THE ORIGIN AND SPREAD OF DEMENTIA PARALYTICA

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PART I

DEMENTIA paralytica[1] is a declining disease. Deaths due to it in England and Wales were first recorded by the Registrar General in 1901 and since that year, when the number was 2,272, the annual figure has fallen steadily until in 1957 it was only 68. Moreover, there is evidence (adduced below) that not more than a small part of this decline can be attributed to improvements in medical treatment. The fear that there might be a recrudescence of dementia paralytica as a result of the spread of syphilis during the second world war has not so far been realized and it seems likely that what is now, in Great Britain at all events, an obsolescent disease will soon become a rarity. Yet there are many unsolved problems in its history. We do not know, for example, why the alleged references to this striking disease were so few and so inadequate until the third decade of the nineteenth century. We do not know why its recognition in many countries was so tardy in spite of the clear description given by the French alienists. Nor do we know why the disease, which at the start of the nineteenth century seems to have been predominantly one of males, has gradually—and at different rates in different countries—become much more evenly distributed between the sexes.

The principal aim of the present essay is to recall some aspects of the history of dementia paralytica. It is a history of which psychiatrists may very properly be proud but which, perhaps, is less well known in general medicine than it deserves.[2] A modern Oxford historian has observed that, as all history

[1] The disease which all English-speaking physicians recognize by the term "general paralysis of the insane" or "G.P.I." has suffered from a plurality of names. Calmeil, in 1826, called it "paralysie générale des aliénés", which was no doubt an improvement on Bayle's "arachnitis chronique" of 1822, in that it did not assume an unproved pathological cause. But later, when Baillarger and others believed they had discovered cases of general paralysis without insanity, a new name seemed necessary, and Falret in 1853 advocated "folie paralytique". However, Calmeil's term was by that time fairly entrenched and remained the favourite in spite of Salomon's quip (1862) that "he who is generally paralysed is certainly dead". Salomon suggested the alternative "general paresis"—a term which has enjoyed a considerable vogue in America. Mickle, in his authoritative English textbook on the subject (1880), gave a list of eight English and nineteen French synonyms, but his book is still entitled *General Paralysis of the Insane*. Krafft-Ebing and other German writers favoured the name "dementia paralytica"; and in adopting this name, which I believe to be the most satisfactory one, I have had in mind not only that it over-rides the barriers of national language but also that (*a*) Salomon's criticism of the term "general paralysis" is unanswered, (*b*) the word "insane" is a legal rather than a medical term and has since 1930 been largely expunged from English statutes, and (*c*) the criticism that the initial letters of dementia paralytica may be confused with those of dementia praecox is no longer a valid one. Yet during the period with which this essay is mostly concerned (that is, broadly, the nineteenth century), "general paralysis of the insane" or more simply "general paralysis" was the common English usage.

[2] It has been strangely neglected by the historians of medicine. Neither the early history of the disease nor the name of Antoine Bayle (who is universally credited with the principal part in its delineation) are so much as mentioned in the histories of Garrison (1929), Guthrie (1945), Castiglioni (1947) or Major (1954); and there is only a passing reference in Mettler (1947). Henry, in his *History of Medical Psychology* (Zilboorg and Henry, 1941) gives a good account, but the story should have a place in the general history of medicine.

must be a selection from the facts, its presentation is often made more pointed by ordering the facts to illustrate some general theory or interpretation of the events. In the hope of adding new interest to an old tale, I have adopted this method and shall bring forward evidence to suggest: first, that dementia paralytica, from being a rare disease or even non-existent, suddenly assumed epidemic prevalence in northern France soon after the Napoleonic wars; second, that from France the new disease spread slowly across Europe and to the New World, gradually changing in its clinical manifestations; and third, that over and above the effects of treatment and prevention there has been a natural decline in its prevalence during the past fifty years. As far as they can be upheld, these points will support the well-known hypothesis that dementia paralytica is due to a special "neurotropic" strain of the syphilitic virus, for they will allow us to put forward the view that a mutation giving rise to the neurotropic strain occurred in northern Europe towards the end of the eighteenth century; that the spread of this mutant strain explains to some extent the curious time lapse before the disease was recognized in other countries; and that, comparably with the great epidemic of syphilis in the late fifteenth century, the new disease slowly changed in its prevalence and clinical manifestations.[1] It must be admitted that the neurotropic hypothesis has never had a great appeal for the best authorities on the subject. Nevertheless, it has not been discredited and still provides a possible explanation of some of the historical facts about dementia paralytica which are otherwise very difficult to explain.

The clinical and pathological characteristics of dementia paralytica were first clearly delineated during the third decade of the nineteenth century by physicians working in the mental hospitals of Paris. These men took the view that the disease which they described had always been in existence and that it had simply escaped the notice of earlier workers. Thus, in his *Maladies du Cerveau* (1826, Introduction, p. xxiii), Bayle[2] says that chronic meningitis, which was very common in the insane and which he first described in 1822, "had never been noticed before". Georget (1820, p. 130) simply states that among demented patients "the commonest disorder of muscular power is weakness, general or partial, of voluntary movement" and makes no suggestion that there has been a recent increase in prevalence of this disorder. Calmeil (1826, p. 7) says: "The species of paralysis that I wish to describe under the title of general paralysis of the insane is far from rare; however, as far as I know, its natural history has not yet been traced in detail." By the time Esquirol wrote his *Des Maladies Mentales*, dementia paralytica had become a well-recognized condition; yet he refers (1838, vol. 2, p. 263) to the writings of Calmeil and Bayle as only confirming "the sad truth to which I drew attention in 1805" (which was, the incurability of insanity complicated by paralysis), and this observation does not suggest that Esquirol thought there was anything

[1] The view that the fifteenth century outbreak of syphilis was due to a mutant strain of the spirochaete has been succinctly put in the *Lancet* (1957). See also Hirsch (1885), Mott (1908), Morris (1912), Sudhoff (1926), Whitwell (1940), Lees (1950). Some of the arguments for and against the neurotropic hypothesis of dementia paralytica are summarized by Hutton (1941) and Wilson (1941, Vol. I, Ch. 17). Curiously, however, neither of these writers makes reference to the suggestive (though limited) epidemiological evidence mentioned in support of the hypothesis by Stewart (1924). The present essay is, in one sense, an attempt to add to this epidemiological evidence.

[2] The life, character and works of Bayle and of other eminent French psychiatrists have been described by René Semelaigne (1894, 1930). The relevant parts of Bayle's inaugural thesis of 1822 on which rests his claim to have given the first clear description of dementia paralytica have been translated into English by Moore and Solomon (1934).

new in the occurrence of paralysis in the insane. This belief in the antiquity of dementia paralytica persisted through much of the nineteenth century. Writing what he claimed to be the first separate volume on the subject by a British author, Thomas Austin states (1859, p. 1), "General paralysis, though it had doubtless existed from the earliest period of insanity, eluded observation or at least never so fixed the attention of those who must have witnessed it, as not to be recognized and described as a distinct disease till the early part of the present century." Sankey, that sound and erudite lecturer on mental diseases to University College, London, says (1866, p. 178), "It is quite a settled point that the disease was not recognized till a comparatively recent date but distinct allusions to the symptoms may be found in authors of very ancient times"; and he later gives his opinion that the "apparent novelty" of the disease is largely due to slowness in its recognition. Writing the chapter on Progressive General Paralysis in Charcot's *Traité de Médecine*, Ballet and Blocq (1894) observed that—"The discovery of general paralysis as a distinct disease with its own characteristic lesions . . . dates from 1822 . . . Before this, general paralytics had been observed and certain peculiarities of their illness noted, but no one had thought to isolate it as a morbid entity distinct from other nosographic species recognized at the time."

Yet there is strong evidence, marshalled by Kraepelin (1913, p. 163; 1927, p. 1135), that dementia paralytica must in fact have been rare before the Parisian outbreak. We may therefore consider why the earlier writers should have taken the view that it had always been prevalent, a view not uncommonly accepted even today. Two reasons may be brought forward. In the first place, it was generally believed during the eighteenth century that diseases, like plant and animal species, were fixed and immutable. The works of Linnaeus had encouraged naturalists to study with increased attention the attributes of living organisms so that each could be classified into its particular species, order and genus. This stimulus soon spread to medicine and the study of *nosography*, the classification of diseases into distinct and related types, became a popular and respected specialty.[1] But in the days before Darwin and Wallace it would not have occurred to the physician that a disease (especially a chronic disease) might arise *de novo* any more than the naturalist would have expected to find a newly created species. In the second place, the syphilitic origin of dementia paralytica was unsuspected or unproved during the nineteenth century; the principal causal factors were thought to be alcoholic and sexual excess, and those who upheld this view could scarcely have believed that the disease was a new one in history.[2]

[1] What Linnaeus had done for botany and Cuvier for zoology, Cullen of Edinburgh (1769) attempted for general medicine and his pupil, Thomas Arnold, for insanity. Arnold's *Observations on Insanity* (1786) does not appear to have exercised much influence on his contemporaries and remains a curious relic of the attempts to classify on philosophical grounds "those disorders of the *mind* which still resist the discriminatory powers of our scientific age". Philippe Pinel, a friend of Cuvier, also published a classification of mental diseases, but though his *Nosographie philosophique* (1798) proved in the end as sterile as Arnold's *Observations*, these works may serve to indicate one significant point: that during the latter part of the eighteenth century, mental disorders were carefully studied with a view to the classification of syndromes and we may pardonably be astonished that so striking a disease as dementia paralytica, if it had been anywhere near as prevalent as it later became, could have escaped notice.

[2] Maudsley was the weightiest proponent of the theory of sexual excess. In the first edition of his *Physiology and Pathology of Mind* (1867, p. 360) he takes the very moderate view that the commonest cause of dementia paralytica is intemperance, alcoholic or sexual, and, acknowledging that these are nevertheless not infrequently absent, adds that then "some sort of hereditary taint is likely enough to be present". In 1873 his views are more definite and his contribution to an aetiological discussion is reported in the *Journal of Mental Science* (1873)

The nineteenth century belief that dementia paralytica had always existed led to search for descriptions of its symptoms and signs in the writings of earlier physicians. A consequence of this search is the frequency with which Thomas Willis is quoted as having given the first description in 1672. The evidence for his claim is worth re-examining. I have been unable to discover who first drew attention to the relevant passages in the *De Anima Brutorum*, but Sankey (1864) refers to them and thereafter most writers, especially English ones, quote them as a matter of course.[1] The passages are as follows:

"I have observed in many that when, the Brain being indisposed, they have been distemper'd with a dullness of mind and forgetfulness, and afterwards with a stupidity and foolishness, after that have fallen into a Palsie, which I oft did predict; to wit, the Morbific matter being by degrees fallen down, and at length being heaped up somewhere within the Medullar Trunk (where the Marrowy Tracts are more straitned than in the Streaked Body) to a stopping fulness. For according as the places obstructed are more or less large, so either a universal Palsie, or an half Palsie of one side, or else some partial resolutions of members happen . . .

"The oppilative or stopping Particles being fallen down from the Brain and carried forward into the oblong Marrow, enter into the Nerves destinated to the Muscles of some parts of the Face, and by obstructing the ways of the Spirits in them, bring forth the Palsie in the Tongue, and sometimes a loosening of these or those Muscles of the Eyes, Eye-lids, Lips and other parts."[2]

It is, in truth, hard to see why this extract should have come to take so prominent a place in accounts of the history of dementia paralytica. A "half palsie of one side" or palsy of the tongue and eyes are not at all characteristic of the disease; Griesinger (1861, p. 396) for example says, "It is only in exceptional cases that we observe greater weakness in one half of the body, an inclination of the tongue to one side, obliquity of countenance . . . Strabismus and disorders of movement of the eyes generally scarcely ever occur." Much of the description would fit the case of arteriosclerotic dementia with its slowly progressive amnesia punctuated by cerebro-vascular attacks associated with paralysis. Certainly, of the illustrative case histories which Willis gives later (pp. 174–6), most show either intra-cerebral haemorrhage at post-mortem or a satisfactory response to treatment. A scrutiny of the rest

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thus: "He would by no means venture to say that sexual excess was the sole or entire cause of general paralysis . . . but of the efficiency of sexual excesses as an exciting cause he entertained no doubt"; the excesses he had in mind were not sudden outbursts of sexual activity but "that quiet steady continuance of excesses over months or years, by married people, which was apt to be thought no vice or no harm at all." By 1879 (*Pathology of Mind*, 1st edition, p. 432) his opinion on the most frequent exciting cause is—"Sexual excess I hold confidently to have that evil pre-eminence"; and in 1895 (2nd edition, p. 465): "Were it right to ascribe it to any single cause, I should fix on sexual excess and still hold the opinion despite the dissent of those inquirers who find no evidence of such excess." Although, from our later knowledge, these extracts might tempt us to reflect on the puritan strain in Maudsley and on the Victorian attitude to sex, yet, until the weight of evidence associating dementia paralytica with syphilis became overwhelming, the theory of sexual excess explained the facts as well as any other theory and better than most. At times, however, the attempt to reconcile fact and theory strains even Maudsley's ingenuity: commenting on the rarity of general paralysis in the highlands of Scotland, "where there is of course no deficiency of women or whisky", he asserts that an open-air life and "a great deal of bodily exercise" make people less likely to be provoked into excesses and more capable of withstanding them.

[1] Mickle (1880, p. 2) assigns the chief merit of the discovery of general paralysis to "Willis, Haslam, Bayle and Calmeil, especially the first three". I doubt whether any Frenchman would agree.

[2] Most writers quote in the original Latin, but for the benefit of those whose Latin is as rusty as my own, I give the translation made by Samuel Pordage in 1684. The "streaked body" is, of course, the corpus striatum. Willis's explanation of paralysis is based on the theory that normal functioning of the nervous system depends on the unimpeded flow of vital spirits from the brain down through supposed channels in the nerve tracts. A "morbific" process manifested itself by the generation of "stopping" particles (or "oppilative" particles, from the Latin, *oppilare*, to stop up) in the brain, and these, carried down into the narrower nerve channels, tended to clog them and so impede or prevent the flow of vital spirits.

of the chapter shows that Willis's concept of "palsie" was a wide one and included simple exhaustion and weakness. "Long and immoderate sadness, a Consumption, a Scorbutic Atrophy or wasting, being long fixed in Bed, unhealthy old Age . . . at length brings on a *Palsie*" (p. 165). Again, on a different aspect, he says (p. 166), "They who are frequently and grievously obnoxious to the Colick at length become also paralytic. The cause is so frequent here, that the succession of this Disease is accounted among its *prognosticks*." This passage may suggest lead poisoning,[1] but certainly not dementia paralytica. In the case of the "young and handsome woman" who, after suffering "a most cruel and continual Colick", became "molested with a stupefaction", Willis observes again that such distempers often forerun a "palsie", which indeed followed here so that "not only all her greater Members, as her arms and legs, but almost every lesser joynt or limb was almost wholly loosened that she could not move hand nor foot or the fingers or toes of either". Yet after a month or two the young lady recovered completely. From such examples we may reasonably conclude that Willis, in observing that states of "stupidity" were sometimes followed by "palsie", had in mind diseases altogether different from dementia paralytica. Moreover, if brief generalizations are going to be adduced as evidence for the existence of dementia paralytica, why pick on Willis? Other passages from much earlier writers might equally well be adduced. Thus Hippocrates (quoted by Whitwell, 1940) says, "Mental weakness associated with a shaking voice, a tongue and voice tremulous, indicates a grave form of mental disorder",[2] and Whitwell quotes similar passages from Celsus, Aretaeus, Galen and Avicenna; one from Boerhaave in 1761 seems closer to the mark than Willis's: "if in an apparently healthy young man noticeable tremor occurs about the lips or eyelids with stammer, then paralysis will follow and death from apoplexy." Such passages have been ignored (rightly enough), yet the references to Willis continue. Morton's *Medical Bibliography* (1954), for example, states simply that Willis's *De Anima Brutorum* "includes a description of general paralysis, probably the first definite recognition of the condition"; Garrison (1929, pp. 263 and 827) makes a similar assertion. These continued claims on Willis's behalf are the more surprising as they are contrary to the authoritative opinion of Robertson (1923); Robertson thought it "much more likely that Willis refers to senile or arteriosclerotic dementia". The fact is that no claim for the recognition of a disease can safely be based on a brief generalization; it must rest on detailed case-histories of which one *may* be sufficient but more than one is always preferable. Willis indeed gives us case-histories, but these serve only to weaken still further the claim that he described dementia paralytica.[3]

[1] Griesinger (1861, p. 172) wrote: "In lead poisoning the excitement passes frequently into stupor; besides, there are often cramps and paralysis: the prior existence of lead colic . . . may assist in forming the diagnosis". Meryon (1864), discussing a case of plumbism, says: "for nearly two years the characteristic colic of lead-poisoning preceded the paralysis; and such is the invariable course of the disease." In the seventeenth and eighteenth centuries, not only was industrial plumbism common but "outbreaks of lead poisoning occurred throughout Western Europe as the result of the addition of lead to wine to promote fermentation and because of its employment in the manufacture and storage of cider and in materials for cooking vessels and other household articles" (Cantarow and Trumper, 1944).

[2] Bucknill and Tuke (1858, p. 17) also refer to this passage from the *Corpus Hippocraticum*: "We might recognize here" (they say) "the symptoms of incipient general paralysis."

[3] That a single case may be sufficient is illustrated by another of Willis's case histories in the same chapter "On Palsie" of the *De Anima* (p. 167). The "prudent and honest Woman" with the "spurious Palsie" who, when she spoke too long or too eagerly, became as mute as a fish for an hour or two, must surely, as Guthrie (1903) pointed out, have suffered from myasthenia gravis.

A much more likely contender for the first English account of the disease is John Haslam, apothecary to Bethlem Hospital. In 1798 the first edition of Haslam's *Observations on Insanity* was published, and his Case 15 (p. 115) is usually upheld as the most convincing pre-Parisian description of dementia paralytica. Robertson (1923) says it "presents a clinical and pathological picture so typical that no one has ever doubted the diagnosis". Now we are told that the patient, a man of 42, admitted to Bethlem Hospital in 1795, "had some years before travelled with a gentleman over a great part of Europe" and therefore, if the case was one of dementia paralytica, we can imagine that he might have acquired the disease from the same source as, on our hypothesis, led to the Paris outbreak. On the other hand, we are dealing with an isolated case and authorities are in agreement (see, for example, Krafft-Ebing, 1894, pp. 75 and 78; Kinnier Wilson, 1954, Vol. 1, p. 553) that in any single instance the differential diagnosis on clinical and gross anatomical grounds between dementia paralytica and cerebral syphilis may be impossible; indeed, the facts that in Haslam's case the first sign of illness was a sudden headache and that the mouth was "drawn aside" are perhaps more suggestive of the latter condition. Moreover Leigh (1955) has commented on the post-mortem aspects of this case that "it is impossible to hold that he (Haslam) has given a recognizable description of the macroscopic anatomy of general paresis". A more serious objection to the establishment of our hypothesis is the much-quoted observation of Haslam on paralytic affections of the insane. The passage below is taken from the first edition (1798, p. 120) of the *Observations on Insanity*, the sentences in brackets being those added in the second edition (1809, p. 259).

"Paralytic affections are a much more frequent cause of insanity than has been commonly supposed (and they are also a very common effect of madness; more maniacs die of hemiplegia and apoplexy than from any other cause). In those afflicted from this cause we are, on inquiry, enabled to trace a sudden affection, or fit, to have preceded the disease. These patients usually bear marks of such affection, independently of their insanity: the speech is impeded and the mouth drawn aside; an arm or leg is more or less deprived of its capacity of being moved by the will; and in by far the greatest number of these cases the memory is particularly affected. (Persons thus disordered are in general not at all sensible of being so affected. When so feeble that they can scarcely stand they commonly say they feel perfectly strong and capable of great exertions. However pitiable these objects may be to the feeling spectator, yet it is fortunate for the condition of the sufferer that his pride and pretensions are exalted in proportion to the degradation of the calamity which affects him.) Very few of these cases have received any benefit in the hospital; and from enquiries I have been able to make at the private houses where they have been afterwards confined, it has appeared that they either died suddenly from apoplexy or have had repeated fits from the effects of which they have sunk into a stupid state and have gradually dwindled away."

This passage is usually taken to indicate that dementia paralytica must have been common at Bethlem Hospital as early as 1798; but I shall attempt to dispute that view.

First, Haslam's description differs in many respects from the classical descriptions of dementia paralytica. In dementia paralytica, the mental changes are usually observed before, not after, the onset of paralysis; the paralysis develops gradually, not suddenly; it is rare for a single limb or the ipsilateral limbs only to be involved; and while apoplectiform fits are common, persistent hemiplegia is rare and death in apoplexy is also rare. As the clinical signs of dementia paralytica have changed somewhat during the past century, I will support my assertions by quoting from early, but authoritative, writers. As regards the relation between the time of onset of the mental and of the paralytic

symptoms, Calmeil (1826, p. 336) says that "at Charenton, paralysis almost always appears after the onset of the mental disturbance", and Prichard (1835, p. 106) says: "It results, from a great number of observations purposely made by MM. Calmeil, Esquirol and others, that general paralysis commences sometimes long after mental derangement; in other instances simultaneously with it; while in comparatively a few cases it precedes the manifestation of disorders in the mind." As regards the mode of onset of the paralysis, the disease runs its course "gradually and even slowly, the symptoms appearing and developing themselves in a regular succession" (*ibid.*, p. 105). As regards the mouth, Calmeil (1826, p. 10) says that the mouth and face preserve their natural position, and Westphal (1868), who gives a very careful and thorough account of the motor symptoms of dementia paralytica, says, "Unilateral paralyses of the tongue or of the face either do not occur at all, or, where they have been observed, play but an unimportant part in so far as they exhibit as a rule merely transitory, suggestive and incomplete phenomena." Westphal also observes that the apoplectiform and epileptiform attacks of dementia paralytica frequently result in unilateral or bilateral paralyses but "all these paralyses have the peculiarity that they very soon, in the course of a few hours or days, either entirely or almost entirely disappear . . . In exceptional cases they remain persistent." As regards hemiplegia and apoplexy as a cause of death, Skae (1860) examined 78 patients dying of dementia paralytica but could attribute only one death to apoplexy and one other to exhaustion from a succession of epileptic fits; Calmeil (1826, p. 79) had earlier said that death seldom follows as the simple consequence of cerebral disease.

Second, Haslam's remarks could equally well be taken to apply to other diseases, notably chronic alcoholism. "Of all forms of chronic insanity", Griesinger (1861, p. 570) wrote, "drunkenness especially appears to possess much in common with general paralysis"; and indeed the similarity gave rise to the name "alcoholic pseudo-paresis". We know, too, that chronic alcoholism had become very common in England towards the end of the eighteenth century from the recently developed habit of dram-drinking, and its mental effects were far more common than in France, where wines rather than spirits were the national beverage. Thus Prichard (1835, p. 204) says, "Drunkenness is a much more prevailing vice in England and in Germany than in France, Italy and Spain . . . In public lunatic asylums in England, it is generally known that, in a great proportion of cases, dram-drinking is the exciting cause." In 1844, this proportion was given as 18 per cent. by the Lunacy Commissioners (Bucknill and Tuke, 1858, p. 44), though at Bethlem Hospital Sir Alexander Morison found it only 12 per cent. However, to quote Griesinger again (1861, p. 171), "it is generally recognized that in later times the abuse of spirits in England has very much diminished". We may conclude that insanity due to alcoholism must have been very common in England in Haslam's time; moreover, the increase in prevalence had only recently occurred, so that the cause of the associated dementia and paralyses might often have been missed.

Third, the case records of Bethlem Hospital have been preserved (though somewhat incompletely) since the year 1816 and provide original and impartial evidence on the frequency with which paralysis was diagnosed by Haslam's immediate successors. I have examined these records for the three years 1816 to 1818 and find that, of 295 cases admitted during those years, paralysis or a "suspicion of paralysis" is mentioned in 19 (16 male, 3 female). However, the word "paralysis" is clearly used in the same loose sense in which Willis used it.

Any weak, stuporous or troublesome patient was liable to be called paralytic.[1] Thus a 60-year old ironmonger remains "motionless and silent . . . like an immovable statue" for many months, though his health and appetite are good; yet Dr. Tuthill says, "from the extreme slowness of manner and dumbness of this patient, I apprehend something of a paralytick nature has already taken place". A sailor aged 22, suddenly taken ill seven months before admission, is "occasionally violent, threatens to hang himself, swears a great deal, is dull and heavy but in good health"; Dr. E. T. Monro then notes that "some suspicion of paralysis is to be attached to this case and more especially as he appears to have been wounded in the head". A lace-maker of 46 becomes weak and tremulous and develops anasarca of her legs: she is reported as "dropsical or paralytick" and is later said "to be approaching a state of paralysis or to have already suffered from it". It is noteworthy that, of the 16 males described as paralytic, three were innkeepers. Four of the 19 cases are said to have had exalted or grandiose ideas and one of these was an innkeeper. Altogether, I think the diagnosis of dementia paralytica can be seriously considered only in 5 cases (though a further 4 cases, of which the notes are perfunctory, could possibly have been paretic). Of these 5 cases, one is under some suspicion on account of his youth (26 years)—another because he was, after a year's stay in the "curable establishment", accepted as a chronic patient (which implies that he had violent or dangerous propensities). I conclude that, although the occur-

[1] There was a rule at Bethlem that patients who developed fits or became paralytic could be discharged immediately as incurable. In the Minutes of Evidence of the Committee appointed by Parliament in 1815 to consider the better regulation of madhouses in England there occur the following curious exchanges, which suggest that a diagnosis of "paralysis" might be no more than a mere administrative convenience. The Committee were questioning Wallet, at that time steward of Bethlem Hospital, concerning the early discharge of patients subject to fits or paralysis. Wallet replied (p. 64):

"—I remember a woman who was discharged as paralytic, who came from Hoxton; the nurses said at the time that she was the strongest patient in the house; she was returned to Miles's.

Do you know Sarah Payne?—Yes.

Was she a strong healthy-looking person?—Very much so.

Was she a violent patient?—She was.

By whose order was she sent to Hoxton?—She was discharged by the medical gentlemen as paralytic.

Had she any paralytic attack during the time she was in the Hospital?—I never heard of any attack.

Had she, in your opinion, the appearance of a person who suffered under paralysis?—I do not know that she had; I saw the difficulty they had in taking her away, in putting on a strait waistcoat; she was very strong."

The matron of Bethlem, Elizabeth Forbes, was also questioned on Sarah Payne (p. 76):

"While she was with you, had she any paralytic attack?—She was much worse when she went back than when she came; she was more violent and unhappy and distressed, always asking if she was going to be murdered and such things; Mr. Haslam thought she was paralytic.

Had she a fit?—I never knew her to have a fit.

No contraction of limbs?—No.

No want of articulation?—No, not at all; but she was always kept handcuffed lately, and chained.

She was sent out in a considerably increased state of violence than when she came in?—Yes, which Mr. Haslam attributed to paralytic (sic.).

Was she very strong?—Very strong; it required three or four people to move her; she was brought to the side-room every day, but there was great difficulty in moving her, she wanted her liberty I believe."

Later still in the Inquiry, Haslam himself was questioned about Sarah Payne (p. 128):

"What became of her?—I do not know; she was discharged from the Hospital; she was paralytic.

She was discharged as paralytic?—She was in a general state of tremor. We apprehended she would soon die; she was incurable. Patients becoming sick and weak, and not being able to undergo the discipline of the house, are immediately discharged."

rence of dementia paralytica at Bethlem Hospital during this period was possible and even probable, it was certainly not common.[1]

[1] Of the nineteen cases stated to be paralytic, the three which seem to me the most suggestive of dementia paralytica are as follows:

(1) Male, age not stated, admitted 18 Jly. 1816.

"Disordered about 5 weeks. Was disordered 2 years ago and recovered. Talks incoherently —not mischievous. Comes from the Parish of New Windsor, played the Serpent in the Earl of Dartmouth's Band. Staffordshire Militia 2 or 3 years ago.

July 20th. A Tremor observable in this case with great incoherence of discourse. 23rd. From the evident tremor of his limbs and lips it is to be feared that Paralytick symptoms may come on in this case.

Aug. 3rd. He imagines that he is the greatest of singers and that he performs at Covent Garden Theatre every night at the present time. 15th. Remains as heretofore. 20th. Either he has already suffered some slight Paralytick attack or the probability is that he will suffer it ere long.

Sept. 10th. Remains in the same condition and is a hopeless case, I fear. 26th. Becomes worse—trembles much and stammers in his speech sometimes—is very much lost in his mind. Has very grand ideas—considers according to Dowie's account that he has four millions of money.

Oct. 30th. He continues to exhibit symptoms of some Paralytick attack which has deprived him of his intellect. He continually harps on his wealth and musical abilities. The use of Calomel keeps him in an equable state.

November. Evident symptoms of Paralysis exist in this case and the grand line of operation appears to be the prevention of any fresh accession of similar attacks. His health is pretty good at this time.

December. The imbecility of mind which accompanies or rather succeeds Paralytick symptoms was never more obvious than in this case. His answers to questions will vary every minute. He will call his wife by 3 different names and give the most incoherent account with a stammering and tremulous voice."

(No further notes.)

(2) Male, age 26, admitted 20.11.1817.

"Disorder'd six months. This is the first attack. He imagines himself a great Commander, being a Jew Lawyer.

Dec. At the latter end of this month, he faulter'd very much in his speech and was evidently partially Paralytick.

Jan. There can be no doubt that some slight degree of paralysis has occurred in this case. The stammering tongue, staring eyes, great incoherence of speech and general demeanour evince this plainly.

Feb. This patient shows repeated proofs of his having suffer'd from some attack of paralytick tendency. His spirits are ever good.

March. He continued very cheerful during this month altho' evidently shattered in his mind and Paralytick. He has an exceedingly good appetite, and is ready to shake hands with everybody. No coherence of speech.

May. It appearing that this patient was altogether paralytick, and that his malady arose solely from this cause, no prospect appearing of rendering him any advantage, he was this day (Discharged as an Improper Object.

(signed E. T. Monro)."

(3) Male, aged 40, admitted 2.7.1818.

"This man has been disordered only 4 months and married only 6 months. He has been 3 weeks at Mr. Pell's Somers Town. He has lived 8 years with Messrs. Rundell & Bridge, Ludgate Hill. He has attempted suicide and is a native of Scarborough. He has a brother who threw himself over Blackfriars Bridge. He had a most excellent character.

Aug. 22. This man has one of the most remarkable craniums Dr. Monro ever saw. There still remains a great propensity to suicide and he appears to be partially paralytick.

Sept. He has an idea that his food and everything else he takes is poisoned. He is a truly deplorable object in every respect.

Oct. A little improvement is observable in this case since the last account. He talks less and is not so much agitated in his general demeanour. He is described as cleanly in his person.

Nov. A very miserable object, decidedly liable to attacks of Paralysis. Stammers in his speech and is extremely confused in his ideas. Very zealous in defence of his master.

Dec. Troubled with a Dyarrhoea about this Period.

Jan 11. Died of Apoplexy.

Appearance observed on examining the Body, 11th Jan. 1819:

All the vessels of the Dura and Pia Mater were loaded with blood. The surface of the latter membrane was copiously moistened with a serous Effusion. The arachnoid coat was thick and opake over the convexities of the cerebral hemispheres, and the Texture of the Pia Mater generally distended with fluid. The lateral Ventricles were considerably larger than usual and contained an increased quantity of fluid; but they were not distended.

(signed Wm. Lawrence, E. T. Monro)."

Finally, it cannot be without significance that none of Haslam's younger contemporaries credit him with the discovery or even the description of dementia paralytica, although they were certainly well acquainted with his works. Burrows, commenting somewhat sceptically on Haslam's and Esquirol's assertion of the great prevalence of paralysis among the insane, says (1829, p. 175): "In adopting the term paralysis, as it occurs in connection with insanity, we are not sufficiently precise. Paralysis, like apoplexia, comprises very different states of disease."[1] A passage in Prichard's *Treatise on Insanity* suggests that the Bristol alienist's silence on Haslam was not mere oversight. Haslam had resigned his post as apothecary to Bethlem in 1815 but Prichard, writing of general paralysis in 1835 (p. 109), says, "At Bethlem I was assured by the house-steward . . . that he has in many instances recognized the early symptoms of this disease . . . The disease, as it occurred in Bethlem, is characterized by the same symptoms as at Charenton, viz. by imperfect muffling articulation, by tottering in the gait, weakness and inaccuracy in the voluntary movements. Monomania, with pride and the illusive belief in great possessions, is the mental disease which has been noticed in the majority of the cases." In his Croonian lectures of 1849, Conolly not only makes no reference to Haslam but says (p. 38), "it is extraordinary that scarcely a trace, if even a trace of a description of a paralysis, so distinct and peculiar in its character, should be found until we come to the writings of physicians yet living"; but Haslam had died in 1844. Bucknill and Tuke, in their *Manual of Psychological Medicine* (1st edition, 1858) do not mention Haslam in connection with general paralysis, nor for that matter do Falret (1853), Griesinger (1861) or Krafft-Ebing (1866). Baillarger (1860) referred to Haslam's case, but did not attach much significance to it as "very many similarly precise passages have been buried for centuries without being noticed until they were dug up by historians". In 1866 Sankey (p. 178) observes, though without further comment, that "to (Esquirol) is due the credit of attracting attention more pointedly to this disease, though Esquirol himself attributes the merit to Haslam".[2] It is from this time (so far as I can determine) that Haslam's claim begins to be more definitely and generally asserted, not only by English writers (Mickle, 1880, p. 2) but by the French (Bonnet and Poincaré, 1868, p. 4) and the German (Krafft-Ebing, 1894). Yet I cannot but think that the silence of Haslam's contemporaries,

[1] The terms *palsy* and *paralysis* have given rise to some confusion in the history of medicine. They have been used to cover: (*a*) general enfeeblement of movement arising from any cause (e.g. Willis's "being long fixed in bed"); (*b*) all degrees of muscular weakness attributable to special disease rather than to general debility (e.g. Parkinson's "shaking palsy"); and (*c*) complete or nearly complete loss of voluntary power (e.g. Salomon's usage, where the term *paresis* is reserved for partial loss of power). The Parisian physicians who described dementia paralytica were well aware of the semantic difficulty: Delaye in 1824 used the term "paralysie générale et incomplète" and Calmeil (1826, p. 9) adopted the shorter term "paralysie générale" only with reluctance and perhaps because (as Baillarger suggested) it was already in common use.

The term *general* as applied to paralysis was also a source of confusion. See an inconclusive discussion in the *Journal of Mental Science* (1896).

[2] Why, we may wonder, should Esquirol have credited Haslam with a discovery that Haslam's own countrymen denied him? Were it not out of keeping with the magnanimous character of that great Frenchman, we might be tempted to suppose a wish to attenuate the claims of the upstart Bayle, a young man who did not belong to the school of Pinel and Esquirol but had been trained in pathological anatomy by his uncle Gaspard Laurent Bayle and his uncle's friend Laennec. A more reasonable explanation, however, would be that Esquirol, who always thought of paralysis as only a complication of insanity, would have seen no reason to believe that the cases he saw in Paris and which were later delimited by Bayle and Calmeil differed in any fundamental way from other cases of paralysis in the insane already described by Haslam.

who knew and admired his work and who also knew the disease, speaks more eloquently than the historical researches of later times.

Willis and Haslam are, by common consent (at least in English-speaking countries), agreed to have the strongest of the claims put forward for a description of dementia paralytica before the Parisians. I will not, therefore, discuss the claims made for other early writers. Mönkemüller (1911), who studied the subject at the request of Kraepelin, found "only a few cases, mostly very disputable", in the records of the eighteenth and earlier centuries. Among the "Hundred Cases" published by Chiarugi in 1793, Meckel only detected "at least one undoubted case of general paralysis, perhaps even a second"; and Möbius made an interesting observation that during the eighteenth century no famous man died of any illness resembling dementia paralytica, although during the nineteenth century such instances were common—Schumann, Donizetti, Nietzsche and Maupassant, for example (Kraepelin, 1927, pp. 1135 *et seq.*). More noteworthy, perhaps, than the weakness of the positive evidence is the fact that so many able investigators said nothing which can be taken to indicate any acquaintance with the disease. Pinel himself, as late as 1809, when the second edition of his Treatise was published, makes no special mention of dementia in association with paralysis. Yet he was acquainted with Haslam's work (which he praises) and moreover Pinel was, until 1795, Physician to Bicêtre, the Parisian hospital for incurable male lunatics where, if anywhere at that time, dementia paralytica should have been common.[1]

This failure to describe dementia paralytica would—if the disease had been there to describe—be all the more surprising when we take into account the striking clinical syndrome which it commonly presented. Calmeil (1826, p. 326) found the peculiar delusions to be "*infiniment remarquable*". Conolly (1849, p. 39) makes the statement that "of all modifications of mental disorder, the form which is either accompanied from the first with that variety of paralysis which has of late years been observed and described as general paralysis, or eventually supervenes upon such bodily affection, is the most remarkable". Bucknill (1857) says, "The diagnosis of general paralysis is practically of the most facile sort" and "the form of intellectual disorder, moreover, is frequently of the most remarkable kind". Maudsley (1879, p. 432) says, "The group of cases described under this head (general paralysis) unquestionably constitute the most definite and satisfactory example of a clinical variety of mental disease." The egregious characteristics to which these writers draw attention apply principally of course to the grandiose type of dementia paralytica. This type was also called the "classical" type, partly because most of the cases described by Bayle (1826) were of this nature and partly because it was, during most of the nineteenth century, the commonest type.[2]

[1] Browne (1875) says, "It would be difficult to rest satisfied with the belief that, whatever may be the cause, general paralysis did not exist until about 50 years ago, or that it had entirely escaped the cognizance of physicians, general and special; yet it is certain that on examining the works left by Pinel and his predecessors it is impossible to discover any monographic description of this frightful affliction, now so readily detected and diagnosed, although these distinguished men had, for long periods, access to all the experience afforded in Asylums for the Insane." But the Scottish Commissioner in Lunacy cannot have it both ways; either the disease did not exist or it existed but was not recognized.

[2] Between January, 1815 and July, 1823, Bayle (1826, p. 568) collected 189 cases of "chronic meningitis" (i.e. dementia paralytica) among 847 male admissions, and 25 among 606 female admissions to Charenton. His excellent case histories are monotonously similar in their clinical features and no series like them had ever been described before. His patients govern the universe, have 40 million tons of gold, own marble palaces, or build a new paradise. It was, as Bayle says (p. 547), "toujours le même, d'idées dominantes de richesse, de grandeur, de puissance".

The great conceptual advance made by Bayle in 1822 was his belief that the mental symptoms of dementia paralytica and the associated paralysis were both the direct consequence of visible pathological changes in the brain and meninges. We may ask why, if dementia paralytica was always common, such an association between insanity, paralysis and brain change was not noticed earlier. That paralysis was the result of brain change, had of course, long been known, as Willis's cases sufficiently illustrate. The post-mortem examinations made by Chiarugi (Bayle, 1826, p. 383) and Greding (Prichard, 1835, p. 210) showed that vascular engorgement, thickening of the membranes, effusions between the dura and the pia mater and increased fluid in the ventricles were all common findings in the brains of insane patients. No doubt many of these changes were due to agonal infection, prolonged debility, fits, or old head injury; but in the brains of other cases which had shown similar mental symptoms nothing abnormal was to be found. Hence the general opinion arose that post-mortem brain changes were not due to the mental disorder but to its complications—paralysis, phthisis, scurvy, etc. Pinel, according to Prichard (1835, p. 212), "seemed to give up hope of elucidating the pathology of mental derangement by necroscopical research", and this may have been a good reason for his belief (Pinel, 1809, p. 142) that "the primitive seat of insanity is generally in the region of the stomach and intestines and it is from that centre that the disorder of intelligence propagates itself". Esquirol, at least in his earlier years, was of the same opinion and in his article on "Dementia" in the *Dictionnaire des Sciences Médicales*, 1814, says, "The opening of the body teaches us nothing with regard to (the seat of dementia) and all the organic alterations of the brain belong less to insanity than to its complications. I possess many observations on anatomical pathology which, compared with the history of the illness, prove that madness existed before any organic lesion of the brain and that when the organic lesion took place it showed itself by convulsions or paralyses which are present as complications." Such a view is understandable if organic causes of mental disorder were rare or associated only with simple dementia; but if dementia paralytica had always been common one might have expected that the constant association between its mental and physical signs and its obvious pathological brain changes would have been noticed by the many able investigators who looked for such associations before 1822.

The evidence thus far may be summarized as follows: (1) no very satisfactory or unequivocal accounts of a disease corresponding to dementia paralytica had been given before those of the Parisian alienists in the early nineteenth century; (2) yet by 1823, Bayle found that a fifth of all male admissions to Charenton conformed to his description of—"l'aliénation mentale avec paralysie incomplete par suite de meningitis chronique", while Esquirol (1838, p. 272) gives this proportion in 1826–28 as more than a quarter; (3) in noting the absence of earlier accounts, we must bear in mind not only the striking clinical and pathological features of the disease but also the fact that insanity had been carefully studied during the late eighteenth century from the aspects of nosology and brain pathology. One explanation of these observations is that dementia paralytica, from being a rare or non-existent disease, suddenly became very prevalent in Paris during the second decade of the nineteenth century. It was not recognized before because it had rarely or never occurred before; it was recognized by the Parisian alienists because it became so common there that it could not be missed[1]; it was not thought to be a new disease

[1] This would of course in no way lessen the merit of its first describers. The efflorescence of genius which led to and was evoked by the discovery of dementia paralytica is one of the

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because physicians believed that diseases, like species, were enduring and immutable.[1] Another explanation, however, was put forward by Robertson (1923) in his excellent essay on the discovery of general paralysis. He considered that the Napoleonic wars must have produced "a large harvest of cases of general paralysis", many of which would come to the two great mental hospitals of Paris, Bicêtre and Charenton (the latter catering particularly for army officers). These hospitals had been re-organized by or under the influence of Pinel, who had introduced kindness and orderliness into the regime and insisted on full and careful case-records. "The symptoms of general paralysis", says Robertson, "are so striking that the great number of similar cases thus collected together could scarcely have been overlooked when Pinel's method of caring for the insane was adopted." This may be conceded and is not incompatible with the first explanation; but, unlike the first explanation, it does not account for the later history of dementia paralytica and for the evidence which suggests that, from its origin in northern France, the disease spread in a fairly well-defined manner across Europe, then to America and later still to less highly industrialized countries.

PART II

The earliest definite reference to dementia paralytica in France is, I think, that of Esquirol, who in 1814 wrote: "When paralysis is a complication of dementia, all the paralytic symptoms appear one after the other; first of all, articulation of sounds is laboured; soon after locomotion is made with difficulty; finally, there is loss of control of the excretions." The disease was certainly common at Charenton in 1816, when the cases described by Bayle began to be admitted; and we have Esquirol's word for it that by 1828 one-sixth of all admissions to Charenton were paretic and the disease was common at

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most astonishing and glorious chapters in psychiatry. Baillarger (1860) considered this discovery the most important single achievement in the history of mental disease; Harrington Tuke (1859) wrote of Calmeil's *De la Paralysie* that it described general paralysis "with a terseness and success that may be considered as rendering his work unrivalled in medical literature". Robertson is no less emphatic: referring to the publication in 1826 of Bayle's *Maladies Mentales* and Calmeil's *De la Paralysie*, he says—"The appearance in the same year of two such books . . ., both dealing with a newly discovered disease in so masterly a fashion, is unique in the history of medicine. And, although much has been written about general paralysis during a century, the disease is described in these two books so fully, so faithfully and so convincingly that future additions to our knowledge seem little more than details. No other book devoted to this subject alone was written for two generations afterwards, nor was there any needed." I wish I could add the commendation of some *general* physician.

[1] We might even hazard the guess that the honour of being the eponymous discoverer of dementia paralytica went to Bayle because, not being a pupil of Esquirol and having no great experience of mental disease, he saw his patients' behaviour without the preconceptions of instruction or of habit. Bayle was only 19 when he became interne under Royer-Collard at Charenton, and only 23 when he submitted his inaugural thesis—"Recherches sur les maladies mentales" (1822). But Georget, Delaye, Falret and Calmeil would be thoroughly familiar with the classification and opinions of their great teacher, Esquirol, and of *his* great teacher, Pinel; they were for many years unable to conceive that paralysis could be other than a mere epiphenomenon of insanity, as scurvy or phthisis might be; and Esquirol himself never abandoned that view (Baillarger, 1859, 1860). "There is a suspicion", says Robertson, "that antagonism to Bayle existed because he did not belong to the school of Esquirol." This is too mild. It is obvious that intense passions were aroused. Esquirol's pupils went out of their way to pour scorn on Bayle's ideas and to belittle his achievements. According to Toulouse (1922), even Pinel pronounced his work "premature and useless". We read with sorrow but without surprise that after his term of office as interne at Charenton ended in 1823, Bayle "drifted away" from the study of mental diseases to that of general medicine, anatomy, medical history and (*horresco referens*) bibliography. He died in 1858, two years before the writings of Baillarger convinced his compatriots that dementia paralytica might properly be called "la maladie de Bayle".

Bicêtre and at the St. Yon asylum near Rouen (quoted by Prichard, 1835, p. 101). Yet it remained rare in the south of France (Esquirol, 1838, p. 273): between 1822 and 1825 Rech found no case among 132 admissions of insane patients to the hospital at Montpellier; in Toulouse, Delaye found only five cases among 111 patients (no date given); while in north Italy it was rarer still, as Esquirol himself confirmed in 1834. Even in 1849, Lunier concluded from personal observation that dementia paralytica was rare in the south of France. Yet by 1876 it must have become common, for we read that "in the south of France, if we may judge from the official returns, general paralysis has greatly increased during the last generation or two and at present is nearly equal to that in the north" (Eighteenth Report of the Commissioners in Lunacy for Scotland).

Two further observations may serve to suggest that for many years dementia paralytica was uncommon except in the environs of Paris. Salomon (1862) states, "France is the peculiar focus . . . Paris is the headquarters of the disease." Krafft-Ebing (1866) gives a list of the literature concerning dementia paralytica "from the earliest up to the most recent date" and has no reference to any but French writings until 1848. He missed some of the English literature but he is unlikely to have missed any German work.[1] The absence of early German references suggests that dementia paralytica was too rare in that country for the French descriptions to arouse much interest. This is confirmed by Mönkemüller's study (1911) of the case records preserved from the penitentiary and madhouse at the town of Celle, near Hanover. The records cover the period 1750 to 1831 and among 669 cases, Mönkemüller found 31 resembling dementia paralytica. They were distributed over the years as follows:

Years	*Admissions*	*Cases Resembling Dementia Paralytica*
1750–1800	211	0
1801–1810	153	6
1811–1820	188	15
1821–1830	117	10

The diminished number of cases in the last decade is probably accounted for by Mönkemüller's observation that many cases were then being diverted to a new hospital at Hildesheim. It is of interest, too, that "a relatively large number" of the 31 cases were soldiers and had therefore probably been in conflict with Napoleon's armies.

In England, Burrows (1829) seems to have been the first to comment on the new disease. He refers to the descriptions of Georget, Bayle and Calmeil, and then (p. 177) remarks on the "singular discrepancy" in the prevalence of paralysis complicated by insanity in the French as compared with the English hospitals. In the latter, "from inquiry I know the number is comparatively trivial . . . In my own practice, the proportion has not been one in twenty." Conolly (1830), in his *Inquiry concerning the Indications of Insanity*, makes no mention of paralysis in spite of a reference to Bayle's "excellent work".[2]

[1] Meyer (1959) has pointed out that Griesinger, in the first edition of his textbook, 1845, drew attention to the occurrence of "so-called general paralysis" in Germany.

[2] Conolly confirms Bayle's observation that many patients dying of consumption show "spes phthisica". The reference is not, of course, to the pathologist Gaspard Laurent Bayle, who wrote the famous *Recherches sur la phtisie pulmonaire*, but to Gaspard's nephew Antoine and his *Maladies du Cerveau* (p. 551).

Prichard (1835) went to some pains to determine whether Burrows's opinion was correct but (p. 108) he "met with considerable difficulties in obtaining satisfactory information". He concluded, however, that the disease was "comparatively rare in private asylums" and, in the one public asylum (Gloucester) for which he gives figures, only 16 cases had been observed since 1828. Yet by 1849 the situation must have changed, for Conolly in his Croonian lectures says that general paralysis was common in all the asylums of England, France, Belgium and Germany, though rare in Italy and Spain. We may consider, too, the progress of the disease in one particular asylum, the Middlesex Lunatic Asylum at Hanwell, from figures given by its superintendents. Sir William Ellis makes no mention of dementia paralytica in his *Treatise on Insanity* of 1838. Two years later Millingen (1840) finds only twelve cases of paralysis among 1,000 patients and contrasts this with the high prevalence at Charenton. By 1849, however, Conolly finds that among 690 deaths at Hanwell over the last ten years, the proportion of those due to general paralysis was 37 per cent. in males and 11 per cent. in females. These figures for a London asylum were probably well above the average for the country, as in 1876, when the annual reports of the Commissioners in Lunacy first give separate statistics, the proportion of deaths from general paralysis in all the asylums of England and Wales was 14 per cent. in males and 3 per cent. in females.[1]

The disease does not seem to have appeared in Scotland until 1839, nor was this due to lack of knowledge of it. "I saw the disease in Paris in 1832", says Browne (1875), "but did not recognize it in this country till 1839." It soon became fairly common in Edinburgh and Glasgow (Workman, 1858) but elsewhere remained rare or unknown for many years. Thus Skae (1860) says that his former pupil Howden, who had been well acquainted with the disease in Edinburgh, could not find a single case among the 300 patients of the Montrose Asylum; and during the years 1869 to 1872, among 200 admissions to the Fife and Kinross Asylum, Batty Tuke discovered only four cases (Bucknill and Tuke, 1874, p. 127). As late as 1879, Maudsley could remark that general paralysis was "hardly ever met with in the highlands of Scotland". In that same year, however, the proportion of deaths due to general paralysis in all the asylums of Scotland was officially given as 18 per cent. in males and 3 per cent. in females.[2]

In the United States, dementia paralytica was not recognized until after 1840. I have been unable to consult the original reference of Luther Bell (his Annual Report for the McLean Asylum, Boston, 1843), but that he was the earliest to record the disease is confirmed by several writers. Thus Bucknill and Tuke (1874, p. 323) say: "The late Dr. Bell of America, writing in 1844, said it was only within three years that patients had been admitted to the McLean Asylum labouring under general paralysis. On looking over the register for the past years he could not find a case the description of which resembled

[1] Nevertheless, in some asylums in England and Wales there were whole decades when a quarter or more of all the male admissions were paretic. These cases pursued a slow but relentless course to complete dementia and death, and it is not hard to imagine that the unrewarding and dispiriting task of nursing them was one reason why the high standards of humane care set up by the pioneers of non-restraint and moral management seem gradually to have deteriorated during the latter half of the nineteenth century.

[2] See the 41st Annual Report of the General Board of Commissioners in Lunacy for Scotland (1899, App. A, Tab. X). We may calculate a crude mortality rate for general paralysis in England and Wales and in Scotland, using the figures given in the Board of Control Reports for the year 1876 and the estimated population of the two countries in this year. Expressed as deaths per million of the population, the figure for England and Wales is over 50, for Scotland it is under 20.

the manifestations so graphically described by many English and Continental authors." Chase, writing in Philadelphia in 1902, says (p. 21): "As an illustration of the former rarity of the disease in this country, it is said that the eminent alienist, the late Dr. Luther Bell, of Massachusetts, at the time of his first visit to England about fifty years ago, had never recognized a case of general paresis, a statement which seems almost incredible considering its rapid increase and spread in late years, especially during the past quarter of a century." There was no further report of cases of general paresis in the States until that of Pliny Earle in 1847 (MacDonald, 1877; Wagner, 1902). Recognition was even more tardy in Canada. "When I entered the Toronto Asylum in 1853", says Workman (1858), "there was not a single case, as far as I could judge, in the institution but it was not long before it began to make its appearance." That there was a characteristic mode of spread of the disease suggested itself very strongly to his fellow-countryman MacDonald (1877).[1] MacDonald says, "A curious point in the history of the disease is its gradual extension from one country to another and its gradual increase in localities where it has once appeared"; and he gives a table of asylum reports indicating that general paresis was still rare in the western and southern states compared with its prevalence in the central states and those of the eastern seaboard. In his own institution (the New York State Asylum) the numbers of paretics were increasing annually and although some of the increase might be explained by familiarity, yet "when all due allowance is made on this account there is still abundant evidence that the disease is steadily and rapidly extending". His observations led him to believe that in any one place the disease progressed in a manner shown by: first, its appearance and recognition in males; then, increased frequency in males and its appearance in females; increased frequency in both sexes with an increased proportion in females; and finally, changes in the nature of the disease, such as its duration and the age of patients attacked. He also quotes figures to show that dementia paralytica was at that time much more prevalent in Britain than in the United States; in 1874–76, for example, the percentage of cases in the asylums of Great Britain was 14·1 for males and 3·2 for females whereas in the U.S.A. the figures were 4·1 and 0·4. Workman had reached similar conclusions in 1878. Observing that there

[1] Macdonald, Workman and Mickle were Canadians and had all studied at the Toronto School of Medicine. Mickle, who emigrated to England and became Superintendent of Grove Hall Asylum, London, was unimpressed by the American statistics of his two compatriots and dismissed them with the remark that "many statistics are utterly misleading . . . merely an index of the varying capacity of medical men to recognize the disease". But when we remember that this disease was recognized in America only at a time when every psychiatrist must have been familiar with its textbook description, and that the progress of any infectious disease across that vast and largely unopened continent must have been relatively slow, we may think the Americans had a better opportunity than Europeans of observing the spread of dementia paralytica.

Another statistical sceptic was Spitzka, professor of medical jurisprudence at New York, and originator of the maxim that general paresis was due to the three W's—wine, women and worry. He severely disapproved of "the widely circulated error" that general paresis was "travelling" from east to west of the American continent. His opposition to MacDonald's statistics was based (1883, pp. 183, 208): (1) on the fact that in the German and French asylums, "where the diagnostic acumen of the medical officers is unquestionable", the disease was said to be increasing only very slightly; and (2) on the *ad hominem* argument that MacDonald had not only attempted to support the ridiculous theory of the Englishman Austin that in general paresis an affection of the left pupil was associated with mania and of the right with depression, but that he had got this association the wrong way round, so that his figures instead of supporting Austin's theory were at complete variance with it—a careless error which, says Spitzka, "constitutes a significant commentary on the reliability" of the author's work in general. Yet in fact it was not MacDonald but Spitzka who was the careless one, inasmuch as Austin (1859, p. 31) claimed mania to be associated with contraction of the left, MacDonald (1877) with dilatation of the right pupil.

were markedly fewer paretic deaths in the Toronto Asylum during the eighteen-seventies than in English asylums of comparable size, he adds, "I have carefully examined over 130 reports of United States and Canadian asylums for the last 3 years. In more than half of this number I have found that paresis was either totally unmentioned or but very exceptionally noted in the obituary tables. I believe it is a recognized fact that in the Southern and farthest Western States the disease is unknown; or at least it has been unnoticed . . . To an English superintendent, who numbers his paretics by the score and shows a paretic death proportion of one in three or four, this fact could not fail to appear marvellous." During the next twenty years, however, dementia paralytica spread and increased in both Canada and the States, so that by 1894 Ballet and Blocq could write, "Central and Western Europe and North America have the unhappy privilege of furnishing the greatest number of cases." Dayton's figures (1940, p. 468) show that, of first admissions to the mental hospitals in the State of Massachusetts between 1917 and 1933, the proportion of paretics was 10·6 per cent. for males and 3·0 per cent. for females.

The spread of dementia paralytica among the negro population of North America is also worth noting. Long after it had become common among whites, the disease was still rare in negroes. As late as 1883 and 1886, asylum superintendents in North Carolina and in Georgia could claim never to have met with general paresis among their coloured patients (Moreira and Penafiel, 1907). In the New York Asylum, Spitzka (1883, p. 180) found the proportion of cases lower among negroes than among whites and indeed used this finding to support his belief that general paresis was "more frequent with races of a high than of a low cerebral organization". Berkley, in 1893, drew the same conclusion for the Northern States generally; but a few years later, in his *Textbook on Mental Diseases* (1900, p. 194), he writes of dementia paralytica in the negro: "Before the civil war and for some few years afterwards the disease was unknown among them. Little by little the number of cases grew in frequency. Such patients were at first regarded as curiosities, but at present in Baltimore paretics represent approximately the same percentage, according to the total population, in negroes as they do among Caucasians; nor do the general types of the disease differ materially in the two races." Emil Kraepelin (1913) quotes an investigation "very kindly undertaken for me by Hoch in New York" which showed that in seven large asylums the average rate for paresis in negroes was over twice that in whites. Green (1914) wrote, "For many years it was claimed that general paresis was seldom met with in the negro race. That this claim is untrue is generally accepted today"; at the Georgia State sanitarium he found the proportion of general paresis among negro admissions was twice that of the whites. Plaut, in 1926, again found a higher rate of general paresis among negroes than whites in America, and in the same year Kraepelin (1926) lent the weight of his authority to the "remarkable fact" that general paresis had been extraordinarily rare in North American negroes forty to fifty years earlier but was now very common among them. Figures quoted for Massachusetts mental hospitals from 1917 to 1933 by Dayton (1940, p. 411) and for New York State Hospitals in 1935 by Rosanoff (1938) indicate that general paresis continued at least twice as common among negroes as among whites; while recent work (Malzberg, 1953) indicates that in New York State this comparative factor has risen to more than five.

The spread of dementia paralytica in certain other countries may be mentioned more briefly. In Ireland, the disease was generally acknowledged to be rare at least up until the eighteen-seventies. Thus Ashe (1876) found no cases

in the asylums of Belfast or Cork and only one in Londonderry and drew the conclusion that "general paralysis is scarcely to be found in Ireland". Deas, in 1879, echoes "the undoubted fact that general paralysis is all but unknown in Ireland", and seven years later Mickle (1886, p. 259) can still say that "Ireland enjoys an extraordinary immunity from general paralysis". Yet the Reports of the Inspectors of Lunatics (Ireland) in 1890 (the first year in which separate figures are given) indicate 30 deaths—more than 3 per cent.—from general paralysis, a number and proportion which increases in later years. In the Isle of Man, the immunity to the disease seems to have lasted even longer, Richardson (1891) reporting that "during the past six years I have seen no instance of it in a patient of Manx parentage", though two cases had occurred in immigrants. In Denmark, figures given by Heiberg (1932) suggest that dementia paralytica was uncommon there until the late eighteen-sixties. The number of paretic deaths at the St. Hans Hospital, Copenhagen, in 1866 was five; but the average annual deaths for the decades from 1866 until 1925 were 8·6, 14·0, 23·1, 35·8, 41·3 and 51·7. Heiberg also gives reasons for believing that the figures represent "with a rather high degree of accuracy" the actual number of paretic deaths in the city of Copenhagen. Smith's figures (1926) for admissions to the Kommune Hospital in Copenhagen from 1876 to 1926 show the same general trend (Table I).

TABLE I

Numbers of Cases of Dementia Paralytica Admitted to the Kommune Hospital, Copenhagen (from Smith, 1926)

Year	1876 –80	1881 –85	1886 –90	1891 –95	1896 –1900	1901 –05	1906 –10	1911 –15	1916 –20	1921 –25
Males	88	138	139	188	202	222	169	316	308	305
Females	3	23	37	57	89	104	97	149	121	116
Ratio M/F	29	6·0	3·8	3·3	2·3	2·1	1·7	2·1	2·5	2·6

Similar trends are to be found in reports from other countries. In Brazil, according to Moreira and Penafiel (1907), there were five cases of paresis admitted to the National Hospital for the Insane in Rio de Janeiro in 1889; but the average annual number admitted during the 3 quinquennia from 1890 to 1905 was 10·1, 17·4 and 21·2, while the percentage of paretic admissions increased from 3·1 to 4·0 and 5·3. They also observe that the disease was commoner in immigrants than among natives, a differential prevalence which held true of other countries until quite recent times. Thus Lennox (1923) observes that although syphilis was three times as common in China as in America, the incidence of neuro-syphilis was less than one-seventh as great; and he quotes "writers of experience" who, during the years 1907–1916, hardly ever saw general paresis in Chinese, and where it occurred the patient was found to have been infected from a non-Chinese source. Although Lennox thought the rarity of neuro-syphilis among the Chinese might to some extent be due to lack of facilities for diagnosis, yet he concluded that this would "probably not account for all the observed racial differences". Stewart (1924) quotes a report by Christidis of 1922 that among 3,000 cases of syphilis in Persia he did not find a single paretic; paresis was also rare in European residents who had acquired syphilis in Persia but was common in those infected from outside sources.

The general facts related above always appeared sufficiently remarkable to contemporary workers to demand an explanation. Before considering some

of the earlier explanations, I will suggest that these facts seem broadly explicable on the hypothesis that a mutant neurotropic strain of the syphilitic spirochaete appeared in northern France and then spread by venereal infection along the trade routes of the world. On this hypothesis, the new disease would tend to spread first to those countries having the closest commercial intercourse with the country of origin; and on reaching a new country overseas, would appear first in the port towns and only later spread inland. Again the disease would tend to spread more quickly among peoples of similar cultural and ethnic group and only move slowly to other groups. The facts that dementia paralytica is a chronic disease and that a variable interval of five to twenty years separates the initial infection from the appearance of symptoms would account for the absence of any explosively obvious outbreak of cases. Such an epidemiological hypothesis could hardly have been put forward before 1913 as until then the infectious nature of dementia paralytica was unsuspected or unproved; and by 1913 the disease had become fairly evenly distributed over the civilized world and it was easy to dismiss the older statistics as valueless because they had not been based upon objective methods of diagnosis.

The diagnosis of dementia paralytica became objective during the years 1896 to 1912, when the specific reactions of the cerebrospinal fluid were elucidated by Babcock, Alzheimer, Wassermann and Lange. Before this, diagnosis during life had to be made entirely on clinical grounds, though post-mortem examination added much to the accuracy. (It is worth noting that, according to the reports of the Commissioners in Lunacy, the proportion of post-mortem examinations carried out on patients dying of general paralysis in the asylums of England and Wales between 1901 and 1911 was over 70 per cent. We have no post-mortem figures for earlier years, but no reason to suppose they were less.) No doubt in the statistics of dementia paralytica were included some cases of arteriosclerotic, alcoholic and epileptic dementia, cerebral syphilis, cerebral tumour, pellagra and plumbism; but it had been recognized almost from the start that these conditions entered into the differential diagnosis, while conditions that were differentiated only later, such as the dementias of Pick and Alzheimer, were too rare to be of statistical importance. No doubt, too, the diagnosis was made more carefully in some centres than in others, but this is true of all diseases. The consequence would be that the edges of the statistical picture were blurred by a penumbra of misdiagnoses and the problem is—whether the size of this penumbra was such as to fog the true picture beyond recognition.[1] In assessing the value of these nineteenth-century statistics, it is perhaps useful to reflect that the diagnosis of dementia paralytica at that time was probably much more accurate than is the present day diagnosis of schizophrenia,[2] for the former disease presented not only mental changes

[1] Kraepelin (1927, p. 1137) discusses the unreliability of the nineteenth century statistics on dementia paralytica and gives his opinion that "they are set about with so many sources of error as not to allow any definite conclusion on the actual alterations in frequency of the disease". Nevertheless, he in fact permitted himself to draw general conclusions: for example (p. 1145), "from these considerations we may take it as very probable that dementia paralytica was formerly uncommon, then underwent a progressively rapid increase from the beginning of last century and for some time now has been gradually diminishing"; and again, discussing the sex incidence (p. 1150), "although the figures may be considerably influenced by the sources of error mentioned above, yet there can be no doubt of the overall increase in the danger to the female sex from dementia paralytica".

[2] It is sometimes urged that the present-day diagnosis of schizophrenia is too uncertain for epidemiological studies of this disease to be meaningful. The history of dementia paralytica suggests that we should be unwise to neglect such studies. In 1857, Esmarch and Jessen had drawn attention—rather apologetically—to the statistical relations between syphilis and paresis. Another early piece of evidence for the syphilitic hypothesis was provided by Sankey,

but physical signs and characteristic post-mortem appearances and was uniformly fatal within a few years. Although it seems probable that before 1906 there was some degree of confusion as to what should be included in the diagnosis of dementia paralytica, yet I cannot find that, on the whole, there was any sudden fluctuation in the reported incidence or mortality of the disease after the introduction of objective methods of diagnosis.[1]

It is a curious historical fact that during the nineteenth century each generation of psychiatrists was confident of its own ability to diagnose dementia paralytica but was very ready to doubt the diagnostic accuracy of its predecessors. Thus an anonymous reviewer of the 41st Annual Report of the General Board of Commissioners in Lunacy for Scotland (*Journal of Mental Science*, 1907), referring to the continued increase in admission rate and deaths of general paralysis during the past 25 years, says: "The reviewer is convinced that a few years ago many of the cases now returned as having died from general paralysis would have been described as cases of cerebral softening, disseminated sclerosis, and cerebral paralysis."[2] Twenty-one years before this, Mickle had

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who, in 1866, pointed out the close association between the incidence of syphilis and of paresis in different social classes. But this delicate flower was withered by the scorn and authority of Mickle, who, in his textbook (1880, p. 105) dismisses it with the inappropriate remark that "even if true this does not establish any connection between the syphilis and the general paralysis". Krafft-Ebing, on the other hand, was so impressed by the statistical evidence that he was emboldened in 1894 to inoculate nine paretic patients with syphilis; but, as Berkley (1900, p. 174) and others observed, this proved nothing, for persons infected with syphilis do not necessarily develop symptoms, patients with longstanding syphilis may acquire the infection anew, and other investigators (see Diefendorf, 1906) repeated Krafft-Ebing's work with contrary results. Yet this doubtful experiment caught hold of the popular fancy, convinced many who had been sceptical of all the patiently accumulated statistics, and is still regularly quoted as one of the landmarks in the history of dementia paralytica.

[1] The difficulties of clinical diagnosis were indicated by the problem of "pseudo-paralysis" (see, for example, Hyslop, 1896). It is likely that these difficulties increased at the end of the nineteenth century on account of the rapid changes in the proportions of the different clinical types of dementia paralytica. However, it seems that the difficulty lay more in the initial than in the final diagnosis: Kraepelin says of the period 1892–1907, "at that time we had the tendency to diagnose the condition as early as possible from the clinical picture. . . . Consequently we made many wrong diagnoses later discovered by regular follow-up" (1927, Vol. I, p. 958).

Objective diagnosis became common after Wassermann's demonstration, in 1906, that his complement-fixation test was given by the cerebrospinal fluid of paretics; and was further refined after 1912 when Lange discovered the specific reaction of the fluid to colloidal gold. With these facts in mind we may note that in England and Wales:

1. The Registrar General's figures from 1901 onwards for deaths due to general paralysis of the insane show no change other than a continued downward trend (Fig. 2);

2. The change in sex ratio of deaths from general paralysis of the insane is closely paralleled by that from tabes, the accurate diagnosis of which was probably little influenced by the new techniques (Fig. 1);

3. First admissions to asylums of cases diagnosed as general paralysis of the insane are recorded in the annual reports of the Board of Control. These show a sudden decrease in the numbers in both sexes for 1914, an occurrence which may be attributed to the outbreak of the first world war; otherwise, neither the numbers nor the sex ratio show any sign of short term change between 1900 and 1928.

[2] This reviewer seems to have been particularly unguarded in his assertion. The Annual Report gave a table of deaths, not only from general paralysis but also from "apoplexy and paralysis" and the numbers in this latter table did not vary over 30 years and showed no sex difference: clearly the Scottish doctors had been at pains to separate "cerebral softening" and "cerebral paralysis" from general paralysis. As for disseminated sclerosis, the Reports of the Commissioners in Lunacy give the number of deaths in England and Wales from cerebral and spinal sclerosis in 1901 as 8, in 1906 as 18, in 1910 as 9; the number in Scotland would be proportionately less and it seems clear there had been little variation in the statistically negligible number of such cases. Again, a fellow-reviewer writing twelve years earlier on the 36th Annual Report (*Journal of Mental Science*, 1895) had said, "There can be no reasonable doubt, even after making due allowance for possible greater certainty in diagnosis, that of late years there has been a steady and by no means inconsiderable increase (in general paralysis), notably in the male sex."

written (1886, p. 248), "It is difficult to say how far the apparent increase of general paralysis among women of late years is due to a former defective recognition of it and faulty diagnosis, owing to the less salient features and less dramatic course of general paralysis as it occurs in women than as in men." Twenty-six years before this, Skae (1860) had said, —"for many years (general paralysis) must have been imperfectly known and recognized even in large asylums, if we may judge from the small proportion of cases mentioned in the annual reports of these asylums, compared with the large number which now figure in the tables of these reports. The only other explanation of this fact is that the disease has been increasing in frequency in this country of late years." And twenty-five years earlier than this, Esquirol (1838, p. 274) took Burrows to task with the words: "This worthy writer attributes the frequency of paralysis in Paris to our bad management and our failure to take proper precautions in guarding our insane from exposure to inclement weather; whereas in England, he says, the patients are very well cared for . . . I am convinced that once the symptoms of paralysis complicating insanity are better understood, there will be found in England and particularly in London as many paralytic insane as there are in Paris."

Although the statistics of earlier authors could always be dismissed as unreliable, yet the reported variations in the prevalence of dementia paralytica at any one time could not be so dismissed, because they were again and again confirmed by experienced psychiatrists from personal observations.[1] Of the explanations offered, however, none was adequate and many were self-contradictory. The lower consumption of alcohol was held by Lunier (1849) to account for the lower prevalence of dementia paralytica in southern France; by Wise (1869) for the "remarkable rarity" of the disease among the natives of India; and by Kraepelin (1913) for its rarity in upper-class European women, in "non-Europeanized" peoples and in Mahommedans. Yet this explanation would certainly not account for the low prevalence of dementia paralytica in Northern Scotland and in Ireland, nor for the observation that "the Irishman has to go to America to be attacked by it, for at home he seems immune" (Berkley, 1900, p. 193). Clouston (1883, p. 379) considered "hard muscular labour" was among the exciting causes of dementia paralytica, yet Maudsley (1879, p. 433) attributed its rarity in Scottish highlanders to their taking "a great deal of bodily exercise". An attack of malaria or relapsing fever soon after syphilitic infection has been held to account for the rarity of dementia paralytica in the tropics, but McCartney (1946) has pointed out that neuro-syphilis is rare in the Marshall Islands where there is no malaria; and malaria would not explain the rarity of dementia paralytica in many colder countries such as Ireland and Norway. Towards the end of the nineteenth century the association between syphilis and dementia paralytica became increasingly well-established and the importance of the former as an exciting cause of the latter disease was summed up in the famous "civilization and syphilization" aphorism of Krafft-Ebing at the Moscow Congress in 1897. But as Mott pointed out in

[1] One of the strongest objections to the Theory of Evolution was that, as no one could see evolution taking place, the theory was merely a hypothetical explanation of events long past and incapable of proof or disproof; and a recent demonstration that the evolutionary process can actually be observed today in certain species of seabirds has been claimed as valuable additional evidence. In the same way, many nineteenth century psychiatrists found it hard to believe that the prevalence of dementia paralytica in different countries could have changed significantly during the century; but its rapid increase among American negroes, a phenomenon that took place under the very eyes (so to speak) of Kraepelin, was a practical and almost irrefutable demonstration that such changes could occur.

1900, dementia paralytica was rare in some countries (Persia, Japan, Egypt) where syphilis was very common, a fact with which Kraepelin (1913) concurred and which he was at a loss to explain. The belief that "civilization" was a factor determining the prevalence of dementia paralytica had long been held, though there was disagreement whether the effects were due to the excessive sensitivity of more highly civilized beings or to their degeneracy. Salomon (1862) thought the peculiar susceptibility of Frenchmen to the disease was the result of their "insatiable thirst after 'la gloire' ". Mickle (1880, p. 97) taught that "a life absorbed in ambitious projects, with all its strenuous mental efforts, its long-sustained anxieties, deferred hopes and straining expectation . . . chagrins, forced erethism of the intellectual faculties . . . exposure to constant sources of annoyance—all these predispose to general paralysis". Stewart (1896) considered the recent increase in the disease as due to "increasing moral and physical decadence, lessening power of resistance and diminishing vitality, and increasing tendency to premature and rapid racial decay"; though a few years later (1901), when subsequent figures indicated a slight fall in the number of paretics, he was happily able to conclude that the tendency to racial decay in England and Wales had undergone a reversal.[1]

Kraepelin (1913, 1926, 1927) was much occupied with the problem presented by variations in prevalence of dementia paralytica in different countries. When in Java in 1904, he had been unable to discover a single case among the natives and he did not believe that the reported variations in prevalence could be explained by variations either in the prevalence of syphilis or in the recognition and diagnosis of paresis. He admits that the theory of a special strain of syphilis would explain the otherwise very difficult fact that dementia paralytica is rare in some countries where syphilis is common but he rejects this theory on two counts. The first count is that "we see Europeans become paretics after infection with the same syphilis to which the nervous tissue of the natives is immune". He gives no reference for this statement and it would clearly never be easy to establish that a European acquired syphilis from a native rather than from an immigrant or in another country. The second count is that "in Constantinople the different races show a very different susceptibility for paresis although the syphilis of the Turks, Greeks, Jews and Armenians is certainly the same". From this statement it would appear that Kraepelin conceived of different strains of syphilis being statically distributed in different countries and that he did not have in mind the concept of a new

[1] Nineteenth century ideas on the aetiology of dementia paralytica provide material for a historical study which might illustrate our contemporary views on a disease such as schizophrenia where the aetiology is still obscure. Not only do many of these ideas seem very strange to us now, but they led to the advocation of "rational" methods of treatment and prevention which might seem even more strange were it not that the history of medicine is full of such things. For example, the hypothesis that dementia paralytica was caused by sexual excess led to the prophylactic advice that wives should be "cautioned against being too loving to their lords" (*Journal of Mental Science*, 1873). Of course, not everyone agreed with such a view; Mickle (1880, p. 105) was contemptuous of it, on the grounds that married women were not lascivious bacchantes and stood in no need of such advice.

For a long time, one of the most unlikely of these speculations was that dementia paralytica was due to syphilis. The statistical and epidemiological evidence in favour of this view, however, became increasingly strong at the end of the nineteenth century. But statistical evidence is never proof and as late as 1902 Nonne could state that in his opinion "progressive paralysis is not a specific syphilitic disease of the brain". Kraepelin, in 1904 (and this was two years before Wassermann showed that his antigen reaction was given by the spinal fluid of paretics), was bold enough to commit himself absolutely to the syphilitic hypothesis, but for the more cautious or less statistically-minded psychiatrist there was no sure path through the speculative labyrinth until the autumn of 1912, when, in the paretic brain sections sent to Noguchi by Moore, the pale visage of a few spirochaetes sufficed to disinherit chaos.

strain in the process of spreading from Europeanized to non-Europeanized countries; yet it is on this latter concept that most of the facts seem explicable.

The same belief in a static distribution of a neurotropic strain is evident in Kinnier Wilson's writings. In his *Neurology* (1941, Vol. I, p. 462; 2nd edition, Vol. I, p. 485), he states: "Another allegation, often quoted by those who believe in the dualist theory, is to the effect that in certain countries where syphilis is rife, neuro-syphilis is conspicuous by its relative absence . . . But most of such claims are proving visionary in the light of advancing knowledge. In 1926 Plaut showed that the incidence of general paralysis among American negroes is actually higher than among whites." Wilson seems here to be supposing that the earlier statistics on the scarcity of dementia paralytica in negroes were simply false. He was not alone in such a belief, for there are many references in the literature to the "legend" that dementia paralytica did not occur or was very rare in certain communities and to the "advancing knowledge" which showed such legends to be false (see, for example, Barnes, 1891, quoted by Moreira and Penafiel, 1907; Samuels, 1916; Marie, 1922). Yet Kraepelin definitely rejected the "legend" theory,[1] and it would seem altogether more reasonable that real increases in the prevalence of dementia paralytica occurred; and it would then be at least as satisfactory to explain these increases in terms of the spread of a neurotropic strain as by such vague hypotheses as "unknown protective influences" or "factors incidental to civilization" (Wilson, *op. cit.*, pp. 536, 486).

Changes in Sex Ratio

From the time of its discovery, dementia paralytica has always appeared to be more common in men than women, but the figures given for the proportion of male to female cases have varied widely in different times and places. "The comparative figures can vacillate between one to two and one to seventeen or even higher values", said Kraepelin (1926); he thought the variation could not be attributed to sex differences in the incidence of syphilis but, apart from suggesting that a low consumption of alcohol might account for the rarity of the disease in upper-class European women, he offered no explanation. The statistics have been discounted as fallacious but otherwise there has not, as far as I know, been any general attempt to explain these variations in sex ratio.

In hazarding a partial explanation, I suggest that if factors of time and place are taken into account it becomes possible to discern a fairly constant pattern of change, similar to that suggested by MacDonald in 1877, viz. that when dementia paralytica first appears in a country the sex ratio (males to females) is high but gradually falls to a more or less steady value of between

[1] "In countries where the social care of the insane is not adequately carried out, only a fraction of the psychotic patients enjoy medical attendance, but it is highly improbable that general paretics will be missing amongst these few, all the more so as their symptoms are usually very disturbing. If accordingly I experienced that, in a hospital containing several hundred native patients, not one case of general paresis could be found by excellently trained medical officers, we must infer that the disorder cannot in any way be as common in those parts as it is at home" (Kraepelin, 1926).

A more recent example of the "legend" theory is provided by two studies made in Bosnia and Herzegovina. In 1888, Gluck and others had reported that although syphilis was widespread in these "remote provinces", only 0·65 per cent. of native-born syphilitics developed dementia paralytica, compared with 9 per cent. of the foreign-born (Kraepelin, 1927, p. 1149). The investigation was repeated by Kojog (1939) who found that the proportion of paretics to syphilitics was the same as in Europe (5–10 per cent.). Kojog drew the conclusion that Gluck's work was entirely inaccurate; but the different findings might alternatively reflect the fact that the first world war and the general development of communication had made this part of Yugoslavia a much less remote place.

four and two to one. This is the pattern which would be expected on the hypothesis of the spread of a neurotropic strain of spirochaete. On this hypothesis, the strain would tend to reach a new country by the agency of travellers and seamen; from these men the infection would pass principally to prostitutes in the coastal towns and from them to native males. As the number of male clients is in general much higher than the number of prostitutes, the disease would at first show a preponderance of males and would only gradually spread to other females. In time, however, a balance would be reached and thereafter the sex ratio of dementia paralytica would tend to be more stable. The rapidity with which a steady ratio is reached seems to have varied markedly from country to country, and this could possibly be explained by variations in cultural attitudes to sexual behaviour. I will quote figures to indicate the early rarity and later increasing proportion of female cases in different countries.

In Paris, the sex ratio was never very high and seems to have fallen to a low level in a short time. Bayle (1826, p. 568), at the Charenton Hospital, found the ratio of males to females eight to one during the years 1816 to 1823; at the same hospital from 1823 to 1826 Calmeil (1826, p. 370), as the result of a "scrupulous examination", found the ratio to be three to one; a decade later, Foville found it 2·3 to one (Griesinger, 1861, p. 400). In 1886 (p. 245), Mickle quotes the proportion in France as 2·5 to one and a similar figure is given by Idanoff (1894). In Germany, Neumann (1859) believed that women were "very seldom" the victims of dementia paralytica. Other early writers put the ratio in Germany as 10 to one (Griesinger, 1861, p. 400); Sander (1870) found this ratio at the Charité Hospital, Berlin. In 1877, Krafft-Ebing put the figure at eight to one but twenty years later (1894) concluded that the proportion of females had considerably increased. By 1913, Kraepelin (p. 142) could say that "the relative number of women is certainly increasing in Germany" and that whereas the sex ratio had been seven or eight to one in earlier decades it had fallen to between five and two to one. In the St. Hans Hospital, Copenhagen, Heiberg's figures for paretic deaths during the years 1876 to 1890 show a gradually increasing proportion of females from 12 per cent. to 30 per cent.; from then on (to 1930) this proportion remains almost constant. Smith (1926) has given figures for the annual admission of paretics to the Kommune Hospital, Copenhagen, from 1876 to 1925; the numbers in quinquennial periods are shown in Table I, and from this it is evident that the relative proportion of male cases was at first very high but after the end of the nineteenth century remained steady at about 2·5 males to one female.

In England, the sex ratio of deaths seems to have been fairly steady at about four to one for most of the nineteenth century. In the earliest reference to the subject which I can find, however, Prichard (1835, p. 110) records that of the 16 cases seen at the Gloucester asylum since 1828 only one was female. Conolly (1849) says that at Hanwell Asylum during the decade 1839 to 1849 there were 146 male and 33 female deaths from general paralysis, adding that "in private practice I have never yet met with a case of general paralysis in a woman". Similar figures for provincial asylums are given by Wilson (1857) and Boyd (1865). From 1876 the Annual Reports of the Commissioners in Lunacy give statistics for general paralysis of the insane in England and Wales; these indicate a relatively constant sex ratio of about four to one until the second decade of the twentieth century when there is a slight increase; from 1925 there is a progressive decrease until by 1945 the ratio is 2·3 to one. These recent trends are reflected in the Registrar General's reports (Fig. 1). Discussing his earlier experiences of dementia paralytica in Scotland, Browne

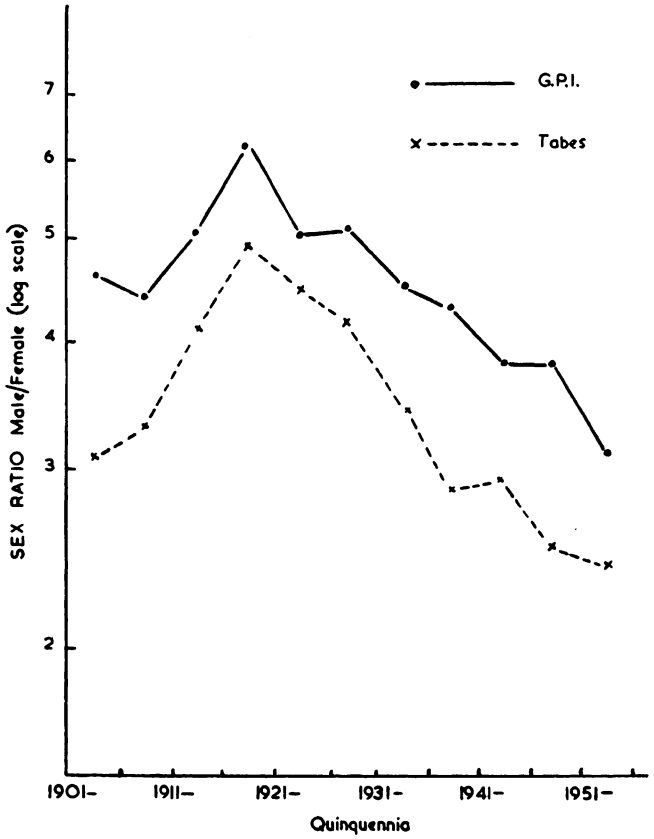

FIG. 1.—Sex ratio, by quinquennia, of deaths from General Paralysis of the Insane and from Tabes (from the Registrar General's Annual Reports for England and Wales).

(1875) said he had never been able to convince himself of the presence of the disease in the female, and Skae (1860) said that at the Royal Edinburgh Asylum he had "very seldom more than one female paralytic under my care at any one time" but rarely fewer than 22 to 25 male cases. From the Annual Reports of the General Board of Commissioners in Lunacy for Scotland, however, we learn that the male-to-female ratio of deaths was soon in the region of four to one and continued at this level into the early part of the twentieth century.

The same picture of dementia paralytica being at first rare in females and later much more common seems evident in North America. Between 1841 and 1843, Luther Bell (quoted by MacDonald, 1877) found 16 cases of the disease at Boston, but only one of these was female. Workman (1858) wrote: "In five years I have not in the Toronto Asylum met with a single case of general paralysis in a female . . . Why is it that in America general paralysis of the insane is almost if not entirely confined to males and why in Europe is there so considerable a number of exceptions to this rule?" Twenty years later (1878), Workman wrote on the subject again: during the period 1865 to 1877 he had had 95 cases of general paresis at Toronto, of whom only eight were female; and in the New York State Lunatic Asylum at Utica, where "the records are perfectly reliable", the sex ratio of paretic deaths from 1849 to 1877 was

16 to one and in New York itself the ratio was between 15 and 20 to one. "Why a New York city asylum should show a lower proportion than an English asylum, I fail to understand." MacDonald's opinion (1877) on the gradual increase in the proportion of female cases has already been noted and his figures suggest a higher sex ratio in the Western than in the Eastern States. Figures for various asylums in the United States during the latter decades of the nineteenth century show a ratio of about eight to one (Wagner, 1902) and Berkley (1900, p. 171) makes the observation that the sex ratio had decreased during the past ten to fifteen years from nine or ten down to seven or eight. The ratio continued to decrease. Dayton's figures (1940, p. 468) show that in Massachusetts mental hospitals between 1917 and 1933, the male-to-female ratio was about four to one. In New York State hospitals between 1932 and 1941 this ratio decreased progressively from four down to three (Arieti, 1945), and figures of the U.S. Bureau of the Census (quoted by Iskrant, 1945) show the ratio for paretics in all mental institutions in 1940 was three to one.

The commonest—indeed the only—general explanation put forward to account for the increasing proportion of female paralytics in any one locality and their varying proportion in different countries was that the statistics were misleading. Thus Austin (1859, p. 59) thought the disparity had been "overstated"; Mickle (1886, p. 245) asserted that, as the relative proportion of male to female cases in England was four to one, Krafft-Ebing's earlier estimate of an eight-to-one rate was "inaccurate"; and the anonymous reviewer in the *Journal of Mental Science* (1907) believed that the increasing proportion of females was due to the fact that in this sex "the disease is now diagnosed with greater accuracy". However, we should note that although dementia paralytica may have been less dramatic in females than in males, it was not therefore less well diagnosed, for in both sexes the simple dementing type and the depressed type had been clearly described by Calmeil in 1826 and the hypochondriacal type by Baillarger in 1857. Again, if the clinical diagnosis in the female was more difficult and less often made, we should expect to find that when objective methods of diagnosis were developed early in the present century the proportion of female cases would appear to increase, but in England, at any rate, the opposite occurred, as is shown by the reports of the Board of Control and the Registrar General. The change in sex ratio of dementia paralytica during the early twentieth century is unlikely to reflect any change in diagnostic habit, as a very similar change occurred at the same time in tabes (Fig. 1).

Changes in Type and Prevalence

When a population is exposed to infection by a new virulent organism, the resulting disease tends in the course of years to undergo an evolution from forms which are acute and severe towards those which are milder and more chronic. This seems to have happened, for example, in the great fifteenth century epidemic of syphilis. If some such evolution can be shown to have occurred in dementia paralytica since its definite recognition 140 years ago, this may be taken to support the hypothesis that it was at that time a new disease. I will briefly consider evidence for supposing that there has been a gradual change in the proportion of clinical types of dementia paralytica and, more recently, a natural decline in its prevalence.

Both Bayle and Calmeil recognized that in its early stages dementia paralytica could be characterized either by grandiose delusions or by depression or by simple dementia, but neither of them had any doubt that of these three

types the grandiose was much the commonest. Thus Bayle (1826, p. 547) says that although not every case shows monomania yet "exceptions are very rare and are probably due to the fact that detailed observation was lacking during the first two stages of the disease". Calmeil (1826, p. 325 ff.) considered that ideas of grandeur were present in "a very great number" of insane paralytics and that simple dementia and depression (or *lypémanie* as he then called it, following Esquirol's classification) were rare. Falret, in his *Recherches sur la Folie Paralytique* (1853, p. 29), still stated that expansive delusions were the commonest mode of onset of the disease. During the second half of the century, however, changes in the relative proportion of the types began to be observed. In 1859 Calmeil published his second major work on dementia paralytica, the *Traité des Maladies Inflammatoires du Cerveau*; here (Vol. I, p. 276) he states that the depressive type had become more common during the past twelve years until now it was almost as common as the expansive type. According to Westphal (1868) "it is now established beyond contradiction that ideas of the most varied, yea even opposite description, frequently exist during the whole course of the disease or only for a certain period of it", and he adds that Bayle's belief in the overwhelming preponderance of the grandiose type "must be considered as completely refuted". Krafft-Ebing, in his monograph of 1894 (p. 25) observes that "comparison between past and present is misleading because for several decades the nature of general paralysis has been changing and in place of the classical, dramatic, obstreperous type we see more and more of the simple, dementing type". Of the various German and Austrian figures quoted by Kraepelin (1913), none puts the proportion of the expansive type as higher than 30 per cent.; the percentages of the depressive type range from 10 to 20, and of the demented type from 40 to 60.

The same gradual changes are apparent in Great Britain, though the classical type seems to have remained common for a longer time than on the continent. Thus Conolly (1849) says, "The disease is so generally associated with ideas of wealth and grandeur that when these prevail strongly in any patient we expect the paralysis to supervene. It is scarcely ever combined with melancholia." The low proportion (45 per cent.) of the grandiose type found by Austin (1859, p. 59) is perhaps to be explained by the unusually large number of females (nearly one-third) among his 135 cases[1], for as late as 1871 Blandford, lecturer in psychological medicine at St. George's Hospital, still taught that "almost all, certainly nineteen out of twenty, paralytics are full of ideas of their greatness, importance and riches" (p. 260). Bullen (1893), from observations at the Wakefield Asylum, Yorkshire, between 1880 and 1890, concluded that the grandiose type was diminishing and the depressed and simple dementing types increasing in frequency (the proportion among his cases over a decade being 64 per cent., 13 per cent. and 21 per cent. respectively); he also quotes Claye Shaw as saying, "I have no doubt that we get more cases of the demented and paralysed form than we used to, and that the percentage of these is not only greater, *quoad* other forms of insanity, than formerly, but that amongst general paralytic cases it is the most common form." A later study at the Wakefield Asylum by Baird (1905) for the years 1896 to 1902 showed the proportion of grandiose cases to have fallen to 46 per cent., with corresponding increases in other types, principally the melancholic. Clouston of Edinburgh, in the sixth edition of his textbook (1904, p. 342) says of the

[1] All authorities have agreed that grandiose delusions were less common in female paretics. According to Stoddart (1921, p. 433) this peculiarity was ascribed by Krafft-Ebing and Regis to the relative poverty of ideation in women.

simple dementing type, "about one-third of all the cases of the disease that I used to see were of this character, and nearly all the older medical officers of asylums say that this type is increasing while the classical grandiose type is diminishing in frequency". In a study at Brentwood Mental Hospital, Power (1930) found that between 1907 and 1922 there was a slight decrease in the number of grandiose cases, from 43 to 40 per cent. and an increase in the demented type from 30 to 50 per cent. Stoddart (1921) makes the generalization that the depressed form "is almost as frequent as, if not at present more frequent than, the expansive form".

More recent continental work indicates a continued decrease in the proportion of the classical grandiose type, though a newly distinguished type —"euphoric dementia"—appears. Thus Bostroem (1930), in 1,218 cases studied at Munich between 1920 and 1930, found the grandiose type in 10 per cent., euphoric dementia in 30 per cent., simple dementia in 34 per cent. and the depressed type in only 7 per cent. Among 680 paretics admitted to the St. Hans Hospital, Copenhagen, between 1922 and 1935, Lomholt (1944) found 14 per cent. expansive or grandiose, 2 per cent. depressive, but 60 per cent. with fatuous, euphoric dementia. Froshang and Ytrehus, studying paretics admitted to hospitals in Oslo between 1915 and 1954, found that the proportion of the classical type gradually decreased from 10 to 4 per cent.

Although a distinction between the various types of dementia paralytica is not always easy to make (especially as, during the course of the illness, the clinical picture may fluctuate) yet it seems reasonable to detect certain major changes during the past 140 years. The grandiose type, from being much the most common, has gradually become uncommon and indeed rare. The depressive type, originally rare, became more common during the latter half of the nineteenth century (between 20 and 50 per cent. of cases) but has again become rare. That there have been changes in the relative proportion of types, few if any authorities have seriously questioned. The changes cannot be accounted for merely by changes in the sex ratio, for in England they occur during a period when the sex ratio was constant; nor can they be held due to changes in prevalence of the disease, for the decline in proportion of the grandiose type continued when the prevalence was increasing during the nineteenth century and when it was decreasing during the twentieth.

There is some evidence that this decline in prevalence of dementia paralytica in the present century cannot, in England at least, be altogether or even principally ascribed to the effects of medical intervention. Figure 2 shows the mortality in England and Wales from dementia paralytica, tabes and aortic aneurysm since 1901 (the first year for which the Registrar General's reports list general paralysis of the insane and tabes separately). In 1940, the Registrar General adopted the Fifth Revision of the International List for the classification of causes of death (in which "aneurysm of the aorta" replaced the previous comprehensive category of "aneurysm") and also in the same year changed the method of selecting the assigned cause from the death certificate ("the choice now being in the main that inferred from the statement of the certificate instead of being determined by arbitrary rules of precedence"). In 1950, the Sixth Revision of the International List was adopted, by which "aneurysm of the aorta" excluded both dissecting aneurysm and aneurysm specified as non-syphilitic. These changes in method of classification account for the breaks in the curves of Figure 2. They are of little consequence for the mortality from dementia paralytica and tabes; but they imply that the figures for aortic aneurysm must, in the earlier years, have included many deaths from

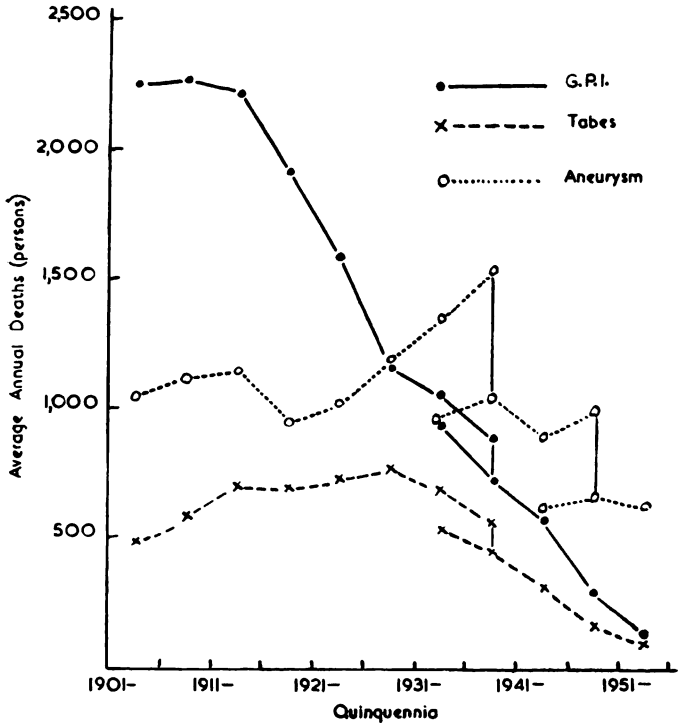

FIG. 2.—Average Annual Deaths, by quinquennia, from General Paralysis of the Insane, Tabes and "Aneurysm" (from the Registrar General's Annual Reports for England and Wales). The breaks in the curves are explained in the text.

non-syphilitic aneurysms, so that the real decline (if any) in mortality from syphilitic aneurysm must be less than that represented by the curve (indeed, for females, the Registrar General's actual figures of average mortality from 1946 to 1955 are higher than those from 1901 to 1910). This comparatively slight decline (or perhaps rise) in mortality from aortic aneurysm is in accordance with the figures quoted by King (1958) that the number of cases of syphilis of more than a year's duration showed no appreciable decline between 1931 and 1952. The decline in mortality from dementia paralytica and tabes cannot, therefore, be attributed to the prevention or early treatment of syphilis. Yet the decline in mortality from tabes cannot be attributed to any specific treatment, for until penicillin was introduced after 1945 no specific treatment was known[1]; this decline has probably, therefore, been a natural one. From the close similarity between tabes and dementia paralytica we might argue that the decline in mortality from dementia paralytica has also been a natural one. Even if we disallow this argument, the decline is far greater than could be attributed to the effects of malarial treatment. Thus Nicole (1943) found that of 401 paretics receiving malaria only 32 per cent. were finally discharged from hospital and the same proportion is mentioned by Hutton (1941) and, from the U.S.A., by Iskrant (1945). Even if none of the discharged cases was recorded as dying from dementia paralytica, this would only lead to a mortality reduced from pre-malarial days by a factor of 1·5 whereas the mortality has in fact

[1] Walshe (1947, p. 174) says that he "cannot claim ever to have been satisfied that anti-syphilitic treatment influences the course of tabes".

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been reduced by a factor of 18. There remains a further possibility. The paretics who remained in hospital after treatment and who died perhaps years later of intercurrent disease may not all have been recorded as dying from dementia paralytica. If the proportion of such cases was sufficiently high, this could account for the reduction in mortality. Yet it would not explain the fall in mortality that occurred before malaria therapy was introduced, nor would it explain the continued fall in mortality after the therapy had become established. Moreover, no explanation of reduced mortality in terms of treatment would account for the very general experience that the morbidity has been declining for many years and that nowadays a case of dementia paralytica is almost a rarity. I am informed by the Board of Control that the numbers of admissions (including re-admissions) of general paralysis of the insane to mental hospitals in England and Wales fell from 1,246 in 1930 to 408 in 1950.

Conclusion

Sir Humphrey Rolleston (1927) observed that many diseases have undergone modifications in form, in severity and in prevalence during historical times. Such modifications may be ascribed either to changes in the habits or constitution of the host, or to changes in an infecting organism. The disappearance of chlorosis, for example, was probably related to the disappearance of the fashion for tightly-laced corsets; the diminished prevalence of urinary calculus can be attributed to changes in dietary and drinking habits. Diphtheria, on the other hand—"a disease so sharply cut that it can hardly have been overlooked until Brettonneau of Tours" (who gave the first clear description of it in 1821)—is seen by Rolleston as probably arising *de novo* from the mutation of a hitherto harmless diphtheroid. In the same way, it may be suggested that dementia paralytica may also have been a new disease arising from a mutation in the syphilitic virus towards the end of the eighteenth century. In summary, this hypothesis is based on four considerations:

1. There is evidence (not universally accepted) that the syphilitic virus underwent some change at the end of the fifteenth century and that this was responsible for the great epidemic of that time. With regard to other changes in the nature of syphilitic disease, Klotz (1926) pointed out that there are no satisfactory descriptions of aortic aneurysm until the beginning of the sixteenth century when they become common.

2. Although dementia paralytica presents (or did present, when it first became prevalent) a very striking clinical picture, yet there is no clear description of it and certainly no evidence that it was at all common until the Parisian outbreak described by Esquirol, Georget, Bayle and Calmeil.

3. The hypothesis of a mutant strain of spirochaete spreading by venereal infection from a centre somewhere in northern France would largely explain the varying times at which dementia paralytica was recognized in different countries and the variations in prevalence and sex ratio reported in these countries during the years after its first recognition.

4. There is evidence that during the past 140 years the disease has shown gradual modifications in clinical form and a recent natural decline in prevalence. These changes are comparable with the changes that took place in the clinical course of syphilis during the years that followed the fifteenth century epidemic.

The existence of a neurotropic strain of treponema must, in the absence of laboratory proof, remain only a more or less probable hypothesis. The

attempt to support this hypothesis has been my excuse for drawing attention to the history of dementia paralytica. It is a disease which, in a relatively short time, has shown marked changes in its prevalence, distribution and clinical characteristics; and whatever may be the explanation of these changes, they permit us to reflect on a theme which it is perhaps the business of medical history to emphasize—the mutability of disease.

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REFERENCES

ARIETI, S., "General Paresis in Senility", *Amer. J. Psychiat.*, 1945, **101,** 585.
ARNOLD, T., *Observations on the Nature, etc. of Insanity*, 1786. London.
ASHE, I., "Some Observations on General Paralysis", *J. Ment. Sci.*, 1876, **22,** 82.
AUSTIN, T. J., *General Paralysis, its Symptoms, Causes and Seat*, 1859. London.
BALLET, G., and BLOCQ, P., in *Traité de Médicine*, ed. by Masson, G., 1894, Vol. 6, p. 1011. Paris.
BAILLARGER, M., "Délire hypocondriaque des déments paralytiques", *Gaz. des Hôpitaux*, 1857, pp. 55, 218, 477.
Idem, "De la découverte de la paralysie générale, I", *Ann. Méd.-Psychol.*, 1859, **5,** 509.
Idem, "De la découverte de la paralysie générale, II", *ibid.*, 1860, **6,** 1.
BAIRD, H., "Statistical Observations on General Paralysis", *J. Ment. Sci.*, 1905, **51,** 581.
BAYLE, A. L. J., *Recherches sur l'arachnitis chronique, la gastrite et la gastro-entérite chroniques, et la goutte, considerées comme les causes de l'aliénation mentale*, 1822. Paris.
Idem, *Traité des Maladies du Cerveau*, 1826. Paris.
BERKLEY, H. J., "Dementia Paralytica in the Negro", *Johns Hopkins Hosp. Bull.*, 1893, **4,** 94.
Idem, *A Treatise on Mental Disease*, 1900. New York.
BLANDFORD, G. F., *Insanity and its Treatment*, 1871. London.
BOSTROEM, A., in *Handbuch der Geisteskrankheiten*, ed. by Bumke, O., 1930, Vol. 8, p. 165. Berlin.
BONNET, H., and POINCARÉ, —., "Recherches sur l'anatomie pathologique et la nature de la paralysie générale", *Annal. Méd.-Psychol.*, 1868, **12** (4th series), 169.
BOYD, R., "Vital Statistics, etc. in the Somerset Lunatic Asylum", *J. Ment. Sci.*, 1865, **10,** 491.
BROWNE, W. A. F., "New Cerebro-psychical Diseases", *Amer. J. Insan.*, 1875, **32,** 198.
BUCKNILL, J. C., "The Diagnosis of Insanity", *J. Ment. Sci.*, 1857, **3,** 141.
Idem and TUKE, D. H., *A Manual of Psychological Medicine*, 1858, p. 17. London.
Idem, *ibid.*, 1874, 3rd edition. London.
BULLEN, F. ST.J., "Inquiries into a Variation of Type in General Paralysis", *J. Ment. Sci.*, 1893, **39,** 185.
BURROWS, G. M., *Commentaries on the Causes, etc. of Insanity*, 1829. London.
CALMEIL, L. F., *De la Paralysie considérée chez les Aliénés*, 1826. Paris.
Idem, *Traité des Maladies Inflammatoires du Cerveau*, 1859. Paris.
CANTAROW, A., and TRUMPER, M., *Lead Poisoning*, 1944. Baltimore, p. vii.
CASTIGLIONI, A., *A History of Medicine*, 1947. 2nd edition. Translated by Krumbhaar, E. B. New York.
CHASE, R. H., *General Paresis*, 1902. London.
CLOUSTON, T. S., *Clinical Lectures on Mental Diseases*, 1883. London.
Idem, *ibid.*, 1904. 6th edition. London.
CONOLLY, J., *An Inquiry concerning the Indications of Insanity*, 1830. London.
Idem, *On Some Forms of Insanity*, 1849. London.
CULLEN, W., *Synopsis Nosologiae Methodicae*, 1769. Edinburgh.
DAYTON, N. A., *New Facts on Mental Disorders*, 1940. Illinois.
DEAS, P. M., "Five Years of Statistics, etc.", *J. Ment. Sci.*, 1879, **25,** 8.
DIEFENDORF, A. R., "The Etiology of Dementia Paralytica", *Brit. med. J.*, 1906, *ii*, 744.
ELLIS, W. C., *A Treatise on the Nature, etc. of Insanity*, 1838. London.
ESMARCH, F., and JESSEN, W., "Syphilis und Geistesstöring", *Allg. Ztschr. f. Psychiat.*, 1857, **14,** 20.
ESQUIROL, E., Article on "Dementia" in the *Dictionnaire des Sciences Médicales*, 1814.
Idem, *Des Maladies Mentales*, 1838. Paris.
FALRET, J., *Recherches sur la Folie Paralytique*, 1853. Paris.
FROSHANG, H., and YTREHUS, A., "A Study of General Paralysis with special reference to the Reasons for the Admission of these Patients to Hospital", *Acta Psychiat. Neurol. Scand.*, 1956, **31,** 35.
GARRISON, F. H., *An Introduction to the History of Medicine*, 1929. 4th edition. London.
GEORGET, E. J., *De la Folie*, 1820. Paris.
GREEN, E. M., "Psychosis among Negroes—a Comparative Study", *J. nerv. ment. Dis.*, 1914, **41,** 697.

GRIESINGER, W., *Mental Pathology and Therapeutics*, 1861. Translated in 1867 by Robertson, C. L., and Rutherford, J., London.
GUTHRIE, D., *A History of Medicine*, 1945. London.
GUTHRIE, L. G., " 'Myasthenia Gravis' in the Seventeenth Century", *Lancet*, 1903, *i*, 330.
HASLAM, J., *Observations on Insanity*, 1798. London.
Idem, *Observations on Madness and Melancholy*, 1809. London.
HEIBERG, P., "Variations in the Number of Reported Cases of Syphilis and in the Number of Deaths from General Paresis", *Acta Psychiat. Neurol. Scand.*, 1932, **7**, 189.
HIRSCH, A., *Handbook of Geographical and Historical Pathology*, 1885. London. Vol. 2, Ch. 2. Translation from the 2nd edition by Creighton, C.
HUTTON, E. L., "Recent Advances in the Aetiology and Treatment of Neurosyphilis", *J. Ment. Sci.*, 1941, **87**, 1.
HYSLOP, T. B., "Pseudo-General Paralysis", *ibid.*, 1896, **42**, 303.
IDANOFF, I. D., "De la Paralysie Générale chez la femme", *Annal. Méd.-Psychol.*, 1894, **19**, 382.
ISKRANT, A. P., "The Economic Cost of Paresis in the United States", *J. ven. Dis. Inf.*, 1945, **26**, 175.
Journal of Mental Science, Discussion on "The Causation of General Paralysis", 1873, **19**, 164.
Ibid., Review of the 36th Annual Report of the General Board of Commissioners in Lunacy for Scotland, 1895, **41**, 116.
Ibid., Discussion on "Pseudo-General Paralysis", 1896, **42**, 646.
Ibid., Review of the 48th Annual Report of the General Board of Commissioners in Lunacy for Scotland, 1907, **53**, 154.
KING, A., " 'These Dying Diseases'; Venereology in Decline?", *Lancet*, 1958, *i*, 651.
KLOTZ, O., "Concerning Aneurysms", 3rd Gordon Bell Memorial Lecture, University of Toronto Studies, Pathological Series (quoted by Rolleston, 1927b), 1926.
KOJOG, F., "Die endemische Syphilis in Bosnia und Herzegowina", *Dermatologica*, 1939, **79**, 361.
KRAEPELIN, E., "General Paresis", *Nervous and Mental Diseases Monograph No. 14*, 1913. New York. Translated by Moore, J. W.
Idem, "The Problems presented by General Paresis", *J. nerv. ment. Dis.*, 1926, **63**, 209.
Idem, *Psychiatrie*, 1927. 9th edition. Vol. 2. Leipzig.
KRAFFT-EBING, R. VON, "Zur Geschichte und Literatur der Dementia Paralytica", *Zeitschr. f. Psychiat.*, 1866, **23**, 627.
Idem, *Die Progressive Allgemeine Paralyse*, 1894. Vienna.
Lancet, "A new disease?", 1957, *ii*, 285.
LEES, R., "Syphilis—a historical and modern problem", *Trans. Med.-Chir. Soc. Edin.*, 1950, **129**, 58.
LEIGH, D., "John Haslam, M.D., 1764–1844, Apothecary to Bethlem", *J. Hist. Med.*, 1955, **10**, 17.
LENNOX, W. G., "Neurosyphilis among the Chinese", *Arch. Neurol. Psychiat.*, 1923, **9**, 26.
LOMHOLT, M., "Clinic and Prognosis of Malaria-treated Paralysis", *Acta Psychiat. Neurol. Scand.*, 1944, Suppl. 30.
LUNIER, M. L., "Recherches sur la paralysie générale progressive", *Annal. Méd.-Psychol.*, 1849, p. 183.
MCCARTNEY, J. L., "Why is Neurosyphilis uncommon in the Tropics?", *Mil. Surgeon*, 1946, **99**, 21.
MACDONALD, A. E., "General Paresis", *Amer. J. Insan.*, 1877, **33**, 451.
MAJOR, R. H., *A History of Medicine*, 1954. Oxford.
MALZBERG, B., "Mental Disease in Negroes in New York State, 1939–41", *Ment. Hyg.*, 1953, **37**, 450.
MARIE, M. A., in *La Paralysie Générale, Centenaire de la Thèse de Bayle*, 1922. Vol. 2, p. 139. Paris.
MAUDSLEY, H., *The Physiology and Pathology of Mind*, 1867. London.
Idem, *The Pathology of Mind*, 1879. London.
Idem, *ibid.*, 1895, 2nd edition. London.
MERYON, E., *Practical and Pathological Researches on the Various Forms of Paralysis*, 1864. London, p. 153.
METTLER, C. C., *A History of Medicine*, 1947. Philadelphia.
MEYER, A. "A Note on the Concept of Dementia Paralytica at the time of Robert Schumann's death in 1856", *J. Ment. Sci.*, 1959, **105**, 116.
MICKLE, W. J., *General Paralysis of the Insane*, 1880. London.
Idem, *ibid.*, 1886. 2nd edition. London.
MILLINGEN, J. G., *Aphorisms on the Treatment and Management of the Insane*, 1840. London, p. 46.
MÖNKEMÜLLER, —., "Zur Geschichte der progressiven Paralyse", *Zeit. f. d. ges. Neurol. Psychiat.*, 1911, **5**, 500.
MOORE, M., and SOLOMON, H. C., "Contributions of Haslam, Bayle and Esmarch and Jessen to the history of Neurosyphilis", *Arch. Neurol. Psychiat.*, 1934, **32**, 804.
MOREIRA, J., and PENAFIEL, A., "Contributions to the Study of Dementia Paralytica in Brazil", *J. Ment. Sci.*, 1907, **53**, 507.
MORRIS, H., "Observations on the History of Syphilis", *Lancet*, 1912, *ii*, 497.

MORTON, L. T., *Garrison and Morton's Medical Bibliography*, 1954. 2nd edition. London, p. 418.
MOTT, F. W., *Arch. Neurol. (London)*, 1900, **1**, 166.
Idem, "Recent developments in our knowledge of Syphilis in relation to Diseases of the Nervous System", *Brit. med. J.*, 1908, *i*, 10.
NEUMANN, H., *Lehrbuch der Psychiatrie*, 1859. Quoted by Krafft-Ebing, 1894.
NICOLE, J. E., "Malaria in Neurosyphilis, 1923–1943", *J. Ment. Sci.*, 1943, **89**, 381.
NONNE, M., *Syphilis und Nervensystem*, 1902. Berlin, p. 543. Quoted by Zilboorg and Henry, 1941.
PADGET, P., and MOORE, J. E., "Syphilis, a review of the recent Literature", *Arch. int. Med.*, 1936, **58**, 901.
PINEL, P., *Nosographie Philosophique ou Méthode de l'Analyse appliquée à la Médecine*, 1798. Paris.
Idem, *Traité Médico-philosophique sur l'Aliénation Mentale*, 1809. 2nd edition. Paris.
PLAUT, F., *Paralysestudien bei Negern und Indianern*, 1926. Berlin, p. 25.
POWER, T. D., "The Aetiology of General Paralysis of the Insane", *J. Ment. Sci.*, 1930, **76**, 524.
PRICHARD, J. C., *A Treatise on Insanity*, 1835. London.
Report together with the Minutes of Evidence and an Appendix of Papers from the Committee appointed to consider of Provision being made for the better Regulation of Madhouses in England (1815). London.
RICHARDSON, —., "Asylum Reports for 1890", *J. Ment. Sci.*, 1891, **37**, 604.
ROBERTSON, G. M., "The Discovery of General Paralysis", *ibid.*, 1923, **69**, 1.
ROLLESTON, H., "Changes in the Clinical Aspects of Disease", *Brit. med. J.*, 1927a, *i*, 87.
Idem, "Clinical Variations in Disease from the Historical Point of View", *ibid.*, 1927b, *ii*, 205.
ROSANOFF, A. J., *Manual of Psychiatry*, 1938. 7th edition. New York, p. 341.
SALOMON, E., "On the Pathological Elements of General Paresis", *J. Ment. Sci.*, 1862, **8**, 365.
SAMUELS, W. F., "General Paralysis of the Insane in the Federated Malay States", *ibid.*, 1916, **62**, 411.
SANDER, W., "Die paralytische Geistesstörung beim weiblichen Geschlecht", *Berlin Klin. Woch.*, 1870, **7**, 81.
SANKEY, W. H. O., "The Pathology of General Paralysis", *J. Ment. Sci.*, 1864, **9**, 467.
Idem, *Lectures on Mental Diseases*, 1866. London.
SEMELAIGNE, R., *Les Grands Aliénistes Français*, 1894. Paris.
Idem, *Les Pionniers de la Psychiatrie Française*, 1930. Paris.
SKAE, D., "Contributions to the Natural History of General Paralysis", *Edinburgh med. J.*, 1860, **5**, 885.
SMITH, J. C., "Notes on the Appearance of Dementia Paralytica and the relation between its Frequency and the Antisyphilitic Treatment", *Acta Psychiat. Neurol. Scand.*, 1926, **1**, 346.
SPITZKA, E. C., *Insanity, its Classification, Diagnosis and Treatment*, 1883. New York.
STEWART, R. M., "General Paralysis; its unsolved problems", *J. Ment. Sci.*, 1924, **70**, 33.
STEWART, R. S., "The Increase of General Paralysis in England and Wales; its Causation and Significance", *ibid.*, 1896, **42**, 760.
Idem, "Decrease of General Paralysis of the Insane in England and Wales", *ibid.*, 1901, **47**, 41.
STODDART, W. H. B., *Mind and its Disorders*, 1921. 4th edition. London.
SUDHOFF, K., *Essays in the History of Medicine*, 1926. New York, Ch. 22, p. 259.
TOULOUSE, E., in *La Paralysie Générale, Centenaire de la Thèse de Bayle*, 1922. Paris, Vol. 2, p. 11.
TUKE, HARRINGTON, "On General Paralysis", *J. Ment. Sci.*, 1859, **5**, 575 and **6**, 200.
WAGNER, C. C., "The Comparative Frequency of General Paresis", *Amer. J. Insan.*, 1902, **58**, 587.
WALSHE, F. M. R., *Diseases of the Nervous System*, 1947. 5th edition. Edinburgh.
WESTPHAL, C., "On the present state of our knowledge regarding General Paralysis of the Insane", *J. Ment. Sci.*, 1868, **14**, 162.
WHITWELL, J. R., *Syphilis in Earlier Days*, 1940. London.
WILLIS, T., *De Anima Brutorum*, 1672. Translated in *Dr. Willis' Practice of Physick*, by Samuel Pordage, London, 1684. Part II, "Concerning the Soul of the Brutes", Ch. 9, *et seq.*
WILSON, J. H., on "General Paralysis of the Insane", *Liverpool Med.-Chir. J.*, 1857, p. 231.
WILSON, S. A. K., *Neurology*, 1941. 2nd edition, 1954, edited by A. N. Bruce, London.
WISE, —., "General Paralysis of the Insane", *Indian med. Gaz.*, 1869, **4**, 75.
WORKMAN, J., "Pathological Notes", *Amer. J. Insan.*, 1858, **15**, 1.
Idem, "On Paresis", *Canada Lancet*, 1878, **10**, 357 and **11**, 1.
ZILBOORG, C., and HENRY, G. W., *A History of Medical Psychology*, 1941. London, Ch. 13.