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Review

Sack and sugar, and the aetiology of gout in England between 1650 and 1900

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Abstract

A marked increase in gout was observed in England during the 17th to 20th centuries. Many have ascribed this rapid increase in gout to the introduction of wines that were laced with lead. In this article, we suggest another likely contributor, which is the marked increase in sugar intake that occurred in England during this period. Sugar contains fructose, which raises uric acid and increases the risk for gout. Sugar intake increased markedly during this period due to its introduction in liquors, tea, coffee and desserts. We suggest that the introduction of sugar explains why gout was originally a disease of the wealthy and educated, but gradually became common throughout society.

Key words: gout, uric acid, sucrose, fructose, lead.

Introduction

Between the 17th and 20th centuries there were many reports of gout in England, and it became a common topic for artists and authors [1, 2]. Gout was more common among royalty, the rich and educated, and affected many leaders of the day, including William Harvey (1578–1647), John Milton (1608–74), Thomas Sydenham (1624–89), Isaac Newton (1643–1727), Lord Chesterfield (1694–1773), Samuel Johnson (1709–84), George IV (1762–1830) and Alfred Lord Tennyson (1809–82). During this period there were many paintings and drawings depicting the wealthy, obese, plethoric individual, drinking his port wine and suffering from the gout (Fig. 1) [1–3]. An increase in the frequency of gout was also observed in Holland during this time. Known as the 'king of diseases and the disease of kings', gout was the disease of the rich, the 'offspring of luxury and intemperance', or as the wit Ambrose Bierce (1842–1913) wrote, 'gout is a physician's name for the rheumatism of a rich patient'.

The cause for the increased reports of gout that occurred in England during this period has been largely attributed to lead poisoning. Alfred Baring Garrod, who discovered that gouty subjects had high uric acid levels in their blood, was well aware of the association of lead with gout and kidney disease [4, 5]. Chronic lead poisoning can result in reduced urinary urate excretion and hyperuricaemia, and is a known cause of gout (saturnine gout) [6]. One source of lead was from paints, especially for those with the habit of licking their brush between paint strokes [7]. A more common source of lead was liquors. Cider was one example, as it is an alcoholic drink made from apples in which the presses were often made of lead. Acute lead poisoning was responsible for an outbreak of abdominal colic (the Devonshire colic) that occurred in the 1760s in Devonshire, England [8]. Another source of lead was from port and wines brought in from Portugal, the Canary Islands and the Madeira Islands. Fortified wines such as port or sherry were often made with brandy that in some cases was distilled using lead-containing equipment [9]. Many of these wines were also shipped in wooden barrels with lead-lined lids or lead fastenings. The physician Gene Ball brought attention to this latter source of lead in an article in which he analysed some old port and wines produced between 1770 and 1820. Two bottles from Portugal and the Canary Islands had high lead content (830–1900 mg/l) that was 5 to 10 times the levels found in current wines from these locations [9].

While we do not contest the importance of lead in the epidemic of gout that occurred in England during the 17th–20th centuries, we believe there is another contributor that has not received due attention, and that is the introduction of sugar. In this article we review evidence that sugar intake may have had an equal, or perhaps an

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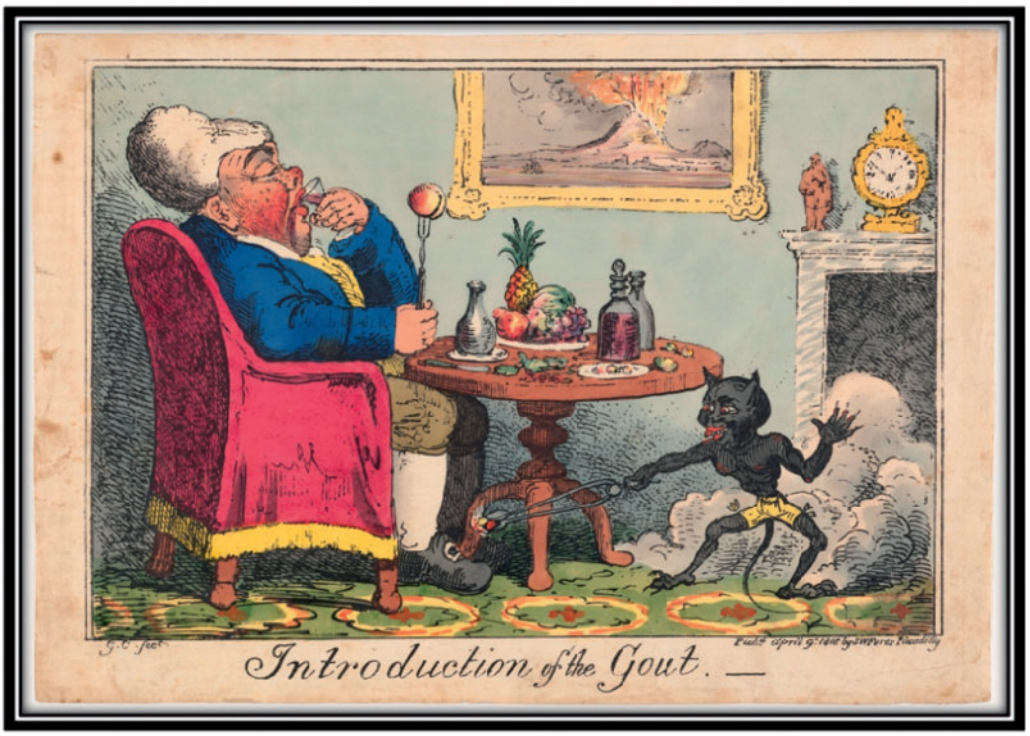
Fig. 1 The introduction of gout.



A painting from 1818 by George Cruikshank shows a wealthy man who is eating fruits and drinking wine and is about to be introduced to the pleasures of gout. Note the eruption of Mount Vesuvius in the background as a premonition for this special event. Reproduction made from a copy held by the Harvard Medical Library in the Francis A. Countway Library of Medicine.

even more important role in the outbreak of gout that occurred in England. A more detailed presentation on the history of sugar as it relates to obesity and gout is available for those interested in this subject [10].

Sugar increases serum uric acid levels and increases the risk for gout

Sugar, or sucrose, is a disaccharide containing fructose and glucose. Upon ingestion, the enzyme sucrase, which is present in the small intestine, converts sucrose to monosaccharides, which are then absorbed. The metabolism of glucose and fructose is similar except for the first few enzymic steps, and this is key in our understanding of how sugar raises uric acid. When glucose is metabolized by glucokinase, the initial phosphorylation of glucose is carefully regulated, and adenosine triphosphate (ATP) levels are always maintained in the cell. In contrast, the metabolism of fructose by fructokinase C, the principal isoform of fructokinase, results in the rapid phosphorylation of fructose to fructose-1-phosphate, resulting in transient depletion of intracellular phosphate and ATP. As intracellular phosphate falls, the enzyme adenosine monophosphate deaminase is activated, resulting in the shunting of adenosine monophosphate to inosine monophosphate, inosine, hypoxanthine and eventually uric acid [11]. The rise in intracellular uric acid is marked, and results in a spillage into the circulation and a rapid rise in uric acid levels. The ability of fructose to acutely raise uric acid levels has been so consistent that it has been developed as a test (fructose tolerance test), as some individuals, such as those with gout and hypertension, show a greater increase than that observed in the otherwise healthy individual [12–14]. In addition, chronic ingestion of fructose also turns on the *de novo* synthesis of uric acid [15].

Consistent with these findings, subjects chronically fed sugar (or fructose) show an increase in fasting serum uric acid levels [16, 17]. Epidemiological studies have linked increased intake of sugary soft drinks with elevated serum uric acid levels and increased risk for gout [18, 19]. In contrast, the relationship of fruits (which also contain fructose) with gout is less strong, perhaps because many fruits are rich in vitamin C (ascorbate), which lowers serum uric acid and stimulates urate excretion [20, 21]. Nevertheless, physicians such as Sir William Osler felt that restricting fruit intake was critical in the gouty patient to prevent recurrent arthritic attacks [22].

Sugar consumption increases in Shakespearean England

Sugarcane was originally grown in India in the Ganges River Valley, where it was harvested as early as 500 BC.

Nevertheless, sugar remained largely unknown to Europe until the Middle Ages, when some of the earliest reports came from the Crusaders fighting in the Holy Lands. By approximately 1000 AD, however, sugar was entering Europe from Egypt and Ceylon primarily via the port of Venice [23].

At first sugar was so expensive that it was available only in small amounts and was primarily used as a medicine. For those who were rich, however, sugar became a special, sought-after food. Many kings loved sugar. For example, court records showed that King Edward I of England ordered 1877 pounds of sugar in 1287 and 6258 pounds of sugar in 1288 [24]. Saint Thomas Aquinas of Italy declared that sugar, while being a medicine, could be eaten during the fast [25]. Aquinas went on to become extremely fat himself.

Beginning in the 1400s sugar production was occurring in southern Spain, as well as by the Portuguese in the Madeira Islands and Sao Tome off the coast of Africa [26]. The discovery of Hispaniola by Columbus and of Brazil by Cabral led to a further expansion of the sugar industry. By 1505 the first boat carrying slaves from Africa arrived in the Americas, primarily to work in the sugarcane fields, and by 1516 the first boats loaded with sugar were returning to England [24]. A triangle of trade developed in which slaves were sent from Africa to the Americas to produce sugar that would then be sent to Europe, followed by the shipping of manufactured goods to Africa. During the next three centuries between 10 and 20 million African slaves were brought to the Americas, creating one of the darkest periods of history.

While Spain and Portugal initially received much of the imported sugar, these countries largely lost control of the sugar trade to England during the 1500s. There were likely multiple reasons, including the rebellion (the Dutch Revolt) of the Low Countries from Spain in the 1560s and the loss of the Spanish Armada to England in 1588. By 1544 England had also established its first sugar houses in London [23]. This was fuelled by increasing shipments of sugar to England from Barbados and other islands in the West Indies. England imported 1200 barrels (termed hogsheads) of sugar in 1660, 50 000 barrels in 1700 and 11 000 barrels in 1753 [24].

The only other country that was importing sugar to the same extent was Holland, due largely to the formation of the Dutch East Indies Company in 1602. The Dutch brought sugar to Amsterdam from the East Indies. One of the major sources was Java, where the number of sugar mills increased from 20 in 1650 to 130 in 1710.

Sugar becomes increasingly available to the English

As sugar imports increased, sugar prices fell and it became increasingly available to the common man. The intake of sugar in England increased 5-fold between 1700 and 1800, whereas it remained unchanged in France (Fig. 2) [27]. Per capita intake of sugar increased from an average of 4 pounds/year in 1700, to 18 pounds in 1800 and to 90 pounds in 1900 [28]. While part of this increase was driven by increasing sugar imports, the tax on sugar was also stepwise reduced until it was completely eliminated in 1874.

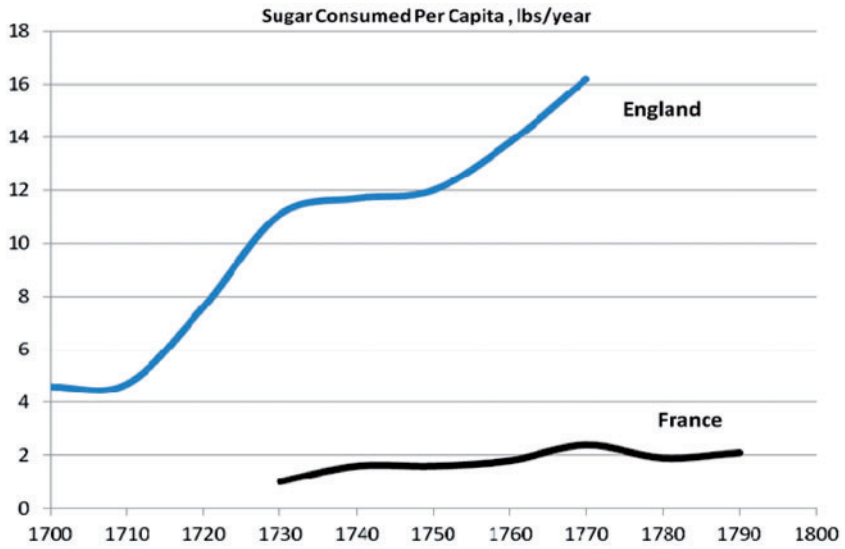
One of the first uses of sugar was in drinks, particularly sweet wines and sweet ciders (Fig. 3). Some wines, such as those from Portugal and the Madeira Islands, were often rich in sugar content. Spain and the Canary Islands were also famous for producing sack, in which spirits from grapes, sugar beets or sugarcane were added to the wine. If the spirits were added before fermentation was complete, then the wine would have a high residual sugar content. Sack was imported to England in relatively large amounts beginning around 1517 and was often combined with additional sugar to make the famous sack and sugar drink. Sack became a common drink available in taverns in England by the late 1500s, where it could cost as little as 2 shillings a gallon. Falstaff, a character in several of Shakespeare's plays, took the nickname of Sack and Sugar because of his love for this drink, and perhaps not surprisingly, developed gout in the play Henry IV (Fig. 4). Another common drink was hippocras, in which sugar, cinnamon and nutmeg was added to wine. By the early 1630s, punch became a common drink in which initially wine and brandy, and later Jamaican rum, were combined with sugar, lemon and spices. Rum is derived from sugarcane and became the official drink of the British Navy following the fall of Kingston, Jamaica, to the British in 1655.

Sugar was also commonly used in foods (sweetmeats) and desserts (such as sack posset, which was a custard-like dessert made from cream, eggs and wine). One of the more common uses of sugar, however, was to add it to tea or coffee. Interestingly, the habit of adding sugar to tea or coffee was introduced in England in the mid-1600s, and by the turn of that century the first teahouses and coffee houses were present in London [27, 29].

Other potential causes of gout in England (1650–1900)

While sugar and lead are two factors that likely contributed to the frequency of gout during this period, it is important to mention the potential contributory role of alcohol and purine-rich foods. Alcohol is known to increase serum uric acid by at least two mechanisms. First, the metabolism of alcohol is associated with increased nucleotide turnover in the liver [30]. In addition, chronic alcohol intake can reduce urinary uric acid excretion, likely due to the production of lactate that stimulates reabsorption of uric acid via an organic anion exchange mechanism [31]. Epidemiological studies suggest that the risk of hyperuricaemia from alcohol is greatest for beer, followed by hard liquor, and the risk of gout from wine is relatively low [32, 33]. Interestingly, experimental studies show that both alcoholic beer and non-alcoholic beer can increase uric acid levels [34–36]. This is probably because beer also has a high purine content [36], in part because of

Fig. 2 Sugar intake increases in England in the 18th century.



England controlled much of the sugar that was imported from the West Indies during the 18th century. During this period sugar intake increased dramatically in England. In contrast, in countries such as France, sugar intake remained low. During this time obesity and gout became much more common in England than in France. As William Wadd wrote, 'For one fat person in France or Spain, there are one hundred in England' [42]. Data are from Austen and Smith [27], reproduced with permission from the *Fat Switch* by Richard Johnson (Mercola.com, 2012).

Fig. 3 The Crown and Sugar Loaf.

Sugar and fruits were commonly added to alcohol-containing drinks in 17th- to 19th-century England. This is a pub in the vicinity of St Paul's Cathedral in London that dates back to at least the early 1800s. Sugar or fruits were commonly added to a wide variety of drinks, including sack and sugar, punch, hippocras and beer.

the purines present in the yeast used in the process of making the beer.

In addition to alcohol, it is well known that purine-rich foods can increase the risk for gout [37]. It is likely that the wealthy would have been able to more readily afford many of the purine-rich foods such as caviar, anchovies, shellfish and organ meats. Some authorities during this period suggested such purine-rich foods might be contributing to the frequency of gout in the English population [38, 39]. Unfortunately there are inadequate epidemiological data

Fig. 4 Sir John Falstaff.

Sir John Falstaff was a braggart and drunk in several of Shakespeare's plays. His nickname was Sack and Sugar, after his favourite drink of sherry wine (sack) mixed with sugar and cinnamon. Falstaff developed gout in *Henry IV*. Painting by Adolf Schrödter, 1867 (public domain).

to know the importance of the role of purine-rich foods for the increased frequency of gout that was observed during this period.

Conclusions

Lead is a well-known cause of gout. However, sugar intake is also recognized as a cause of gout. It is striking that the rise in gout parallels the rise in sugar intake in England and Holland. Indeed, writers during this period linked the development of gout with sugared wines and ciders [4, 40]. Stephen Blankaart, a physician in Holland, wrote in 1683 that the importation of sugar into Amsterdam was associated with a marked increase in gout, as well as caries and obesity [41]. We would therefore suggest that those who love the sweet wine, may enjoy the bitter gout with time.

Rheumatology key messages

- Gout was epidemic among the rich and wealthy in England between 1650 and 1900.
- Gout was historically attributed to purine-rich foods, alcohol or low-grade lead poisoning.
- Recent studies suggest that fructose-containing sugars also contributed to the gout epidemic in England.

Disclosure statement: R.J.J. has patent applications related to blocking fructose metabolism or lowering uric acid, a means to prevent or treat features of the metabolic syndrome. He also has a patent on lowering uric acid with allopurinol in the treatment of hypertension and has written two books, the *Sugar Fix* (Rodale, 2008) and the *Fat Switch* (mercola.com, 2012), that discuss the role of sugar and fructose in the obesity epidemic. M.A.L. has patent applications related to the blockade of fructose metabolism to prevent or treat metabolic syndrome. All other authors have declared no conflicts of interest.

References

1 Rodnan GP. A gallery of gout. Being a miscellany of prints and caricatures from the 16th century to the present day. Arthritis Rheum 1961;4:27–46.

2 Graham W, Graham KM. Our gouty past. Can Med Assoc J 1955;73:485–93.

3 Rodnan GP, Beneder TG. Ancient therapeutic arts in the gout. Arthritis Rheum 1963;6:317–40.

4 Garrod AB. Observations on the blood and urine of gout, rheumatism and Bright's disease. Med Chir Trans 1848; 31:83.

5 Garrod AB. The nature and treatment of gout and rheumatic gout, 2nd edn. London: Walton and Maberly, 1863.

6 Lorimer G. Saturnine gout, and its distinguishing marks. Br Med J 1886;2:163.

7 Lancereaux E. Note relative a un cas de paralysie saturnine avec alteration des cordons nerveux et des muscles paralyses. Gaz Med Paris 1862;17:709–13.

8 Wedeen RP. Irregular gout: humoral fantasy or saturnine malady. Bull NY Acad Med 1984;60:969–79.

9 Ball GV. Two epidemics of gout. Bull Hist Med 1971;45:401–8.

10 Johnson RJ. The fat switch. Chicago: mercola.com, 2012.

11 van den Berghe G, Bronfman M, Vanneste R, Hers HG. The mechanism of adenosine triphosphate depletion in the liver after a load of fructose. A kinetic study of liver adenylate deaminase. Biochem J 1977;162:601–9.

12 Perheentupa J, Raivio K. Fructose-induced hyperuricaemia. Lancet 1967;2:528–31.

13 Stirpe F, Della Corte E, Bonetti E, Abbondanza A, Abbati A, De Stefano F. Fructose-induced hyperuricaemia. Lancet 1970;2:1310–1.

14 Rutkowski B, Tylicki L, Manitius J, Lysiak-Szydlowska W. Hypertensive nephropathy—an increasing clinical problem. Miner Electrolyte Metab 1999;25:65–8.

15 Emmerson BT. Effect of oral fructose on urate production. Ann Rheum Dis 1974;33:276–80.

16 Reiser S, Powell AS, Scholfield DJ, Panda P, Ellwood KC, Canary JJ. Blood lipids, lipoproteins, apoproteins, and uric acid in men fed diets containing fructose or high-amylose cornstarch. Am J Clin Nutr 1989;49:832–9.

17 Israel KD, Michaelis OE 4th, Reiser S, Keeney M. Serum uric acid, inorganic phosphorus, and glutamic-oxalacetic transaminase and blood pressure in carbohydrate-sensitive adults consuming three different levels of sucrose. Ann Nutr Metab 1983;27:425–35.

18 Choi JW, Ford ES, Gao X, Choi HK. Sugar-sweetened soft drinks, diet soft drinks, and serum uric acid level: the third National Health and Nutrition Examination Survey. Arthritis Rheum 2007;59:109–16.

19 Choi HK, Curhan G. Soft drinks, fructose consumption, and the risk of gout in men: prospective cohort study. BMJ 2008;336:309–12.

20 Gao X, Curhan G, Forman JP, Ascherio A, Choi HK. Vitamin C intake and serum uric acid concentration in men. J Rheumatol 2008;35:1853–8.

21 Huang HY, Appel LJ, Choi MJ *et al*. The effects of vitamin C supplementation on serum concentrations of uric acid: results of a randomized controlled trial. Arthritis Rheum 2005;52:1843–7.

22 Osler W. The principles and practice of medicine. New York: D. Appleton and Co., 1893.

23 Moseley B. A treatise on sugar, 2nd edn. London: John Nichols, 1800.

24 Mintz S. Sweetness and power. New York: Penguin Books, 1986.

25 Conway P. Saint Thomas Aquinas of the order of preachers (1225–1274). London: Ongmans, Green and Co., 1911.

26 Galloway JH. The sugar cane industry. Cambridge: Cambridge University Press, 1989.

27 Austen RA, Smith WD. Private tooth decay as public economic virtue: the slave-sugar triangle, consumerism, and European industrialization. Social science history, Vol. 14. Durham: Duke University Press, 1990:95–115.

28 Deer N. The history of sugar. London: Chapman and Hall, 1949–50.

29 Smith WD. Complications of the commonplace: tea, sugar and imperialism. J Interdiscip Hist 1992;23:259–78.

30 Faller J, Fox IH. Ethanol-induced hyperuricemia: evidence for increased urate production by activation of adenine nucleotide turnover. N Engl J Med 1982;307:1598–602.

31 Lieber CS, Jones DP, Losowsky MS, Davidson CS. Interrelation of uric acid and ethanol metabolism in man. J Clin Invest 1962;41:1863–70.

32 Choi HK, Curhan G. Beer, liquor, and wine consumption and serum uric acid level: the third National Health and Nutrition Examination Survey. Arthritis Rheum 2004;51:1023–9.

33 Choi HK, Atkinson K, Karlson EW, Willett W, Curhan G. Alcohol intake and risk of incident gout in men: a prospective study. Lancet 2004;363:1277–81.

34 Gibson T, Rodgers AV, Simmonds HA, Toseland P. Beer drinking and its effect on uric acid. Br J Rheumatol 1984;23:203–9.

35 Ka T, Moriwaki Y, Inokuchi T *et al*. Effects of allopurinol on beer-induced increases in plasma concentrations and urinary excretion of purine bases (uric acid, hypoxanthine, and xanthine). Horm Metab Res 2006;38:188–92.

36 Yamamoto T, Moriwaki Y, Takahashi S *et al*. Effect of beer on the plasma concentrations of uridine and purine bases. Metabolism 2002;51:1317–23.

37 Choi HK, Atkinson K, Karlson EW, Willett W, Curhan G. Purine-rich foods, dairy and protein intake, and the risk of gout in men. N Engl J Med 2004;350:1093–103.

38 Haig A. Uric acid as a factor in the causation of disease. A contribution to the pathology of high arterial tension, headache, epilepsy, mental depression, gout, rheumatism, diabetes, Bright's disease, and other disorders, 1st edn. London: J & A Churchill, 1892.

39 Luff AP. The Goulstonian lectures in the chemistry and pathology of gout: delivered before the Royal College of Physicians, March, 1897. Br Med J 1897;1:838–42.

40 Warner F. A full and plan account of the gout. London: T Cadelll, 1768.

41 Blankaart S. Borgerlyke tafe. Amsterdam: Om lang gesond sonder ziekten te leven, 1683. Jan en Hoorn, Boekverkooper over het Oude Heeren Logement.

42 Wadd W. Cursory remarks on corpulence or obesity considered as a disease with critical examination of ancient and modern opinions relative to the causes and cure, 3rd edn. London: Smith and Davy, 1816.