

Bark's Bite: did 18th century pharmacopeia complicate Thomas Jefferson's headaches?

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ABSTRACT

Thomas Jefferson, the 18th and 19th century revolutionary, statesman, and third President of the United States, suffered numerous debilitating headaches throughout his lifetime. These headaches, or 'fits' as he called them, have fascinated historians. They have alternatively been identified as migraines, tension, or cluster headaches; yet, despite Jefferson's copious personal records and correspondence, his headaches continue to defy classification.

While the cause of Jefferson's headaches remains debatable, Jefferson was explicit regarding his choice of headache pharmacotherapy. His records catalogue numerous purchases of 'bark', referring to an 18th century fever-treatment called Jesuit or Peruvian bark. Jefferson's choice of this treatment provides insight into 18th century headache medicine. Likewise, an understanding of Jesuit Bark, and its biologically active component, quinine, permits a novel reexamination of Jefferson's headaches.

KEYWORDS

Thomas Jefferson, headache, Jesuit Bark, quinine, *Cinchona*

Introduction

Thomas Jefferson was a formative figure in the history of the United States of America. He was also a fastidious record keeper, and maintained regular correspondence with his friends and acquaintances. In many of these preserved records, President Jefferson complained of debilitating headaches, often at critical points in his career. These records have been a gift to medical historians, who have written extensively about Jefferson's cephalalgia. While he often wrote extensively of his headaches, his symptoms do not fit the standard definitions of primary headache syndromes.

While his headaches are confusing, his headache remedies are well described, and only lightly tread upon by historians. His pharmaceutical of choice, Jesuit (also called Peruvian) bark, was a popular 18th and 19th century fever drug from *Cinchona* trees, and the first popular vec-

tor of quinine in Western medicine. As we discuss Jefferson's headaches, we will consider Jesuit bark's contemporary usage. We will also consider the side effects of quinine, and how drug toxicity may be one of the reasons Jefferson's cephalalgia resists classification.

Development

For basic biographical data and previous articles on Jefferson's headaches, we searched PubMed using the search terms, "Thomas Jefferson," and "Headaches." These search criteria were also entered into Google Scholar, and the JSTOR database. To search for articles discussing the contemporary use of *Cinchona* bark, we performed PubMed searches for "bark," "Jesuit bark," "Peruvian bark" "Cinchona," and "quinine" in association with "headache." Original correspondence and records from Jefferson's library were obtained from

public databases maintained by <http://www.monticello.org>.

Discussion

The Second Continental Congress convened in Philadelphia, Pennsylvania on 10 May 1775. At first, the Virginian Peyton Randolph was appointed president of the congress. However, he soon returned home to preside over the Virginia House of Burgesses. In his place, Thomas Jefferson was named a delegate for Virginia (Figure 1).

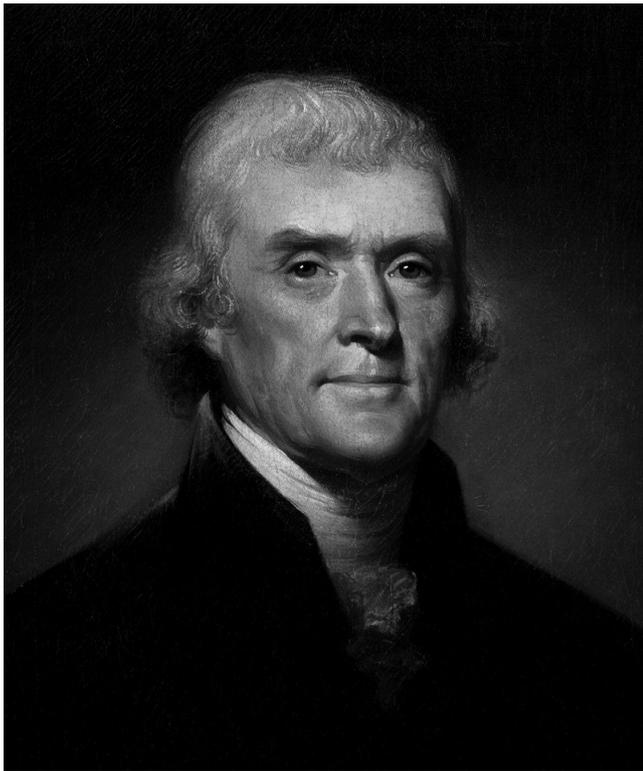


Figure 1. A portrait of Thomas Jefferson, by Rembrandt Peale (1778-1860), painted in 1800, held by the White House Historical Association. Public domain image.

In the spring of 1776, with tensions between the Crown and the Colonies coming to boil, Jefferson found himself in a state of personal loss and physical pain. His mother had passed away, and he was suffering a bout of severe headaches lasting five weeks between April and May of 1776.¹ Only after his recovery was he able to return to Philadelphia, where he was subsequently

named as an author of the *Declaration of Independence*, a remarkable incidence where a headache almost changed history.

Thomas Jefferson's headaches began in his twenties.² His first episode, like many subsequent, began with a personal stressor; in this case, it was his failed courtship of Ms. Rebecca Burwell. During the rest of his life, he suffered at least five other major bouts of headache, each lasting weeks at a time. A headache episode in the spring of 1776 was coincident with stress of the Second Continental Congress and the death of his mother.³ A flight from Monticello to evade the British army and political maneuvering by rivals were associated with a headache in June of 1781.³ Yet further headaches struck in 1789, at the end of his service in France. This episode, too, was coincident with a failed courtship, this time of Ms. Maria Cosway.² He had episodes of headache in the early 1790s in his service as Secretary of State, which were noted to occur during difficult negotiations with Alexander Hamilton. He had a hiatus of several years, with his headaches returning during his presidency, including a severe bout in 1807.⁴ After leaving public office, his headaches seem to resolve, or at least no further headaches were noted in his personal correspondence.

Jefferson never described his headaches in clinical detail. From records, we gather that his headaches could occur several times daily and last for hours.² Clearly, they were severe: he mentioned delays in correspondence, difficulty reading, and delaying travel and social activities, all because of his pain. He described shutting himself in a dark room and refraining from physical activity. During his first episode, he even noted some positional character, with his headaches worsening when he looked down.⁴

Historians of Jefferson's headaches generally favor one of three diagnoses: migraine, tension, or cluster headaches. A diagnosis of migraine, as defined by the International Headache Society (IHS), requires at least 5 attacks, lasting between four and seventy-two hours, with any two of the following: unilaterality, pulsating quality, moderate-to-severe intensity, and exacerbation by physical activity. Chronic tension headaches have a more complicated set of criteria but are defined as occurring more than fifteen days a month for more than 3 months a year, and can last hours, or even be continuous. They should not have migrainous features, and

must have two of the following characteristics: bilaterality, a non-pulsating pressure quality, mild-to-moderate intensity, or lack of relationship to physical activity. Cluster headaches must be severe-to-very-severe, last up to 3 hours at a time, and occur in clusters up to 8 per day. They must also be accompanied by a unilateral autonomic manifestation. Common to all primary headaches is the caveat that the pain must not be attributable to another disorder.⁵

Unfortunately, with the sparse descriptions Jefferson provides for his headaches, it is hard to match with contemporary diagnosis schemes. Certainly his headaches were debilitating—moderate-to-severe in character. They were, however, long in duration, often lasting weeks. He describes no migrainous features, or autonomic character, but he often ceased all activity to avoid his headache pain. They share features of each primary headache syndrome. This ambiguity is why Jefferson's headache diagnosis remains a debate among contemporary medical historians.

Diagnosis aside, Thomas Jefferson did not suffer without treatment. His most commonly referenced headache remedy was 'bark', referring to Jesuit or Peruvian bark, from trees of the *Cinchona* genus of the *Rubiaceae* family (Figure 2). Initially described by Jesuit missionaries in South America, this bark became popular in Europe in the 17th and 18th centuries.⁶ It captured the interest of physicians and chemists of the day, and numerous extractions and preparations were available.^{7,8} It was popularized by Thomas Sydenham for fevers, likely related to malaria. The active ingredients were quinine and quinidine alkaloids, in concentrations ranging from 3%-13%, depending on the *Cinchona* species used.⁶

While principally a fever drug (likely because of quinine's efficacy against malaria), Jesuit bark became something of a cure-all in Europe and its colonies. Indeed, it even received a formal endorsement for headache treatment: Jefferson's contemporary, Gerard van Swieten, a European physician credited with the first clinical description of cluster headaches, advocated for its use in this presentation of cephalalgia.⁹ It is unsurprising, given Jesuit bark's popularity, that Jefferson's ledgers note multiple purchases of the drug between 1790 and 1807, indicating longstanding and frequent use.^{4,10}

Jesuit bark was not the only popular headache medication of the era, and indeed it was not principally used

for headaches, but rather for fever.^{6,7} Other popular pain remedies of the 18th and 19th century included liquor and laudanum.¹¹ One of Jefferson's physicians even recommended using ammonia.² These are among the more discrete pharmaceuticals; there were numerous proprietary mixtures as well, the medical ancestors of the 'snake oil' of the 19th century.¹² Despite the myriad options, Jefferson's principle remedy, as recorded in his ledgers, was *Cinchona* bark.

Though well intentioned, Jefferson's use of Jesuit bark may not have been benign. In fact, quinine toxicity was originally called cinchonism, a term derived from the *Cinchona* bark that Jefferson used so readily. Also called quinism, quinine toxicity presents in acute and chronic forms, and can manifest with gastrointestinal disturbances, vasodilatation, and sweating.¹³ Two symptoms of cinchonism, however, stand out for Thomas Jefferson: headache and diarrhea.^{2,3,13}

While we have no means of calculating Jefferson's quinine intake, both acute and chronic toxicity can cause headache. Since the quinine concentration in different species of *Cinchona* was so variable, toxicity could have occurred unpredictably and inadvertently.^{5,13} A superimposed quinine headache could have prolonged Jefferson's headache bouts and caused symptoms that were unrelated to an underlying primary headache. An additional diagnostic consideration is the IHS class of medication-overuse headache. Such headaches must be present for more than fifteen days a month, require over three months of use of a medication for headache, the headaches must develop or worsen with medication, and the headaches must return to their previous pattern with discontinuation of the medication.⁵ Prolonged quinine use as an analgesic could potentially have caused a medication-overuse headache, which could account for the amorphous symptoms and prolonged duration of Jefferson's cephalalgia.

Jefferson did not suffer only from headache. Episodic diarrhea was another lifelong malady, and was even implicated in his demise.³ Less popular a topic of discussion than his headaches, Jefferson's diarrhea provides for an interesting differential. Jefferson, himself, attributed his loose stools to shellfish. Other contemporaries suggested inactivity, and recommended horseback riding as a therapeutic. Some modern authors have suggested irritable bowel syndrome, a disease often comorbid with headache.³

His first recorded diarrhea episode occurred in his 30s, several years after his first headache. However, diarrhea is a known complication of both acute and chronic cinchonism. His diarrhea continued through his peak bark consumption years between 1790 and 1807. Jefferson treated his diarrhea with laudanum.^{3,14} Long term



Figure 2. A photograph of bark from *Cinchona officinalis*, of the many species of quinine containing trees that could have been distributed as Jesuit or Peruvian bark. "Cinchona officinalis, the harvested bark," by H. Zell, licensed under CC by-SA 3.0.

opium use in the setting of cephalalgia is now known to cause narcotic-overuse headaches—though this is not as well established in cluster headaches.⁵ Also, the IHS acknowledges that analgesia, even when used for non-headache purposes, may cause a medication-

overuse state in vulnerable patients. As with the possibility of secondary headache from cinchonism, headache from laudanum could certainly muddle features of primary headaches.

Conclusion

While there is no doubt that Jefferson suffered from a primary headache syndrome, the etiology remains a matter of debate. Given their severity, and his degree of incapacitation, migraines and cluster headaches are the most likely candidates, and historians continue to debate the merits of these diagnoses. However tempting, we will avoid offering our own primary headache diagnosis. Jefferson's records are too sparing in clinical detail and his symptoms do not offer a definitive answer. The fact that his headaches are amorphous, however, raises a question: did Jefferson's headache remedies mask his presentation?

Jefferson's use of quinine suggests a possible secondary headache syndrome. Jesuit bark could, either acutely or chronically, have led to headaches as a direct toxic effect. Toxicity aside, chronic quinine use as an analgesic could have caused a medication-overuse headache. Likewise, Jefferson used laudanum to treat chronic diarrhea, another side effect of quinine. Even if quinine were not the cause of his diarrhea, the use of laudanum could have caused an analgesic, or narcotic-overuse syndrome as well. Secondary headache can mask the clinical features of primary headache syndromes, which can readily explain why Jefferson's headaches defy definitive characterization.

Conflicts of interest

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