Rheumatology and the adolescent patient

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Background

Adolescence can be a time when rheumatological conditions present to the general practitioner for diagnosis and management. Diagnosis of rheumatic disease during adolescence and earlier childhood often brings additional challenges such as those relating to body image, schooling and recreational activities, friendships and relationships, compliance with medications and independence with healthcare needs.

Objectives

This article highlights rheumatological conditions that have relevance during adolescence and describes the approach to the history, examination and investigation of young people with rheumatic disease. Some common management issues that may arise when assessing adolescent patients in the primary care setting, including indications for referral to a rheumatologist, are outlined.

Discussion

The transition from one of dependence to self-management is a complex but important process as many adolescents with rheumatic disease will have persistent disease activity or ongoing sequelae continuing into their adulthood.

Adolescence is a period of developing independence, whereby a young person makes the developmental and physiological transition from child to adult.[1] It can be variable in its age of onset and duration, and is recognised as an age during which even healthy young people can be vulnerable to the perceived stresses and expectations placed on them by not only themselves but also their peers, parents, teachers and wider community. For young people with a chronic illness, having to negotiate through this age can therefore be all the more demanding, and can be a challenging time for the young person, their family and caregivers alike, including medical practitioners.[2–4] Furthermore, there is the impact of having to deal with the realisation that their medical condition and/or its sequelae may be lifelong.[5]

Common rheumatological conditions of adolescence

Juvenile idiopathic arthritis

Juvenile idiopathic arthritis is a chronic arthritis of at least six weeks' duration in children younger than 16 years of age for which no other cause is found.[6] The categories of juvenile arthritis are based on clinical and laboratory characteristics, which influence management decisions and estimation of likely course and prognosis. The International League Against Rheumatism (ILAR) classification system is the most widely accepted, and although all subtypes of juvenile idiopathic arthritis can present in adolescence, some are more relevant.[7]

Rheumatoid–factor positive polyarticular arthritis, which accounts for 2–7% of juvenile idiopathic arthritis cases, more commonly presents in girls aged 9–11 years.[8] Similarly to adult-onset rheumatoid arthritis, it typically presents with symmetrical involvement of small and large joints.[8] This form of juvenile arthritis requires aggressive treatment, which may require escalation to biologic medications as there is potential for deformity and significant disability if the disease is uncontrolled.

Long-term immunomodulatory therapy that spans the duration of adolescence into adulthood is likely, as this group is the least likely to achieve remission without medication.[9]

Rheumatoid–factor negative polyarticular juvenile idiopathic arthritis accounts for 20–25% of all juvenile idiopathic arthritis cases, many presenting during adolescence.[10] Compared with patients who have rheumatoid–factor positive polyarthritis, there are generally fewer joints involved, and the pattern is more asymmetric. Up to one-quarter of these patients may achieve remission by the age of 16 years; however, most patients require systemic therapy and can have ongoing disease activity into adulthood.[10]

Enthesitis-related juvenile arthritis (ERA), unlike other forms of juvenile idiopathic arthritis, is typically seen in adolescent boys aged 10–13 years, and is associated with human leukocyte antigen B27 (HLA-B27) positivity.[11] There may be a family history of ankylosing spondylitis. The disease most commonly involves the lower limbs, and can affect the spine and sacroiliac joints. Enthesitis – pain at the sites of attachment of ligaments, tendons or joint capsule to bone – is common and should be carefully examined, particularly if there is a history of heel or foot pain. The approach to the management of ERA is unique. Enthesitis may require treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and orthotics, and patients with axial involvement often require biologic medications. ERA is part of a spectrum of disease that extends into adulthood and, in particular, may progress to ankylosing spondylitis.[12] Current treatments for ERA have not been shown to alter the progression of ankyloses.[8]

ERA can be associated with acute uveitis, presenting as a unilaterally painful, erythematous eye, contrasting with the more common form of uveitis seen in younger children with oligoarthritis, which is asymptomatic and frequently bilateral.[13]

Reactive arthritis

Reactive arthritis, although not a form of juvenile idiopathic arthritis, can present in adolescence, and like ERA, has an association with HLA-B27 positivity. The classic triad of arthritis, conjunctivitis and urethritis is not present in all cases. Enteric or genitourinary infections, including sexually transmissible infections (STIs; eg chlamydia), are typical triggers and should be considered in adolescents presenting with arthritis and relevant symptoms on systems review.[14] The pattern of arthritis is variable; however, it most commonly involves the lower limbs, and prominent pain and erythema are classically described. Differentiating reactive arthritis from juvenile idiopathic arthritis can be challenging; however, reactive arthritis is generally self-limited, requiring treatment with NSAIDs only.

Systemic connective tissue disorders

Any of the systemic connective tissue disorders seen in adult rheumatology clinics can also occur in childhood. The peripubertal or adolescent age groups are particularly prone; for example, 20% of patients with systemic lupus erythematosus (SLE) present before the age of 18 years. Scleroderma, juvenile dermatomyositis and some forms of vasculitis, including granulomatosis with polyangiitis and Takayasu's arteritis, may also present in adolescence. Discussion of each of these conditions is beyond the scope of this paper; however, a summary of the epidemiology and clinical features are noted in Table 1.

Idiopathic chronic musculoskeletal pain

Musculoskeletal chronic pain syndromes in children are common, accounting for approximately 12% of rheumatology clinic referrals.[15] These syndromes more commonly present after the age of 12 years, are four times more common in females, and are more common in Caucasian children.[15] The precise mechanism of idiopathic pain syndromes is not well understood; central sensitisation of a peripheral stimulus is a commonly used explanatory model of pathophysiology. These syndromes can be localised, referred to as chronic regional pain syndrome (CRPS). Patients with CRPS may have a history of a minor trauma to a peripheral body part, preceding the onset of pain, swelling and vasomotor changes. Disuse and immobilisation of the painful limb perpetuates the pain and vasomotor instability, which necessitate intensive desensitisation and rehabilitation for successful treatment. Generalised pain syndromes, referred to as diffuse musculoskeletal pain or juvenile fibromyalgia, require a multidisciplinary rehabilitation approach with a combination of pharmacotherapy, physical and psychological therapy.[16]

Approach to the rheumatological history and examination of a young person

History

As an episode of arthritis can be a component of an array of differential diagnoses, a detailed and thorough history is essential. Questions are not only relevant to the symptomatic joint(s) (eg site, duration, morning stiffness, interference in function), but the history should also include questions considering extra-articular symptoms (eg skin rash, gastrointestinal features, fevers, menstrual issues). Family history may include important aspects such as spondyloarthropathies or autoimmune predisposition. A HEADSS (ie home, education, activities, drugs, sexuality, suicide) assessment should be considered as part of the routine history, as this might have particular relevance (eg drug and alcohol use when medications such as methotrexate are in indicated). Sexual history and contraceptive information may be relevant to medication use and consideration of STI-related reactive arthritis. Chronic illness may be associated with poor self-esteem and mental health morbidity, and screening for relevant symptoms is required.

It is important to understand the functional impact the disease may have on typical adolescent activities. Small-joint disease of the hands can affect writing and computer skills, and aids may need

Table 1. Connective tissue diseases or vasculitides that may present in adolescence[8]

	Paediatric systemic lupus erythematous	Juvenile dermatomyositis	Granulomatosis with polyangitiis	Takayasu's arteritis
Epidemiology	Average age of onset 12 years Female-to-male ratio 4.5–5:1 Higher rates in non-Caucasian populations	Peak age 5–14 years Female-to-male ratio 2:1	Median age 14.9 years (range: 4–19) More common in females than males	More common in adolescence More common in females than males
Clinical features	**Constitutional** Fever, malaise, weight loss, anorexia **Cutaneous** Malar rash, photosensitivity, mouth ulcers, hair loss **Musculoskeletal** Arthritis, myositis **Renal** Hypertension, glomerulonephritis **Neurological** Seizures, psychosis, cognitive deficit, cerebrovascular accident **Cardiac** Pericarditis and effusion, chest pain **Pulmonary** Pleuritic **Gastrointestinal** Ascites, abdominal pain, liver function test derangement **Ocular** Exudates, retinopathy **Reticuloendothelial** Hepatosplenomegaly, lymphadenopathy **Vascular** Raynaud's phenomenon	**Constitutional** Fever, malaise, weight loss, anorexia **Musculoskeletal** Muscle tenderness, arthritis, myositis **Cutaneous** Gottron's papules and plaques, heliotrope rash, malar rash, photosensitivity **Neurological** Proximal weakness, Gower's sign positive **Gastrointestinal** Swallowing dysfunction **Oedema** Subcutaneous tissues **Pulmonary** Interstitial lung disease	**Constitutional** Fever, malaise, weight loss, anorexia **Classical triad:** ***Upper respiratory*** Nasal symptoms, sinusitis, epistaxis ***Lower respiratory*** Haemoptysis, pulmonary nodules, abnormal lung function ***Renal*** Glomerulonephritis, elevated creatinine	**Constitutional** Fever, malaise, weight loss, anorexia **Central nervous system manifestations** Headache, seizures, syncope **Cardiac** Chest pain, claudication, absent wrist pulses, palpitations **Renal** Hypertension **Musculoskelatal** Arthritis, arthralgia, myalgia

to be considered. Joint symptoms from inflammatory disease may affect active hobbies such as sports or dance. It is important to stress that joint pains from non-inflammatory causes are also common in physically active adolescents. The social history is important as relationships and family dynamics can be affected by chronic illness. Financial support and housing arrangements may have an impact on medication and treatment compliance.

Examination

A useful examination tool for the general practitioner (GP) is the paediatric Gait, Arms, Legs, Spine screen (pGALS) for which a downloadable PDF is freely available (www.pmmonline.org).[17] All joints should be assessed for swelling, tenderness and limitation in range of movement. Determining whether the signs are of one or multiple joints, predominantly large or small, symmetrical or asymmetrical, all assist in defining the diagnosis. Gait should be assessed in an area where there is sufficient room to walk with a relaxed stride for several metres. The physical examination includes looking for extra-articular signs, such as growth parameters, skin and nail features of psoriasis, rashes including malar and photosensitive rashes, oral mucosal changes, organomegaly and muscle strength. Range

of motion in the spine and hips, and examining for inflammatory enthesitis at ligament insertions are important in diagnosing ERA. Joint hypermobility, patellar maltracking and retropatellar crepitus are common findings in more mechanical causes of joint pain.

Investigations

Interpreting investigations of adolescents with musculoskeletal complaints can be confusing. Normal findings on investigations, such as rheumatoid–factor negative results or a normal plain X-ray, do not exclude potentially significant arthritis. Conversely, isolated positive results, particularly positive antinuclear antibodies or HLA-B27, are not necessarily diagnostic.[18] Selection and interpretation of appropriate tests will depend on the clinical history and examination; a general guide to investigations in the primary care setting is outlined in Table 2.

Imaging modalities, such as plain radiography, ultrasonography, computed tomography, nuclear medicine and magnetic resonance imaging, can play an important part in the diagnosis and management; however, careful selection and interpretation are required. Discussion with a rheumatologist may assist in the appropriate selection of imaging approaches.

Management considerations for the young person with rheumatic disease

By the very chronic nature of many rheumatological conditions that affect adolescents, these readily fit into the scope of the GP Management Plans program, enabling funded access to various allied health disciplines. This places the GP in a central role in the coordination of care, and should enhance appropriate communication with a rheumatologist.

Treatment compliance

A young person's compliance with medications and appointments can have an impact on disease control and outcome. Barriers to good compliance include:[19]

- lack of understanding and prioritisation of the disease
- medication side effects
- financial issues
- social impact on friendships and relationships.

The route of drug administration, particularly injectable forms, may increase non-compliance because of needle phobia, body image issues and the inconvenience of injections if unable to self-administer. Access to a primary healthcare provider who can administer medication on a regular basis in a convenient time

Table 2. Investigations in the assessment of rheumatological conditions

Investigation	In which clinical setting may this be useful?	How will the result influence diagnosis or management?
Acute phase reactants: ESR, CRP	Recurrent fever, arthritis, clinical features of connective tissue disease	Non-specific marker of inflammation Extreme elevations may broaden the differential diagnosis Serial measurement can be useful for activity monitoring
Rheumatoid factor, anti-CCP	Arthritis in multiple joints	Used for juvenile idiopathic arthritis classification May influence treatment course Present in only 5–10% of children with juvenile idiopathic arthritis
ANAs, anti-dsDNA, ENA, complement levels	Suspicion of SLE or connective tissue disease, rash, fever, arthritis, Raynaud's phenomenon, cytopenias	Diagnostic criteria for SLE Low titres of ANAs are found in up to 30% of the normal population
ANAs	Arthritis in less than four joints	Used to stratify risk of uveitis
HLA-B27	Axial involvement, back or hip pain, enthesitis Family history of ankylosing spondylitis Personal or family history of psoriasis	Used for juvenile idiopathic arthritis classification May influence treatment course Approximately 9% of the normal population carry the gene Reactive arthritis and inflammatory bowel disease can be associated
Urinalysis	Suspicion of SLE or connective tissue disease, rash, fever, arthritis, Raynaud's phenomenon, cytopenias	Early identification of renal involvement with haematuria or proteinuria may influence management and prognosis

ANAs, anti-nuclear antibodies; CCP, cyclic citrullinated peptide; CRP, C-reactive protein; dsDNA, double-stranded DNA; ENA, extractable nuclear antigen; ESR, erythrocyte sedimentation rate; HLA-B27, human leukocyte antigen B27; SLE, systemic lupus erythromatosus

frame to minimise disruption of school and/or extracurricular activities can overcome such issues.

A common medication side effect is nausea with methotrexate. Attempts to minimise this by considering the route of administration, access to anti-emetics and dosing on the least disruptive day for the adolescent are important management issues.

Adherence to medication plans can be difficult to maintain when a young person feels well, is unable to anticipate negative consequences of non-compliance, and perceives the treatment to be an unnecessary burden. In some cases, where the physical signs of disease are less obvious (eg renal lupus), the morbidity associated with non-adherence is potentially high.[20] Non-adherence may lead to disease flares, necessitating treatment escalation and associated time away from study, work and recreational activities. GPs can take a significant role in this regard by confirming the treatment plan with the young person, encouraging adherence, ensuring the adolescent is adequately educated about their disease and its management, and drug monitoring.

Body image and mental health

Body image is an important consideration as physical signs (eg growth and pubertal delay, joint contractures, a limp, swollen painful joint) can affect wellbeing and participation in sports and social activities. Medication side effects, particularly weight gain associated with corticosteroids, may be unacceptable, creating a further barrier to treatment and management compliance.[19]

Anxiety and depression are more common among young people with chronic disease. In the case of rheumatic diseases, this may be multifactorial, with contribution from the disease itself, for example with central nervous system involvement in SLE, along with psychosocial factors and low self-esteem.[20] Chronic pain has a complex association with mental health symptoms and can be both a contributor to, and an outcome of, anxiety and depression.[21]

Sexual and reproductive health

Disease modifying agents (eg methotrexate) are contraindicated in pregnancy because of potential teratogenicity. Hence, routine counselling regarding contraception is important, and disease control during pregnancy must be planned.[20] Cyclophosphamide, if indicated for treating major organ involvement in connective tissue disease, can be associated with reduced fertility; this should be discussed with the patient prior to commencing treatment. Menstrual irregularities (eg menorrhagia and oligo or secondary amenorrhoea) are common, and antiphospholipid syndrome and SLE are associated with an increased risk of miscarriage and other pregnancy-related complications.[20]

Transition to adult rheumatology services

For the young person with rheumatic disease, transition to an adult rheumatology service should occur at a time when they are developmentally ready and have been educated about their disease and the management required.[22] Transition is a recognised time of increased loss to follow-up from the healthcare system, and this can have a negative effect on the disease course and outcome. There are different approaches to transition – some centres use a structured program, whereas others use a graded approach with a combined paediatric/adult rheumatology clinic until the young person is ready to transition to the adult system.[23] In most circumstances, transition is finalised at a convenient time following completion of secondary school.

Barriers to successful transition are complex and include not only patient factors, but also parental factors of unwillingness to 'let go', and systems factors such as gaps in financing, lack of availability of appropriate youth services, and inadequate transfer of documentation between paediatric and adult care.[2] Consensus-based guidelines for transition in rheumatology have been published recently, acknowledging the importance of a comprehensive, structured approach.[24]

Indications for referral to a rheumatologist

Paediatric rheumatology services accept referrals for young people with a range of conditions, including suspected chronic arthritis, connective tissue diseases or vasculitis. In clinical scenarios where the diagnosis is unclear and/or therapy needs are likely to involve intra-articular corticosteroid injections, immunosuppressant therapy or hospitalisation, involvement of a rheumatologist is appropriate. Given the chronic nature of many rheumatological conditions, an ongoing relationship between the GP and rheumatologist will be in the patient's best interest.

Conclusion

Rheumatic disease in adolescence can represent a continuum of chronic childhood-onset illness, or may represent a new diagnosis of an autoimmune disease, vasculitis, connective tissue disease or a chronic pain disorder. To optimise outcomes for young people with rheumatic diseases, consideration of specific management issues in addition to the functional impact of the disease on activities, work, school and relationships should be considered.

Key points

- A thorough history, including a HEADDS assessment, is important for the diagnosis and management of adolescents with rheumatic disease.
- pGALS is a useful screening tool for the examination of young people with musculoskeletal complaints.
- Investigations for rheumatic disease should be ordered and interpreted only in the context of the history and examination findings.
- Management considerations include functional impact on the young person, medication compliance, body image and mental health, sexual health and transition to adult care. The GP Management Plan can be initiated to assist optimal care of many adolescents.

- Juvenile idiopathic arthritis, systemic connective tissue disease, vasculitis and chronic pain syndromes may present in the adolescent age group.

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