

The Madness of King George

Variegate porphyria has also been known as the Royal Malady since Macalpine and her coworkers¹² suggested that George III of England (America's last king) suffered from the condition, as had other descendants of Mary, Queen of Scots, who, they argued, had shown clinical signs of the disorder. The 'mad' King's son, George IV, and his granddaughter, Princess Charlotte, were also considered to have suffered from VP¹². The severest critic of Macalpine's diagnosis was, perhaps, Geoffrey Dean, the physician who did so much to put South African porphyria 'on the map'. He argued that the clinical symptoms were atypical and that the deeper colour of the urine, "a pale blue ring upon the glass," might have been due to haematuria¹. Dean felt so strongly about this that, in his review of the monograph by Macalpine and Hunter, he wrote: "This book is a fine illustration of how a story, if repeated frequently enough, comes to be believed even when it is not founded on good scientific evidence"¹. His scepticism was shared by C.E. Dent, the eminent British biochemical geneticist, but supporters of the Royal malady hypothesis included a number of respected British physicians and scientists¹³.

Macalpine's search for VP sufferers among the living descendants of King George proved unsuccessful^{12,14,15}. In spite of having had 15 children, King George left very few descendants. Edward, Duke of Kent, one of his sons and the grandfather of Queen Victoria, appears¹² to have suffered from VP but not to have passed it on to his daughter. The present British Royal Family can, therefore, be presumed not to have VP. Macalpine *et al.*¹² did manage to locate and study two descendants from common ancestors of the King: one had suffered a proven attack of porphyria and laboratory tests established its presence in the other¹².

In the recent film *The Madness of King George*, starring the South African-born actor Nigel Hawthorne, the King is portrayed, in the words of Hawthorne, as "a man of the people [who] really believed that in order to keep the monarchy it had to be special, and so he inaugurated a lot of court manners, behaviour and protocol. He was an ordinary man who loved farm life and was known as Farmer George." The King gains the audience's sympathy as he battles bouts of madness, the first (of five) occurring when he was 50 years old. His attacks of mental derangement were widely discussed in parliament as well as by the medical profession and the whole populace, engendering in doctors and the public a humanitarian concern for the fate of the mentally ill. The birth of psychiatry can arguably be traced to the madness of King George. Macalpine and Hunter were, in fact, researching the history of psychiatry when they came upon voluminous sources relating to the King's illness. The King's physicians had concluded that his mental illness was part of a physical disorder and not psychological. Macalpine and Hunter agreed with the royal physicians and arrived at the posthumous diagnosis of porphyria variegata. The recent film highlights the primitive state of medicine at the end of the eighteenth century: physical examination was carried out in the most rudimentary manner and the physicians, to observe protocol, were unable to ask the King any questions (including those pertaining to his health) unless they were addressed first! The film concludes with the words "The colour of the King's urine suggests that he was suffering from porphyria, a physical illness that affects the nervous system. The disease is periodic, unpredictable and hereditary." Patients with porphyria pass urine that, on standing, acquires a port wine colour; the name porphyria was derived from the Greek 'porphuros,' meaning reddish purple, because of the colour of the urine.

Macalpine & Hunter¹⁴ conclude that "George's malady was not 'mental' in the accepted sense, in whatever old or modern terms it may be couched. His long and sorrowful illness in which he suffered severely from his affliction, pitifully from his treatments, and miserably from his management, takes on a new importance in the annals of medical history as the first description of a rare metabolic disorder not even today fully understood".

The cloning of the *PPO* gene makes it possible to return to the case of George III and the Royal malady. It can no longer be assumed that Royalty and other persons of 'high social station' will refuse to cooperate in an historically interesting investigation aiming to posthumously diagnose the illness of King George. After all, the Duke of Edinburgh recently participated in DNA investigations to authenticate the remains of Tsar Nicholas II and his family (ref. 16). At the time, Paul Debenham¹⁷ wondered "whether the graves of many mysteries will now be genetically probed". The first step in trying to solve the mystery of George III's illness would be to test living relatives for a *PPO* mutation. It might also be possible to obtain DNA from the remains of King George III himself.

History is rarely objective and the behaviour of a long dead monarch may be viewed with more sympathy if it were confirmed that (s)he suffered from a genetic disorder, characterized by bouts of 'madness' with which physicians of the time were unable to deal, let alone diagnose correctly. Some prominent people, afraid of what future biographers might say about them, have been known to destroy their papers before they die. Will there come a time when behavioural genetics has progressed so far that prominent (and not so prominent) people will dictate that when they die their bodies must be cremated and the ashes scattered to the winds because of their concern that history might judge them to have been genetically unsuited for the position they occupied in society? T.J.

IMAGE
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REASONS

King George (Nigel Hawthorne, centre) is calmed by Queen Charlotte (Helen Mirren, left) as he takes an interest in Lady Pembroke (Amanda Donohoe, right). (*The Madness of King George*, The Samuel Goldwyn Co.)

