What is a frozen shoulder?
Marked limitation of shoulder movement as a result of contraction or fibrosis of the capsule of the glenohumeral joint may follow chronic inflammatory arthritis, previous trauma, or prolonged immobilisation or may be idiopathic. The condition is seen more commonly in diabetics and in patients after myocardial infarction or stroke. Patients typically have a history of chronic shoulder pain with inability to lie on the affected side, followed by progressive stiffening of the shoulder in all ranges of motion, especially external rotation. Most cases resolve over a few months after mobilisation exercises and a corticosteroid infiltration. Recovery may be prolonged, taking up to 2 years, especially in diabetics.[5]

Cervical spine pathology is a common cause of referred pain to the shoulder.

How often is the shoulder joint involved in systemic or generalised arthritic disorders?
The most common inflammatory arthropathy involving the shoulder joint, including the rotator cuff, is rheumatoid arthritis. Shoulder involvement is also seen in seronegative spondyloarthritis (SpA), affecting about 30% of patients with ankylosing spondylitis. Gouty involvement of the shoulder is uncommon. Glenohumeral osteoarthritis is rare and should prompt a search for secondary causes, such as chronic rotator cuff tear, acromegaly, previous trauma or underlying inflammatory arthritis.[5]

What is the Milwaukee shoulder?
This is a condition seen in elderly women due to calcium hydroxyapatite deposition, resulting in an haemorrhagic effusion, severe rotator cuff degeneration and rapidly progressive destructive arthritis of the shoulder joint.[5]

What is enthesitis?
This is inflammation at sites of tendon, ligament, capsular or fascial insertion into bone. It may occur after injury, in repetitive use syndromes and in certain inflammatory conditions such as SpA and HIV-associated arthropathies.[6]

What are the common causes of medial and lateral elbow pain?
Enthesopathy at the origin of the common wrist flexor is characterised by pain at the medial aspect (golfer's elbow) with tenderness just distal to the medial epicondyle and pain that worsens with wrist flexion. Enthesopathy at the origin of the wrist and finger extensors presents with pain and tenderness over the lateral epicondyle exacerbated by resisted wrist extension (tennis elbow). Management may include steroid infiltration if the patient does not respond to conservative measures.[7]

Which conditions need to be considered in patients with nonspecific distal arm pain in the absence of obvious pathology?
Repetitive strain injury is usually a diagnosis of exclusion, with occupational overuse being an important risk factor. Some consider this condition to be a variant of fibromyalgia, as patients tend to have associated fatigue and sleep disturbances. Conditions such as carpal tunnel syndrome (CTS) and a small ganglion within the wrist need to be excluded.[8]

What are the signs of carpal tunnel syndrome?
Typically, patients present with sensory loss or paraesthesia along the radial aspect of the ring, middle and index fingers and the thumb. Symptoms may be reproduced by tapping over the carpal tunnel (Tinel's sign) or by full flexion of the wrist for 60 seconds (Phalen's sign). Thenar atrophy may be present, implying chronicity. Predisposing conditions are inflammatory arthropathy, acromegaly, diabetes, hypothyroidism, overuse syndromes and pregnancy.[7,8]

What is De Quervain's disease?
This is tenosynovitis of the first dorsal compartment of the wrist, which presents with pain on the radial side of the wrist and the base of the thumb. Pinching or grasping movements of the thumb produce pain. A clinical test – Finkelstein's manoeuvre – is positive if pain is reproduced along the first dorsal compartment, when the wrist is moved in an ulnar direction with the thumb clasped in the palm. Local steroid infiltration into the tendon sheath may be required if conservative measures with NSAIDs and wrist/thumb splint fail.[7,8]

What is trigger finger?
This is tenosynovitis affecting the flexor tendons of the fingers or thumb, resulting in fibrosis or nodule formation. It interferes with the normal smooth movement of the tendon, 'catching' or locking as the tendon passes under the A1 pulley in the region of the metacarpophalangeal joint. Patients may have tenderness at the base of the finger with a palpable nodule. Pain is exacerbated by stretching the tendon in extension or resisted flexion.

Patients may benefit from local steroid infiltration. Conservative measures include immobilisation for 4 - 6 weeks, with a repeat steroid infiltration; if symptoms persist for more than 6 weeks surgery should be considered.[7,8]

Summary
- Upper limb pain syndromes may be due to a wide variety of local or systemic factors, many of which may be effectively managed in primary care.
- Due consideration has to be given to referred pain so as not to miss pathology elsewhere.

References available at www.cmej.org.za

Fibromyalgia

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Over the past decade there have been major advances in our understanding of fibromyalgia (FM). The identification of alterations in the levels of many neurotransmitters has resulted in newer targets for therapeutic intervention in this condition.

FM is a chronic disorder characterised by widespread musculoskeletal pain. According to the American College of Rheumatology (ACR) fibromyalgia classification criteria (1990)[1] patients must have a history of widespread pain that has been present for at least 3 months. The pain can be elicited on digital palpation by manual pressure of

Table I. The 2010 fibromyalgia clinical diagnostic criteria[4]

- **Widespread pain index (WPI)**
  The WPI score depends on the number of sites where the patient had pain in the last week (score: 0 - 19)
  The 19 sites are (R - right; L - left):

Shoulder girdle R/L	Hip (buttock, trochanter) R/L	Jaw R/L	Upper back
Upper arm R/L	Upper leg R/L	Chest	Lower back
Lower arm R/L	Lower leg R/L	Abdomen	Neck

- **Symptom severity (SS) scale**

Fatigue	Waking unrefreshed
Cognitive disturbance	General somatic symptoms

  The score for each of the 4 symptoms is allocated as 0 (no problem), 1 (slight), 2 (moderate) and 3 (severe). The total score ranges from 0 to 12

- **Patients are classified as having fibromyalgia if:**
  WPI >7 and SS score >5 *or* WPI between 3 and 6 and SS score >9

  The new diagnostic criteria do not require a physical examination and can be self-administered

approximately 4 kg/cm^2 at 11 or more of the 18 defined tender points. The pain is considered to be widespread if it involves both sides of the body and occurs above and below the waist. In addition, axial skeletal pain (cervical spine, anterior chest, thoracic spine or low back) must be present.

These criteria were developed for use in clinical trials. It is increasingly recognised that the diagnosis of FM does not rely solely upon eliciting tender points, and features such as fatigue, sleep disturbance and cognitive dysfunction are prominent.[2]

FM affects mainly middle-aged women; however, adolescents, men and older people are also affected. It is far more prevalent than inflammatory arthritis, e.g. rheumatoid arthritis.

Chronic widespread pain is the characteristic symptom in patients with FM. Only about 50% of patients with chronic widespread pain fulfil the criteria for FM.[3] It is unclear how patients with chronic widespread pain who do not fulfil the tender point criteria should be classified, and the role of the tender points in the diagnosis of FM has been challenged by many authors.

Diagnosis

The 2010 fibromyalgia clinical diagnostic criteria[4] were recently proposed by Wolfe and colleagues and depend on the widespread pain index and the symptom severity scale as shown in Table I.

Pathogenesis

Functional MRI imaging studies have shown that low-intensity stimuli, which would not normally produce pain, activate areas of the brain that process pain and result in pain sensation in FM patients. In addition, areas of the brain which are activated by low-intensity stimuli in FM patients are only activated by high-intensity stimuli in controls.[3]

Biochemical abnormalities that have been noted in FM patients include:[3]

- Substance P is raised 2 - 3-fold in the CSF. Increased levels lead to heightened awareness of pain.
- Brain-derived neurotropic factor (4-fold increase) and glutamate are elevated.
- Serotonin levels are low. This has been linked to poor sleep, pain perception, headaches and mood disorders.
- Dopamine levels are low. This plays a role in pain perception and natural analgesia.
- Noradrenaline levels are low.

These biochemical abnormalities result in whole body hypersensitivity to pain and suggest that FM is a disorder of central pain processing or a syndrome of central sensitisation.[3] Therefore, in FM, some of the neurotransmitters which increase pain are high and others, which may inhibit pain, are too low.

Clinical aspects

Several risk factors have been identified, including genetic factors, gender, age, poor sleep, physical de-conditioning and neuro-endocrine and autonomic dysregulation. Approximately 50% of patients with FM state that their symptoms began after a precipitating event, including chronic stress, emotional trauma, physical injury, surgery and motor vehicle accidents.[3]

The dominant symptoms are widespread muscle and/or joint pain, fatigue, sleep disturbances, impaired memory and concentration, cognitive impairment, depression and paraesthesia.

The spectrum of abnormalities seen in FM extends beyond widespread pain and overlaps with other syndromes, such as:[2,3]

- regional pain syndromes, e.g. non-cardiac chest pain, dyspepsia, headaches, irritable bowel syndrome, chronic pelvic pain, temporomandibular joint pain
- other central sensitivity syndromes, such as chronic fatigue, irritable bowel, pelvic pain, tension headaches, migraine, restless legs syndrome
- allergic symptoms, such as nasal congestion, hives and welts
- mood disorders, including anxiety, depression and personality disorders.

Management

A thorough history and physical examination is the basis of making a confident diagnosis, as radiological and laboratory tests do not assist in confirming it.

Conditions which must be considered in the differential diagnosis include hypothyroidism, polymyalgia rheumatica, systemic lupus erythematosus, rheumatoid arthritis and myositis.[5]

Patient education. FM should be explained as a symptom, such as headache or backache. It is important for patients to be told that they have a real problem which is a biologically based disorder.

Psychological and behavioural management, including cognitive behavioural therapy and relaxation techniques, should be employed at the outset.

Physical therapy improves pain and functional ability and should include strength training, developing flexibility, balance and endurance.

Diet. Important considerations are vitamin D supplementation, emphasis on bone health and reaching an optimum weight.

Pharmacological management. Evidence for the efficacy of different classes of drugs has been categorised as follows:

- Strong evidence – tricyclics (amitriptyline); dual re-uptake inhibitors (SNRI/NSRI – venlafaxine, duloxetine, milnacipran); alpha-2-delta ligands (pregabalin, gabapentin)
- Modest evidence – tramadol; selective serotonin re-uptake inhibitors (SSRIs); dopamine agonists; gamma-hydroxybutyrate
- Weak evidence – growth hormone; 5-hydroxytryptamine; tropisetron, S-adenosyl-L-methionine
- No evidence – opioids; NSAIDs; corticosteroids; benzodiazepine and non-benzodiazepine hypnotics; melatonin; guanifenesin; dehydro-epiandrosterone.

References available at www.cmej.org.za

Use of biological agents in rheumatic disease

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In a large number of rheumatic diseases the disease process is driven by the immune system. In the past few decades, there have been great advances in our understanding of the immunopathology and pathogenesis of the rheumatic diseases. At the same time, there have been similar advances in the development of drugs, particularly in the field of biopharmaceutical drugs that can target specific components of the immune response central to these diseases. Biological drugs can be monoclonal antibodies or proteins produced by living cells that bind with receptors on various cells to block formation or action of various cytokines or cell mediators, or in other ways change cell function.[1,2]

The area where there has been the most use of these drugs in research and later in the clinical setting has been in the treatment of inflammatory arthritis, particularly rheumatoid arthritis (RA), but also in the treatment of ankylosing spondylitis (AS), undifferentiated spondyloarthritis, reactive arthritis, psoriatic arthritis (PsA) and juvenile idiopathic arthritis (JIA). In these diseases, the biological disease-modifying anti-rheumatic drugs (DMARDs) have made a great difference to patients who have failed conventional synthetic DMARDs, not only in improvement of symptoms and function, but by inhibiting structural damage to joints.[2,3]

The first biological DMARDs to be used in the treatment of inflammatory arthritis were the TNF-alpha blockers. There are now several different TNF-alpha blocking drugs available in South Africa. Infliximab (Revellex) is given as an intravenous infusion every 8 weeks at a dose of 3 mg/kg (5mg/kg for AS), etanercept (Enbrel) is given subcutaneously at a dose of 25 mg twice a week, and adalimumab (Humira) subcutaneously at a dose of 40 mg every second week. All three drugs have been shown to be equally effective in the treatment of inflammatory arthritis and are indicated for these diseases.[3]

The main safety concerns with these drugs, as with any that affect the immune system, have been the potentially increased risk of infection. Clinical trials have shown that the infection risk was comparable to placebo groups on the whole as far as most infections were concerned. The infection of concern, particularly in a high-risk country, is tuberculosis (TB). There is a risk of reactivation of latent TB infection (LTBI) as well as newly acquired infection. TNF-alpha plays a specific role in the formation of granuloma that contains the TB organism in LTBI, and inhibition can lead to breakdown of the granuloma and release of the organisms. All patients are tested for LTBI before starting a biological drug and are treated if the infection is present. The risk of TB has been reduced using this approach, but it is still something to be looked for every time a patient on a biological agent is assessed at follow-up. Other safety concerns are the risk of malignancy and lymphoma, which do not seem to be increased compared with the background population of patients with severe inflammatory arthritis. There have been a few cases of demyelinating disease and patients with any suspicion of such a disease should not receive these drugs. Another contraindication is heart failure, as it can be worsened. Safety in pregnancy has not been established, although specific abnormalities related to the drug have not been seen in babies born to patients on these drugs during pregnancy.[2]

Other biological drugs have become available, namely abatacept (Orencia), rituximab (MabThera) and tocilizumab (Actemra). Abatacept is a selective co-stimulation modulator that inhibits the co-stimulation of T cells important in the RA disease pathogenesis. It is given at a dose of 750 mg or 1 000 mg, depending on the mass of the patient, as an intravenous infusion every month. Rituximab is an anti-CD20 monoclonal antibody which depletes CD-20 positive B cells in the body. The dose for RA is two 1 000 mg intravenous infusions given 14 days apart every 6 months or when a patient again starts to show symptoms of active disease. Abatacept inhibits the cytokine IL-6 and is given with a dosing schedule of 4 or 8 mg/kg every 4 weeks as an intravenous infusion. In clinical trials, the response to all three drugs has been comparable to that seen with the TNF-alpha blockers. The safety of these drugs is similar to that of the TNF-alpha blockers, with the risk of infection remaining the main concern, although the risk of TB seems to be decreased.

The use of biologics in other connective tissue diseases has not been as widely studied. Most are anecdotal studies, as most diseases are uncommon and the clinical picture is variable, making randomised controlled trials difficult. Rituximab has shown promise in treating several connective tissue diseases where conventional therapies have failed, including systemic lupus erythematosus (SLE), various types of vasculitis, Sjögren's syndrome and possibly scleroderma.

The biological drugs have opened new horizons for the treatment of rheumatic diseases and will continue to be important drugs. Unfortunately the technology used to make these drugs is expensive, which