

Papers and Originals

The "Insanity" of King George III: a Classic Case of Porphyria

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"The attacks of George the Third are invested with peculiar interest," wrote Ray (1855). "Five times" was the king "struck down by mental disease . . . and twice the recurrence of his disorder gave rise to a degree of political feeling that has seldom been equalled, and to political discussions that settled for ever a vital principle in the British constitution." No illness had such profound effects on the nation and its institutions as the "madness" of George III, and indeed no other has received so much attention from commentators, biographers, and historians. The royal malady also influenced the history of psychiatry, not least by dragging the "mad-business" into the limelight (Hunter and Macalpine, 1963).

Strangely only two clinical studies have been devoted to it, both by psychiatrists and both American: Ray in the mid-nineteenth century and Guttmacher in the mid-twentieth. From the latter historians have adopted as fact that "His insanity was a form of manic-depression [*sic*]" (Namier, 1955) or, as in a recent narrative of the regency crisis 1788-9, that "the king's disorder was undoubtedly psychotic, of a manic-depressive type . . . caused by an underlying conflict . . . exacerbated by violent frustrations, annoyances and emotions" (Trench, 1964). This diagnosis is challengingly unsatisfactory not only because it leaves many mental symptoms unaccounted for, but because it ignores the physical symptoms which were a major part of the king's sufferings.

New Medical Evidence

The discovery of new medical evidence in the journals and correspondence of the king's physicians made it possible to fit together all pieces of the enigma—200 years after what is generally assumed to have been the first attack in 1765. Four primary sources are drawn on for the first time in a clinical study: 47 volumes of Willis manuscripts at the British Museum (B.M. Add. MSS. 41690-41736, first catalogued 1959); 8 volumes and 10 boxes of Queen's Council Papers at Lambeth Palace Library; Sir Henry Halford's daily record of the illness, October 1811-January 1812, in the Royal Archives at Windsor; and Sir George Baker's diary in the possession of Sir Randle Baker Wilbraham.¹ The royal malady now assumes an unsuspected significance which gives it a unique place in the annals of medicine. The new diagnosis may also necessitate revision of historical judgments and notions concerning the character and conduct of this "much maligned monarch" (Namier, 1955).

The Bias of History

For many reasons the illness is difficult to study, foremost paradoxically because of the abundance and diversity of sources, printed and manuscript, spread over almost the sixty years of the reign which span the recurrences of the illness. It was

a period teeming with great men and great events, and never had there been so many diarists, correspondents, and chroniclers who may have noted pertinent facts not recorded elsewhere.

Physicians' Daily Bulletins

The public bulletins were made colourless out of respect for the royal family and designed to allay alarm rather than record medical facts. They were intended to reveal no more than was



Statuette of King George III.

"sufficient for every good or loyal purpose" (Nisbet, 1817), as, for instance, "His Majesty has had a restless night, and is this morning much indisposed" (14 December 1788). Nor were the physicians explicit when they meant to be informative, as in a report to Prime Minister Spencer Perceval: "He is under

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¹ In the condensed form of this paper it was not possible to give the reference to every quotation, particularly in the case history, which is mainly based on these sources.

a great degree of irritation, and the whole frame is so much disturbed, as to make us consider Him in some danger" (24 December 1810). "The report of the physicians," complained Lord Grenville on 8 October 1811, "is worded as foolishly as ever" (Jesse, 1867). What they did contain was not always reliable, since many were a compromise between dissenting medical opinions, as parliamentary committees criticized. When party strife centred on a regency, the physicians found themselves arbiters of government, and everything hung on their answers to whether they thought "the State of His Majesty's Health does, or does not . . . render His Majesty incapable, either of coming to Parliament, or of attending to Public Business" (Report 1789). Not surprisingly they were also suspected of party political bias.

Eighteenth Century Practice

Another difficulty is that observations were made and couched in the theory and language of a bygone age. Organ pathology could make little headway against the old humoral pathology in the absence of a science of physical signs. Little was known of neurology short of involvement of higher centres by injury, infection, strokes, and fits. The physicians had no stethoscope, no knee-jerk hammer, not even a clinical thermometer. Laboratory medicine did not exist but excretions were inspected. Diagnosis was made on what Dr. George Fordyce (1794) called "an estimate of symptoms and appearances"; the doctor listened to the patient's complaints, inquired into his "animal functions" and general health, felt the pulse, and looked at the tongue.

Even within this limited range of fact-finding the royal physicians were peculiarly handicapped. They were expected to observe protocol however ill or delirious the king was: if they were not addressed first they could ask no questions. Whole visits were spent in fruitless silence, as they reported to the Queen's Council on 8 January 1812: "His Majesty appears to be very quiet this morning, but not having been addressed we know nothing more of His Majesty's condition of mind or body than what is obvious in his external appearances."

Mental Symptoms

The highpoint of this great drama of human, psychiatric, and national history was reached in 1788, when the 50-year-old king went "mad." Naturally the mental symptoms at once moved to the centre of the public stage in what became an intricate complex of medical and political controversy in which confusion extended far beyond the patient's mind, and so gave the illness its lasting stigma. They were the loudest, the most dreaded, and of greatest concern to government and country alike, since it was the king's mental state which determined

whether he was competent to rule. And they gained added prominence because whoever came in contact with the king could, and did, form his own opinion of them.

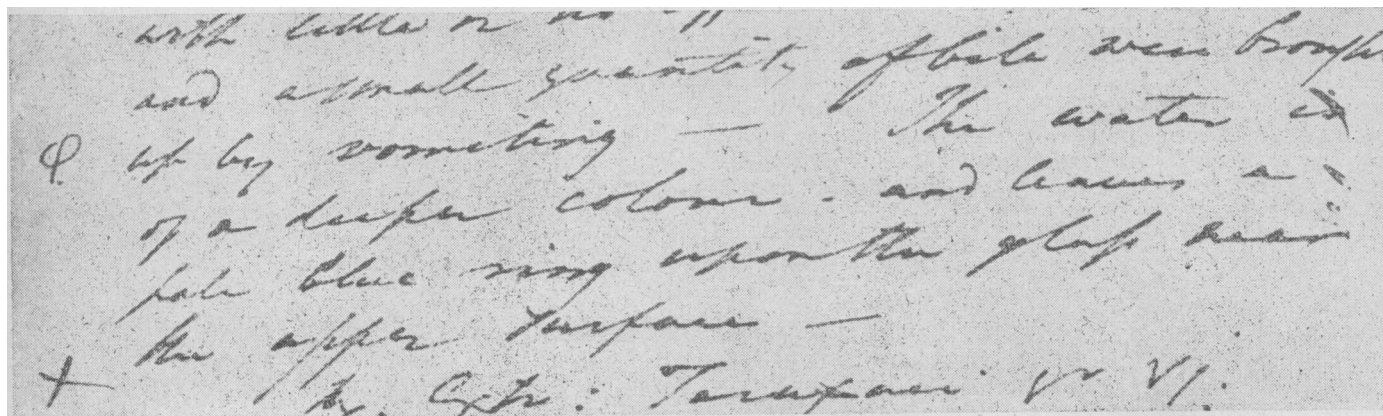
The physical symptoms in contrast, though at times so severe that his life was in danger, did not enter the political or social arena. They receded into the background less in fact than emphasis and came to be regarded as incidental or the result of the mental illness, if not actually manufactured to hide the true facts. The seal was set on this historic bias when in December 1788 "Persons who have made this Branch of Medicine their particular study," as "mad-doctors" were referred to in parliament, were called to take charge of the king's management. While the balance was thus weighted against the physical side of the illness, the door was closed to the real diagnosis.

The Problem

The problematic nature of the illness emerges clearly from the sequence of events in the 1788-9 attack. It started in June with severe abdominal pain, diagnosed as "biliary Concretions in the Gall Duct." In July and August the king was excitable. Colic returned in October, followed by aches and pains, muscular weakness, and stiffness, diagnosed as "rheumatism," and as "gout" when the legs were badly affected. His condition deteriorated with more colic and constipation, racing pulse, sweating attacks, cramp, lameness, and hoarseness, attributed to "fever." Intractable insomnia, incessant talking, excitement, confusion, and fits supervened, diagnosed as "delirium" or—since the physicians could not agree whether there was fever—as "mental derangement" caused by some severe bodily disease. By November he was "under an intire alienation of mind" and considered "mad." Parliamentary committees interrogated the physicians about his competency to continue as head of State and the prognosis. In January 1789 a regency for which the party of the Prince of Wales had been agitating was accepted as unavoidable. The Bill had passed the Commons and was in progress through the Lords when the king unexpectedly began to recover. On 12 February "a progressive state of amendment" was announced, and on 26 February "the cessation" of the illness. Thanksgiving prayers were offered, and, though "emaciated and enfeebled," the king "resumed personal exercise of His Royal Authority" on 10 March. On 23 April services were held for "delivering our most Gracious Sovereign from the severe illness with which He hath been afflicted" and the painful chapter closed. Twelve years elapsed before the next major attack.

Original and Consequential Madness

Was the "aberration" part of a physical disease or purely mental? The physicians thought in terms laid down by Dr. William Battie, one time president of the Royal College of



Part of a page from the Willis papers: entry in the hand of Sir Henry Hallford recording the colour of the king's urine.

Physicians, in his *Treatise on madness*, published in 1758—that is, within living memory.² He taught "that Madness with respect to its cause is distinguishable into two species . . . viz. *Original and Consequential* . . . The first is solely owing to an internal disorder of the nervous substance: the second . . . owing to the same . . . being disordered *ab extra*." In modern terms he differentiated the functional psychoses from the organic mental states due to brain disease. The best known among the latter was febrile delirium and "mental derangement," which was milder—to-day called toxic confusional states. Harper for instance wrote in 1789 under the impact of the king's disorder: "morbid matter, or . . . acrimonious, stimulating particles settling on the brain, has likewise been accounted capable of producing Insanity" by "translation of morbid cause."

Mania or Delirium ?

Dr. Robert Darling Willis summed up the problem for the parliamentary committee in December 1810: "I consider the King's derangement more nearly allied to delirium. . . . In delirium, the mind is actively employed upon past impressions . . . which rapidly pass in succession. . . . There is also a considerable disturbance in the general constitution; great restlessness, great want of sleep, and total unconsciousness of surrounding objects. In insanity, there may be little or no disturbance, apparently, in the general constitution; the mind is occupied upon some fixed assumed idea . . . and the individual is acting, always, upon that false impression . . . also, the mind is awake to objects which are present. Taking insanity, therefore, and delirium, as two points, I would place derangement of mind somewhere between them. His Majesty's illness, uniformly, partakes more of the delirium than of insanity."

Prognosis

The physicians grappled with the diagnosis not as an academic exercise nor as a guide to treatment but as the clue to prognosis. "Original Madness," mania, or insanity was considered not amenable to art and spontaneous recovery uncommon, whereas "Consequential Madness," delirium, and derangement were expected to subside with the underlying condition, rarely leaving a defect state called "fatuity" or dementia. Insanity and delirium represented opposite poles of hopefulness and despair. The *Morning Chronicle* of 28 November 1788 reassured its readers: "Although the disorder has deranged the head, it is not, as was once dreaded, a mental incapacity called Insanity, for that calamity will not admit of a sudden and effectual cure." While the king's "agitation," "hurry of spirits," and changeability from confusion with excitement to insight and composure pointed to delirium, doubt arose when the condition persisted. This looked like insanity with its chronic course, and disheartened the most sanguine supporters of the fever/delirium theory. At this juncture all medical and political parties were confounded by the king's swift and complete return to clarity and reason as if it had been delirium all along.

Physicians' Dilemma

In this quandary it is not surprising that the physicians remained evasive though hard pressed by government and

parliament. Only two took a definite stand and both had sufficient political motive for their views. Dr. Richard Warren, Whig sympathizer, and physician also to the Prince of Wales, confided in a letter: "*Rex noster insanit; nulla adsunt febris signa; nulla mortis venturae indicia*"—our king is mad; there are no signs of fever; no danger to life (8 November 1788). The Reverend Dr. Francis Willis, Tory "mad-doctor" brought down from Lincolnshire with his sons by Pitt, told the parliamentary committee in December 1788 that he had "great Hopes of His Majesty's recovery" because in his practice he cured "Nine out of Ten . . . Persons . . . afflicted with the Disorder," implying, as his grandson Dr. Francis Willis explained 35 years later, that he diagnosed "*delirium and derangement cum febre*." Dr. Anthony Addington, who had looked after Earl Chatham, was hopeful that it was not mania "from this Circumstance—that it had not for its Forerunner that Melancholy which usually precedes a tedious Illness of this Sort" (Report 1788).

What Other Contemporary Doctors Thought

John Hunter, surgeon extraordinary to the king, who though not consulted kept himself fully informed, thought it a systemic affection which "would probably come to some sort of crisis, by which it would appear whether there was strength enough in the constitution to prevail over the disease," and estimated "that the chances were nine to one in his [the king's] favour" (Grenville, 1788).

Other medical men joined in the controversy in print. Jones (1789) diagnosed "nervous fever" and proposed methods of treatment and prevention. Rowley (1790) concluded that the king suffered from what he had described in 1788 as "a new species of temporary madness," a "derangement" without fever caused by "some prevailing irritating acrimony," to-day called toxins. Pargeter (1792) argued that "this case could not have been *maniacal*," since undoubtedly fever had been present and by ancient usage insanity was "delirium without fever." In the king's last illness Sutcliffe (1824) proposed a trial of his "herbaceous tranquillizer," because of its success with "maniacal patients."

Diagnosis in Last Illness: A Singular Case

The physicians in attendance from 1810 were equally non-plussed. They thought his mental state more characteristic of delirium—but symptomatic of what? R. D. Willis had "never seen a person . . . labouring under a similar complaint" but found the "symptoms of bodily indisposition sufficient to account for all the derangement of mind." Henry Revell Reynolds, who had seen all attacks from 1788, considered it insanity but had never known "exactly a case parallel to the king." William Heberden junior thought it "a derangement attended with more or less fever, and liable to accessions and remissions" due to "a peculiarity of constitution, of which I can give no distinct account." In October 1811 he replied to the Queen's Council's quarterly questionnaire: "For want of terms more accurately defined respecting disorders of the human mind, His Majesty's present state might be called Insanity but . . . appears . . . to differ materially from ordinary cases . . . by that perplexity and confusion of ideas, which belong more properly to delirium." In January 1812 he admitted that it "is different from any other case that has occurred to my own observation." And Sir Henry Halford told the Council: "The King's case appears to have no exact precedent in the records of insanity."

Their guarded answers were wiser than they could have known. But by then the need for a diagnosis had lost its immediacy. The regency had been established in February 1811 and the 72-year-old blind monarch had begun to show

² It remained the standard work for over 50 years. Dr. Matthew Baillie, called to the king in 1810, wrote from Windsor for it "and the old Dr. Monro's *Remarks upon that Treatise*" (Baillie Collection, R.C.S.). (Dr. Monro had attended the king once in 1788.) And Sir George Baker, the king's regular physician and the first to be called in 1788, proudly informed the parliamentary committee that he had walked the wards of St. Luke's Hospital for Lunatics with Bartie.

signs of "fatuity." Dr. Baillie reported in January 1812: "I cannot state that His Majesty's recovery is altogether without hope, but I think it . . . extremely improbable . . . His memory seems to be impaired."

Later Studies

In the eighteenth century physicians dealt with both physical and mental illness alike unless a patient became unmanageable, as Dr. Reynolds explained: "If no Restraint is necessary . . . every Physician of Experience will, I have no Doubt, think himself competent to conduct . . . such a Case" (Report 1789). This changed with the establishment of mental hospitals. Two orders of disease were then created and psychiatry became estranged from medicine—a development reflected in later studies of the royal malady.

Acute Mania

The first asylum doctor who studied George III's illness was Isaac Ray (1855). In a paper to the Association of Medical Superintendents of American Institutions for the Insane he gave an account of all attacks from printed sources then available. Concerned with the phenomena of mental illness, he considered diagnosis—"the form of disease"—only in connexion with the royal physicians' dilemma between delirium and insanity: "They sought no doubt to give the impression that it was simply a case of delirious wandering produced by bodily disturbance, which would readily pass away with the condition on which it depended. It is impossible to see any ground for this opinion. This attack [1810] closely resembled the others. It was manifested by hurry, restlessness, caprices, indiscretions, violence, and delusions. In one word, it presented all the characters of ordinary acute mania." But he added a significant caveat: "Few men would have seemed less likely to be visited by insanity. His general health had always been good; his powers were impaired by none of those indulgences almost inseparable from the kingly station; he was remarkably abstemious at the table; and took much exercise in the open air. Insanity had never appeared in his family, and he was quite free from those eccentricities and peculiarities which indicate an ill-balanced mind."

Manic-depressive Psychosis

By the 1930s psychiatric emphasis had shifted from description to classification, and Jelliffe (1931), applying the Kraepelinian criteria of excitement and recurrence, diagnosed "manic-depressive psychosis" with the manic element paramount.

Guttmacher (1941) built his full-scale medico-historical study on this diagnosis—"a disturbance of mood, rather than of mentation"—and proceeded to explain the onset of the attacks in psychopathological terms: "Self-blame, indecision, and frustration destroyed the sanity of George III . . . Had 'farmer George' . . . been a country squire, he would, in all probability, not have been psychotic." The somatic symptoms are dismissed as subterfuges to hide the embarrassing nature of the illness. Of the 1765 attack Guttmacher wrote, "In all probability, the disorder was purely mental and the clinical reports were falsified"; of the 1788-9, "Physical symptoms were invented or, at least, exaggerated further to fool the public." Only when the press mentioned mental symptoms "did the court cease manufacturing reports of various baffling physical symptoms." He even believed that the king "abetted by the false interpretations of those about him . . . was trying to delude himself into viewing his illness as primarily physical." Tachycardia, sweating, colic, hoarseness, are rated

accompaniments of manic states; pain, paresis, stupor, fits as "hysterical."

The wheel had turned full circle from the royal physicians puzzling what physical illness had caused the mental disturbance to twentieth-century psychiatrists explaining the physical disturbance as the guise or somatic expression of mental illness.

Neurotic Personality and Heredity

To support his thesis, and in contrast to Ray, Guttmacher held that the king was predisposed by a neurotic personality and a hereditary taint: "This unstable man . . . this vulnerable individual" whose "neuroticism" made him take the "job of kingship too seriously" so that he "broke under the strain," was "a victim of neuropathic tainting . . . the list [of affected members] is . . . frightening." This he modified in 1964 to "The family history is not very impressive psychiatrically."

No medical study has since been made. Historians had therefore to rely on the diagnosis of manic-depressive insanity or psychosis with all it implies.

Case History

It is usually stated that there were five attacks: January-July 1765, age 26/7; October 1788-February 1789, age 50; February-March 1801, age 62; January-March 1804, age 66; and from October 1810 to his death on 29 January 1820 in his 82nd year. This was also punctuated by "accessions" and "remissions," which in the first year or two gave rise to hopes of full recovery.

In addition, minor attacks can be established in: May-June 1762, age 24; January-February 1766; in the summer of 1790; in December 1795; and there were probably others. These can be checked by his absences from Privy Council meetings and references in his own letters. Furthermore, during convalescence from major attacks he had "occasional paroxysms of his disorder, though short and slight" and "periods of flurry" (Report 1810).

All attacks were "of the same general character" (Report 1810) and most started in winter. They left him "wasted," "weak," and "aged."

Systemic and Neurological Disturbances

Attacks were ushered in by cold, cough, and malaise, quickly followed in the first attack by anginoid pains ("stitches in the breast") and in all others by abdominal colic with constipation ("very acute pain in the pit of the stomach shooting to the back and sides"); tachycardia up to 144 beats a minute; hoarseness (his voice "croaking," "rasping," "hardly audible"); painful weakness and stiffness making him unable to walk and even stand unaided or hold a cup or pen; tormenting "cramps"; paraesthesiae ("complained of heat and burning"); hyperaesthesia (could not bear the touch of clothes or bedding, wig or tie); hypalgesia ("scarce sensible of the Blisters applied to His legs").

There were episodes of generalized "tremor"; localized pain in head, face, and neck; dysphagia ("foaming at the mouth," "tasted his food but could not eat"); visual disturbances ("could not read"); and in his last illness nystagmus ("eyes exhibit rapid vibrations"); he was also "dizzy," "speechless," and incontinent.

Vasomotor disturbances were marked with profuse sweating and suffusion of the face ("he changed countenance and flushed so much that water stood in his eyes from the excessive heat"). At times he had oliguria, polyuria, polydipsia, pale stools, swelling of legs and feet, and once "great weals on his arms."

Cerebral Involvement

Simultaneously signs and symptoms of encephalopathy appeared: agitation, talking "with uncommon rapidity and vehemence," sensitivity to light and sound, emotional lability, uninhibited behaviour, and nocturnal confusion. Total insomnia supervened; at one time he had no sleep for 72 hours, at another he rambled incessantly for 26, and to his death his physicians reported his sleep in quarters of an hour. "Great irritability of frame and temper" was accompanied by "turbulence" and frank delirium: "he baffled all attempts to fix his attention," showed "gross errors of judgment," was aimlessly "occupied adjusting his bedclothes" or "sorting his papers."

Illusions, delusions, and hallucinations followed: "impressed by false images," "continually addressed people dead or alive as if they were present," lived "in a world of his own," "delirious all day," "engrossed in visionary scenery," "his conversation . . . like the details of a dream in its extravagant confusion," "total alienation."

"Extraordinary excitement and irritation" led to "stupor," "insensibility," incontinence, and convulsions, so that his physicians feared "a paralytic stroke" or "imminent dissolution."

Last Years

As age and illness took their toll he became more "tranquil," "cheerful and good-humoured" or "trifling and silly," "tears and laughter in quick succession." Two delusions, fleetingly expressed in 1788, came to the fore, one connected with Lady Pembroke, the other with Hanover: "His Majesty's adherence to certain erroneous notions with some degree of consistence partakes of the true character of Insanity," noted Heberden in 1811.

Blindness attributed to cataract became complete about 1812 and later he also went deaf. Long periods of being "silent and weak on his legs" were interrupted by paroxysms of abdominal and limb pains of which "he complained loudly," hoarseness, tachycardia, and insomnia accompanied by "great perturbation in his system." In his last attack, one month before he died, he spent 58 hours without sleep and gave other "remarkable proof of the extraordinary energies of his constitution." Thereafter he sank and quietly "expired without pain."

Suddenness of Change and Insight

"Throughout this long and severe illness the suddenness of opposite changes has been frequent and most remarkable," wrote Greville. One morning in November 1788 he was "composed, conversed with very little inconsistency," and in the afternoon "more agitated than ever, pulse very quick, determined frenzy." In July 1811 he deteriorated so rapidly that his physicians at Windsor, in their "very great anxiety, found it absolutely necessary to give some written account of the King at the door of the Castle" without waiting for sanction from Whitehall.

On his recovery in 1765 he requested parliament to make provision for a regency in case "it should please God to put a Period to my Life, whilst my successor is of tender Years." After severe attacks he realized that he had "lost track of time and events," as he told his friend George Rose. At the beginning of the 1801 attack he confided to the Reverend Thomas Willis: "I do feel myself very ill, I am much weaker than I was, and I have prayed to God all night that I might die, or that He would spare my reason . . . should it be otherwise, for God's sake keep from me your father [Dr. Francis Willis]." And on recovery he wrote to his friend Richard Hurd, Bishop

of Worcester, that he had "after a most tedious and severe illness . . . most wonderfully escaped the jaws of death . . . though I cannot boast of the same strength and spirits I enjoyed before."

Treatment and Restraint

No account of the illness can disregard the king's treatments and how far the "turbulence" he displayed were provoked by the repressive, coercive, and punitive methods by which he was ruled. In 1788 the senior Willis boasted to the king's equerry that "he broke in [patients], as horses in a menage." For any non-compliance, as refusing food, not going to bed, or throwing off his bedclothes, he was clapped in a "winding sheet," or a restraint chair which he bitterly dubbed "his coronation chair," or mostly in a straitwaistcoat with his legs tied to the bed. "His Majesty quarrelled with His tea and dinner and was confined"; "He threw off His wig and tie and resisted them being replaced and was restrained," read typical entries in the log of the Willises.

Besides mechanical restraint he was subjected to a medicinal regimen to bring down his "fever" and "turbulent spirits." He had to submit, often only after "a formidable struggle," to vomits, purges, bleeding, blistering, cupping, the application of leeches, and so on. In the last illness Drs. Baillie, Heberden, and Halford repeatedly protested to the Archbishop of Canterbury, as head of the Queen's Council, against "the unvaried tediousness of His silent and solitary confinement" enforced by Dr. Willis's sons, Robert Darling and John, to "minimise excitement." They pleaded for "a milder and more liberal system of management," and that the king should at least be permitted to "converse." "He has been kept in unedifying confinement and seclusion," wrote Heberden in September 1811, which had itself "become a source of irritation" and excited "a fresh accession of His disorder." That harsh treatment and enforced inactivity make violent and mischievous patients was only learnt later in the 19th century—in the king's time his obstreperous behaviour was taken as the ebullition of furious mania and his violent dislike of the Willises as delusional.

Acute Intermittent Porphyria

The clinical picture revealed by the physicians' daily record makes the diagnosis of manic-depressive psychosis untenable. Evidently his excitement lacked the cardinal feature of exaltation (Kraepelin, 1921), and his physical sufferings were an integral part of the illness.

By the triad alone of abdominal symptoms, polyneuritis, and mental disturbance the condition is at once recognizable as acute intermittent porphyria.³ Reviewed in this light the symptomatology and course of the royal malady reads like the description of a text-book case: colic and constipation; painful paresis of arm and legs; vocal paresis, visual disturbances and other signs of bulbar involvement; radicular pain; autonomic disturbances with marked tachycardia and sweating attacks; and encephalopathy ranging from insomnia to excitement, raging delirium, stupor, and fits. The only feature not recorded is hypertension, because blood-pressure was not measured, but the repeated crises threatening "a stroke" may have been hypertensive.

In keeping with acute intermittent porphyria are also: age of onset; attacks precipitated by mild infections; rapid fluctuations; protracted convalescence; excess of symptoms,

³ Lead poisoning, which also causes colic, palsy, and encephalopathy, can be excluded by absence of anaemia and presence of tachycardia; and distinct attacks over many years without other members of the household being affected. Nor would Sir George Baker have missed plumbism, since it was he who demonstrated that lead poisoning was the cause of "the endemic colic of Devonshire" (1767).

and hence complaints, over signs which make patients appear demanding, irascible, and difficult to manage.

The commonest misdiagnoses to-day were also considered in the king's case: biliary colic for abdominal pain; rheumatism for neuropathy; psychosis for encephalopathy. Of Goldberg and Rimington's (1962) 50 patients 29 had mental symptoms; 14 were "depressed, nervous, hysterical, lacrymose, peculiar"; 9 "confused, hallucinated, disorientated"; 6 "legally certified." According to Saint (1963) patients "show any of the stigmata of acute toxic confusion psychosis, displaying agitation, sleeplessness and hostility towards the medical attendant, and suffering visual or auditory hallucinations." Five of his 16 patients had been admitted to mental hospitals with diagnoses of "depression, schizophrenia, delirium tremens, and acute anxiety state." Holt's (1963) description of a patient in an attack as "ill, paralysed, delirious, and in agonising pain" exactly fits George III.

Urinalysis

To-day the diagnosis would be clinched by finding abnormal metabolites in the urine or observing its characteristic blue, blood-red, purple, or "dark" colour. Though one could hardly hope that such an observation, even if made, would have been recorded, we succeeded in locating four references to discoloured urine: 18 October 1788, Sir George Baker: "urine bilious" (Diary); 6 January 1811, Sir Henry Halford: "The water is of a deeper colour—and leaves a pale blue ring upon the glass near the upper surface" (Willis MSS.), and 14 January 1812, "Bluish 8 and 9 [ounces]" (Royal Archives); 26 August 1819, report of Drs. Baillie and John Willis: "His Majesty has passed . . . bloody water . . . during the last 16 hours," of which "no tinge" remained the following day (Queen's Council Papers; Willis MSS.). All these observations were made during paroxysms when the excretion of porphyrins and porphobilin-like chromogens is known to be greatest.

Inborn Error of Metabolism

Acute intermittent porphyria is usually transmitted as a Mendelian dominant, and in a patient so severely ill as George III one would expect other members of the family to be affected (Waldenström, 1937). To review the medical history of the House of Hanover is, however, a major task if only because of the number of probands (George III's father was one of eight children, George III one of nine, and himself the father of 15), many of whom lived abroad. But one outstanding case was his youngest sister, Caroline Matilda (1751–75), the hapless, banished queen of Denmark and Norway.⁴

The mysterious illness to which she succumbed within one week in her 24th year started with malaise, followed rapidly by paralysis of legs, arms, and bulbar centres, so that in her last hours she lay motionless, and though conscious was able to communicate only by moving her eyes. There was no fever but tachycardia of 133 before the pulse became uncountable. She had had two similar, milder yet "dangerous" attacks before. Her puzzled physicians thought she had died of a malignant throat infection which impeded articulation, swallowing, and breathing. But since there was no other case, it was rumoured that she had been paralysed by poison. To scotch this depositions were taken from eye-witnesses, and these allow the diagnosis to be made to-day (N. W. Wraxall, 1799; C. F. L. Wraxall, 1864).

The picture of acute ascending paralysis is not uncommon in fulminating porphyria. Interestingly she manifested the disease at the same age as her brother, whom she also resembled in features and in "a degree of quickness" of speech.

⁴ Two sibs overtly affected among nine (three of whom died in their teens) would in fact accord with the transmission of a dominant character.

Summary and Conclusions

This study allows the certain conclusion that George III'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 to-day fully understood. Moreover, the royal malady is unique for the continuity of its documentation over 58 years—indeed, in the last illness four of the physicians who had attended the king in earlier attacks had been replaced by their sons.

The assumption that the king was "neurotic" will also have to be revised, since porphyria may render its victim restless, hurried, agitated, and impulsive, especially in minor attacks which go unrecognized. Finally, by implication this diagnosis clears the House of Hanover of an hereditary taint of madness imputed to it by the long-sustained but erroneous interpretation of George III's illness.

The extract from Sir Henry Halford's clinical journal, which is in the Royal Archives, was supplied to us, and is now published, by gracious permission of Her Majesty the Queen.

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Mineral Metabolism in Mania

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In a previous paper (Coppen and Shaw, 1963) we showed that depressive illness is associated with a considerable increase in residual sodium (intracellular and a small amount of bone sodium), which returns to normal after recovery. We have now extended these investigations to patients suffering from mania. This paper reports our findings in this condition and also in some of these patients who had recovered from their illness or who had swung from mania into depression. We have also compared these findings with our previous results in depression.

Methods

Twenty-two patients suffering from mania who were admitted to Graylingwell Hospital during a 12-month period were selected for this investigation on the basis of the diagnosis of mania which was made by the consultant psychiatrist in charge of the case and was confirmed by another consultant psychiatrist. Details of age and sex of the patients are shown in Table I. Those patients who were suffering from physical illness, or were over the age of 75, or had taken lithium during the six weeks prior to admission were excluded from the study. One woman who developed diarrhoea and vomiting during the initial illness tests has been rejected from the series. All patients ate a normal ward diet and were up and about the ward and hospital for at least three whole days prior to the initial biochemical test.

The biochemical tests were carried out on the first Friday after admission and were repeated four weeks later if the patient was still in hospital. Height was measured on admission and the weight was recorded on the morning of the tests. Clinical assessments were made at the same time as the biochemical tests, but the results were analysed in different centres and were not compared until the investigations on all patients had been completed.

Two methods of assessment were employed on the first and fifth Tuesday and Friday after admission. One of us (R. C.) assessed each patient for mood, activity, and talk by means of

a nine-point scale for each factor. The second method was to give part of the Hildreth feeling and attitude scales (Hildreth, 1946). As the two feeling scales are the most effective in discriminating between normal and affectively disturbed patients (Fisher, 1949; Campbell, 1957; Shapiro, Campbell, Harris, and Dewsbury, 1958), we used these in the assessment of mood. Each scale consists of 10 statements: the patient was asked to tick the phrases which described his feelings most closely at that particular time. The statements in the feeling scales contain ones which would be chosen by depressed, normal, and elated subjects. Each choice has an empirically determined weight ranging from 0.1 to 9.6.

In feeling scale 1 we found that one of the higher-scoring "manic" responses—"swell"—was not used at all by the patients, probably because it was an Americanism avoided by even the most exuberant patient. This disturbed the balance of the scale, so the results were analysed on feeling scale 2 alone. Patients scoring between approximately plus or minus one standard deviation from the mean for normals (5.90; Campbell, 1957) were regarded as normal. Those scoring below 5.1 were regarded as depressed and those above 6.9 as manic. Manic patients vary rapidly in clinical condition, and therefore the biochemical tests were compared with the Hildreth and clinical assessments performed on the same day. It will be seen that nine patients had changed rapidly after admission and were no longer rated manic on the occasion of their first biochemical tests. The clinical assessment and the classification according to the Hildreth scale showed good agreement but the results were analysed according to their classification on the Hildreth.

The distribution of electrolytes was determined as described previously (Coppen and Shaw, 1963) with the exception that exchangeable sodium was estimated from both urine and a 1 in 3 dilution of plasma. Close agreement was found between these duplicate estimations.

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