

The evolution of gout (an old lifestyle disease)

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Abstract

Background: Few diseases that confront the 21st century clinician have documented history which dates back to early human era.

Methods: We reviewed how the understanding of the aetiology, symptomatology, diagnosis and treatment of gout including myths have evolved and discussed the implications thereof.

Results: Gout has been recognized as a clinical entity before 2000BC with Hippocrates describing the five aphorism of gout. Between the 1st and the 6th century AD, the role of genetics and the association of gout with an indulgent lifestyle and tophi were described. Hemodactyl (a source of colchicines) was also first identified during this period. "Gout" was coined from the Latin word "Gutta" in the 13th century and the microscopy of uric acid crystals and gout symptomatology were the focus of investigations between the 17th and 18th centuries. Several drug treatments were developed between the 19th and 20th centuries including salicylates, probenecid and allopurinol. Gout as a risk factor for metabolic syndrome, NIDDM and cardiovascular disease is a challenge for the 20th century and the future.

Conclusion: The understanding of gout has evolved with human development but the challenges for the future will include how to deal with the associated cardiovascular co-morbidities.

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Gout in ancient Egypt

Gout was known among the Egyptians as Podagra (foot pain) as early as 2640 BC and was described by Hippocrates in the fifth century BC as the "unwalkable disease", mostly affecting the rich.¹ Hippocrates noted that gout did not affect eunuchs, was uncommon in pre-menopausal women and youth before coitarche, acute attacks subsided within 40 days, and affected more people in the spring and autumn. Hippocrates further wrote: "Persons affected with the gout who are aged, have tophi in their joints, have led a hard life, and whose bowels are constipated are beyond the power of medicine to cure".² The low prevalence of gout among eunuchs at that time could be explained by their non-indulgent lifestyle. Modern-day understanding suggests that gout has little or nothing to do with a hard life or constipation, but with tophi in the joints and indulgent lifestyles. Interestingly, modern management offers no cure – a difficulty observed several centuries ago.

Gout between the first and sixth century AD

By the first century AD, a Roman senator named Seneca highlighted the role of genetics in gout. He noted that women were becoming increasingly afflicted by gout, supposedly based on women's rivalry with men in living lavish lifestyles. Around the same time, Galen described 'tophi' as the manifestation of longstanding gout, and by the sixth century a physician named Alexander of Tralles discovered hermodactyl

(a source of colchicines) while searching for a laxative. He was the first to use it to treat gout.²

The name "gout"

"Gout" was coined by a monk named Randolphus of Bocking in the 13th century from the Latin word "gutta" (which translates into "drop").¹ Randolphus thought that gout resulted from the excess of one of the four humours that maintained health. This "drop" was thought to flow into the joint, causing pain.

Between 17th and 18th century AD: Gout microscopy, symptomatology and uric acid

Around 1679, Antoni van Leeuwenhoek described the microscopic picture of tophi as follows: "I observed the solid matter which to our eyes resembles chalk, and saw to my great astonishment that I was mistaken in my opinion, for it consisted of nothing but long, transparent little particles, many pointed at both ends and about 4 'axes' of the globules in length. I can not better describe that by supposing that we saw with naked eye pieces from a horse-tail cut to a length of one sixth of an inch". This observation is consistent with modern microscopy of uric acid crystals, and today observing uric acid crystals in joint aspirates is a criterion for the diagnosis of gout.

In 1683, Thomas Sydenham gave a detailed description of the symptomatology of the acute disease, based on his personal experience

both as a physician and gout sufferer. He wrote: "The patient goes to bed and sleeps quietly until about two in the morning when he is awakened by a pain which usually seizes the great toe, but sometimes the heel, the calf of the leg or the ankle. The pain resembles that of a dislocated bone.... and this is immediately succeeded by a chilliness, shivering and a slight fever ... the pain ..., which is mild in the beginning ..., grows gradually more violent every hour ... so exquisitely painful as not to endure the weight of the clothes nor the shaking of the room from a person walking briskly therein."

In 1734, William Stukeley described the crystal from a tophaceous joint and 42 years later, uric acid was identified by Scheele (a Swedish chemist). In 1763, colchicines was rediscovered by Prof Baron von Stoerk in Vienna, while in 1797 Woolaston confirmed that tophi consisted of uric acid deposit,³ using tophi from his own ear. It was almost a century later that McCarty and Hollander used polarised microscopy to confirm that joint fluid of gout sufferers contain monosodium urate.

Gout in the 19th and 20th centuries

Though gout was uncommon among black South Africans,^{4,5} Mody and Naidoo reported that a case report on a black South African sufferer was published as early as 1807 by Andrew.⁶ Cassim et al also reported an increase in HLA B14 antigen among black South Africans with gout compared to those without.⁵

The USA pharmacopaedia listed colchicine in 1820 and it was not until 1859 that Sir Albert Baring Garrod hypothesised that "urate deposit is the cause and not an effect of gout". He advocated a diet low in purine-rich food for the treatment for gout. Between 1894 and 1897, Haig was reported to have conducted several experiments on himself (being a gout sufferer), to show that hyperuricaemia could be lowered by lowering the intake of purine-rich diets, and similarly Freudweiler proved that injecting urate into joints and subcutaneous tissues precipitated gout and tophi respectively.¹

Uricosuric agents, especially salicylate, were used to treat gout towards the end of the 19th century, but salicylate was abandoned because of uric acid retention at low doses and toxicity at high, uricosuric dosages.

In 1931, Sir Archibald Garrod (Sir Albert Garrod's son) suggested that gout should be included in the class of diseases of in-born error of metabolism and by the 1940s aspirin was used for the treatment of gout. The year 1951 saw the introduction of probenecid and by 1963, allopurinol was used for the treatment of gout.² George Hitchings and Gertrude Elion were awarded the Nobel Prize for developing allopurinol, azathiopine and other drugs in 1988.

Gout in the 21st century: An old disease with a new challenge

In the 21st century, gout remains the most common inflammatory arthritis in men over 40 years old and the incidence is on the increase across all races.^{5,7} This is attributable to factors such as dietary changes, increasing longevity, sub-clinical renal impairment and increases in the use of diuretics and other drugs causing hyperuricaemia. A recent study identified gout as an indicator of increased risks for metabolic syndrome, non-insulin-dependent diabetes mellitus (NIDDM) and adverse cardiovascular outcomes,⁸ and this constitutes a serious concern within the context of a global epidemic of NIDDM and coronary heart diseases. An increase in all causes of mortality from coronary heart disease has also been found among men with gout compared to controls.⁹ In the

same light, increasing servings of fructose-rich drinks in contrast to diet soft drinks has been associated with increasing the risk for gout.¹⁰

The indulgent lifestyles that predispose to gout are also risks for most cardiovascular diseases. However, a prospective study on coffee consumption suggests that it appears to protect against the development of gout. This protection increases with the number of cups of coffee consumed per day, with maximum protection at six cups, irrespective of caffeine content [RR = 0.41; 95% CI (0.19–0.88)].¹¹

Gout and sick role

Although King George III never had any gouty attacks, he possibly had raised urate blood levels because four of his sons and one daughter had the clinical disease. This highlights the role of heredity and the concept that hyperuricaemia does not necessarily equal the clinical disease. King Louis XIV of France, his father and grandfather all suffered from gout. The sick role offered by acute gout attack has been reportedly faked by John Hancock, a governor of Massachusetts, to stay away from ratifying the constitution to unite all the states of the USA.

Conclusion

As human lifestyle changes, the challenge for the future will not only be how to control pain and lower urate levels effectively, but also the associated cardiovascular co-morbidities in patients with gout.

NB: Our next article will review the management options for the gouty patient.

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