

## General Paralysis of the Insane (GPI): Redefining Psychiatry and Disease

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General Paralysis of the Insane (GPI) is an organic, severe neuropsychiatric condition following infection by the bacterium *Treponema pallidum*. Today, GPI (alongside tabes dorsalis, a similar disease lacking psychiatric manifestations) is generally referred to as neurosyphilis, though caution must always be exercised in linking medical conditions of one time period with another, despite their similarities. General paralysis of the insane received many different names in various countries throughout the seventeenth and eighteenth centuries, reflecting different aspects of the condition. For example, 'general paralysis of the insane' emphasized the aspect of insanity and psychiatric symptoms, while terms like 'general paresis' instead highlighted the motor disturbances that patients faced. Other terms such as 'paralytic dementia' or 'Ménigite chronique' highlighted neurological aspects of the condition. With the sheer number of synonyms presented by William Julius Mickle as early as 1886, one can imagine the wide variety of neurological, physical, and psychiatric symptoms presented in this complex, nuanced disease state (Mickle 1). In fact, general paralysis of the insane presented a peculiar case for nineteenth century psychiatry, as psychiatrists first recognized that alterations in the brain physiology of GPI patients led to psychiatric, neurological and physical manifestations.

Common psychiatric symptoms observed in GPI patients included mania and impulsivity, and neurological symptoms included

cognitive and memory deficits in addition to epilepsy (Pearce 273-4). The key symptom of GPI, however, was a devastating physical manifestation - the complete loss of will to move, hence the term 'paralysis' or variants in the many synonyms for the disease (274). GPI patients took up a significant proportion of asylum admissions, and the prognosis was grim. The pathogenesis of general paralysis of the insane as described by Antoine Bayle, who first identified GPI, as a distinct disease rather than a complication of insanity, was divided into several progressive stages with unique symptoms, although the concept of concrete, well-defined pathological stages is often a generalization at best when dealing with progressive disease (274). Despite criticism from many researchers at this partitioning, references to particular stages of GPI are commonplace in primary and secondary source literature, and some researchers such as E. Salomon of Sweden even sought to section general paralysis of the insane into various stages themselves (Mickle 3-5). For instance, Bayle's stages of general paralysis of the insane included "ambitious monomania, mania, and dementia," which can be contrasted against Salomon's stages of chronic lepto-meningitis, chronic diffuse periencephalitis, cerebral cortex degeneration, and finally, atrophy of the cerebral cortex (5). Despite reference to the same disease, the descriptions of these stages are drastically different and even use different models (psychiatric contrasted to neuroanatomical), which truly highlights the variable nature of general paralysis of the insane's pathogenesis.

Despite the rich history associated with GPI, it appears to be somewhat overlooked by the medical community, as well as the historical community. In my essay, I will argue that general paralysis of the insane was a fundamental and radical disease in the context of the developing fields of psychiatry and disease, further legitimizing psychiatry as a valid medical field, while highlighting a significant knowledge gap in the context of medical microbiology, including diagnostic criteria. The circumstances surrounding an individual's diagnosis of general paralysis of the insane were often

influenced by the social and financial standing of European patients; therefore, the disease was nearly a privilege to receive, at least in the sense that it separated patients from other psychiatric conditions with greater negative stigmas (Artvinli 130). Henry Williams identified general paralysis of the insane early on as a disease that the intellectual members of a community were disproportionately affected by (Williams 744).

### ***Social Status and the diagnosis of General Paralysis of the Insane***

Alongside the already complicated myriad of potential symptoms in this poorly understood disease, the diagnosis of general paralysis of the insane was often multifaceted, as the social status of a patient was an important contributing factor to whether a patient would be diagnosed with GPI, or another form of neurological or psychiatric disease such as dementia or insanity. Concerns from medical professionals already existed due to the sheer number of possible symptoms associated with general paralysis of the insane, and the excessive social profiling of patients performed in the nineteenth century only further complicated matters (Wallis 11). The societal component of a general paralysis of the insane diagnosis was much more prominent in European countries than in other countries, most likely as a result of popular European morals and societal expectations (Artvinli 130). To this extent, many have repeatedly referred to general paralysis of the insane as a “disease of civilization” (O’Connor 68). German psychiatrist Richard von Krafft-Ebing took this concept one step further, denoting GPI as a combination of both civilization and syphilization; a disease of “brain workers,” such as poets, physicians and teachers, could only be found in civilized cities (Artvinli 130). Raşid Tahsin, a Turkish psychiatrist, also correlated general paralysis of the insane with individuals of the higher socioeconomic classes, reinforcing the concept across Europe that general paralysis of the insane was a

disease of the wealthy, “worldly” man (130). Others, while holding a similar view, do not hold the condition in such a high regard and would rather choose to emphasize the aspect of moral corruption and dangers of excess wealth (Braslow 584). Albert Campbell speaks of general paralysis of the insane as a disease that “localizes where traffic in immorality is greatest,” which O’Connor argues may have been one of the only references to prostitution in the context of GPI, despite the rich involvement of syphilis in both the etiological debates of GPI, as well as prostitution and contagious diseases acts during the nineteenth century (O’Conner 69). This social profiling rampant in the early history of general paralysis of the insane as a clinical disease inevitably led to the misdiagnosis of GPI patients who simply did not fit the social profile of GPI as a disease. Later reports of general paralysis of the insane tend to shift away from class-based diagnostic criteria, and more reports of lower-class general paralysis of the insane patients, as well as female general paralysis of the insane patients, made their way into the literature (Artvinli 133).

### ***The Controversy of General Paralysis of the Insane as an Organic Disease***

The proposed linkage between organic brain damage, such as the result of persistent inflammation of the meninges, with a host of physical, neurological and psychiatric manifestations, was nothing short of groundbreaking in the context of the history of psychiatry, then known as alienism. Prior understanding of general paralysis of the insane before being recognized as a distinct disease by Bayle, such as by French alienist Jean Etienne Dominique Esquirol, suggested that the signature paralysis associated with GPI was simply a complication of insanity, and thus, was not of organic origin (Pearce 274). Historian E.M. Brown argues that this dismissal by Esquirol may have been due to the timeframe of the disease progression; paralysis followed the observable psychiatric

symptoms of insanity (Brown 243). Observations of insanity by John Haslam, who retrospectively may have been the first to document GPI symptoms in asylum patients, described a variety of pathological hallmarks now known to be found in GPI cases (Moore and Solomon 806-7). However, despite clearly describing what would be identified as general paralysis of the insane decades later, Haslam and the medical profession as a whole did not seem to regard the findings as anything more than complications of insanity (806-7). Alienism had always sought empirical, scientific methods to legitimize their profession as one of medicine, and not one founded on quackery; historically, psychiatry as a profession was often viewed with skepticism and distrust. Bayle's medical thesis, which described an organic brain condition not only in terms of neurological symptoms but also psychiatric symptoms, challenged alienism's view and directly contradicted the highly regarded work of Esquirol, as well as that of Philippe Pinel (808-9). Bayle's bold thesis received tremendous attention—including scathing attacks and criticism, even forcing him to leave the discipline of alienism—but nonetheless, changed the trajectory of psychiatry (Pearce 275). Bayle, due to his bold theories and overconfidence, was not viewed in a favourable light, despite the magnitude of his proposal claiming general paralysis of the insane as an organic disease. This positive attention instead went to Louis Calmeil, who published a similar piece on general paralysis of the insane in 1826, but was overly cautious in his statements, as opposed to Bayle's grandeur. Calmeil also worked to explain the organic brain lesions observed in postmortem GPI patients in such a fashion that it would not reject the popular works of Esquirol and Pinel, concluding his research with a statement that the brain lesions observed during autopsy were unable to sufficiently explain the psychiatric symptoms observed in the GPI patients during their life (Brown 239-240, 250). Calmeil would then receive the utmost praise from the very same alienists who criticized Bayle, notably Georget, who viewed Bayle's thesis as a direct attack on his mentor, Pinel, as well as the profession of psychiatry as a whole (250-51).

## ***General Paralysis of the Insane and *Treponema pallidum****

The pathogenesis of general paralysis of the insane as a disease was not the only factor of controversy. Since the proposal of syphilis as the etiological agent of general paralysis of the insane by Esmarch and Jessen in 1857, numerous arguments and debates during the nineteenth century sprung forward (Artvinli 127). Prior research on syphilis by venereologist Phillippe Ricord shed light on the disease state progression, including the partitioning of syphilis into three distinct stages of disease (Stewart et al. 60). Tertiary syphilis was a debilitating condition obtained following years of harbouring an untreated *Treponema pallidum* infection, known to affect many organs of the body, including the brain and muscles; descriptions of tertiary syphilis could easily account for a large portion of the varied symptoms observed in GPI patients. It was not the work of Esmarch and Jessen, however, that garnered the attention of the medical community, but rather the work of Alfred Fournier, Ricord's pupil, who statistically related GPI to syphilis infections. Emil Kraepelin, a German psychiatrist, declared that without a doubt, syphilis must be the essential cause of general paralysis of the insane (Braslow 581). This sentiment was echoed by Italian alienist and physician Luigi Mongeri, who determined that syphilis was a necessary prerequisite for the development of general paralysis of the insane after careful examination of 144 patients (Artvinli 129). English neuropathologist Sir Frederick Mott was also a strong supporter of the syphilitic etiological theory, and had managed to utilize anatomical as well as clinical evidence of a linkage between syphilis and GPI.

Despite growing support for the syphilitic etiology of general paralysis of the insane, many physicians were hesitant to correlate general paralysis of the insane with any form of venereal disease. O'Connor argues specifically that this hesitance may have been a result of the moral and societal characteristics associated with the

class of patients receiving a general paralysis of the insane diagnosis; to link married and employed middle-aged men of society with something as taboo as syphilis would have had consequences for physicians (O'Conner 68). Stewart et al. make a similar argument; physicians would often disguise or hide symptoms of syphilis to not endanger the moral reputation of their patients (Stewart et al. 77). Henry Williams, medical superintendent of Randall's Island hospitals located in the United States of America, writes the following regarding syphilis in his musings of the devastating toll of general paralysis of the insane: "the chief causes of paresis are habits and excesses that I cannot properly more than hint at here, working on a foundation laid by a disease whose name I may not mention because it is in itself a synonym for immorality" (Williams 752). It is key to note here that Thomas Clouston, then president of the Royal College of Physicians of Edinburgh, publicly diminished the role of syphilis in the pathogenesis of general paralysis of the insane, and instead suggested alternative etiological factors such as hard work (O'Conner 69). There is some idea, in the historiography regarding general paralysis of the insane, that the refutation of syphilis as the contributing factor to general paralysis of the insane by the esteemed Clouston was motivated not by belief, but by fear of repercussions by the financial supporters of the Royal Edinburgh Asylum of London (69). Judging by the hesitation expressed by Williams, this is entirely plausible. Williams himself chose to focus on 'excessive action' as an etiological agent of GPI, detailing apparent strain in the brain's blood vessels that would have eventually led to paralysis due to an individual overthinking (Williams 752). By relating general paralysis of the insane to a venereal disease, Clouston risked tarnishing the reputation of the respectable individuals diagnosed with general paralysis of the insane as promiscuous and immoral. By choosing to instead pose correlations between general paralysis of the insane and considerable "good" traits, or at least traits with a far less negative stigma, Clouston had protected both his financial and professional interests, as well as the reputation of his many general paralysis of the insane patients.

## ***The Debate Behind the Etiology of General Paralysis of the Insane***

Other etiological factors of general paralysis of the insane are worth exploring, before returning to the debate about syphilis. Speculations about what factors could cause such a terrifying condition were not just restricted to medical reports—public media reports frequently discussed possible etiologies for general paralysis of the insane (O’Conner 70). Notably, mentions of syphilis and venereal disease were rarely, if ever, mentioned. Instead, newspapers opted to discuss the roles of heredity and immorality in the development of the disease (70). Heredity was observed to be a factor in the development of GPI by Bayle in nearly half the cases, Calmeil suggesting one in three cases, and other professionals suggesting much lower proportions (Mickle 251). The diagnostic criteria varied as a result of both class and gender. GPI in wealthy classes was attributed to intense mental activity (as mentioned earlier by Williams), sexual excess, and alcohol abuse, while GPI in lower classes was attributed to prolonged periods of heavy labour, as well as poor nutrition and sleep habits (O’Conner 67). While general paralysis of the insane was diagnosed in men at a much higher rate than women, diagnostic criteria for the identification of general paralysis of the insane in women did exist, suggesting that “domestic troubles” could play a role in the development of GPI in females (67). Mickle addresses the staggering male to female GPI patient ratio by arguing that men were exposed to “greater moral shocks and mental strain” than women (Mickle 247). While Mickle gives an estimate of a 4:1 male to female GPI patient ratio, his colleagues have reported ratios of 8:1 male to female GPI patients (245). Other colleagues would even admit that they had never observed GPI in female patients, causing some to deny the disease’s existence in women (245).

One popular argument against the causative role of syphilis in general paralysis of the insane was the disease’s resistance against



antisyphilitic treatments, including intracranial injections of salvarsan and later, neosalvarsan (Braslow 582). Additionally, respected professors of psychiatry, including Leonardo Bianchi of the Royal University of Naples, claimed that while an etiological link between general paralysis of the insane and syphilis existed, it was not a definitive causative agent (Robertson 25). To support his claims, Bianchi described observing cases where general paralysis of the insane was diagnosed prior to syphilis infections, and that treatment of syphilis in GPI patients still left behind a progressive paralysis (25). W. Ford Robertson, director of the Laboratory of the Scottish Asylums, was a key denier of the etiological linkage between syphilis and GPI, and makes so abundantly clear in his series of lectures on GPI. He argued that most physicians were dissenting from the syphilitic etiology of general paralysis of the insane, and were better spending their efforts investigating alternative etiologies including alcoholism and heredity (3). Interestingly, Robertson did not appear to hold the view that general paralysis of the insane was a disease of immoral lifestyles, asserting that general paralysis of the insane was a disease of both the rich and poor (2). He even went as far as to describe isolating what he believed to be the causative agent from the brains of general paralysis of the insane victims—he termed this *Bacillus paralyticans* in an attempt to disprove the syphilitic theory (17).

The debate regarding the identity of the etiological agent of general paralysis of the insane was not settled until 1913, when syphilitic spirochetes were isolated from the brains of GPI victims by microbiologists Moore and Noguchi (Pearce 273). Possessing definitive knowledge of the biological origin of such a debilitating disease, psychiatrists immediately began looking for new treatment and therapeutic possibilities to put an end to general paralysis of the insane. The race to cure general paralysis of the insane culminated with the novel malaria treatment as described by Julius Wagner-Jauregg, an Austrian physician who discovered that general paralysis of the insane could be alleviated by exposure to malaria-

infected blood and the subsequent high-grade fevers experienced by patients (Braslow 583). Wagner-Jauregg reported 6 remissions out of 9 GPI patients following a test trial of his new therapy, boasting a staggering 67% efficiency rate (584). This is largely considered the first instance of a somatic cure that effectively resolved psychiatric manifestations (579). Wagner-Jauregg would later receive the Nobel Prize in 1927 for his work on curing GPI, and malaria fever therapy was popularized in asylums until penicillin was introduced to asylums (582). Additionally, Julius Wagner-Jauregg was the first researcher to win a Nobel Prize for work in psychiatry; however, the following two decades saw Nobel prizes awarded to several researchers focused on psychiatry and neuroscience.<sup>1</sup>

In conclusion, general paralysis of the insane broke pre-existing models of psychiatry and medicine as a whole with the recognition of an organic brain disease leading to psychiatric symptoms. By shattering the pre-conceived models of alienism, general paralysis of the insane acted as a hallmark disease that revolutionized the integration of psychiatrists in medicine. Not only was general paralysis of the insane the first instance of a disease with psychiatric symptoms with a biological explanation, but it also led to the first instance of a widely effective somatic treatment option in psychiatry (Braslow 579). General paralysis of the insane also contributed to the field of medical microbiology with the attention it garnered towards syphilis, including the Nobel prize-winning malaria therapy introduced by Julius Wagner-Jauregg (579). Finally, the wide variety of possible clinical presentations of general paralysis of the insane, combined with inconsistent etiological information and the fear of medical professions to correlate general paralysis of the insane with venereal diseases such as syphilis, demonstrate the need for standardized, biological disease models with clear diagnostic criteria

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<sup>1</sup> The list of Nobel Prize in Physiology or Medicine awardees is found on the Nobel Prize website.

based upon patient symptomology and medical history, rather than their perceived class standing in society.

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