Learning Objectives

- to provide examples of patient conditions (obesity, hypertension, hyperlipidemia and diabetes) associated with clinical manifestations of gout
- to describe the manifestations of attacks of gout at different stages of development and differentiate them from other kinds of attacks, such as seronegative arthropathies, reactive arthritis, inflammatory bowel disease, and calcium pyrophosphate dihydrate disease
- to describe appropriate treatment for the three stages of the disease

CASE:

A 45-year-old man, employed as a truck driver, visits his family doctor complaining of acute pain, redness and swelling in his left ankle. Three days prior he was awakened in the middle of the night with a pain that he describes as so severe he couldn’t tolerate bedclothes on his ankle. Five years earlier he experienced a similar “attack” in the big toe of his right foot. It lasted two weeks and resolved with ibuprofen. Although he is in good health, he is 20 kg overweight, smokes a pack of cigarettes a day and drinks a case of beer on weekends. His family history is unknown.

EPIDEMIOLOGY AND CLINICAL PRESENTATION

Gout affects about one out of 120 people, predominantly adult men—women are rarely affected before menopause. It is strongly associated with obesity, hypertension, hyperlipidemia and diabetes. The consumption of excess alcohol or low dose ASA can be involved in precipitating acute attacks. The metabolic imbalance underlying gout is hyperuricemia (>340 mmol/dL, >7 mg/dL).

It is important to note that hyperuricemia occurs at least once in at least 5% of asymptomatic individuals and that fewer than 25% of all hyperuricemic individuals will
develop acute gouty arthritis. The risk of gout increases with the degree and duration of hyperuricemia. The incidence of acute gouty attacks is 5% per year with a urate of greater than 540 mmol. Asymptomatic hyperuricemia will not usually require chronic treatment.

The clinical manifestations of gout requiring treatment include recurrent attacks of inflammatory arthritis, accumulation of tophi (on helix of ears, olecranon, fingers etc.), or the development of urate nephropathy. The initial attack of gouty arthritis is often monoarticular and characteristically will affect the first MTP joint of
the foot. An attack can be accompanied by fever, chills and malaise. Subsequent attacks can affect other joints, most often the foot, ankle or knee. A long interval between attacks is typical of acute intermittent gout in its early stages. If untreated, intermittent gout can progress to chronic tophaceous gout with persistent and sometimes destructive joint involvement.

DIFFERENTIAL DIAGNOSIS
Features of gouty arthritis include sudden onset (often overnight), intense pain, redness, heat and swelling. A unique feature is the occasional desquamation of skin overlying the affected MTP. The inflammatory features can subside over several hours if treated at the first sign of an impending attack or they may last several weeks if treatment is delayed. The seronegative arthropathies, such as psoriatic arthritis, reactive arthritis, and enteropathic arthritis, can produce similar attacks and may initially be mistaken for gout. Diagnostic certainty is obtained by obtaining synovial fluid and examining the fluid under polarized light and seeing uric acid crystals.

Pseudogout can produce gout-like attacks characterized by acute localized pain and swelling. The time to peak pain and swelling is often over several days as opposed to hours as in gout. This can be definitively diagnosed by the finding of calcium pyrophosphate crystals in the synovial fluid or presumptively diagnosed by the finding of chondrocalcinosis (deposits of calcium pyrophosphate dihydrate in cartilage) on X-rays of the affected joint. This form of arthritis is most often in people over 60 and often in a hospital setting following surgery or acute vascular accidents (CVA, MI, etc.).

Septic arthritis can be as rapid in onset and equally as painful as gouty

ACUTE GOUT DIAGNOSIS AT A GLANCE
- Risk factors: Male gender, obesity, hypertension, hyperlipidemia, excessive alcohol consumption
- Symptoms: Intense pain in and around affected joints, sometimes fever and chills
- Physical findings: Joint warmth, redness and swelling, visible tophi
- Laboratory findings: Hyperuricemia, uric acid crystals in synovial fluid, tophi on radiography
- Differentiate from: Pseudogout, seronegative arthropathies, septic arthritis
arthritis. Septic arthritis will most often affect joints that have been injured in some way. A high index of suspicion is required and should lead to a rapid joint aspiration for gram stain and synovial fluid culture.

LABORATORY TESTING
Elevated serum urate level, long considered a cornerstone of gout diagnosis, is actually of limited use as the vast majority of hyperuricemic subjects do not develop gout. The serum urate may be normal during the acute attack. Hyperuricemia can be present during attacks of pseudogout.

The definitive diagnosis of gout requires the demonstration of uric acid crystals in synovial fluid or in material removed from a tophus. Any synovial fluid should also be sent for bacterial culture to rule out septic arthritis.

A 24-hour urine collection for urate can be useful to determine if an individual is an overproducer or an underexcreter. This can have some influence in choice of drugs to treat hyperuricemia.

MANAGEMENT
If untreated, gout can progress through three phases over several years. Initially there is asymptomatic hyperuricemia, which usually does not require treatment. This can be followed by acute intermittent gouty attacks that can be separated by years. Rarely (these days) this can evolve into chronic tophaceous gout with persistent arthritis.

The preferred treatment for an acute attack of gout would be an anti-inflammatory drug (NSAID). The drug most frequently prescribed is indomethacin in a dose of 50 mg three or four times a day. Some individuals cannot tolerate this drug due to GI upset or severe headaches. Other NSAIDs in full doses may be used.

Colchicine has been used for many years but has fallen out of favour because of the availability of NSAIDs and its toxicity when used in full therapeutic doses. Corticosteroids are effective in controlling acute attacks of gout. They can be given by intra-articular

WHEN TO REFER
- Gout diagnosis is uncertain and needs to be established or confirmed
- X-rays reveal the appearance or progression of erosions
- There is evidence of renal disease
- Drug treatment is ineffective or drug toxicity/intolerance occurs
injections in monoarticular attacks or by the oral or intramuscular routes for polyarticular attacks. They are also useful in individuals in whom NSAIDs are contraindicated (renal insufficiency, presence of a peptic ulcer, severe ASA sensitivity, etc.).

Allopurinol should never be started during an acute attack of gout. The fluctuation of serum urate levels that this drug produces will actually prolong attacks and make them much more difficult to control.

When the frequency or severity of acute attacks of gout begins to interfere with an individual’s quality of life, then treatment with medications to reduce serum urate levels should be considered. These medications should never be started during an acute attack but only after all acute inflammation is controlled. Fluctuations of serum urate levels can precipitate acute attacks of gout and so prior to initiating hypouricemic therapy, one should initiate low dose colchicine (0.6 mg BID) or an NSAID to prevent acute attacks.

The most frequently used agent to lower serum urate is allopurinol. This drug must be used with caution in the presence of any pre-existing liver or kidney disease. The most frequent side effect is skin rash and in some instances these can be severe (toxic epidermal necrolysis, Stevens-Johnson syndrome). The combination of ampicillin with allopurinol will result in skin rash in 20% of patients. This drug interferes with the metabolism of azathioprine and cyclophosphamide and dose alterations of these medications are required if allopurinol is to be used.

If patients cannot tolerate allopurinol, then other drugs may be used to facilitate urate excretion such as probenecid or sulfinpyrazone.

A decision to initiate treatment with allopurinol or uricosuric drugs requires a commitment to use these drugs for life and not to interrupt therapy if at all possible, as acute attacks would ensue.

**LIFESTYLE MODIFICATION**

Individuals with hyperuricemia or gout should be encouraged to lose weight if indicated. Avoidance of known precipitants of acute attacks is encouraged. This would include avoidance of alcoholic binges, or intermittent use of diuretics and low dose ASA. Dietary restriction of excess purine is useful if intake is excessive (organ meats, e.g. liver, kidneys, brain, sweetbreads or herring, sardines, lentils, lima beans). Patients with gout are also often found to have hypertriglycereidemia and hypertension and these conditions need to be treated aggressively.
GOUT

DIAGNOSTIC SUMMARY

Criteria for acute gouty arthritis
One of the following three criteria:
• Urate crystals in the joint fluid
• A tophus proven to contain urate crystals
• Six or more of the following 12 phenomena:
  – more than one attack of acute arthritis
  – attack of monoarticular arthritis
  – first MTP joint painful or swollen
  – unilateral attack involving first MTP joint
  – unilateral attack involving tarsal joint
  – maximal inflammation developed within a day
  – joint redness
  – suspected tophus
  – hyperuricemia
  – asymmetric swelling within a joint (on radiography)
  – subcortical cysts without erosions (on radiography)
  – negative culture of joint fluid during attack

QUESTIONS

1. What are some key differences between gout and pseudogout?
   On average, pseudogout tends to strike people later in life than gout. Initial attacks of gout are most often in the toes, while pseudogout is most likely to strike the knee. Uric acid deposits (resulting from hyperuricemia) are responsible for the symptoms of gout, whereas pseudogout is associated with calcium-containing deposits.

2. What is the value of a serum uric acid test in diagnosing gouty arthritis?
   Although gouty arthritis is virtually always preceded by hyperuricemia, the converse is not true — that is, hyperuricemia does not progress to gouty arthritis in most cases. Thus, a serum uric acid test is of little value in substantiating a diagnosis of gouty arthritis, except when accompanied by several other criteria for the disease. On the other hand, synovial fluid aspiration can definitively establish a diagnosis if uric acid crystals are detected in the aspirated fluid.