Management of childhood arthritis. Part 2: chronic arthritis

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Classification
Chronic idiopathic arthritis of childhood encompasses a diverse group of disorders. This diversity is reflected in the different classification systems in use in North America and Europe. As concepts have evolved there have been attempts to modify the classification system. This is not just a matter of semantics, but a recognition that it is necessary to develop as much homogeneity as possible in the groupings if there is going to be progress in understanding the cause(s), outcomes, and optimum management of childhood chronic arthritis.

At present it is generally agreed that there are at least the following groups: (a) early onset oligoarticular arthritis, occurring most often in girls less than about 6 years of age, in whom there is a high risk of chronic uveitis; (b) late onset oligoarthritis, affecting mostly older boys, often associated with enthesitis, and which is really a spondyloarthropathy and often a precursor of ankylosing spondylitis; (c) other spondyloarthropathies, a heterogeneous group of disorders, including early onset ankylosing spondylitis, reactive arthritis, and arthritis associated with inflammatory bowel disease; (d) juvenile psoriatic arthritis, which has traditionally been classified with the spondyloarthropathies, but is probably a separate group, in which there is asymmetrical small joint involvement and dactylitis; (e) polyarticular arthritis, which may be further subdivided into rheumatoid factor positive and rheumatoid factor negative subgroups; and (f) systemic onset arthritis, in which there are marked constitutional symptoms, including rash and fever.

Disease assessment
The assessment of children with arthritis has conventionally focused on evaluating disease activity by counting the number of swollen, tender, and limited joints and measuring haemoglobin, platelet count, and erythrocyte sedimentation rate. Disease severity has been assessed by radiography and function by the use of a simple four category scale, the Steinbrocker functional classification. Unfortunately, and not surprisingly, there is poor correlation between each of the individual measures, as well as between these measures and the final outcome of the disease. How a child copes with arthritis, and whether the individual grows up to be functional and happy, is influenced by more factors than can be measured by such simple classifications of disease process and function.

Instruments have now been developed that more accurately assess function and that are sensitive to changing disease activity. The first such instruments were the child and parent questionnaires and physiotherapy assessment scales, known as the Juvenile Arthritis Functional Assessment Report and Juvenile Arthritis Functional Assessment Scale, respectively. These are quick and simple tools measuring the activities of basic daily functioning, suitable for children between the ages of 7 and 17 years. A more complex tool is the Childhood Health Assessment Questionnaire. Based on an adult instrument it can be used for children from about 2 years of age. A more detailed questionnaire that may be particularly valuable for physiotherapists is the Juvenile Arthritis Functional Status Index. These instruments basically only assess functional ability and pain. A more comprehensive tool, which also attempts to assess areas of difficulty in the psychosocial domain, is the Juvenile Arthritis Quality of Life Questionnaire. Still in development is the Childhood Arthritis Health Profile, which attempts to measure both disease specific and generic disorders, including behaviour, well-being, self esteem, the impact of the disease on the family, and functioning in school.

It seems unlikely that any one instrument is going to be able to measure all the factors that affect a child with chronic arthritis. A number of measures such as doctor, parent, and patient global evaluations, functional measures, as described earlier, and more conventional measures such as joint counts and erythrocyte sedimentation rate will be needed in combination to have any hope of accurately assessing whether or not a child is improving. Whether any of these measures, singly or combined, performed early on in the disease course will be able to give useful information about outcome is an important, but unanswered, question.

Drug treatment
There have been some important advances in the pharmacological management of chronic arthritis in childhood, in particular the earlier use of intra-articular corticosteroids and of the
so-called slow acting antirheumatic drugs (SAARDs).

Several studies have now shown that intra-articular corticosteroids are effective drugs in childhood. Triamcinolone hexacetonide in a dose of about 1 mg/kg body weight for large joints and about half that dose for smaller joints can be used for children with a few swollen joints if the arthritis does not improve within a few weeks of starting non-steroidal anti-inflammatory drugs (NSAIDs), or if the joint(s) are very swollen and painful. Intra-articular triamcinolone could possibly be used alone without NSAID treatment for oligoarticular disease; there is only anecdotal evidence to support such an approach, but it could certainly be justified in a child who is having difficulty in tolerating NSAIDs.

Several workers have suggested that the conventional ‘pyramid’ treatment approach, in which treatment is started with an NSAID and a SAARD only used if the disease continues to progress, is suboptimum. There are a number of reasons to question the conventional approach. Firstly, it does not appear to be effective in preventing the long term progression of the disease. Childhood arthritis is a much less benign disease than used to be believed, with about 40% of children from all disease subtypes continuing to have active joint inflammation and 20% of children having severe functional limitations after 10 or more years of follow up. There may be a relatively limited window of opportunity in the first two years of disease to limit joint damage; beyond this time cartilage loss is inevitable as the damage has already been done.

Secondly, in adults NSAIDs are more toxic relative to SAARDs than previously recognised. Whether this is true in children is not known, but it is certainly a possibility. Thirdly, the additional use of methotrexate to the therapeutic armouramentarium has revolutionised the management of childhood chronic arthritis, as it appears to be an effective drug, with much less toxicity than was originally feared.

At the present time it is still appropriate to begin treating a child with chronic arthritis with an NSAID. We usually start with naproxen 15 mg/kg/day divided twice a day for most patients, but we have a bias that tolmetin (30 mg/kg/day divided three times a day) may be more effective for children with probable spondyloarthopathies (older boys, with their legs affected, often with enthesitis). We wait 6–8 weeks before deciding if the NSAID is efficacious, though if the child has a very swollen or painful joint(s) we may well inject him or her with triamcinolone hexacetonide.

We have a low threshold for starting treatment with a SAARD, using methotrexate within a few weeks of the onset of the disease if we suspect that the child is likely to have a severe disease course. For incompletely controlled mild disease we might try hydroxychloroquine (5 mg/kg/day) before using methotrexate, as it does not require routine blood tests to monitor for toxicity. Although ocular toxicity used to be a concern, there seems to be a negligible risk of eye damage at this dose. We also use sulfasalazine (50 mg/kg/day divided three times a day), which is probably more effective than hydroxychloroquine, but more toxic, requiring initially two weekly to monthly tests to monitor for bone marrow suppression and liver and renal toxicity. Sulfasalazine may be particularly effective in patients with a spondyloarthropathy or with psoriatic arthritis. There is some evidence that it is effective as a single drug without NSAIDs in children with various forms of chronic arthritis.

As methotrexate is such an effective drug, it is important not to wait too long before starting it. The initial dose is about 0.15 mg/kg/week as a single dose, increasing over a few weeks to 0.3–0.5 mg/kg/week (approximately 10 mg/m²). Doses considerably in excess of this may be necessary and are usually well tolerated, particularly if the child receives a small dose of folic acid (1 mg/day). If the liver enzymes increase, the dose can be stopped or reduced temporarily. Discontinuing the concomitant NSAID often allows the methotrexate dose to be increased without the enzymopathy recurring. Intramuscular or subcutaneous methotrexate can be used in children requiring higher doses of methotrexate in whom there are problems with toxicity or uncertainties about absorption.

Many patients with polyarticular disease benefit from a small dose of prednisolone (0.1–0.2 mg/kg/day given once or twice a day) while waiting for the NSAID and SAARD to start working. In systemic onset disease we almost always have to use moderate dose prednisolone (0.5–1 mg/kg/day divided three times a day) to control the systemic symptoms. Although there are proponents of high dose intravenous methylprednisolone pulse treatment in systemic disease and in severe polyarticular disease, our experience has been that the response to such pulses is limited, to only a few days’ duration, unless corticosteroids are continued by mouth. Although many authorities advocate the use of alternate day doses of prednisolone as maintenance treatment, my bias is that it does not usually adequately control the disease, with symptoms breaking through on the ‘off day’. Unfortunately, there are no good studies comparing the use of different corticosteroid regimens in childhood arthritis. There is some evidence that both gold and sulfasalazine treatment in the acute systemic phase may be associated with the development of a rare, but potentially fatal, disorder known as macrophage activation syndrome, in which there is hepatic encephalopathy with disseminated intravascular coagulation. This disorder usually responds to very high doses of prednisolone alone, but may require cyclosporin treatment.

Although not always successful, the philosophy is to try and completely suppress all evidence of active arthritis. Continuing inflammation, even if low grade, eventually leads to permanent joint damage which could possibly be avoided with earlier, more aggressive intervention. Whether the development of the so-called ‘biologics’ will lead to a greater ability to control inflammation is an exciting but uncertain prospect.
Rehabilitation

Simply suppressing the inflammation is often insufficient to return the child to normal functioning. Some children develop disabling joint deformities, not due to damaged joints, but due to inadequate attention being paid to the soft tissue contractures that develop as a consequence of having a painful, swollen joint. It is therefore essential that the doctor works closely with physiotherapists and occupational therapists to institute an appropriate rehabilitation programme. Optimally, this requires a coordinated team approach, with regular reassessments of the therapeutic goals.

Childhood is a period of rapid physical growth and treatment must focus on controlling deviations from expected patterns of development, such as leg length discrepancies, valgus/varus deformities, and gait abnormalities. The danger of excessive rest causing muscle wasting, joint contractures, and osteoporosis is now well recognised. Increasingly, the importance of maintaining overall physical fitness for the child’s long term physical and psychological wellbeing has been emphasised.32–35 Therapeutic options include stretching, strengthening, gait retraining, serial casting, orthotics, and other devices to help activities of daily living. Surgical interventions are much less often required if there is an early, well coordinated treatment programme. Open synovectomies are positively harmful and arthroscopic synovectomies of limited benefit. Unfortunately, an occasional child has continuing poorly controlled disease and becomes a candidate for surgical procedures that include soft tissue releases, operations to correct leg length differences and angular deformities, and joint replacements. Any surgery requires careful planning between the surgeon, doctor, and therapists.

Finally, the importance of managing the whole child and the child’s environment (family, school, peers) cannot be over emphasised. The development of chronic arthritis alters the child’s and child’s parents perceptions of themselves as individuals and as a family unit. It affects plans for the future as well as day to day functioning, and has major financial implications for the family.38–41 Dealing with these complex psychosocial issues is difficult, requiring input from sources including schools, colleges, and universities. Although the data are limited, the evidence suggests that most children with chronic arthritis grow up to become well adjusted and contributing members of society.42 The factors which contribute to a good outcome, even in the face of severe arthritis, and the factors which lead to a poor outcome need to be a focus of continuing research.32 54–35

This paper has attempted to give an overview of the issues involved in managing children with chronic arthritis. Many issues have, by necessity, been discussed in a fairly superficial manner. For more detailed, theoretical, and practical information there are a number of reference books available.1


