Gout Malcolm Persey MD FRCP

Anyone who has suffered gout will recognize the description, given by a physician, Thomas Sydenham, of his own attacks, as long ago as 1683:

The victim goes to bed and sleeps in good health. About 2 o'clock in the morning, he is awakened by a severe pain in the great toe; more rarely in the heel, ankle or instep. This pain is like that of a dislocation, and yet the parts feel as if cold water were poured over them. Then follows chills and shiver and a little fever. The pain which at first moderate becomes more intense. With its intensity the chills and shivers increase. After a time this comes to a full height, accommodating itself to the bones and ligaments of the tarsus and metatarsus. Now it is a violent stretching and tearing of the ligaments-- now it is a gnawing pain and now a pressure and tightening. So exquisite and lively meanwhile is the feeling of the part affected, that it cannot bear the weight of bedclothes nor the jar of a person walking in the room.

Gout has an even longer history than this, with evidence of gout in ancient Egyptian skeletons from as long 4000 years ago. Hippocrates, he of the famous oath taken by newly-qualified doctors, wrote of gout in around 400 BC.

The next few paragraphs will try to provide to some of the commonly asked questions about gout, aiming to make this painful condition and its treatment more understandable to its sufferers.

Who gets gout?

Anyone! While gout has traditionally been associated with drinking a lot of alcohol, eating a lot of meat, and other indulgences, this is by no means necessary and most people who suffer gout nowadays are just 'average'. It is true that gout is unusual before the age of about 30 years, and more common in men (almost 4 times as common in men as in women), but this favouring of men tends to even out with age, with the problem affecting women increasingly after the menopause. Overall a little over 1% men will suffer gout. The reasons for these differences will to some extent become apparent when we discuss later why gout occurs. It is true that some people will be more likely to get gout because of what they eat or drink, or because of drugs they have to take for other conditions, or because it runs in the family. Some of these might be possible to modify after discussion with your doctor, but you cannot change your parents!

In discussing how to prevent gout later, we will make a distinction between common primary gout, which is large determined by your family genes, and rarer secondary gout, where an underlying alternative cause for the problem can be identified.

The gout attack ('acute gout')

Most people who suffer gout would use much less elegant language than Dr Sydenham to describe the severe pain that they suffer! The description he gives is nevertheless very accurate of what most people suffer. For reasons that are unknown

attacks usually do start in the early hours of the morning, often waking the patient, with increasing pain over a few hours. However, people rarely describe having a fever or a temperature, but the attacks do most commonly occur in the big toe (more than 50%) or ankle. Other joints can be affected (knee, elbow, wrist, hand joints), but it is unusual to have gout affecting the hip, for example, or shoulder. The swelling is usually very marked, and the whole foot is often affected, so that it is difficult to tell that the problem stems from the big toe. It is almost always accompanied by redness ('erythema') and warmth, the area feeling hot to the touch, and the area is extremely tender, to the extent that even the lightest of touches can make you jump, the pressure of the bed clothes unbearable. It will be very difficult to walk, and almost impossible to take weight on the affected foot.

What happens next?

Once upon a time, there was no effective treatment for gout, although doctors were often unwilling to admit as much. We therefore know that if you do nothing about an attack of gout**, the pain and swelling peak at around 24 hours**, is at its most severe for a couple of days, and then gradually improves over 7 to 10 days. As the swelling and redness disappear then the overlying skin sometimes flakes, leaving a trail of dead skin flakes on the floor or in the bed, like scales. By 2 weeks after the attack started everything looks and feels back to normal. Doctors refer to this period after an attack, or if you are unlucky, between this attack and the next, as the 'intercritical period.'

Will it happen again?

Once you have had one attack of gout, there is a good chance that it will happen again (about 80% of people within 2 years), but it is impossible to predict how often or when. As we will see below, this is very important to appreciate when discussing the different types of treatment. If you have attacks very infrequently, we would be thinking about treatment very differently from someone who has attacks every few weeks.

Recurrent attacks

A small number of people have attacks frequently. As mentioned above, there may be identifiable reasons for this which can be modified, but regular medication may be required to prevent recurrent attacks. If attacks are recurrent and no treatment instituted the attacks tend to become more frequent (the 'intrecritical period' becomes shorter) and can involve more than 1 joint at a time.

Chronic tophaceous gout

An even smaller number of people develop something called chronic tophaceous gout. As we will discuss, gout is usually associated with high levels of a chemical called uric acid in the blood. If levels of this are very high for many years this can cause not only the attacks of gout which we have described, but the uric acid can be deposited in a form outside the joints (called in medical terminology 'extra-articular'gout, meaning outside the articulation or joint). Tophi are deposits of a form of uric acid under the skin as a white, cheesy material, most commonly in the ear lobes and behind the elbows, but can occur almost anywhere. These deposits are not usually

painful, but are unsightly and can get in the way. If large, or if they catch on things, they can leak their cheesy material, which is messy, and can become infected and painful. Most importantly, this can mean that similar deposits are occurring unseen within the body, such as in the kidneys, where they can cause damage. If tophi occur it is therefore important to look at measures which lower the level of uric acid in the blood and so reverse this process. In people who suffer recurrent attacks of gout, and who do not have treatment to lower the blood uric acid level, it is estimated that 12% of them will develop tophi in the next 5 years, and 20% over 20 years. Conversely it is therefore important to realise therefore that most people who have recurrent attacks of gout, do not go on to get tophaceous gout.

Another important manifestation of extra-articular gout is kidney stones. There are many types of kidney stone, but chemical analysis allows a medical laboratory to determine if a stone contains uric acid. If so this would therefore suggest the need to look at and lower the uric acid level in the blood.

Extra-articular gout can cause damage to the kidneys even without the formation of stones. Such kidney damage will be detected by blood tests of kidney function. However, these can only determine that kidney damage is present, not what causes it, and again, there are very many other causes of kidney damage, other than a high uric acid level in the blood. This is a difficult situation to interpret as kidney damage is itself often associated with failure to efficiently excrete excess uric acid efficiently in the urine. As a result the uric acid level rises in the blood. Faced with blood tests showing both a high uric acid level and a degree of kidney impairment it can be impossible to determine which came first.

What causes gout?

Uric acid is one of the many chemical floating around in our bloodstream. We are all making and breaking down DNA constantly and uric acid is a natural breakdown product of this, and we get rid of it mostly in urine. All animals produce it; birds get rid of it as the white stuff in bird pooh. Most mammals can convert it into something which dissolves very readily in urine. The problem for man (and some apes) is that this ability to convert it into something very soluble was lost somewhere in evolution. As a result, if the concentration in blood rises too high, it will not dissolve and tends to form crystals like salt crystals. Perhaps fortunately, it does not tend to form crystals in the bloodstream itself, but seems to like building up deposits in the lining (‘synovium’) of joints.

This may never cause any problems, but if the uric acid level in the blood is high for many years, the deposits build up to critical levels and can then break down, often for no apparent reason, and the crystals leave the lining and enter the joint itself. Joints are generally very sensitive to having anything unusual in them and they recognize the uric acid crystals as something which should not be there. They react to them rather as they would a germ or bug, and send in lots of extra cells and chemical to try and destroy the crystals. It is this reaction which causes the swelling, warmth, redness, tenderness and pain, which together comprise inflammation. The inflammation is thus a normal and healthy reaction to the crystals in the joint, and it is very effective at dealing with them, which is why the inflammation settles down over 7 to 10 days.

In many cases, nothing further will happen, but the underlying problem persists, namely high levels of uric acid in the blood, building up in the lining of joint, and the attack could recur at any time.

Why is the level of uric acid level high?

There are many factors which influence the level of uric acid in the blood. Rather like someone's height, in most cases your average level is set by your genes and there is little that you can do about it. However, variations in the level around your average are influenced by diet, alcohol consumption (and type of acholol), medication, obesity and other illness. Where a secondary cause of a high uric acid level can be identified it can be classified as causing overproduction of uric acid, or under excretion, both of which will cause the uric acid level in the blood to rise.

Why do attacks happen when they do?

This is very poorly understood. Attacks often appear to have no clear precipitant, but sudden changes in the level of uric acid in the blood, up or down, (eg eating certain foods, alcoholic binges, crash diets, a new medication) can precipitate an attack. They often seem to follow trauma, surgery, starvation or dehydration.

Treatment of the attack

Gout is associated with very intense inflammation. Treatment of an attack ('acute treatment') needs to be aimed at suppressing inflammation to be successful. Keeping the affected area still, raised, iced (eg with a packet of frozen peas), and simple pain killers like paracetamol, may give some relief but will not shorten the attack.

One of the oldest and best established treatments to reduce inflammation is a drug called colchicine. This may have been described as a treatment for gout as early as the 6th century. Colchis was a community on the Black Sea coast, from which the meadow saffron plant, or *Colchicum autum*, derived its name. Colchicine is an extract of this plant. It was little used as a treatment in the 'modern' era until it became available as a tablet in 1936. While undoubtedly effective and safe when given by mouth, it often causes diarrhea if used in doses large enough to be effective (at least 3 500 microgram tablets daily) and takes longer to work than other treatments.

Nowadays the most widely used treatment for an attack of gout is a class of drug called non-steroidal anti-inflammatories, or NSAIDs for short. There are many varieties of NSAIDs, the oldest being aspirin, although this is now rarely used for this purpose. Other common examples are ibuprofen (Nurofen® is a common brand), diclofenac (Voltarol®, Diclomax®), indometacin (Indocid®) and naproxen (Naprosyn®). There is little to choose between these in terms of their effectiveness provided they are given in adequate dose. For example, the standard dose of diclofenac is 50 mg three times daily, but many doctors will suggest taking 100 mg for the first dose, technically an overdose, to combat the intense inflammation associated with gout. Typically the drug should be started as early as possible in an attack and usually settle the attack within 3-5 days, although some relief is apparent

much sooner. The drug should be continued for a few days after the symptoms have settled.

There are some circumstances where these drugs may not be safe and hence should be avoided, although sometimes, as the course is typically short, provided you are made aware of the risks, your doctor may feel the risk justified. Situations where these drugs are considered less safe include in the elderly (over 70 years), if there is significant kidney disease or heart failure, severe high blood pressure, asthma, a history of ulcer in the gut, liver failure, or treatment with warfarin. Each case should of course be discussed with your doctor.

In recent years a modified form of NSAIDs have become available, known as COX 2-II specific NSAIDs. These have been 'tweaked' to try and reduce the incidence of the most common serious side effect of these drugs, namely bleeding from the upper gut, and ulcers in the stomach and upper gut. They undoubtedly have a lower incidence of these serious side-effects, and in effect allow a larger dose of anti-inflammatory to be given, but their popularity has been mitigated by their greater expense, and some concerns about other rare side effects. However, they are very effective at treating gout, the most widely available being eterocoxib, or Arcoxia®, given at a dose of 120 mg od, and patients often feel better after only a single dose, although it can be continued for up to 10 days.

For patients where colchicine or NSAIDS cannot be given, are not tolerated by the patient, or appear to be ineffective, steroid treatment is often the most effective. Many people are nervous of steroids, but the side effects about which one hears are only relevant when the dugs are given for long periods. Short sharp courses given to treat gout, provided these are not too frequent, are rarely associated with such side effects. Typically, the steroid is given by mouth (eg 20 mg daily for 10 days). However it can also be given as a single injection into the buttock, or even directly into the affected joint. This latter route can be highly effective, and may also allow fluid to be taken from the joint for analysis and confirmation of the diagnosis. However, as discussed below, this is rarely necessary and the procedure, while short-lived, is quite painful, and not all doctors will be proficient in it. Steroids are a very effective and safe treatment for acute attacks of gout.

It is important to realize that these 3 treatments (colchicine, steroids and NSAIDs) are the only treatments effective at reducing inflammation and shortening the duration of an attack.

If I treat the attack and suppress the inflammation will I be allowing damage to occur?

This is a reasonable question, in that the inflammation happens because the body is attempting to rid itself of potentially damaging crystals. However, the inflammation probably inadvertently causes as much damage as the crystals themselves, so suppressing the inflammation has a net benefit, as well as getting rid of the pain!

Treatment of recurrent attacks and tophaceous gout

As we have already suggested, one or even several attacks of gout do not require treatment beyond the anti-inflammatory treatments we have discussed.

However, there are a number of circumstances where it may be recommended to have a form of treatment which will lower the uric acid level in the blood, and so prevent further attacks; this is termed prophylactic therapy.

These situations are where attacks are frequent (eg more than 3 times per year); the anti-inflammatory treatments cannot be given, for whatever reason, or are ineffective, or where there is evidence that the gout is causing trouble outside the joints, as in tophi or in the kidneys, either as kidney stones or impairment of kidney function.

If there is an obvious reason for having high uric acid levels ('secondary gout') which can be adjusted, this is one avenue to explore. A common example of this is where water tablets (diuterics), which raise the uric acid level in the blood, are being used to treat high blood pressure. In such circumstances it is often possible to use an alternative blood pressure tablet which does not have this effect. Low dose aspirin is frequently prescribed to reduce the risk of heart disease; while often necessary, with few alternatives as safe and cheap, it is sometimes prescribed when not strictly required.

Causes of secondary gout

As discussed briefly above, causes of high uric acid levels can be classified as causing overproduction of uric acid, or preventing its excretion in the kidneys. Some such as alcohol operate through both mechanisms.

Overproduction

Certain cancers and their treatment

Psoriasis

Hemolytic anaemia

Alcohol

Fructose (in many soft drinks)

Rarely warfarin, vitamin B12

Under excretion

A large number of drugs:

Low dose aspirin

Cyclosporin

Diuretics

Alcohol

Kidney disease

An interesting example of gout caused at least partly by under excretion of gout is ‘saturnine gout’. This is now of largely historical interest but when lead poisoning was a common problem (lead in water from lead piping, children ingesting lead paint, or in ancient Rome, the use of lead salts to sweeten wine) the lead prevented excretion of uric acid and caused gout. Gout was a common problem in Ancient Rome!

How can I and my doctor be certain it is gout?

When you describe what has happened to you to your doctor he/she will try and elicit a history of the symptoms from you. This information will include the site of the pain, its severity, if there was swelling, how long it lasted, if it has happened before, if there is a family history, your alcohol consumption, and medication you may be taking etc. The doctor will then examine you, and if suspecting gout this will generally involve examining the affected area, but also anything else relevant arising from the history you have given, and also an examination for tophi, the soft tissue deposits of uric acid. If you have given a typical history, of very severe pain and swelling, lasting 7-10 days, affecting a big toe, there is usually little room for doubt about the diagnosis, as few very other conditions behave in this manner. If there are atypical features eg an unusual joint affected, or longer attacks than expected, other possibilities may need to be considered, but even here, it is usually a matter of excluding these conditions, rather than confirming gout.

What tests do I need?

It follows from the previous paragraph, that often no specific tests are needed to make a diagnosis of gout. Nevertheless, both patients and doctors may feel more comfortable if some tests are performed to confirm the diagnosis, particularly if there are some unusual features.

Aspiration of the affected joint

This refers to taking a sample of fluid from the affected joint with needle and syringe. Sometimes this **must** be done eg if there is concern that the joint is inflamed because of an infection, rather than gout. However, it is often painful, can be difficult to perform, and will rarely be done outside a hospital setting.

Blood tests

We have discussed how most patients who suffer gout will have high uric acid levels in the blood. How, it is usually unhelpful to perform blood tests at the time of an attack. This is because, as a result of the intense inflammation, uric acid is excreted more effectively during an acute attack, and the levels of uric acid level in the blood actually falls, and can be misleadingly normal. It is more helpful to measure the uric acid level in the blood about 6 weeks later. This will be more representative, and your doctor will usually take the opportunity to check you for impairment of kidney, high cholesterol and diabetes, all of which are more common in gout sufferers. It is

important to realize however that uric acid levels can vary quite widely on day-to-day basis and treatment should not be based on a single measurement.

X-rays and scans

These are rarely helpful. Unless you have had gout for many years, with recurrent attacks, X-rays are normal. Uric acid deposits are not visible on X-ray or in any type of scan, and it takes many years for any damage to occur, which might be visible on an X-ray. If X-rays of a big toe are performed they almost inevitably show some osteoarthritis ('wear and tear') affecting the big toe joint, as this is as common as wrinkles on the forehead. This may in part explain why gout occurs commonly in the big toe, as it seems to have a predilection for worn joints, but such wear and tear is by no means necessary for it to occur.

Prevention of recurrent attacks

What can I do?

As already mentioned, there may be obvious reasons why gout attacks continue to recur, such as medication, obesity, or excess alcohol consumption. These may well be modifiable and should be discussed with your doctor.

Many people are keen to address their diet to reduce their risk of recurrent attacks. In practice, most dietary modifications have only a small effect on uric acid levels in the blood and hence only a small effect on the risk of recurrent attacks of gout. In general foods rich in chemicals called purines (which in turn are found in high levels in protein-rich foods), which are broken down in the body to uric acid, tend to raise the urate level in the blood. A diet low enough in purine to reduce the blood uric acid level by only 10-15% is very difficult to stick to and some might argue that the diet is so unpalatable that they would rather suffer gout! Adequate treatment of recurrent gout, on the other hand, often requires the uric acid level to be *consistently* lowered by 50%; this is very difficult to achieve and maintain long term through dietary modification. To complicate matters further, the effects of dietary modification are sometimes unpredictable; for example, yoghurt is high in protein, but a yoghurt-rich diet tends to lower uric acid levels, although again only by modest amounts.

It is of course possible to measure the effect of dietary modifications by checking the blood level of uric acid before and after a dietary modification, but it is important to remember that the modification would need to be sustained long-term.

To be sceptical about the effects of diet is not to deny that certain foods which affect the urate level sharply might not precipitate acute attacks; people will often discover these precipitants for themselves, but common culprits are sardines, offal and shellfish. Further dietary information is available from the UK Gout Society (www.ukgoutsociety.org).

In practice, most patients with recurrent gout and high uric acid levels need medication to successfully reduce the uric acid level enough to prevent attacks.

Medication to prevent recurrent attacks

Drugs are available which reduce over-production of uric acid, as well as drugs to enhance excretion through the kidney (called uricosuric drugs). In theory therefore, which drug is used can be tailored to the cause of high uric acid levels (over-production or under excretion). In practice, in many cases the cause is a bit of both, and the drug used to treat over-production (allopurinol, Zyloric®) is much more effective and better tolerated than uricosuric drugs, and so is usually first choice. It is worth noting that if significant kidney function impairment is present, uricosuric drugs cannot further increase the amount of uric acid excreted in the urine.

Do I have arthritis?

You may hear your condition referred nto as arthritis (eg acute gouty arthritis). There are many forms of arthritis, which simply means inflammation in a joint. Other than this gout has little in common with other forms of arthritis such as rheumatoid arthritis. (An interesting medical curiosity is that gout is very rare in patients with rheumatoid arthritis). If properly treated there is no reason why it should cause the sorts of problems which people with rheumatoid arthritis suffer.

What else might it be

What else is it called?

Gout has few alternative names. We have already referred to acute gouty arthritis; it may also be called urate arthropathy, or ‘the’ gout. ‘Podagra’ means pain in the foot but historically severe pain in the foot was often called gout, even if many cases were probably not, and the term has stuck as name for gout affecting the foot.