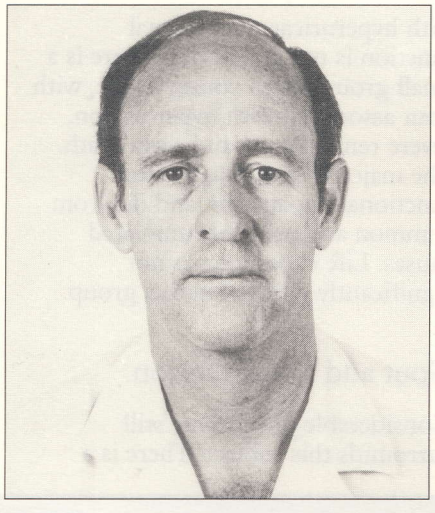
Gout and Hyperuricaemia

– Prof SW Brighton



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Curriculum vitae

Prof SW Brighton studied at the University of Pretoria and received the MBChB in 1963. After some years in hospitals in Durban and London (UK) and then general practice in Pretoria, he joined the staff of the Department of Physical Medicine, University of Pretoria 1975-1979, obtained the M Med degree, and since 1980 has been attached to the Department of Rheumatology (UP). In 1979 Prof Brighton was elected Fellow of the Faculty of Physical Medicine of the College of Medicine of SA. He has published in many medical journals, in RSA and abroad, and is actively involved in research work at the University of Pretoria.

Summary

The causes of gout are basically either the increased formation or decreased excretion of uric acid. Certain causes and risk factors, aspects of its pathophysiology and epidemiology are all explained in order to assist the GP in understanding and treating his patients.

S Afr Fam Pract 1990; 11: 292-5

KEYWORDS:
Gout; Uric Acid; Life style; Diet; Alcohol Drinking.

In the prevention and management of gout it is good to understand some of its epidemiology and pathophysiology. The causes of gout (table 1) are basically twofold, the increased formation and decreased excretion of uric acid.

Frequency of Clinical Gout

In industrialised societies most studies give an overall prevalence of 2,6 cases per thousand population, but this varies greatly. It is also known that hyperuricaemia (and gout) can change and often in a very short time in a population, owing to environmental and particularly dietary factors.

Plasma levels are low in children with no difference between the sexes. Levels then rise after puberty, more so in boys than in girls. After middle age, values for women rise to approach those of men.

A rigid definition of hyperuricaemia is not possible. In general terms and for practical purposes the upper limit or normal may be taken as 420 umol/l (7 mg %) for men and 360 umol/l (6,0 mg %) for women.

Gout and the Kidney

In former times when no effective therapy was available, gouty patients invariably developed kidney complications. It is much less today, at least in its more gross form.

Table I: Causes of Hyperuricaemia

I	*Increased formation of uric acid.*
	Specific enzyme abnormalities
	Increased turnover of nucleoprotein
	Diet
	Exogenous chemicals.
II	*Decreased excretion of uric acid*
	Renal function and fluid volume
	Drugs
	Starvation and ketosis
	Essential hypertension
	Lead Poisoning
	Hypercalcemia
	Myxoedema
III	*Other factors*
	Race, sex and age
	Genetic factors
	Body weight
	Social class and intelligence
	Alcohol
	Cardiovascular disease
	Diabetes

... Gout and Hyperuricaemia

Three clinical entities are recognised:

i) uric acid nephrolithiasis

ii) acute uric acid nephropathy

iii) urate nephropathy

i) *Uric acid nephrolithiasis*
Estimation of stone formation among gouty patients vary from 4 to 20%. Many factors play a role, but is more common in warm climates with relative dehydration. Patients with chronic diarrhoea and ileostomies who have low urinary pH values are a special high risk group.

ii) *Acute uric acid nephropathy.*
This is a consequence of excessive nucleoprotein degradation occuring most commonly after chemotherapy for lymphoma or leukaemia.

iii) *Urate nephropathy.*
Interstitial deposition of urate may lead to renal function impairment, but abnormalities of tubular function may also lead to hyperuricaemia. It is often difficult in an individual patient to establish the sequence of events which has taken place. The effect of hyperuricaemia per se, as contrasted with hyperuricaemia on renal function is not at all clear. There is a small group, often young in age, with gout associated with hypertension, severe renal disease and early death. The majority show slight renal functional impairment and die from common and probably unrelated causes. Life expectancy is not significantly reduced in this group.

Gout and Hypertension

Considerable uncertainty still surrounds this subject. There is a

definite subset of young subjects with gout, severe hypertension and renal failure. For the majority of other patients with gout, mild hypertension is common. Up to 43% in some series. An association between hypertension, hyperuricaemia and renal blood flow has been documented. The hyperuricaemia in this hypertensive population is probably a reflection of hypertensive vascular disease.

Gout and Hyperlipidaemia

There have been a number of studies claiming an association between hyperuricaemia and hypercholesterolaemia, but other studies have not confirmed this. Patients with a raised triglyceride level in type IV hyperlipoproteinaemia often have a raised serum urate level, and hypertriglyceridaemia is common in patients with gout. Obesity is to some extent a common factor as well as alcohol intake. There does not appear to be a direct causal mechanism. There is increasing evidence of genetic factors. Gout and

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hypertriglyceridaemia may be related by the close proximity of disease specific - alleles.

Gout and Cardiovascular Disease

The problem of uric acid and vascular disease also remains to be clarified. A relationship between hyperuricaemia and atheroma has been suggested in the past, but not borne out by clinical experience or epidemiological studies. Many hyperuricaemia patients have an increased burden of other cardiovascular risk factors such

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Most patients with gout, also have mild hypertension

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as hypertension, smoking and obesity making it very difficult to establish if hyperuricaemia per se made an independant contribution to risk.

Gout and Diabetes

Apart from the well known fact that diabetic ketoacidosis like any other form of ketosis can give transient hyperuricaemia because of impaired renal excretion of urate, the relationship between glucose, uric acid, lipid metabolism and body weight is difficult. An association has been claimed between gout and diabetes but the general clinical impression and epidemiological studies have not shown such an association.

Serum urate levels are higher in executives than in craftsmen. PhD scientists have higher urate levels than supervisors, and they in turn have higher levels than craftsmen. Among university professors and business executives, urate levels showed a positive correlation with drive, achievement, range of activities and leadership. The significance of these associations is unknown although gout in the overweight, overindulgent business executive may in part, be due to diet. It has been suggested that the development of intelligence in primates has been enhanced by evolutionary loss of uricase, urate perhaps bestowing a certain intellectual stimulation. There is no direct evidence for such an hypothesis. On the other hand hyperuricaemia is also associated with mental deficiency eg the Lesch-Nyhan syndrome.

Diet

Almost without fail, gout patients regard eating and drinking two of the great pleasures in life. A diet rich in purines is well known to raise serum uric acid levels eg organ meats (liver, kidney) pate, fish roe, shellfish, herring and sardines. Many of the so called health foods (yeast products etc) as well as large dosages of ascorbic and nicotinic acid may raise the urate levels. The hyperuricaemia of beerdrinkers is partly due to ingested purines as well as the hyperuricaemic effect of alcohol itself. The actual energy content of the diet is also of importance. The relationship of body weight to hyperuricaemia has been shown in numerous epidemiological studies.

Alcohol

The age old belief that some gout patients are over indulgent in alcohol has been corroborated. Alcohol has a very high calorific value and in itself

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Serum urate levels are higher in executives than in craftsmen

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leads to obesity. Alcohol may also raise the serum uric acid level independent of weight changes. It can now be assumed that chronic

consumption of alcohol produces an increased synthesis of urate, with acute intoxication providing an additional element of decreased tubular clearance.

Diuretics

Diuretics may both inhibit tubular secretion as well as more avid reabsorption of urate. The gout produced by long term diuretic use may present as a classical acute gout but more often a chronic polyarthritis is seen. This may be mistaken for rheumatoid arthritis or osteoarthritis. Tophi may form and are commonly

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A definite relationship between body weight and hyperuricaemia

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seen around the distal interphalangeal joints of the fingers mimicking Heberden nodules. The pulps of the fingers are also a common site for tophi.

Lead Poisoning

The bones of ancient Romans contain high quantities of lead derived from lead lined water pipes as well as the making of wine in lead containers. They also had a high prevalence of gout. The available evidence indicates that exposure to lead can cause renal damage, a particular feature of which is a tubular defect leading to uric acid retention.

Aided by knowledge about gout and its associations and causes, we are more easily able to answer the questions of our patients and reduce the incidence of this life-style disease.

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