammation, while often elevated, are unreliable at measuring disease activity in most JRA patients. A positive rheumatoid factor, found in most patients with adult RA, is infrequently seen other than in older children with PoO disease. The antinuclear antibody, seen in almost all patients with lupus, may be positive in up to 1/2 of patients with PaO or PoO JRA, at times causing physicians to mislabel a JRA patient as having lupus. The gene HLA-B27, seen in most patients with AS, is positive in about 1/2 of older children with PaO disease.

X-ray studies of involved joints are most useful to assess for joint damage, evaluate the growth status of a limb, and exclude other diagnoses. Because of concerns regarding radiation exposure in children, these studies are ordered less frequently than in adult patients. Magnetic resonance imaging (MRI) may be used if evaluating for a bone or soft tissue tumor but is not routinely needed to diagnose JRA.

## **Therapy:**

The goals of therapy for JRA are to reduce symptoms but more importantly prevent or at least minimize the long-term complications of the disease, namely joint damage and loss of function. Just as JRA has many forms, the treatment required to achieve these goals also consists of many different strategies.

Non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen (Motrin) and naproxen (Naprosyn) are often sufficient to treat milder JRA. In fact, over 1/2 of patients will respond to such therapies, and an additional 1/2 that fail will respond to treatment with a different NSAID. Responses are generally seen within 1 to 3 months, after which time other therapies must be considered. Depending on the age of the child, oral suspensions or syrups may be preferred over pills.

Corticosteroids such as prednisone are effective in JRA but must be used with caution. While these medications rapidly reduce swelling and pain in involved joints and reduce signs of SO JRA, there is a risk of infection, weight gain, weakening of the bones, as is the case with adults taking these medications long-term. An additional consideration in children is that steroids slow down growth when given for prolonged periods of time. For these reasons, corticosteroids are often best used for temporary treatment of disease flares. An additional role of steroids is to administer by joint injection in patients with PaO disease where one or two joints are swollen. The procedure is best performed under general anesthesia in younger children. This approach may reduce contractures of the limb or limit problems with growth of a limb.

Disease modifying anti-rheumatic drugs (DMARDs) should be started in a child with JRA failing to respond to NSAIDs after 2 to 3 months of therapy. Methotrexate (MTX), given as a once weekly dose, is the drug many physicians prefer due to the evidence that this agent improves function and limits joint damage in JRA. Children with PoO or SO JRA are given this medication more frequently than those with PaO JRA. Reduction in blood counts, elevation of liver enzymes, and susceptibility to infection are potential side effects to monitor but generally are less frequent in children than in adults.

Other DMARDs that are often effective in JRA include sulfasalazine (Azulfadine), hydroxychloroquine (Plaquenil), cyclosporine (Neoral), azathioprine (Imuran), and leflunomide (Arava). In general, less evidence is present to support the effectiveness of these therapies in JRA, but for PaO JRA, sulfasalazine appears to be particularly effective in certain patients.

Tumor necrosis factor (TNF) antagonists such as etanercept (Enbrel), infliximab (Remicade), and adalimumab (Humira) have recently been shown to be quite effective in treating JRA. While only Enbrel is approved by the FDA for treating JRA, the other agents in this class also appear to be equally effective. As in adults, a risk for infection does seem to be increased in patients using these medications. Because of the cost of these therapies and the need for either injection or intravenous infusion, TNF

antagonists are generally used in patients resistant to standard therapies, particularly for children with PoO disease.

A recent preliminary observation is that anakinra (Kineret), a medication that blocks the effects of a chemical known as IL-1, seems to be quite effective in treating SO JRA. This medication must be given by daily injection, is expensive, and does somewhat increase the risk of infection. Nonetheless, the promising early results suggest that Kineret may play a prominent role in treating SO JRA resistant to other medications.

Occasionally, iritis or a manifestation of SO JRA involving another part of the body may guide therapy more so than the joint disease. In this event, preventing vision loss or damage to different organs must also be factored in as a goal of therapy. Fortunately, the above medications generally treat these features of the disease as well, but a more aggressive approach may be needed in children with some of these complications of JRA.

Physical therapy is another important addition to the treatment of JRA in many children. Maximizing strength and function in diseased joints and splinting or stretching to minimize contractures or deformities are reasonable approaches to treating this disease and allow the child to actively participate in his or her recovery.

Finally, because many children with JRA feel isolated from their peers due to their limitations, activities in the community sponsored by the Arthritis Foundation or other such organizations can play a valuable role by providing support. Information for the child's teachers and classmates provided by the Foundation can also assist in their understanding of the disease. Arthritis camps, support groups for families, and other programs help the child and the family realize that they are not alone with JRA. Much can be done for JRA, but it must first be recognized and appropriately treated. As education of the community and medical professionals improves and therapies continue to be developed, hopefully so will the care provided to children suffering from various forms of JRA improve.

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