

currently severely limits their use, but it is hoped that the price will improve and that we will be able to give the benefit of another type of treatment to a greater number of our patients with rheumatic disease.

### Summary

- The biological drugs have made a major impact on the way rheumatic diseases can be treated.
- They have been used mainly in the treatment of inflammatory arthritis.
- Some biologicals show promise in the treatment of other connective tissue diseases, particularly vasculitis and lupus.
- Several of these drugs block cytokines, such as the TNF-alpha blockers and IL-6 blockers, while others block activation of cells that produce cytokines or produce apoptosis in cells (e.g. abatacept and rituximab).
- Currently available drugs are in injectable form used at different time intervals.
- The main concerns in the use of biological drugs have been increased infection rate, particularly activation of tuberculosis.
- On the whole the biologics are relatively safe drugs offering real benefit in previously difficult-to-treat diseases.

References available at [www.cmej.org.za](http://www.cmej.org.za)

## Gout – an overview

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Gout (urate crystal deposition disease) is considered by some to be the most painful and most frequent of all inflammatory joint conditions.<sup>1,2</sup> If not well managed, it may lead to extensive polyarticular joint damage, systemic complications and functional loss.

The initial symptoms are usually acute with joint and soft-tissue inflammation of the foot and first MTP joint in more than 80% of cases. Urate crystals are deposited in multiple peripheral joints and soft tissue as a result of chronic raised uric acid. The disease progresses as the urate pool in the body increases over a period of approximately 10 years from initial asymptomatic hyperuricaemia to a monoarticular attack. Attacks increase in frequency and extensiveness and the disease eventually becomes chronic, tophaceous and polyarticular with systemic complications and nephropathy. Kidney stones in over-producers are common and may provide

a clue to the diagnosis of gout. The clinical picture of longstanding gout may mimic rheumatoid arthritis and it is one of the most mismanaged conditions in rheumatology.

The uric acid pool increases with purine intake and internal production related to the breakdown of nucleic acids. Xanthine oxidase is important in the oxidation of hypoxanthine to xanthine and uric acid. In the majority of cases the uric acid is raised owing to impaired renal excretion and transport. Dehydration, alcohol and many drugs that depend on renal excretion may influence the serum uric acid levels. A small amount of uric acid is excreted through the gut and has an enterohepatic circulation. Normal serum uric acid levels range from 0.12 to 0.55 mmol/l and normal urate excretion in the kidney ranges from 1.5 to 4.4 mmol/l in 24 hours. It is interesting to note that uric acid acts as a danger signal in the body when tissue is damaged and is a strong inducer of acute inflammation.<sup>3</sup>

Effective management of gout should aim to prevent joint damage and systemic complications. Early intervention and prevention of repetitive attacks improve the outcome. It is possible to decrease the uric acid pool or prevent it from accumulating. With long-term lowering of uric acid the tophi may decrease in size and the volume and kidney function may improve. Two important pillars in the management of gout include lifestyle modification and drug therapy.

Treatment should be tailored according to the individual patient. The following factors should be considered in the management of each patient:<sup>4-7</sup>

- The specific risk factors that relate to gout, including serum urate levels, history of previous attacks and radiographic signs of joint damage.
- The clinical phase of gout.
- General risk factors that predispose the patient to other complications that are commonly noted in the gout patient. Risk factors for cardiovascular and kidney disease include the patient's age, sex, body mass index, fat distribution and related conditions such as hypertension, hypercholesterolaemia, type 2 diabetes and lifestyle factors (smoking, diet and alcohol consumption). It is important to consider drug interactions that may influence urate levels.

The non-pharmacological management of gout is a critical component that is mostly neglected by the practitioner, but may bear the most fruit in the long term. A major goal is reached if the patient understands the basic mechanisms of the disease and feels motivated to comply with treatment and lifestyle adjustments. The patient should be motivated regarding weight loss, diet modifications, fluid intake and alcohol

consumption. Adequate water intake prevents dehydration and the precipitation of urate. It is important to note that excessive protein (in any form) may precipitate acute gout – not only red meat. Legumes, nuts and some vegetables are high in protein.<sup>8</sup> Excessive intake of fruit may precipitate acute gout. The basic rule is moderation and a healthy lifestyle.

Drug therapy is limited and the need exists for newer therapies. More drugs are expected to be available in the near future, but may be costly. Prophylactic therapy is indicated when frequent attacks occur and when complications or tophaceous gout are present. Xanthine oxidase inhibitors are effective in over-producers and under-excretors. Allopurinol reduces the production and load of uric acid that needs to be excreted by the kidneys. Gout may worsen when treatment is initiated in patients during an acute attack or precipitated in the patient with high uric acid levels. It is wise to initially give low doses of allopurinol and slowly titrate to higher doses, while covering the patient for acute attacks with low doses of (0.5 - 1 mg) daily colchicine and non-steroidal anti-inflammatory drugs (NSAIDs). The uric acid levels should be monitored monthly and should ideally be lowered to levels below 0.35 mmol/l. It may be necessary to give more than 300 mg of allopurinol daily and in rare cases up to 900 mg daily. Increase by 50 mg to 100 mg monthly according to the serum uric acid and monitor the kidney function and full blood count.

In patients in whom allopurinol toxicity occurs, options include other xanthine oxidase inhibitors (febuxostat), a uricosuric

agent (probenecid), or allopurinol desensitisation (only in cases of mild rash). Note that probenecid is contraindicated in kidney disease and when a history of kidney stones is present. The daily colchicine may be discontinued when the target uric acid levels have been reached.<sup>9</sup> Colchicine may then be given as needed for an acute attack at doses of 0.5 mg three times daily until the attack subsides. NSAIDs may also be given, as well as corticosteroids (systemic or intra-articular). It is important to note that corticosteroids have many adverse effects and are often misused to the detriment of the gout patient. It is better to continue the allopurinol during an acute attack rather than discontinuing the drug. This will lead to less fluctuation of drug levels and better control of the disease.

Management of co-morbid conditions in the gout patient is important. There is a higher risk of atherosclerosis and patients are prone to have hypertension, glucose intolerance and hypercholesterolaemia. These conditions should be treated aggressively. Hypertension may be resistant to treatment and it is not always possible to discontinue diuretic therapy. A useful drug for hypertension that increases the urine excretion of uric acid is losartan.<sup>10</sup> The key to successfully managing gout is early and aggressive treatment that includes education, motivation and lifestyle modification.

#### In summary

- Gout is strongly modified by the lifestyle of a patient. Education, motivation and lifestyle modification play a major role in treatment.
- Gout progresses through different stages that are related to the total amount of uric acid that accumulates in the body over time.
- The eventual outcome in the poorly managed patient is polyarticular joint damage, functional impairment, nephropathy and cardiovascular complications.
- Treating acute attacks only will not prevent the eventual outcome of the disease.
- Effective management of gout should aim to prevent joint damage and systemic complications by lowering and maintaining the uric acid levels to a target of below 0.35 mmol/l.
- Corticosteroids are often used without considering the detrimental side-effects and do not lower uric acid levels, while contributing to worsening the co-morbid diseases that frequently occur in patients with gout.
- Xanthine oxidase inhibitors are effective in under-excretors and over-producers by decreasing uric acid levels and lightening the load of uric acid to be excreted.
- Xanthine oxidase inhibitors should not be discontinued in the event of an acute attack in the patient who is on treatment.

- Probenecid should be used with caution in patients with a history of kidney stones and nephropathy.
- Many drugs influence the excretion of uric acid and may precipitate acute attacks, while losartan is a good choice in the management of hypertension because of its uricosuric characteristics.

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### Lower limb pain syndromes

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Lower limb pain is a common presenting complaint in primary care with aetiological factors such as trauma, repetitive strain injury and systemic inflammatory disorders. This review focuses on some commonly encountered problems when dealing with patients who present with lower limb pathology.

#### What are the common causes of referred or radicular pain in the lower limb?

Intra-abdominal, gynaecological, urological and lumbar spine pathology may be referred to the lower limbs. Lumbar spine pathology is a common cause of radicular pain, with disc herniation at L4 - L5 or L5 - S1 being the most frequent levels of involvement. Sensory loss and paraesthesia in the typical dermatomal pattern, or loss of reflexes (L3 - L4: loss of patellar tendon reflex or S1: loss of Achilles tendon reflex)<sup>1</sup> may be clinically evident.

#### What are the causes of hip pain in children and adolescents?

Participation in sports and related activities needs to be considered in this age group. Labral tears, in particular, present typically with anterior hip pain or groin pain. There may be associated symptoms of clicking or locking of the hip. One of the most common problems in young patients is a slipped capital femoral epiphysis. The patient usually complains of pain in the groin, thigh or knee with limitation of external rotation and leg length shortening. Idiopathic avascular necrosis (AVN) of the femur (Legg-Calvé-Perthes disease) may occur in children,

commonly boys between the ages of 4 and 9 years.<sup>2</sup>

#### Causes of avascular necrosis of the femoral head in adults

Systemic steroids and alcohol are well-recognised causes of AVN in adults, but conditions associated with hypercoagulable states such as systemic lupus erythematosus, antiphospholipid syndrome, sickle cell disease, primary coagulopathies and metabolic disorders such as diabetes need to be considered. A high index of suspicion is needed for the early detection and diagnosis of AVN as initial clinical features are nonspecific, with insidious onset of progressive hip pain exacerbated by weight bearing with normal range of motion.<sup>3,4</sup>

#### How do you diagnose and treat bursitis around the hip?

Two important bursae may lead to hip pain: iliopsoas and greater trochanteric bursa. The iliopsoas bursa lies between the iliopsoas muscle/tendon and the pubic eminence. Typically patients have pain and tenderness in the groin with pain on resisted flexion of the hip. The more common bursal lesion is trochanteric bursitis. Patients have difficulty lying on the affected side with localised tenderness over the greater trochanter. They also have pain on adduction and passive internal rotation of the hip. The ischial bursa lies over the ischial tuberosity in close proximity to the sciatic nerve. Common presenting symptoms include buttock pain worsened by sitting and associated paraesthesia down the back of the leg. Treatment may include non-steroidal anti-inflammatory drugs (NSAIDs), analgesia and local steroid infiltration under ultrasound guidance for the deep bursae.<sup>3,4</sup>