

Research Article

Neurosyphilis. Historical Perspectives on General Paresis of the Insane

Jesper Vaczy Kragh*

Department of Public Health, University of Copenhagen, Denmark

*Corresponding author

Jesper Vaczy Kragh, Department of Public Health, CoRe, University of Copenhagen, Karen Blixens Plads 8, DK-2300, Denmark, Tel: 45 29792902; Email: jvk@sund.ku.dk

Submitted: 15 September 2017

Accepted: 19 September 2017

Published: 23 September 2017

Copyright

© 2017 Kragh

OPEN ACCESS

Abstract

In the early nineteenth century general paresis of the insane (GPI), also known as general paralysis or dementia paralytica, was described as a new psychiatric disorder. It soon became one of the most dreaded mental disorders. Large numbers of patients with GPI were admitted to mental hospitals in the nineteenth and early twentieth century. The inevitable outcome of the disease was death within a short period of time. The cause of GPI was unknown until the late nineteenth century, and there was no effective treatment. The development of accurate diagnostic methods was introduced in the early twentieth century, and it was confirmed that GPI is a syphilitic disease. New effective treatment options eventually made GPI a rare diagnosis in psychiatry. Nowadays, GPI is an uncommon disease, but the history of the disorder and its treatment offers important historical lessons.

Keywords

- Neurosyphilis
- General paresis
- Penicillin
- Malaria fever therapy
- History of psychiatry

ABBREVIATIONS

GPI: General Paresis of the Insane; **AR Pupil:** Argyll Robertson Pupil

GENERAL PARESIS OF THE INSANE

GPI first appears to be reported in Paris during the Napoleonic Wars [1-3]. It was also in France that the earliest descriptions of GPI as a disease were published. The paralysis consisted of relatively constant and progressive physical features: disturbance in articulation, typically causing tremulous and indistinct speech; unsteadiness of gait leading to staggering; and eventually complete paralysis of voluntary movements, inability to swallow, incontinence and gangrene [4]. Argyll Robertson pupil (AR pupils) was also observed. Physicians of the nineteenth century noted that the disease usually struck people (mostly men) in their thirties and forties. The early sign of GPI was the speech defects, the patients had difficulties pronouncing certain words. Furthermore, the patients often suffered from depression and personality changes, especially megalomania claiming to be kings, emperors, God etc. Memory and intellectual impairments also occurred. In the later stages of GPI paroxysms with seizures occurred, and the patients' condition would gradually get worse. It was observed that the patients usually died two or three years after being admitted to the mental hospitals [5].

The paralytic symptoms were described by Jean-Étienne Esquirol (1772-1840) in 1816, but it was the young French physician Antoine-Laurent-Jesse Bayle (1799-1858) who first identified GPI as a distinct disease in his medical thesis of 1822 [1,6,7]. Georget E] (1795-1828) and other French psychiatrists

also studied GPI in the early nineteenth century, noting the fatal course of the disease and the increasing number of cases of GPI [2]. Esquirol reported that one-sixth of all admissions to Charenton in 1828 were paralytic patients, and the disease was also common at Bicêtre and the St. Yon asylum near Rouen [3]. Large numbers of GPI cases were also reported from the US and the UK, where as many as 20 percent of British male asylum admissions received this diagnosis, and in Denmark [1,5,6]. In some countries such as the Netherlands, the number of GPI admissions appears to have been lower [8]. However, during the early nineteenth century the syphilitic origin of GPI was unknown, the principal causal factors were thought to be alcoholic and sexual excesses [3].

CAUSES

In 1857, Peter Willers Jessen (1824-1912) and Friedrich Esmarch (1823-1908) of Schleswig published the first international article suggesting syphilis as the possible cause of GPI [3,5,9]. In the article, "Syphilis und Geistesstörung" [Syphilis and mental disorder], they noted that little could be found in the psychiatric literature about syphilis and its relation to psychosis. They claimed to have obtained evidence at the mental hospital Hornheim that syphilis could produce mental disturbance. Jessen and Esmarch reported that in "nine subsequently observed cases [of GPI] a previous syphilis was demonstrated in all except one case, in which only a visit to a brothel could be ascertained". Consequently, they proclaimed that "these facts probably justify the hypothesis that syphilis is the foundation of dementia paralytica" [10]¹. However, Jessen and Esmarch were well aware of the fact that the small number of cases described in the article

did not demonstrate, in a convincing manner, that syphilis was the cause of GPI, but they hoped that their article would “stimulate similar observation and differences of opinion” [10].

Jessen and Esmarch’s study inspired the Danish psychiatrist Christian Magdalous Jespersen (1844-1873) of St. Hans Mental Hospital in Zealand to conduct a large study of GPI [11]. In 1873, Jespersen completed his doctoral thesis entitled *Skyldes den almindelige fremskridende paresis syphilis?* [Is the common progressive paralysis due to syphilis?] Jespersen noted that only a few psychiatrists before him had reached the conclusion that the main cause of GPI was syphilis. The Swede Gustav Kjellberg had asserted, in an 1863 study, that general paresis did not “develop in an organism which is entirely free from hereditary as well as acquired syphilis” [12]; and the Norwegian Ole R. A. Sandberg stated in an 1868 article, that syphilis had “the first rank among the causes” of GPI [9,13]. Jespersen emphasised that very few psychiatrists outside Scandinavia had pointed to syphilis as the cause, and he could only bring

Translation from German to English by the author to mind a single German physician, Theodor Simon, who was inclined to share this view [14].

Christian Jespersen’s enquiry was the hitherto most extensive epidemiological study of patients with GPI. His material consisted of 123 patients who had been admitted to St. Hans Mental Hospital [15]. Jespersen personally examined 34 paralytics resident in St. Hans Hospital for signs of previous syphilis. He also went through the medical records of all the patients to find out if the patients had been treated for syphilis previously. Moreover, he collected information from general practitioners and interviewed the relatives of the patients in order to gather information about the paralytic patients. He eventually reported that 77% of 123 patients had a past syphilitic infection. These findings supported his conclusions that “general progressive paralysis does not occur in a person unless he has formerly had syphilis” and GPI “is a syphilitic brain disease” [5,11,15].

In 1884 the Congrès Périodique International des Sciences Médicales was opened in Copenhagen and the question of syphilis and GPI was one of the main topics [16]. Jespersen’s results were discussed in detail at the Congress. Jespersen was supported by Oscar Rohmell (1845-1912) of St. Hans Hospital. In a study of 194 patients with GPI, Rohmell found that 77% had syphilis [17]. Rohmell was backed up by other Scandinavian psychiatrists at the conference, whereas medical doctors from Russia, Holland and France stressed other causes of GPI. At the Congress the famous defender of the degeneration doctrine, Valentin Magnan (1835-1916), of the Hôpital St. Anne in Paris [18], criticised the Scandinavian studies. He maintained that at St Anne, where an average of 300 paralytic patients were admitted annually, only 30-40 syphilitics were found among the patients with GPI. And he declared that “syphilis, chronic alcoholism and excesses of any kind are only determining factors” which act on the background of a hereditarily conditioned predisposition [9,19].

After the Congress the quarrel about the cause(s) of GPI continued. In France, Magnan was challenged by Alfred Fournier (1832-1914), who conducted extensive studies in order to prove that GPI was “a syphilitic madness” [20]. Fournier was supported

by Emil Kraepelin (1856-1926) and other notable psychiatrists, and by the turn of the century, psychiatrists more commonly accepted that syphilis was the essential cause of the disease [6].

However, it was not until the early twentieth century that the exact cause of GPI was discovered, viz. the bacteria *Treponema pallidum*. The bacteria were finally seen with the human eye in 1905, when Fritz Schaudin (1871-1906) observed the small organism under his microscope [21]. One year later, the first blood test for detecting syphilis was developed by August von Wassermann (1866-1925); and in 1913, Hideyo Noguchi (1876-1928) and co-workers at the Rockefeller Institute of New York were the first to discover *Treponema pallidum* in the brain of a patient with general paralysis [22,23].

TREATMENT

Effective treatments for GPI were still lacking in the early twentieth century. The first cure for primary syphilis, Salvarsan (arsphenamine), discovered by Paul Ehrlich in 1909, had no effect on GPI, and the same applied for other psychiatric treatments of the time. However, this changed during the First World War. In the summer of 1917, Julius Wagner-Jauregg (1857-1940) conducted his first experiment on malaria fever therapy for GPI at the Psychiatric University Clinic in Vienna [24]. Prior to this experiment in 1917, he had studied various methods of inducing fever in psychiatric patients. In the late 1880s and 1890s, he had begun using tuberculin and other bacterial proteins to produce fever, and he also had suggested using malaria in an 1887 publication, but eventually gave up this plan [7,25]. It was a chance event caused him to take up the plan again thirty years later. While World War I was raging, a soldier from the Macedonian front was admitted to the hospital in Vienna. The soldier had tertian malaria with chills, sweating and regular attacks of fever; and Wagner-Jauregg considered the possibility of using the soldier’s blood to induce fever in the hospital’s patients with general paralysis. During an attack of fever Jauregg drew blood from the soldier and injected it subcutaneously between the shoulder blades of two patients with paralysis. Then he used the blood from the two patients to inoculate a new group of patients with GPI. After the blood was injected, the patient’s first fever attack occurred about a week later. After going through seven to twelve fever attacks, the patients were given quinine to terminate the malarial infection [26].

One year after the first trial, Julius Wagner-Jauregg reported that 67% of the paralytics had improved [6,26,27]. News of malaria fever therapy spread to other countries, and in the early 1920s, the treatment was not only used in Europe, but also in South America and the United States. In an international review of 2460 cases recorded in the literature by 1926, 27.5% of the treated patients were found greatly improved and another 25.6% moderately improved [7]. In 1927, Julius Wagner-Jauregg was awarded the Nobel Prize for Medicine or Physiology for his discovery of the therapeutic value of malaria inoculation in the treatment of general paralysis of the insane. He was the first psychiatrist ever to receive the prize [7,27].

After the introduction of malaria fever therapy other methods of inducing fever in patients with GPI was invented. Treatments with sulphur or milk injections became alternatives to malaria

fever therapy [28]. New treatment devices were also developed. In the 1930s, the air-conditioned cabinet called the hypertherm was introduced in psychiatry. The hypertherm was invented by Charles Franklin Kettering in conjunction with the Fever Research Project at the Miami Valley Hospital in Dayton, Ohio [29]. When the hypertherm was heated up, body temperature would rise to about 40° C, and the patients who received this type of therapy, recovered to the same degree as did the malaria-treated patients. But the hypertherm did not replace malaria fever therapy completely and both methods were used in the 1940s.

Penicillin was introduced in the early 1940s, and the new drug would eventually render both malaria fever therapy and the hypertherm superfluous. In 1943, American doctors reported that they had used penicillin in the treatment of patients with GPI, and one year later it was evident that penicillin also was a success in the treatment of paralytic patients [30]. In the 1940s penicillin was often together with malaria fever therapy and the hypertherm. By the 1950s, the malaria-treatment era was over, but the hypertherm was still used for some time, until it finally became clear to all that penicillin was the best solution [31,32].

In the late 1950s and 1960s, it also became clear that the incidence of GPI was declining rapidly. In the late twentieth century, GPI was no longer among the most dreaded diseases for psychiatrists to fight; and today, GPI only quite exceptionally is evident in psychiatric departments and clinics.

CONCLUSIONS

Even though GPI became a rare disease, it nevertheless played a pivotal role in the development of psychiatry. The unknown cause of GPI thus gave rise to statistical and epidemiological analysis in the 1850s and 1860s; and in the early twentieth century, bacteriological methods were employed in the study GPI. New diagnostic procedures such as the Wassermann test became important tools in the psychiatric clinic. Furthermore, malaria fever therapy provided the background for large empirical studies of psychiatric patients. In order to measure the effect of the treatment it became vital to do large catamnestic studies of treated patients. The study of GPI and the invention of malaria fever therapy resulted in the first Nobel Prize for a psychiatric treatment in 1927.

After the discovery of the cause of GPI and the introduction of malaria fever therapy, hopes were raised in psychiatry that similar methods and results could be obtained with other psychiatric disorders. These expectations, however, were not fulfilled. GPI is no longer considered a major problem in psychiatry, but it is nevertheless important to remember how the disease works. As Gayle Davis reminds us, there are several aspects of current medical debate which suggests that GPI or neurosyphilis should not be confined to the medical dustbin just yet [1]. In the last decade there has been rise in the worldwide rates of primary and secondary syphilis, and syphilis has re-emerged as a health concern in many countries. Concern about a subsequent rise of tertiary syphilis has also been expressed. The early recognition of neurosyphilis is important since patients who are not diagnosed early enough are unlikely to regain previous cognitive performance. Consequently, it is vital not to forget about GPI so that cases can be recognized and treated at an early stage.

REFERENCES

1. Davis G. 'The Cruel Madness of Love'. Sex, Syphilis and Psychiatry in Scotland, 1880-1930. Amsterdam: Rodopi. 2008.
2. Brown EM. French psychiatry's initial reception of Bayle's discovery of general paresis of the insane. *Bull Hist Med.* 1994; 68: 235-253.
3. Hare EH. The origin and spread of dementia paralytica. *J Ment Sci.* 1959; 105: 594-626.
4. Hurn JD. The History of General Paralysis of the Insane in Britain, 1830-1950. University of London, 1998.
5. Kragh JV. Malaria fever therapy for general paralysis of the insane in Denmark. *Hist Psych.* 2010; 21: 471-486.
6. Braslow J. Mental ills and bodily cures. Psychiatric treatment in the first half of the twentieth century. Berkeley: University of California Press. 1997.
7. Brown EM. Why Wagner-Jauregg won the Nobel Prize for discovering malaria therapy for general paresis of the insane. *Hist Psychiatry.* 2000; 9: 371-382.
8. Slijkhuis J, Oosterhuis H. Cadaver brains and excesses in Baccho and Venere: Dementia paralytica in Dutch psychiatry (1870-1920). *J Hist Med Allied Sci.* 2014; 69: 426-460.
9. Neel AV, Ostenfeld I. Contribution to the history of dementia paralytica with special reference to the contributions of Scandinavian, particularly Danish scientists. *Acta Psych Neurol Scand.* 1946; 21: 605-642.
10. Esmarch F, Jessen W. Syphilis und Geistesstörung. *Allg Z Psychiatr.* 1857; 14: 20-36.
11. Kramp P, Gabrielsen G. Skyldes den almindelige fremadskridende parese syfilis? En epokegørende dansk disputats i en videnskabelig brydningstid. *Bibl Læger.* 2002; 194: 154-184.
12. Kjellberg G. Om Sinnesjukdomarnes stadier, utkast til en psychiatrisk diagnostic. Uppsala: AD. Bonnier. 1863.
13. Sandberg ORA. Paralysis generalis. *Norsk Magazin for Lægevidenskaben.* 1868; 22: 1-13.
14. Simon T. Die Gehirnerweichung der Irren. Hamburg: Wilhelm Mauke. 1871.
15. Jespersen CM. Skyldes den almindelige fremadskridende Parese Syphilis? Copenhagen: E. Jespersen. 1874.
16. Lange C. Congrès périodique international des sciences médicales. 8me session-Copenhague 1884. Copenhagen: Gyldendal. 1886.
17. Rohmell A. Le rôle de la syphilis dans le paralysie générale des aliénés. In Lange C .editor. Congrès périodique international des sciences médicales. 8me session, Copenhague 1884. Tome III. Copenhagen: Gyldendal. 1886: 80-86.
18. Dowbiggin I. Back to the future. Valetin Magnan, French psychiatry, and the classification of mental diseases, 1885-925. *Soc Hist Med.* 1996; 9: 383-408.
19. Mangan V. Discussion. In Lange .editor. C. Congrès périodique international des sciences médicales. 8me session, Copenhague 1884. Tome III. Copenhagen: Gyldendal. 1886: 89-90.
20. Quétel C. History of Syphilis. Cambridge: Polity Press. 1990.
21. Hayden D. Pox. Genius, Madness, and the Mysteriums of Syphilis. New York: Basic Books. 2003.
22. Wasserman A, Neisser A, Bruck E. Eine serodiagnostische Reaction bei Syphilis. *Deut Med Wochenschr.* 1906; 32: 744-746.

23. Noguchi H, Moore JW. A demonstration of *Treponema pallidum* in the brain in cases of general paralysis. *J Exp Med.* 1913; 17: 232-238.
24. Whitrow M. Julius Wagner-Jauregg (1857-1940). London: Smith-Gordon. 1993.
25. Albert AR. Fever therapy for general paresis. *Int J Dermatol.* 1999; 38: 633-637.
26. Whitrow M. Wagner-Jauregg and fever therapy. *Med Hist.* 1990; 34: 294-310.
27. Wagner-Jauregg J. Über die Einwirkung der Malaria auf die progressive Paralyse. *Psychiatr Neurol Wschr.* 1918/19; 21/22: 132-134 and 39/40: 251-255.
28. Kragh JV. 'Fumbling in the Dark'. Malaria, sulfosin and metallosal in the treatment of mental disorders in Denmark, 1917-1937". In: Volker Roelcke & Hans-Walter Schmuhl, editors. *Heroische Therapien.* Göttingen. Wallensteins Verlag. 2013: 102-115.
29. Young M. *Encyclopedia of Asylum Therapeutics, 1750-1950.* Jefferson, North Carolina: McFarland & Company. 2015: 131.
30. Shorter E. *A History of Psychiatry. From the Era of the Asylum to the Age of Prozac.* New York: John Wiley & Sons. 1997.
31. Arntsen K, Welner J. Hypertherm treatment of neurosyphilis. Methods of evaluation and prognostically important factors. *Acta Psych Neurol Scand.* 1955; 30: 529-552.
32. Boas J. Introductory lecture. On the treatment of neurosyphilis with artificial fever and penicillin. *Acta Psych Neurol Scand.* 1950; 25: 24-34.

Cite this article

Kragh JV (2017) Neurosyphilis. Historical Perspectives on General Paresis of the Insane. *JSM Schizophr* 2(2): 1013.