

Disease of Distinction

by Stephan A. Schwartz

Diseases have historically significant golden ages. Polio with the 1950s, Malaria with the opening of the Western Hemisphere are two examples. For gout, because effective treatment took so long to develop, there are several peak periods, the last of which is in many ways the most interesting -- the 17th and 18th centuries. And the reason is the role the disease played in America's founding.

John Locke, England's leading empiricist philosopher and an amateur physician, was in many ways the spiritual father of the American revolution. His philosophical writings center on human rights, and influenced virtually every major figure involved in our nation's founding. Locke pursued medicine as avidly as philosophy, and his medical notebooks abound with observations about gout. Like many of his spiritual children in the American Revolution, he suffered gout attacks throughout his adult life.

Franklin, the only person to sign all three founding documents of the United States: the Declaration of Independence in 1776, the Treaty of Paris in 1783, and the Constitution in 1787 was a severe gout sufferer, and had to be carried in a sedan chair to the Constitutional Convention in Philadelphia by convicts.

As was usual with him, he worked out his feelings on the subject by writing about them for publication, beginning by acknowledging the role heavy drinking played in provoking attacks. He told the Abbé Morellet, that "God clearly intended us to be tipplers because he had made the joints of the arm just the right length to carry a glass to the mouth."¹ He even created a dialogue between himself and gout.²

Franklin: "Eh! Oh! What have I done to merit these cruel sufferings?"

Gout: "Many things; you have ate and drank too freely, and too much indulged those legs of yours in indolence."³

The Comte de Vergennes, the French nobleman with whom Franklin worked to obtain the money to finance the American Revolution became

similarly afflicted, and Thomas Jefferson, who also suffered from gout, expressed the odd ambivalence that defined the 18th century view of gout as a prophylactic against more serious afflictions when he described his feelings about the French minister, "We have been some days in much inquietude for the Count de Vergennes," Jefferson wrote in 1787. "He is very seriously ill. Nature seems struggling to decide his disease into a gout. A swelled foot, at present, gives us a hope of this issue."⁴

Franklin, Jefferson, and the Comte de Vergennes may have made such a strong connection because all were sufferers of gout. And they clearly understood the political implications. "The Count de Vergennes has within these ten days had a very severe attack of what is deemed an unfixed gout," Jefferson wrote. "He has been well enough however to do business to-day. But anxieties for him are not yet quieted. He is a great & good minister, and an accident to him might endanger the peace of Europe."⁵

George Mason, the father of the Bill of Rights also suffered from the disease for much of his adult life, and more than once, like Franklin, he worked in spite of the great pain it caused him. Like Franklin, it also limited his involvement at several critical junctures during the Revolutionary period.⁶

Gout attacks were even used as political tactics. Perhaps the most famous example being John Hancock, the revolutionary leader, then the Massachusetts Governor, who was selected to preside over the Commonwealth's ratifying convention when the states were deciding whether to accept the Constitution. He was unable to make up his own mind on the Constitution, and took to his bed with what critics saw as a convenient case of gout.⁷

On the other side of the Revolution, King George III, the British Monarch who was our titular enemy, as well as a long line of British Prime Ministers, all led lives altered by gout.

The physician Aretaeus of Cappadocia captured the essence of gout two thousand years ago: "Pain seizes the great toe, then the forepart of the heel on which we rest; next it comes into the arch of the foot...the ankle joint swells last of all...no other pain is more severe than this, not iron

screws, nor cords, not the wound of a dagger, nor burning fire..."⁸ Like hot needles being slowly pushed into your flesh. Every step's an agony, and the weight of a simple bed sheet is unbearable. In addition to big toes, in the acute stage gout also attacks knees, elbows, wrists, or any other joint. As a chronic condition it leaves chalky deposits, called tophi, that can form like nodules under the skin.

"The pain is caused when white blood cells known as polymorphonuclear leukocytes discover crystals of Sodium Urate in the fluid of the joints," says John Hardin, Chairman of the Department of Medicine, Albert Einstein College of Medicine.⁹

"They start ingesting them, basically eating them, and this causes the release of proteins called Cytokines. It's like a cell level call to arms. 'Come help, we've found an invader. White blood cells come rushing from throughout the body. It's a battlefield, and there's an explosion of inflammation and swelling in the fluid filled space of the joint. That's what causes the pain."¹⁰

"We don't think much about gout today" says Daniel J. McCarty, recently retired as the Will and Cava Ross Professor of Medicine at the Medical College of Wisconsin, and the man who, in 1960, discovered that Sodium Urate crystals -- central to Hardin's explanation -- were in the fluid of a gouty joint.¹¹

"At the research level, medically it is probably the best understood of all diseases and, since it can be pretty well managed, a lot of research interest has now turned elsewhere. Ironically, at the same time many doctors in clinical practise know little about it except that it usually calls for a drug called Allopurinol and another whose principle active ingredient is colchicine. This lack of attention and interest is unfortunate, because there are still mysteries to gout. Many."¹²

The disease today is as prevalent as it was two millennia ago when Aretaeus recorded his observations. Dr. Hardin explains this is because "it is 90 per cent a disease of genetics, and 10 per cent a disease of lifestyle. It is not like small pox which could be eliminated. Until we can control genetics, gout will be with us."¹³

“Heredity and gender.” says John Meyerhoff, Clinical Scholar in Rheumatology at Sinai Hospital of Baltimore, and previously its Chief of Rheumatology.¹⁴ “Overwhelmingly gout is a disease of men. Males, when they go through puberty have the level of their uric acid rise. You need uric acid to make Sodium Urate crystals. Females don’t have increased uric acid levels until after menopause, which is why the small number of gouty women are older. In men it usually takes years for uric acid levels to build up, which is why it starts showing in men in their 30s. Plus you have to come from the gene pool that has the genetic flaw that allows gout to develop.”¹⁵

The genetic key though lies not in uric acid production says Dr. McCarty. “It’s your kidneys. We’ve just learned that.”¹⁶ Excess uric acid, he explains is a waste product usually processed through the kidneys and passed out in urine. “That’s why gout and kidney stones are often linked. How your body processes the excretion of uric acid determines how likely you are to get gout.”¹⁷

“If your kidneys do this efficiently then crystals won’t form,” Dr. Hardin says. “If it doesn’t they may. Although not everyone forms crystals, even when their uric acid levels are high.”¹⁸

Somewhere in the third or fourth interview doing the research for this article, I realize there is an odd disconnect. Most people I mention gout to say, Oh, yeah, I’ve got a uncle/brother/husband/father/guy I’m friends with who has it. He takes something for it and, with that synopsis the conversation goes on to other things. Gout excites little interest in the public mind.

Even researchers in Rheumatology like McCarty, Hardin, and Meyerhoff speak about it with a kind of flat matter-of-factness. To my ear they sound like old CIA operatives talking about KGB during the cold war. An adversary to be respected, but whose basic style holds few surprises. It makes a strange contrast with gout’s place in history.

For over 4,000 years people lay and medical alike talked and thought about gout endlessly. It was the disease that conferred high social status and implied distinction. It was one of the few times in history when a disease was principally defined by its lifestyle context. The only modern

equivalent is the linkage of AIDS with homosexuality in the United States. It even acquired an honorific article: One did not just have gout. One had *the* gout.

Part of what gave gout its special character was that while it tortured, it rarely killed. Indeed, for most of history, when death was a frequent visitor to families it was thought a painful but welcomed prophylactic against diseases which did. England's greatest satirist Jonathon Swift, afflicted with gout himself, whose immortal *Gulliver's Travels* is known to almost every school child, said:

*They give the sick man joy, and praise
The Gout that will prolong his days.*"¹⁹

Gilbert Sheldon, Archbishop of Canterbury under Charles II, in the second half of the 1600s, was reported to have offered £1,000 to any person who would 'help him to gout' to protect his health.²⁰ A century later, the writer Horace Walpole would echo his sentiments saying in a letter, "It prevents other illnesses and prolongs life," adding, "could I cure the gout, should not I have a fever, a palsy, or an apoplexy?"²¹

Because it is partly a disease of lifestyle until modern times, when genetics began to be understood, gout was defined by the lifestyle of its sufferers. Associated with rich high status men and their excessive drinking and rich foods, it also became linked with high I.Q., although the association was controversial. In 1927 the English physician Havelock Ellis, made the point that the linkage could not be random,²² and later research has proven it is not -- sort of.

"Actually the correlation, which is not all that strong, is not between gout and intelligence," says Dr. McCarty.²³ "It's between the level of uric acid in the blood and intelligence. Since uric acid is necessary to form the crystals that cause the pain of gout, I guess you could say the gout intelligence connection is indirect but real."²⁴

There was also a strong sexual component to its reputation, without much medical justification but not surprising, since gifted men who live in luxury and power often take the liberties status affords. And these were not just any rich men.

“Gout is overwhelmingly a disease of adult Caucasian males,” Dr. Meyerhoff points out.²⁵

Until the emergence of modern middle-class democratic cultures, essentially from the classical Greeks, to the height of the British empire, gout was a disease of European men from families with hereditary power. (Although there apparently were pockets, like Switzerland, where gout was notably absent.)²⁶ It played the same role in the third century B.C. aristocracy of Rome, that it would later play in the aristocracies of 17th and 18th century France and England, when each of those countries dominated the world.

It was virtually unknown in Asia until very recently, when those populations began adopting a more western diet. The traditional rice and vegetable based dishes of the East were not high in the purines, which lead to excess uric acid in the system and stimulate gout attacks. In contrast, it would be hard to deliberately design a more purine rich diet than the Western wheat and meat based cuisines of Europe, especially England, whose national dish has been roast beef. Excessive consumption of foods such as sardines, anchovies, herring, mackerel, scallops, most wild game, as well as organ meats like liver, kidney, sweetbreads, brains, meat gravies as well as red wines, particularly fortified wines like port and Madeira, is almost guaranteed to stimulate a gout attack in those already genetically predisposed to it.²⁷ And in both classical and modern times, as general affluence grew, the rich dishes western men loved became increasingly central food choices, and gout amongst the elite correspondingly increased. Conversely, during the period of deprivation and hardship caused by the Second World War it became rare in Europe.²⁸

Because of its genetic distribution gout also developed a powerful moralistic aspect. Europe was the center of Christianity and the concept of sin was a cultural fundamental. Because gout afflicted the rich and powerful and was associated with their loose living and indulgence each case became a parable of Christian ethics. The Italian poet Francesco Petrararch (1304-1374), was one of the first to establish this nuance and it influenced how gout was seen for centuries. The Italian physician and mathematician Geronimo Cardano (1501-76), made the point this way:

“What a man gout makes! Devout, morally pure, temperate, (and) circumspect,” Cardano said, adding, “no one is so mindful of God as the man who is in the clutches of the pain of gout. He who suffers gout cannot forget that he is mortal...”²⁹

The earliest definite evidence of gout was found in 1910, when the mummy of a man was excavated near a temple at Philae, in Upper Egypt.³⁰ Examination revealed that he had suffered from an advanced stage of the disease. Since gout was already well-known when the mummy was a living man, he almost certainly got medical treatment. The Egyptians had already identified gout as a distinct disorder by 2640 B.C. and references to it are found in the earliest medical texts. Both the Ebers and Edwin Smith Papyri describe a condition that is clearly gout.³¹ They were written about 1552 BC but contain information taken from texts a thousand years earlier, and ascribed to Imhotep, a kind of ancient world Leonardo da Vinci, and the great overarching figure of Egyptian medicine.³²

A thousand years later, in the 5th century B.C., Hippocrates (460-357 B.C.), the father of Western medicine, who had studied at the temple of Imhotep at Memphis, and who acknowledged his debt to that training, described how to differentiate what was called *podagra* -- *pous* = foot, ‘*agra*’ = prey: literally a foot-trap -- a disorder of the feet, or *gonagra*, a disorder of the knees, from the more general “arthritis - a disorder of the joints.”³³ All these conditions were seen as products of rheumatism, by which was meant the descent (*rheuma*) of congested humors (a kind of ineffable fluid that influenced the body) into the limbs. Hippocrates clearly knew that while gout was almost exclusively a disease of men, post-menopausal women could contract it, and such knowledge must have been sufficiently common in ancient Greece that Plato could mention the condition without offering a lengthy explanation as to what it was.

Just as with the Second World War, the connection between lifestyle and prevalence of gout was observed by the Romans. In the first decades of that era they noted it was rare, but by the reign of Nero, (37-68 A.D), his mentor Seneca observed that luxurious living had led to its spreading even to women because, “in this age women rival men in every kind of lasciviousness...why need we then be surprised at seeing so many of the female sex afflicted with the gout.”³⁴

Galen, another immortal from the ancient world was born in 129 A.D in the Roman provincial city of Pergamum. He also studied Imhotep, and went on to leave medicine its first description of tophi, the chalk-like excrescencies that plague gout sufferers.³⁵ His views on gout, as well as much else, an idiosyncratic distillation of ancient Greek medicine that came to be known as Galenism, dominated medical thinking for the next 1,000 years.

The term gout was coined in the 13th Century by a man named de Vielehardouin,³⁶ the word being based on the humor theory that a fluid ran down the body into the legs (medieval Latin *gutta*, to drop).³⁷ The first real scientific study of the disease in a modern sense can be traced to 1679 and Antony van Leeuwenhoek, a most unlikely scientist.³⁸ A small tradesman in the Dutch city of Delft he had no higher education and read and spoke nothing but Dutch.³⁹ Particularly he did not know Latin, then the language of scholarship, and medicine. Normally these limitations would have excluded him but van Leeuwenhoek was not deterred by any of it. Some time before 1668, he learned how to grind lenses, and made simple microscopes.⁴⁰ Through his instruments he brought the world awareness of bacteria, sperm cells, blood cells, microscopic nematodes, rotifers, and the chalk like crystals that made gout painful.⁴¹

"...I observed the solid matter which to our eues 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. In a quantity of matter of the thousands of the these long figures, mixed with a small quantity of fluid."⁴²

Sadly, van Leeuwenhoek's work although influential in other areas, initially had little impact on the medical profession's understanding of gout.

In 1734, the physician William Stukeley, following van Leeuwenhoek's microscopy lead described for the first time the uric salts that caused gout's pain. "I doubt not but the poisonous drop of the gout is similar to

that of a venomous bite, as Dr. Mead observ'd it upon a microscopic glass; a parcel of small salts nimbly floating in a liquor and striking out into crystals of incredible tenuity and sharpness, he calls them spicula and darts."⁴³ Stukeley's paper marks the beginning of the long line of research reports that dot modern medical publications.

But gout's literary pedigree extends far outside the bounds of medicine. The disease has a unique profile in Western literature and art. One that is so voluminous that just listing the titles of writers suffering from gout, or referencing it in their work, would look much like a recitation of the canon of English language literature by male authors.

Shakespeare's Sir John Falstaff cries out, "A pox of this gout! or, a gout of this pox! for the one or the other plays the rogue with my great toe," and, in *The Rape of Lucrece* Shakespeare acknowledges the link the disease has always had with age, wealth, and power. "The aged man that coffers-up his gold,/is plagu'd with cramps, and gouts and painful fits."

Gout was such a staple of the culture that it was not just bemoaned, or used for a laugh -- the elderly man lecherously staring at a comely maid, as he is consigned to his chair with gout -- it became a literary device.

Daniel Defoe's *Robinson Crusoe*: "My father, a wise and grave man, gave me serious and excellent counsel.... He called me one morning into his chamber, where he was confined by the gout, and expostulated very warmly with me..."

Charles Dickens used gout over and over in his books. In *Bleak House*, the old country baronet, Sir Leicester Dedlock, lay abed in his ancient oak bedchamber, suffering from it. Sam Weller, in the *Pickwick Papers* cautions his father against excessive drinking fearing it will bring the old man another attack.

Tobias Smollett's *Humphrey Clinker* has gout as a central theme. Sir Walter Scott wrote 23 historical novels, and in three of them gout figures. George Eliot's *Middlemarch* relied on gout, and generations of students know that in Rafael Sanatini's *Captain Blood*, Peter Blood is saved from the terrors of slavery because he gives the British governor of the Barbados relief from an attack of gout.

The famous English artists Hogarth and Rowlandson, both of whom made their reputations portraying the foibles of their time, used gout as a signature. Their images of older debauched and wealthy men in rich surroundings often leering at a young woman as they prominently suffer from gout became a kind of satirical archetype of the age.

Gout, because it was a disease of rich men who shaped the world, and could get things done, was also a font of domestic technological development which only such men could afford.

King Philip II of Spain, a contemporary of Shakespeare, may be the only inventor monarch in history, and gout was his muse. During his attacks, he lived on what is described as “a sort of couch, with movable positions from vertical to horizontal, seven feet long and two and a half feet wide, with a horsehair mattress. The king sat, ate, and slept in it, wearing loose garments that did not put pressure on his arthritic joints.”⁴⁴

More lasting than his couch was the sedan chair, a kind of small box with a seat within that was carried by several men. Eventually the king designed “gout chairs” “for commercial transport that were widely used throughout Europe. Franklin first saw one in Paris in the 1700s.”⁴⁵

Sedan chairs have passed into history now, but the domestic furniture designed because of gout can be seen in American homes to this day, starting with the easy chair.

Until the mid-19th century, the furniture in public rooms was not designed for comfort. Its purpose was to hold the body in a dignified and refined posture.⁴⁶ In an age of wigs, and complex structured clothing it was hard to sit in a respectful upright posture without this support.

As historian John Crowley notes, easy chairs were not originally for “comfortable seating; rather, they were designed for people who could not move easily on their own—chronic invalids, women in the late stages of pregnancy or recovering from childbirth, and men with gout. Their recommended virtues were ‘ease and warm[th]’.”⁴⁷ They were found in bedchambers, where furniture was more accommodating. It may seem odd today to entertain guests after childhood in one’s bedroom, but this

intimate setting was the norm with close friends and family. Many gout chairs even had recliner capability and are the precursors to the La-Z-Boy™ and Barclay Loungers™ that populate the family rooms of America today.

The padded stool that is an easy chair's frequent companion, is also part of our furniture vocabulary because of gout. Its original function was for resting the offended foot. As early as 1600 an anonymous print shows a gout stricken man, his foot on a padded stool, speaking with death. By the 17th century small stools had become almost a visual cliché that instantly set a tone in a picture.

Because powerful men of business and politics found the immobility of gout an unacceptable impediment, the wheel chair, or gout chair as it was first known, was devised. Originally part of a rich man's status paraphernalia (they were very expensive), the wheel chair also began to appear in the social commentary drawings of artists like Rowlandson. Likewise the humble crutch was transformed into a gentleman's accessory and a status symbol, often bejeweled and carved.⁴⁸ The cane or walking stick made it's appearance to help the gout sufferer when he was better able to walk, but still not fully restored.

Like the gout stool the gout sufferer's crutch and cane became a visual cue for comedy, and social criticism. Laurence Sterne's classic comic meganovel *Tristram Shandy*, first published in 1760, includes several scenes of gouty men beating lesser mortals with their walking sticks and crutches. Hogarth himself did illustrations for the novel with all the comic cues of crutches, easy chairs, gout stools; his overweight gentry are a study in porcine overindulgence.

An entire industry of gout "apparatus" had come into being by the end of the 18th century, all designed to relieve the pain of gout, and to increase mobility, and it flourished until the 20th century when medications were finally developed to effectively treat gout.

Treatments for gout have been many and varied, and largely ineffectual, but the strange saga of one drug threads through the entire history of gout. It traces to the sixth century B.C., and the physician Alexander of Tralles, who is the first person known to have prescribed it. He reported

that a preparation made from Autumn crocus, or meadow saffron, which he called hermodactyl, was effective in treating gout. Its active medical ingredient was Colchicum.

Alexander's original clinical insight attracted interest, and was recommended by medical authorities, even as its side effects roused alarm. The dosage was tricky because colchicum could cause severe gastro-intestinal upset, and in still larger doses was poisonous. By the beginning of the Renaissance it had fallen into disuse in spite of its dramatic healing effect during gout attacks. Further sealing its banishment, during the 17th century the English physician Thomas Sydenham (1624-1689), considered "The English Hippocrates,"⁴⁹ and a gout sufferer himself came out against it. He considered the side effects and the question of dosage to be too dangerous and decreed it should not be used.⁵⁰ The result, as W.S.C. Copeman, a modern researcher who has written extensively about gout, notes was "colchicum being banished throughout Europe for the next hundred and fifty years."⁵¹

It got reintroduced by Nicolas Husson, a French army officer who, during the 1770s, concocted a treatment which included colchicum. Sales of his secret formula were very successful, although the potion was highly controversial. Eight years later its sale was outlawed in Paris, although a black market trade continued.⁵²

In 1910, a seemingly reliable form of the medication, cinchophen, was created, and it enjoyed considerable success until in the 1930s when it was found that it caused liver damage. In the 1950s two significant breakthroughs in the pharmacology of gout medications occurred. Probenecid was developed, and it stimulated the body to dump excess uric acid, which reduced the prevalence of attacks. It also helped decrease the incidence of tophi. The other was phenylbutazone which replaced cinchophen and did not produce liver damage. Then in 1963 Allopurinol, a truly functional drug finally emerged, and the final wisps of gout's power to confer cachet were gone.

True to its nature though gout still favors the rich and powerful. American research conducted in the 1960s found that corporate executives, just like their English gentry, or Roman senatorial predecessors, had higher urate concentrations than their blue collar employees.⁵³

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