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Review

Fine Wine and Gout †

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Abstract: From ancient times to the present day, gout has been associated in the popular and scientific literature with wealthy men who overindulge in fancy foods, fine wine, and debauchery. Curiously, amongst diseases, gout was thought to be good, a malady to be accepted because of otherwise beneficial effects on health, and longevity. This narrative review critically examines the history of these associations and explores in detail the pathogenic factors contributing to development of gout prior to the 20th century. While lead toxicity has been previously implicated with wine, the specific association of gout and fine wine can be attributed to lead complexes in products such as sapa, a grape extract used to sweeten wine, in addition to lead nanoparticles leached from crystal glassware and lead glazed dinner plates. The health benefits of gout can be attributed to lead complexes in fine wine and lead nanoparticles from glazed dinnerware. These compounds have excellent antibacterial properties, thereby inhibiting the presence of pathogenic bacteria in foodstuffs. Probing the association of gout and fine wine provides a very well documented example of how the pathogenesis of disease becomes better understood with the passage of time and continuing, persistent scientific enquiry.

Keywords: wine; gout; tophaceous gout; lead; nanoparticles

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1. Introduction

"Gout is one of the Greatest Blessings which can befall mortal man". Philander Misaurus 1720 [1].

For more than two millennia, and down to the present day, gout has been associated with the upper classes of society, the overindulgence of fancy foods, and excessive drinking of fine wine. This perception, often caricatured, had a factual basis up to the 20th century, but no longer.

This narrative review explores the historical contributing factors associating fine wine and gout, focusing on factors contributing to gout's high incidence in 17th to 19th century British high society. In particular, we will focus on these specific associations: why fine wine was associated with gout; why gout preferentially affected wealthy British aristocrats; and why gout was considered a hereditary male affliction amongst nobility. Most interestingly, we will consider why gout, a chronic debilitating affliction with acutely painful exacerbations, was looked upon as a disease with health benefits, keeping other diseases away, and extending longevity.

2. What Is Gout?

"How there can be a doubt about what the gout is, amazes me!" . . . . Horace Walpole, 1781 [2].

Gout, recognized as a specific disease, has afflicted individuals since ancient times [3]. Hippocrates, circa 400 B.C. discussed both gouty arthritis and its acute painful manifestation, podagra. However, as discussed by Porter and Rousseau [4], until the mid-twentieth century there was considerable controversy on just what gout might be. Even after Leeuwenhoek, 1679, demonstrated crystals in tophaceous chalk [5], and after Garrod

in the 1850s showed that crystals in tophi contained urate [6], and that gouty patients had increased blood uric acid [7,8], and even after Barwell [9], 1881, carefully described urate crystals within synovial fluid and on joint surfaces, there were doubts from learned physicians about gout's salient features. Ewart [10] in 1896, and an anonymous commentary [11] in *The British Medical Journal* 11 January 1908, talked of gout and goutiness in terms of an unknown metabolic defect which was accompanied by increased blood uric acid, without mentioning the role of crystals within joints or tophi. Referring to his own illness which had its onset 35 years previously, the famous anatomist Fredric Wood Jones discussed gout in *The Lancet*, 31 January 1948, attributing pathogenesis to an autonomic vasomotor disorder, again without any discussion of crystals [12]. The association of crystals with the pathogenesis of acute gout, universally recognized today [13], was not established until McCarty in 1962 distinguished gout from pseudogout by polarized light microscopy of crystals in synovial fluid. Further, McCarty demonstrated experimentally the inflammatory properties of monosodium urate crystals in vivo [14–17]. As an aside, Barwell, in 1881, described both urate crystals on joint surfaces, and crystals, typical of calcium pyrophosphate dihydrate crystal deposits, within cartilage, but did not recognize that two distinct crystal types were present in the joint, albeit at different histologic sites [9].

3. Gout and Fine Wine

Wine, as a beverage, has accompanied humans since prehistoric times [18]. Fine wines were a feature of the Symposium in ancient Greece, and as gifts amongst wealthy, high ranking Roman individuals, more than two thousand years ago [19]. These cultural traditions still thrive today, worldwide. Through the centuries, as noted by Sieur de Montaigne in France [20], Juch in Germany (morbo dominorum et domino morborum, namely, disease of lords and lord of diseases) [21], and Porter and Rousseau in England [4,22], gout was as frequent a companion to these fortunate folks as was comedy about their arthritic plight. Even allowing that the main audience for the satires were those who were living with gout, the following questions can be asked: What characteristics made wine fine? What were the special properties of fine wine that predisposed to gout? Why was gout less frequent in the rest of the population?

Throughout the ages, wine was, and continues to be, a common beverage amongst all classes in wine drinking cultures. Ordinary wine was consumed in the same year as grapes were harvested. This wine was fermented for short periods, was low in alcohol and was rough in taste. In ancient times, wine, prized as fine wine, was notable for its smoothness, sweet taste, blood red appearance, and conviviality-promoting (alcoholic) effects [23]. Ordinary wine was commonly stored in clay amphorae, but the finest wine was fermented and then stored in much more expensive wooden casks and barrels. Fermenting wine for longer periods increased the conversion of sugars to alcohol at the cost of decreased sweetness. Storing wine in wood casks for prolonged periods facilitated aromatic compounds present in the wood to diffuse into the wine, enhancing taste and smell [24,25]. Wood casks, used in France for over 2000 years, commonly oak [26], were sealed with pine resin. Resin is the waxy substance beneath the bark [27]. Resin is composed of terpenes and other long chain hydrocarbons that are impermeable to water. Resin has a pleasant smell and taste contributing to the sensory pleasure of wine. To enhance sweetness and smoothness, fine wine was adulterated with *sapa* [19]. Sapa was unfermented *must* (grape juice with skins, seeds, stems) boiled to a syrup about one third of the original volume, specifically in lead or lead lined vessels. Lead from the pot surface combined with acetate ions in the wine *must* to yield colorless, sweet tasting, lead acetate, $Pb(C_2H_3O_2)_2$, known as "sugar of lead". Sapa was used to coat the inside of wine casks. Sapa is miscible within the resin. Both sapa and resin are soluble in alcohol, and so the lead concentration in wine increased along with the alcohol concentration and storage time. Lead toxicity has been associated with gout since ancient times [28]. Saturnine gout, acute gout associated with "moonshine", the drinkable product of llicit alcohol distillation and use of lead solder in stills, "continues as atopic of contemporary interest [29]. However, as will be discussed later, caution must be

expressed about a blanket association of slightly elevated blood lead level in the general population with increased lead in the environment [30], and the high association of gout within selected segments of a population.

4. Gout, Fine Wine, Heredity Affecting Male British Aristocrats

The cultural associations of aristocrats drinking fine wine and contracting gout have been a popular subject for satire through the centuries. Gout as a humorous condition, self-inflicted by drinking and dietary excess, still remains a popular, but erroneous perception today [31]. This perception is derived from the continuing popularity of 18th century caricatures by Gillray, Rowlandson, Cruikshank and others, depicting an obese Georgian gentleman at a sumptuous banquet with his bandaged foot resting on a "gout stool" [4]. Because this perception is not the present reality of gout, it is worthwhile examining how this perception came to be entrenched in 18th century Britain. The story begins in 1154, when Bordeaux was acquired by England through the marriage of Eleanor of Aquitaine to her cousin, the future King, Henry II. Wine imports of claret, red Bordeaux wine, became the principal source of income for Henry and subsequent British monarchs, the main market being the nobles and other wealthy folks imitating aristocratic cultural habits [32]. This continued until the War of the Spanish Succession in the early 1700s when sanctions increased the duty on imported French wine. By the Treaty of Methuen 1703, the British worked around this economic obstacle by importing a fortified wine from Portugal, "Port" [33]. Port was stronger in alcohol, than claret. Port, often adulterated, sometimes with lead [34], became even more popular than claret amongst British patricians. Good Port was described as "semper sapidum", (always tasty). Whether the sapidum (pleasant taste) of 18th century quality Port was in part related to sapa remains problematic, as preparation methods were closely-held trade secrets. For the wealthy, drinking fine wine and Port was culturally a part of extravagant feasts which included excessive ingestion of meat, rich in purines [35]. This feasting custom deflected scientific attention about gout pathogenesis from wine to meat, particularly "sweetmeats" which were especially rich in nucleic acids, and to other epigenetic food related factors including fructose-containing soft drinks [36].

Yet, there is much more to the claret and port story. In the 1600s, British prosperity and the scientific revolution brought glassware doped with lead oxide, "crystal", invented by George Ravenscroft, to enhance "sparkle" by increasing the translucency and refractive index of glass [37], and colorful, smooth, shiny, lead-glazed ceramic plates [38] to beautify fancy dinner tables. We now know that the lead particles leached from these prestigious, beautiful objects can contribute to the development of gout.

Because of its high prevalence in males of the British upper classes, gout was thought to be hereditable amongst men in these families. Yet, more often in this group, as in Horace Walpole's case, gout appeared without a family history. This reflects our current knowledge that while gout etiology has various genetic predisposition components [39], environmental factors predominate in disease expression [40,41]. Similarly, while gout is rare in pre-menopausal women, the incidence post menopause approximates gout incidence in elderly men [42]. With the knowledge that life expectancy in the 18th century averaged 37 years, and that typically, gout first appeared in males in their early thirties, the high prevalence of gout in male British aristocrats can be ascribed not to heredity but to the drinking of claret and port, in addition to cultural environmental factors (lead crystal glassware, lead-glazed ceramic dinnerware) associated with their fine dining customs.

5. Gout Was Good; Fine Wine without Gout Is Better

Gout was a singular disease because it was widely perceived as a condition that kept other diseases away [43]. Despite its acute painful episodes, gout was associated with increased longevity. Placed in perspective, life before the 20th century was often short; acquired diseases were commonly infectious. The pain of acute gout episodes could be ameliorated by drinking fine wine and/or potions containing opioids and even colchicine.

6. What Then, If Anything, Was the Scientific Basis That "Gout Was Good"?

Since ancient times, it has been known that metals can protect crops from disease, food from spoiling, and water from causing diseases [44]. For lead, various environmental sources have been associated with lead toxicity (Table 1). As a result, lead is no longer used in water pipes, gasoline, paints, or wine. Where lead is still used in crystal glassware and ceramic glazes, fabrication techniques ensure that lead compounds remain trapped within the product. Recently, the antimicrobial activity of metals has been found to reside, not in the metal itself but in metal ions, metal–organic complexes [45,46] and metal oxide nanoparticles [47]. In this regard, lead ions [48] and lead nanoparticles [49] demonstrate antimicrobial activity. Moreover, the antimicrobial activity varies inversely with lead nanoparticle size [49]. Lead nanoparticles are known to be released from lead crystal glassware and insufficiently fired lead glazed ceramics [3]. It can be hypothesized that these products, ingested with food, functioned as a lead-based mouthwash, contributing both to the antimicrobial effects and the high predisposition to gout in the privileged British male population. The mechanisms of lead toxicity are not fully understood, but a prominent mechanism is thought to be related to the effects of free radicals on membrane function and disruption [44]. Of note, bacteria appear more susceptible to metal toxicity than mammalian cells [44]. Accordingly, metal compounds in concentrations toxic for bacteria may have subclinical effects in humans, manifesting not as acute lead poisoning but as gout.

Table 1. Sources of lead in the environment.

Source	Lead, Molecular State	Notes
Air	Nanoparticles	Industrial (lead product fabrication, e.g., pots, pipes, bullets); Formerly, lead-doped gasoline.
Soil	Ions, complexes, nanoparticles	Industrial, from lead product fabrication; Natural terroir.
Water	Ions	Lead pipes, "soft" water.
Paint	Complexes, nanoparticles	Lead was used to make paint white. Children ingesting lead-containing paint often had lead toxicity.
Crystal glassware	Nanoparticles	Inadequate fabrication techniques; Leaching from wine longstanding in crystal decanters.
Lead-glazed ceramic dinnerware	Nanoparticles	Inadequate fabrication techniques.
Fine wine (sapa)	Complexes, nanoparticles	Sapa to sweeten wine.

7. Conclusions: Fine Wine and Gout in the 21st Century

Lead is no longer used to sweeten wine or food; wine can be imbibed with pleasure without fear of contracting gout. However, historical knowledge of gout's association with fine wine can provide considerable insight into the pathogenesis of gout. First, acute gouty arthritis was commonly superimposed on chronic tophaceous gout, implying a long term increase in the afflicted patients' serum uric acid induced by subclinical lead toxicity from lead complexes and nanoparticles present in fine wine. This observation is important as it discounts acute lead toxicity as a cause of gout. Lead water pipes were common in cities for 2000 years, but in contrast, gout was particularly prevalent only in the wealthy classes. Notwithstanding that chronic lead exposure can impair renal function [50], gout's particularly high incidence amongst the wealthy classes is contrary to the view that pre 20th century population suffered widely from lead toxicity from the water supply via lead pipes. The opinion held for millennia, that gout is induced by excessive fancy food and drink and with a strong hereditary component in males, has now been shown to be only an indirect, nonpathogenic association. However, there is a more general lesson from the long story of gout and fine wine. As better understanding emerges in subsequent generations,

what physicians and scientists consider to be obvious etiologic factors and pathogenic mechanisms for any given disease in former eras, are usually shown to be quite different in later times. For gout pathogenesis then, what will the future bring?

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