Musculoskeletal pain in childhood and adolescence is common and has many causes, including arthritis (acute and chronic), as well as benign conditions, such as hypermobility, and life-threatening conditions such as non-accidental injury and malignancy. Clinical history taking and examination remains the mainstay of the diagnosis of arthritis in young people.

The causes of a group of conditions known as “juvenile idiopathic arthritis” (JIA) are, as yet, poorly understood. Genetic and environmental factors are thought to be important but direct inheritance is not seen. JIA is the main type of chronic inflammatory arthritis in childhood and is defined as arthritis persisting for at least six weeks and before the age of 16 years. It is a heterogeneous group of seven different subtypes (see Panel 1), the most common being oligoarthritis.

**Features, prevalence and impact**

JIA is a different disease from adult rheumatoid arthritis, not least regarding its impact on the growth and development — physical and psychosocial — of a young person. Persistent arthritis during childhood and adolescence will cause localised growth abnormalities. For example, in childhood, persistent arthritis in a knee will lead to bony overgrowth and hence a longer affected leg. Similar arthritis in adolescence could potentially cause premature fusion of the growth plate, resulting in a shorter affected leg. Such leg length discrepancies result in a limp, and potentially lead to scoliosis.

Another important difference is that some subtypes of JIA, particularly oligoarthritis, are associated with the chronic anterior uveitis, which can lead to visual impairment, but this condition does not cause any pain or redness so can be difficult to detect. In contrast, rheumatoid arthritis related eye conditions are all painful and usually result in a red eye. All young people suspected of JIA should, therefore, have a baseline slit lamp examination by an experienced paediatric ophthalmologist.

Other types of inflammatory arthritis occurring in childhood include acute forms, such as septic arthritis (usually only affecting one joint), reactive arthritis (following an infective process and usually self-limiting) and chronic forms (eg, inflammatory bowel disease associated arthritis or arthritis associated with systemic lupus erythematosus). Careful history taking and examination — and the judicious use of a few appropriate investigations (eg, synovial fluid sent for culture where septic arthritis is suspected) — can usually differentiate these from JIA.

There are no blood tests to diagnose JIA (unlike in rheumatoid arthritis, most JIA cases are negative for rheumatoid factor), only ones to help classify the type, assess any systemic inflammatory response and exclude other causes of arthritis.

JIA affects one in 1,000 young people in the UK, and tends to affect females rather than males. It can occur at any age. Although...
Learning & development

the peak onset age is six years, over a quarter of cases present during adolescence. It is a myth that arthritis is linked to injury. Features that can be associated with JIA are:

- Reports of pain may not be explicit (they may depend on the young person’s developmental stage)
- The person is generally unhappy, and may not feel like eating
- A limp or reluctance to walk
- A reluctance to use both hands normally in everyday activities such as play or writing
- Stiffness first thing in the morning

One of the biggest challenges in the care of young people with JIA is securing an early diagnosis. Musculoskeletal pain is common in childhood and is the third most common presentation of teenagers to primary care.1 Young patients and their families — and some health care professionals — are most likely to think that symptoms are “growing pains” or related to strains and sprains from sports. Arthritis, acute or chronic, should be considered with any history of persistent, painful joint swelling, and regular use of band-aids would warrant referral to local rheumatology services.

New standards of care were launched in April 2010 by the British Society for Paediatric and Adolescent Rheumatology (BSPAR) and the Arthritis and Musculoskeletal Alliance (ARMA). The first standard emphasises the need for frontline practitioners who understand the importance of early detection: “All healthcare practitioners likely to come into contact with a child or young person with JIA require the skills to recognise the condition and support the effective management of the condition. This needs to be addressed in medical education and training programmes for other healthcare professionals.”

Up to half of young patients with JIA continue to have joint inflammation as adults, and up to two-thirds continue to have some limitation of their activities of daily living. A Canadian study showed that adult patients with oligoarthritis had the best outcomes, with 47% per cent achieving remission while those with rheumatoid factor (RF) positive polyarthritis had an essentially unremitting course.2

**Management**

It is important to treat JIA effectively, both in terms of appropriate drug therapy and exercise therapy. Limited side effects of therapy may be acceptable in order to avoid joint damage that might become a problem later. The management of JIA is multidisciplinary. The goals of treatment are to:

- Limit the side effects of therapy
- Promote self-advocacy skills
- Educate the patient and his or her family, teachers and other health professionals

**Non-steroidal anti-inflammatory drugs**

Effective anti-inflammatory pain control is indicated for all patients diagnosed with JIA. However, the higher doses of NSAIDs indicated in JIA might cause concern among pharmacists dispensing prescriptions for these patients, especially in the community sector, where there is often no access to patient records to confirm the diagnosis. For example, up to 2.4g of ibuprofen daily is recommended for JIA. (The latest edition of the BNF for Children indicates the specific NSAID doses used in JIA.) It is considered good practice for rheumatology teams to issue patients (or their guardians) with a letter confirming the dose and patients can be asked if they have such a letter. It is, however, important not to express concern about the dose to the patient during confirmation because this could affect future adherence and outcomes. Where in doubt, pharmacists can contact the rheumatology team.

Ibuprofen and piroxicam are the most commonly used NSAIDs. The widespread use of piroxicam in adults was discouraged following Committee for Medicinal Products for Human Use guidance in 2007, but young people tolerate the drug better than adults so its use continues in JIA. (Once they become adults, they are not always switched to an alternative and pharmacists might consider querying this.)

The once-daily dosing of piroxicam dispersible tablets makes them ideal because they do not have to be taken in school hours.

Meloxicam is used in young people aged 12 years and older and, again, is useful because of its once-daily dosing. Indomethacin is occasionally used in systemic JIA to treat fever but use is limited by its side effects, commonly headache and gastrointestinal disturbances.

Slow release preparations given at night may help to reduce morning stiffness.

It should be noted that the maximum effect of NSAIDs may not be seen for up to 12 weeks and, to support adherence, pharmacists should make patients aware of this.

**DMARDs**

Disease-modifying antirheumatic drugs (DMARDs) are used in some subtypes of JIA, but not in most cases of persistent oligoarthritis. The main agents and points related to their use are described in Panel 2.

**Methotrexate**

Methotrexate is well known for its dangers when dosed too frequently. Most regimens call for a weekly dose but there have been notable prescribing and dispensing errors resulting in daily dosing and tragic effects. National Patient Safety Agency guidance on improving compliance with oral methotrexate gives clear requirements to all pharmacy staff regarding the dispensing and checking process for oral methotrexate in arthritis. For example, each patient should be in possession of a methotrexate booklet in which the most recent blood tests are documented in order for the pharmacist to ensure safe dispensing.

In addition, in order to avoid confusion and possible overdose, only the 2.5mg tablets should be provided for arthritis management. However, some patients continue to have problems with taking tablets, necessitating the prescribing of an unlicensed liquid. Like methotrexate tablets, these liquids are available in different strengths so extra care (eg, accurate medication histories) are vital to ensure that the appropriate strength is ordered and made. One of the main difficulties patients with JIA face is the ongoing provision of unlicensed specials. Pharmacists can provide support and reassurance by not raising undue concern about the necessary use of unlicensed products.

**Biologics**

Etanercept, the most commonly used biologic, can be administered at home, and is the only biologic with accompanying National Institute for Health and Clinical Excellence guidance (see Resources; the development of NICE guidance on adalimumab and abatacept for children has been suspended). Adalimumab also supports self-administration.

The administration of some of the new biologics has meant trips to the hospital for young people and their families (eg, the administration of infliximab requires day case admission). The principle of employing care closer to home by using adalimumab was explored by a team in London, who found that young people and their families valued the input of the specialist team and were thus happy to travel for their advice.5 It is important, therefore, to understand the preferences of patients and their families.

**Roles for pharmacy staff**

Pharmacists can support patients with JIA, not only by advising on their medicines but by counselling on issues, such as precautions during treatment (eg, vaccinations and infections), complementary medicines and, in particular, ensuring adherence.

The BSPAR/ARMA guidelines highlight the need for pharmacists and pharmacy technicians in all sectors, as part of the multidisciplinary team, to support children,
young people and families living with JIA in a number of ways, including:

- Referring when JIA is suspected
- Providing treatment information to support shared decision-making
- Supporting adherence to therapy, including compliance aids, such as monitored dosage systems

Organisations such as Arthritis Care recognise the potential for pharmacists to advise people. They highlight the open access to pharmacists without an appointment and their ability to provide medicines both on prescription and over-the-counter. BSPAR/ARMA standards of care cite the pharmacist as a member of the extended care team. The Arthritis Care website highlights, in considerable detail, medicine use reviews and repeat prescription services in community pharmacies. Calls received in 2009 by its telephone helpline about patients aged 0–25 years showed that the fourth most common query type was about medicines, after questions about the type of arthritis, emotional support and severe pain.

The BSPAR and ARMA standards acknowledge the importance of providing young people living with JIA with holistic health information. Topics include sexual health and pregnancy, diet and exercise, dental health, alcohol and drug use, and transition into adult-centred services.

**Alcohol consumption**

Alcohol is not prohibited during methotrexate therapy, but the BSPAR advises no more than five units per week.

**Vaccinations and infections**

Live vaccines (eg, measles, mumps, rubella, Bacillus Calmette-Guérin and varicella) should not be given during methotrexate or biologic therapy. A young patient taking methotrexate, oral steroids, biologics, or all of these, who has not had chickenpox and is exposed to it, or develops chickenpox or shingles, should be referred immediately to a doctor or nurse. Inactivated vaccines can be given as normal.

**Contraception**

Effective contraception should always be used by young people taking methotrexate and biologic therapy, such as etanercept, because they can cause damage to the developing fetus. Young people may also be concerned about future fertility but this is not affected. Advice should promote safe sex as well.

**Complementary therapies**

Patients and their families might also be interested in complementary therapies (eg, glucosamine and fish oils) for JIA, but there is, as yet, no evidence of efficacy for young patients.

**Adherence**

Adherence to medicines for JIA has not been well explored, but it is a crucial factor for meeting the ultimate goals of treatment because DMARDs need to be taken for one or two years beyond remission. Existing studies suggest that side effects of the medicines pose a serious challenge to adherence. Furthermore, patients are usually taking a complex regimen of adjunct medicines, which can include:

- Steroid eye drops for chronic anterior uveitis
- Gastroprotective agents (eg, ranitidine or omeprazole, while taking NSAIDs and prednisolone)
- Anti-nausea therapy (eg, ondansetron) with methotrexate
- Folic acid (5mg weekly or 1mg daily, but not on the same day as methotrexate) to reduce side effects of methotrexate (eg, mouth ulcers)

All the factors above emphasise the importance of involving the young person and his or her family in the treatment decision. It is only through honest discussion that the buy-in needed to secure adherence to long-term treatment can be achieved. Panel 3 (p658) describes a patient’s experience and highlights the trade-offs that might be appropriate so that a young patient remains confident and likely to adhere.

**Transition**

Transition and relocation offers pharmacists a role in discussing ongoing care, including liaison with other healthcare professionals on such matters as supply (including sourcing unlicensed medicines and formulations); identifying possible financial constraints, such as prescription charges; and ensuring that any relocation of care is as smooth as possible.

Nicola Gray and Janet McDonagh will be available to answer questions online on the topic of this article until 20 December 2010.

---

**Panel 2: Features and Challenges of DMARDs Used**

**Non-biological DMARD therapy**

**Methotrexate**

- Takes six to 12 weeks to become effective and effects can increase further over nine to 12 months
- 72 per cent of patients with JIA respond to treatment
- Nausea, vomiting and diarrhoea are common side effects and up to 12 per cent of patients have loss of appetite (folic acid reduces side effects)
- Up to 60 per cent of patients experience a flare up on discontinuation of treatment
- Regular blood monitoring is needed
- National Patient Safety Agency guidelines exist

**Injected (local) corticosteroids** (eg, intra-articular triamcinolone hexacetonide)

- Triamcinolone hexacetonide (available from specialists manufacturers) is effective longer than the acetoxione form (eg, Kenalog, Adcortyl)
- Pain on administration of intramuscular injections
- 2 per cent of patients experience atrophy of fat at the injection site
- Often used in conjunction with methotrexate

**Systemic corticosteroids**

- Use has declined due to concerns about effects on bone health and growth (eg, osteoporosis, delay in puberty, etc)
- Primarily used in systemic JIA, which is associated with fever, skin rash and anaemia, as well as arthritis

**Biological DMARD therapy**

**Etanercept**

- Licensed for JIA patients aged four to 16 years and has National Institute for Health and Clinical Excellence approval for patients who find methotrexate ineffective or intolerable
- 77 per cent response rate
- 36 per cent reach full clinical remission
- Low serious adverse event rate
- All paediatric patients on etanercept should be registered with the BSPAR registry

**Infliximab**

- A dose of 6mg/kg has been shown to have a better safety profile in terms of adverse events than the lower 3mg/kg dose

**Adalimumab**

- Limited licence for use in young people aged 12 years and over
- Particularly effective in combination with methotrexate

---

For personal use only. Not to be reproduced without permission of the editor (permissions@pharmj.com).
important to maximise opportunities for young people to access trusted advice in order to build long-term positive relationships with health professionals.

Vision and challenges

There are a number of challenges that the pharmacy team faces in ensuring that treatments are both effective and safe. The principle of transferring care closer to — or even within — the patient’s home reinforces the importance of accurate information-sharing across interfaces to ensure patient safety and effective treatment. This offers a unique opportunity for healthcare professionals to become actively involved in supporting the delivery of biological therapy in the home through homecare delivery services. This allows the patient to continue to have close contact with the specialist centre while continuing with therapy and further improving adherence.

Part of the pharmacist’s role is to understand the context in which drugs are used, and to reinforce key counselling points, while understanding the patient’s need to discuss other forms of therapy, including complementary medicines. The use of appropriate terminology is vital in gaining patients’ trust, especially regarding the use of cytotoxic drugs such as methotrexate. Inappropriate terminology can undo previous hard work in discussing and negotiating treatment plans with young patients and their families.

Pharmacy staff, in all sectors, have an opportunity to support care of patients with JIA. Information, and the way in which it is presented, is key to ensuring that young people become — and remain — adherent to their treatment. This allows the patient to continue to have close contact with the specialist centre while continuing with therapy and further improving adherence.

Signposting

• Resources for young people on living with arthritis are available at www.arthritis-care.org.uk
• The Arthritis Research UK website (www.arthritisresearchuk.org) contains information about JIA, stories about children and young people, and a parent booklet entitled “When your child has arthritis”.
• “Teens first for health” is a website by Great Ormond Street Hospital for young people (www.childrenfirst.nhs.uk). It has an A-Z section on arthritis, including JIA, and a downloadable methotrexate leaflet.
• The “Kids with arthritis” website (www.cca.org.uk) contains useful facts and helpful advice.

Resources

• The British Society for Paediatric and Adolescent Rheumatology/Arthritis and Musculoskeletal Alliance standards of care for children and young people with juvenile idiopathic arthritis (2010) are available at www.arma.uk.net
• The National Institute for Health and Clinical Excellence guidance on the use of etanercept for the treatment of juvenile idiopathic arthritis (TA35) is available at www.nice.org.

References

3 Beresford M, Baldiam EM. New advances in the management of juvenile idiopathic arthritis. 1: Non-biological therapy. Archives of Disease in Childhood — Education and Practice 2009 Available at http://ep BMJ.com (accessed on 29 November 2010).

PANEL 3: ADHERENCE ISSUES IN A TEENAGER

Sally is a 17-year-old with a history of JIA. For the past two years, she has been stabilised on 25mg subcutaneous methotrexate once weekly, prepared by her specialist centre in a city over 100 miles away from her home. With the launch of a licensed brand of methotrexate, her GP was prepared to take on prescribing, meaning there was no need for her to travel to collect her medicine every three months. After two months, the specialist centre was contacted by Sally in a distressed state. The large volume of the methotrexate in the licensed brand was causing significant pain at the administration site and a skin rash. This was causing her embarrassment during swimming, with a significant loss of self-esteem. The GP was not prepared to prescribe an unlicensed product of methotrexate while there was the licensed brand available.

After discussion with the pharmacist, Sally was determined to stop using the licensed brand and return to using the brand made at her specialist hospital. With good communication in place between the patient and the pharmacist and also between primary and secondary care, Sally is able to co-ordinate collection of her medicine with shopping and theatre trips with her family and friends in the city. She says: “I did miss a lot of school when I was really ill, and I have had to leave my college earlier this year because I had missed too many classes. I was not going to be messed about having to have a painful injection when I knew there was something better.”

Further reading


CPD articles are commissioned by The Journal and are not peer reviewed.

PRACTICE POINTS

Reading is only one way to undertake CPD and the regulator will expect to see various approaches in a pharmacist’s CPD portfolio.

1 Review the doses of NSAIDs that might be seen on a prescription for a young person with JIA, and the non-prescription products that they might buy at a pharmacy.
2 Arrange an awareness-raising session for the pharmacy team of the possibility of young people needing guidance on juvenile arthritis, including symptoms and products that might warrant referral.
3 Gather details of the local resources available in order to signpost young people and their families to specialist diagnostic and care services for juvenile arthritis, and contacts for pharmacists’ clinical enquiries within the local paediatric/adolescent rheumatology team.

Consider making this activity one of your nine CPD entries this year.