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Mosquitoes, Medical Officers and Mental Asylums: Malariotherapy in the UK and the Rise of the Horton Laboratory

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Abstract

Malarial therapy is one of the stranger interventions in the history of psychiatry although it had a serious intent. It was pioneered by Julius Wagner-Jauregg in Austria in the early twentieth century based on observations of improvements in the psychotic symptoms of febrile patients during outbreaks of fever in large asylums. He proposed it as a treatment for patients with general paralysis of the insane, a neuropsychiatric disorder associated with tertiary syphilis which had a progressive and morbid course and was without effective treatment at the time.

This paper examines the implementation of the treatment in Britain and the scientific observations and public concerns underlying the geographical shift of this venture from Scotland and North-West England to London and the South through the 1920s. The centre at Whittingham Hospital in Lancashire which had a major role in the implementation of malariotherapy in the UK, declined and the laboratory newly established at Horton Hospital, Surrey in 1925 under Colonel Sydney Price James, became the dominant UK centre for research on malaria and the production of infected mosquitoes.

The introduction of penicillin in the 1940s led to a rapid decline in cases of general paralysis of the insane, and the use of malaria therapy, although the Horton Laboratory remained open as a malaria reference centre until 1973. This paper discusses the effectiveness of induced malaria as a treatment, which had in James's words 'a tendency to lethality', and the ethical standing of research using infected patients as subjects to further understand malaria, which remains contested.

Keywords

Medical history, General paralysis of the insane, Malaria, Neurosyphilis, Malariotherapy, Horton Laboratory

Overview

Malariotherapy involved the treatment of general paralysis of the insane (GPI) by deliberate infection with the malarial parasite. Although GPI is usually considered today to be the same as neurosyphilis, there are problems with this interpretation of direct equivalence which will be covered below.[1] Malariotherapy was first described by the Austrian Julius Wagner-Jauregg (1857–1940), who won a Nobel Prize for his discovery in 1927.[2] It came into clinical use in the United Kingdom in 1922 and was a routine treatment until the 1940s when superseded by penicillin.[3] It marks a significant, if viewed today as a rather anomalous, era of psychiatric practice. One of the singular features of this development was the rapidity with which a new physical treatment for severe mental illness was adopted by mental hospitals across the country and the technology and infrastructure that sprang into place to support it. Malariotherapy was enthusiastically taken up by many hospitals across the country as a revolutionary physical treatment fuelled perhaps by a professional desire for a biological and medical conception of mental illness.[4]

This innovative experimental zeal is contrary to the orthodox view that the large asylums, later mental hospitals, were inactive and unproductive in terms of research activity. The historian David Cochrane, for example, has suggested the lack of scientific productivity in Britain in the period between the wars was the result of an absence of effective leadership by the medical superintendents of the day. He commented that: 'It had to be acknowledged that a good administrator was not necessarily a good scientist. … Secondly, medical superintendents of the large asylums were too preoccupied with all the endless administrative duties required by the job to pursue sustained enquiry'.[5] The practical application of the novel therapy also demonstrates an unusually close and productive collaboration between two very different branches of medicine: psychiatry and tropical medicine.[6] They were two relatively new medical specialties which were

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[1] Robertson GM. The Morison Lectures, 1913. – General Paralysis of the Insane. *Journal of Mental Science*. 1913; 59(245): 185-221. George Robertson (1864-1932) noted accessory factors believed to assist syphilis in the development of general paralysis, principally alcohol, sexual excess, overwork, worry, trauma, infections, intoxication, and heredity. He later became Professor of Psychological Medicine at University of Edinburgh and President of the Medico-Psychological Association.p. 202-212 - accessory factors p.207.

[2] Whitrow M. Wagner-Jauregg and fever therapy. *Medical History*. 1990, 34(3), 294–310; Wagner-Jauregg J. The treatment of general paresis by inoculation of malaria. *Journal of Nervous and Mental Disease.* 1922; 55(5): 369-389.

[3] Scripture EW. The Treatment of General Paralysis by Malaria. *Journal of Mental Science*. 1923; 69(284): 77-83.

[4] Braslow J. The Influence of a Biological Therapy on Physicians' Narratives and Interrogations: The Case of General Paralysis of the Insane and Malaria Fever Therapy, 1910-1950. *Bulletin of the History of Medicine*. 1996; 70(4): 577-608.

[5] Cochrane D. 'Humane, economical and medically wise': The LCC as administrators of Victorian lunacy policy. In: Bynum WF, Porter R, Shepherd M (eds). *The Anatomy of Madness*, *Vol. 3: The asylum and its psychiatry* London: Routledge; 1988. p.247-272.

[6] Quick T. Once Bitten: Mosquito-Borne Malariotherapy and the Emergence of Ecological Malariology Within and Beyond Imperial Britain. *Bulletin of the History of Medicine.* 2023; 97(1): 67-99.

receiving increased government funding and focus as a result of the First World War (FWW).

It was the Ministry of Health and Board of Control for Lunacy and Mental Deficiency (the successor to the Board of Commissioners in Lunacy) which attempted to control the unregulated spread of the new therapy, apparently prompted by fears of infecting the local populations with malaria. They centralised the geographical base away from the hospitals in the North West of England, including the Whittingham Hospital in Lancashire, whose physicians had done the initial trials collaborating with their academic colleagues at the Liverpool School of Tropical Medicine (LSTM).[7] In 1925, the Board established the Malarial Treatment Centre closer to London at the Horton Hospital near Epsom in Surrey.[8] This paper will explore the differing fortunes of malaria therapy at Whittingham and Horton Hospitals and examine the use of an unconsenting and mentally ill population as experimental guinea pigs for the treatment.

Terminology: general paralysis of the insane and neurosyphilis

General paralysis of the insane was a terrible illness and doubly shameful because of its sexual transmission. Early GPI symptoms included depression, restlessness and tremors but progressed to delusions, grandiose and disinhibited behaviour, memory loss and seizures.[9] It was also known to be incurable and related to the presence of syphilitic changes in the grey matter of the brain. Pre-antibiotic era treatments like mercury and arsenic were highly toxic and could not pass the blood brain barrier.

Acknowledging the anachronism, the historian Gayle Davis decided to use the 1920s term 'neurosyphilis' to cover all neurological disease manifestations of syphilis from GPI, tabes dorsalis, syphilitic insanity and cerebral insanity in her excellent survey of syphilis and psychiatry in Scotland between 1880 and 1930.[10] She demonstrated the obstacles to making a reliable diagnosis of GPI around the turn of the century and determining this from asylum records. The diagnosis might be made on admission based on the medical history, the psychiatric symptoms and the presence of specific physical signs. It could be made after an assessment period or it could be made at post mortem. She identifies the unreliability of the label due to the effects of patient class and affluence on the physician's judgement on whether to investigate appropriately.[11] Asylum doctors associated the contraction of syphilis with lax morals and the working class. Davis writes that physicians appeared to find GPI where they expected to find it.

While some asylum patients had the psychological hallmarks of GPI combined with the physical stigmata, others were not recognised or diagnosed until post-mortem

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[7] Grant AR. The Treatment of General Paralysis by Malaria. *British Medical Journal.* 1923; 2: 698.
[8] Rollin HR. The Horton Malaria Laboratory, Epsom, Surrey (1925–1975). *Journal of Medical Biography*. 1994; 2(2): 94-97.
[9] Purves-Stewart J. Discussion on the Treatment of Neuro-Syphilis. *British Medical Journal*. 1922, 2(3223), 621–627; Craig, M. *Psychological Medicine: A Manual on Mental Diseases for Practitioners and Students.* London: J & A Churchill; 1917.
[10] Davis G. '*The cruel madness of love': sex, syphilis and psychiatry in Scotland, 1880–1930*. Amsterdam and New York: Rodopi; 2008.
[11] Davis. '*The cruel madness of love'*, 2008 (Note 10). p.230.

examination. Her case notes review shows that, even after laboratory testing with the Wassermann test was considered reliable in 1909, the repeated testing required to confirm or reject the diagnosis varied from hospital to hospital.[12] To complicate matters, we now know that positive Wassermann tests can also be found in cases of malaria, tuberculosis and systemic lupus erythematosus. For these reasons, Davis is concerned about the stability of the diagnosis over time. Historian Jennifer Wallis also cautions against 'presentism', the fallacious application of current ideas or present-day perspectives to historical material, in assuming that all of the GPI described in this era is identical to our present-day category of neurosyphilis.[13]

The diagnosis of GPI was a common reason for admission to mental hospitals in the Victorian and early part of the twentieth century. Around this time, nearly 20% of men (but only 3% of women) who died in an asylum did so because of GPI.[14] To clarify the relationship between GPI and syphilis: not all cases of neurosyphilis developed into GPI but the converse was true; GPI only manifested after a previous syphilitic infection. In the UK, contemporary authorities viewed syphilis as an 'essential factor' in the aetiology of disease but other factors were also considered important like 'sexual excess, alcoholism and head injuries'.[15] Despite the limitations of the term, this article will use 'general paralysis of the insane' or GPI throughout, since the focus is on malariotherapy and its historical use as a treatment of GPI.

General paralysis of the insane and malaria

Wagner-Jauregg, then Professor of Psychiatry in Vienna, had reported the effects of the intentional induction of malaria in patients with GPI in 1918.[16] However, these were not his first experiments in the field nor was he the first to publish on the topic. In 'The Effect of Feverish Disease on Psychoses', he reviewed the medical literature in a journal of 1887 and found modern and classical parallels.[17] Fever therapy, or pyrotherapy, was noted in the texts of the ancient Greeks and early physicians like Galen and Hippocrates observed that pre-existing illnesses were often cured after the patient had contracted some sort of fever-inducing disease. The modern literature described a range of anecdotal improvements seen in mental patients with fever caused by cholera, typhoid and erysipelas.

In the years that followed, Wagner-Jauregg had published his trials with various non-infective pyrogenic agents from dead cultures of staphylococcus to tuberculin protein. By 1921, he had collected 150 cases treated with malaria and presented his

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[12] Davis. '*The cruel madness of love'*, 2008 (Note 10). p. 232.
[13] Wallis J. *Investigating the body in a Victorian asylum: doctors, patients and practices*. London: Palgrave Macmillan; 2018. p.10-12.
[14] Hurn J. The Changing Fortunes of the General Paralytic. *Wellcome History.* 1997; 4: 5-6.
[15] Purves-Stewart. Discussion, 1922 (Note 9),; Craig. *Psychological Medicine.* 1917 (Note 9).
[16] Wagner-Jauregg J. Ueber die Einwirkung der Malaria auf die progressive Paralyse. *Psychiatrich-neurologische Wochenschrift.* 1918; No. 21/22: 132-134 & 1919; No. 39/40: 251-255; Whitrow. Wagner-Jauregg*,* 1990 (Note 2).
[17] Wagner-Jauregg J. Ueber die Einwirkung fieberhafter Erkrankungen auf Psychosen. *Jarbücher für Psychiatrie und Neurologie*. 1887; 7: 94-131.

successful results in lecture form and later published these in German and English.[18] Wagner-Jauregg did not know exactly how provoking a high fever had its therapeutic effects. He suggested that the pyrexia might be enough to directly kill the syphilitic organisms in the nervous system, preventing further deterioration and sometimes even reversing the symptoms. Several potential mechanisms of action have been proposed. One possible means is the direct inhibitory effect of increased temperature on microbial activity while others include the effects of hyperthermia on increased organ perfusion and immune system activation.[19]

The introduction of malariotherapy to Britain

There is no definitive account of the ways that knowledge of the discovery of malaria-induced hyperpyrexia made its way to the UK. However, several prominent members of the Medico-Psychological Association of Great Britain and Ireland, the forerunner of the present Royal College of Psychiatrists, attended a meeting of European psychiatrists in Paris in May 1922. This meeting commemorated the centenary of Antoine Bayle's (1799-1858) doctoral thesis of 1822,[20] in which he delineated the neuropathology of GPI, significant as the first description of a visible and definable neuropathological cause of any psychiatric disease. One of the sessions in Paris discussed the relevance of Wagner-Jauregg's work.[21]

Among the British delegates were George Robertson (1864-1932), Professor of Psychological Medicine at University of Edinburgh and President Elect of the Medico-Psychological Association; Helen Boyle (1869-1957), another future president of the Medico-Psychological Association and Dr Hubert Bond (1870-1945), also a delegate of the British government who conveyed a special message from Sir Alfred Mond (1868-1930), the Minister for Health. Robertson, an authority on GPI, headed the delegation and was honoured by being elected Vice-President of the Congress. William McAlister (dates unknown), his assistant at Morningside Hospital in Edinburgh, later became the first British doctor to report the treatment of a patient with GPI.[22]

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[18] Wagner-Jauregg J. Die Behandlung der progressiven Paralyse und Tabes. *Wiener medizinische Wochenschrift.* 1921; 71(25): 1105-09 & 71(27): 1209-15; Wagner-Jauregg. The treatment of general paresis, 1922 (Note 2).

[19] Markota A, Kalamar Ž, Fluher J, Pirkmajer S. Therapeutic hyperthermia for the treatment of infection – a narrative review. *Frontiers in Physiology*. 2023; 14: 1215686; Gao Y, Zhu J, Yin C, Zhu J, Zhu T, Liu L. Effects of target temperature management on the outcome of septic patients with fever. *BioMed Research International*. 2017: 3906032; Evans SS, Repasky EA, Fisher DT. Fever and the thermal regulation of immunity: The immune system feels the heat. *Nature Reviews Immunology.* 2015; 15(6); 335–349.

[20] Bayle ALJ. Recherches sur les maladies mentales. Thèse de médecine de Paris No. 247, 1822. Bibliothèques d'Université Paris Cité. https://www.biusante.parisdescartes.fr/histmed/medica/cote?TPAR1822x247 (accessed 18 Nov 2025).

[21] Anon. Centenary of the Thesis of Bayle. *Journal of Mental Science*. 1922; 68(283): 401-402.

[22] McAlister W. The treatment of general paralysis by infection with malaria. *British Medical Journal*. 1923; 2(3277): 696-698.

McAlister described in depth some of the complexities and practical difficulties that he encountered. The first difficulty was to procure a suitable supply of the malaria protozoa. The help of the local health authorities was enlisted, but an exhaustive inquiry elicited the surprising fact that there was not at that time within the Edinburgh area an uncomplicated case of benign tertian malaria. An approach was then made to the London School of Tropical Medicine, but even had a supply of the organism been available from that source, the practical difficulty of transporting it alive to Edinburgh was deemed insuperable. McAlister wrote:

> Fortuitously, a young man from Burma had been recently admitted to Craig House, another psychiatric hospital in Edinburgh. His mental breakdown was attributed to recurrent severe attacks of malaria, though no accurate information as to the type could be gathered. In due course this patient had a bout of fever which on clinical grounds appeared to be benign tertian malaria, and this was confirmed in the laboratory. As an additional precaution Colonel Marshall, Lecturer in Tropical Diseases in the University of Edinburgh, was called in consultation and confirmed the laboratory findings. But for this propitious coincidence, the initiation of the experiment might have been indefinitely postponed.[23]

Malariotherapy at Whittingham Hospital in Lancashire

Quite why Whittingham Hospital in the North West of England should have become a centre for early trials of malariotherapy may not be immediately apparent. The FWW left the majority of British mental institutions in a parlous state.[24] The need to find accommodation for the large number of servicemen who became psychiatric casualties had caused severe overcrowding in asylums during the war. Overcrowding was compounded by understaffing as doctors and nurses joined the armed forces, and asylum patients suffered from undernutrition and endemic infectious disease, resulting in poor care and many excess deaths. Whittingham Hospital, the largest of the four Lancashire County Asylums and set in rural countryside outside of the county town of Preston, was no exception.

Whittingham was situated in relative isolation and certainly far away from the heavily populated areas of the Midlands and South of England. Its remote location seems relevant to the early adoption of malariotherapy at the hospital. However, despite its isolation, Whittingham's location was connected to a source of live malarial parasites. The hospital had its own private railway line which provided rail connections to towns and cities across England and Scotland and allowed for easy transport of infective materials and patients. Less than 30 miles away the LSTM, established in 1898, was the first institution in the world dedicated to the study of tropical medicine. During the

[23] McAlister. The treatment of general paralysis, 1923 (Note 22).

[24] Lomax M. *The Experiences of an Asylum Doctor: with Suggestions for Asylum and Lunacy Law Reform.* London: George Allen and Unwin; 1921; Groves C, Hilton C. Montagu Lomax: The background and motivation of a 'remarkable man' who spearheaded lunacy reform. *Journal of Medical Biography*. 2023; 31(1) :15-21.

FWW it had been nominated as the national treatment centre for cases of malaria returning from West Africa.[25]

The LSTM's Professor of Parasitology, Warrington Yorke (1883-1943), Figure 1, had an interest in the treatment of malaria and had served in the Royal Army Medical Corps (RAMC) during the war. Yorke later wrote that it was the doctors at Whittingham who first suggested to him to inoculate patients with malaria but clearly there were mutual interests as the infected patients eventually became subjects for malariological research.

Figure 1. Warrington Yorke. Photograph. Wellcome Collection. Reference: 13771i. Public Domain Mark.

The staff at Whittingham included Dr Ronald Clark (dates unknown), the Medical Superintendent, Dr Silverston and Mr Fann, laboratory technician. Alastair Robertson Grant (1891-1986) worked initially as Assistant Medical Officer and later became its Medical Superintendent (Figure 2). He had served as a doctor in the RAMC throughout the FWW and had been mentioned in despatches whilst serving in the Egyptian Expeditionary Force in 1918-19. Malaria had been rife amongst troops serving in the Middle East so that it seems improbable that Grant would not have had practical clinical

[25] Brabin BJ. Malaria's contribution to World War One – the unexpected adversary. *Malaria Journal.* 2014; 13: 497.

experience of malaria. He attributed his own early interest in malariotherapy to the early publications by Wagner-Jauregg and others, many of which were published in German medical journals.[26] However, in his MD thesis of 1924 Grant also noted a discussion of anti-syphilitic treatments at the International Congress of Neurologists in Paris as early as 1920.[27]

Figure 2. Dr Alastair Robertson Grant. Photograph, c1956. Courtesy of Lancashire County Museum Services. Reference: MOLSH.2017.492.

Two patients from Whittingham were transferred to Liverpool and inoculated by Yorke on 21 July 1922 with blood from a patient with quartan malaria contracted in West Africa. Other patients at Whittingham were soon treated with blood from these cases and other centres soon followed, including Rainhill and Winwick Hospitals in the North West. Yorke actively extended the therapy to the Belfast Mental Hospital in January 1924 when according to Graham he 'crossed to Belfast, bringing with him some

[26] Grant AR. The Treatment of General Paralysis by Malaria. *British Medical Journal.* 1923; 2: 698-700.
[27] Grant AR. *Modern methods in the treatment of General Paralysis,* MD Thesis, University of Aberdeen Library Special Collections. 1924. p.23.

mosquitoes which had fed on malarial general paralytics at Whittingham Mental Hospital'.[28]

McAlister at Morningside and Grant at Whittingham reported their initial experiences of malarial treatment in consecutive papers in the same issue of the *British Medical Journal* in October 1923.[29] Emboldened by what appeared to be the remarkable recoveries of some of their patients, yet accepting of a considerable mortality (two of the first twelve patients treated at Morningside died within six months of treatment and six of 40 patients at Whittingham died within fourteen months), both centres continued to treat at pace, reporting their experience to date in January 1924, again in twinned papers.[30] Grant and his colleague, JD Silverston, and Yorke separately, were able to draw out important observations on the therapy. Yorke commented that 'the practice had allowed the observation of malaria in exceptionally favourable circumstances.' He pointed to three important findings: the refutation of the unicity theory of malaria in man; clarification of the incubation period of simple tertian malaria; and an improved understanding of the efficacy of quinine as an anti-malarial agent.[31]

The balance between the effectiveness of the inoculated malarial strain versus its pathogenicity in often already frail patients, had come under scrutiny. The Whittingham collaborators reported their development of the attenuated 'W.' strain of benign tertian malaria through the repeated passage of infected blood from patient to patient:

> The birth of the Whittingham (W.) strain took place on September 8, 1922, when a general paralytic was inoculated with blood from a patient who had contracted benign tertian malaria in India. From this host a long chain of cases of general paralysis and tabes has been infected. During the last forty-two months (three and a half years) the strain has been transmitted by direct subcutaneous inoculation through sixty cultural generations, comprising over one hundred and fifty cases.[32]

Infected blood kept at zero degrees Celsius was found to successfully induce malaria for up to 72 hours and allowed the transfer and use of the W. strain at other hospitals as far away as Leavesden in Hertfordshire, even to Cardiff, Edinburgh and Exeter, aided by Whittingham's own hospital railway which connected to the North West main lines. Further observations were made on the incubation period between inoculation and the

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[28] Graham NB. The Malarial Treatment of General Paralysis. *Journal of Mental Science*. 1925; 71(294): 424-431.

[29] McAlister. The treatment of general paralysis, 1923 (Note 22); Grant. The Treatment of General Paralysis, 1923 (Note 26).

[30] McAlister WM. The Rôle of Infection in the Treatment of General Paralysis. *Journal of Mental Science.* 1924; 70(288): 76–81; Grant AR, Silverston JD. Malaria Therapy in General Paralysis: being Observations on Fifty Cases treated at the County Mental Hospital, Whittingham. *Journal of Mental Science*. 1924; 70(288): 81–89.

[31] Yorke W. The Malaria Treatment of General Paralysis. *Nature*. 1924; 114(2869): 615–616; Grant AR, Silverston JD. The Whittingham (W.) Strain of Artificially Induced Malaria: Observations made during the Treatment of General Paralysis and Tabes Dorsalis. *Journal of Mental Science.* 1926; 72(298): 346–355.

[32] Grant, Silverston. The Whittingham (W.) Strain, 1926 (Note 31).

onset of malarial symptoms and the optimal number of paroxysms of fever required for effect (five to ten) and the enhanced efficacy of quinine as a rescue treatment from induced malaria compared to its disappointing effects in the treatment of servicemen with malaria acquired during the war.

Public anxiety about malariotherapy

Fears that malaria might return to the British Isles began to develop during the FWW and continued during demobilisation. In 1919, the medical correspondent of *The Times* warned that, 'it is quite clear that too little attention is being paid to the discharge of men from the Army who may be the victims of infectious diseases and so may spread these diseases among the civil population'.[33]

Localised outbreaks of malaria had been sporadic but widespread in Britain before the war, particularly in areas of marshland.[34] In 1917, an outbreak of malaria in Kent coincided with the establishment of a military encampment near to mosquito-infested water.[35] The servicemen in the camp were returning from Salonika at the end of the Balkan campaign in which malaria played a critical part.[36] Many had or carried malarial infection and in Colonel Sydney Price James's (1870-1946) view the delayed recognition and diagnosis of malaria had allowed the outbreak to become established, although it had then been quickly controlled by treatment of cases and carriers with quinine. Reflecting on this outbreak and others, James concluded that *Anopheles* mosquitoes remained sufficiently numerous in Britain to allow malaria to take root again: 'These occurrences prove, of course, that in those places the numerical prevalence of anopheles [sic] had not been reduced below the limit at which the disease would spread'.[37]

A further narrative developed in British medical circles that malaria had been the cause of almost all psychiatric casualties of the Balkan campaign. This view was championed by William Kirkpatrick Anderson (1878-1942), Professor of Psychiatry at the University of Glasgow. He subsequently attempted to give evidence in defence of two former servicemen charged with murder in 1923 and 1927 who entered pleas of 'guilty but insane' due to malaria.[38] Anderson went on to write a book *Malarial Psychoses and Neuroses*, published by Oxford University Press in 1927, in which he positioned malaria as the primary cause of several forms of mental disorder.[39] In the public eye, the sensational and high-profile events involving malaria outweighed the

[33] Anon. Menace to Public Health. *The Times*. 2 May 1919. p.9.
[34] James SP. The Disappearance of Malaria from England. *Proceedings of the Royal Society of Medicine*. 1929; 23(1): 71–87.
[35] Walker MD. The last British malaria outbreak. *British Journal of General Practice.* 2020; 70 (693): 182-183.
[36] Brabin. Malaria's contribution to World War One, 2014 (Note 25).
[37] James. The Disappearance of Malaria, 1929 (Note 34). p.87.
[38] Fantauzzo J. 'Malaria Has Spoilt It': Malaria, Neuropsychiatric Complications, and Insanity in ex-Servicemen in Post-First World War Britain. *Social History of Medicine*. 2022; 35(4): 1267-84.
[39] Anderson WK. *Malarial Psychoses and Neuroses*. London: Oxford University Press; 1927.

quiet medical developments in the treatment of GPI taking place in the mental hospitals of the 1920s. Malaria again became a public menace.

In this context, and as the early reports of treatment with malaria were appearing in British medical journals the Board of Control, with responsibility for the administration of mental hospitals in England and Wales, and Sydney Price James, the Adviser on Tropical Diseases to the Ministry of Health, expressed concerns about malariotherapy as a threat to the public health. The possibility of dangerous forms of malaria being communicated to the general population through the infection of mosquitoes local to a mental hospital had been raised by a number of authors, notably Peter Mühlens (1874-1943), Professor at the Bernhard Nocht Institute for Tropical Medicine in Hamburg. James made a proposal for regulation and investigation into potential risks rather than a ban. Taking on the role of investigator himself he demonstrated, with some difficulties, that female *Anopheles* mosquitoes local to the Kent coast could become infected after feeding on a patient with malaria and then successfully convey the infection to another patient.[40]

Mühlens had written to the Board of Control in December 1923, raising fears that the technique of direct inoculation of blood from a known malaria sufferer could inadvertently introduce more virulent strains of malaria, and even other infections, into general circulation and, by repeated use of the same strain for inoculations, cause the development of more virulent forms of the benign strains of malaria selected for use in malariotherapy.[41] Grant and Silverston attempted to refute this view through their observations of *Plasmodium vivax* at Whittingham (Hanwell in London provided similar evidence) which 'indicate that the strain has undergone no change in pathogenicity or virulence or alteration in therapeutic properties during the direct passage from man to man through 60 generations'.[42] But their attempted rebuttal proved to no avail. Acting on James's advice, the Board of Control issued a set of restrictive guidelines in February 1924, essentially preventing further use of the inoculation method and limiting malariotherapy only to those centres able to comply with the Board's requirements.[43]

James insisted that each asylum should be equipped with a laboratory suitable for the daily microscopic examination of the blood of inoculated patients; patients should be monitored and nursed carefully during their illness by staff familiar with malaria, and should be thoroughly treated with quinine to prevent relapse; to prevent stray mosquitoes from biting other patients and subsequently spreading malaria to the general public, all inoculated patients should be kept in mosquito-proof wards during treatment and monitored for several weeks after discharge. In typical British understatement, he suggested that in some cases the malaria strain used previously had been 'of an unusually severe type, accompanied by pronounced complications and with a tendency to fatality'.[44]

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[40] Quick. Once Bitten, 2023 (Note 6).

[41] Letter reproduced in: The Board of Control (England and Wales) and the Malarial Treatment of General Paralysis. *Journal of Mental Science*. 1924; 70(289): 337-341.

[42] Grant, Silverston. The Whittingham (W.) Strain, 1926 (Note 31); Lilly GA. The Treatment of General Paralysis at Hanwell Mental Hospital. *Journal of Mental Science*. 1925; 71(293): 267-278.

[43] The Board of Control, 1924 (Note 41).

[44] The Board of Control, 1924 (Note 41).

The founding and rise of the Horton Laboratory

Horton Hospital and Laboratory are well known to have had a key part in the development of malariotherapy and malaria mosquito research in the UK. The historian and polymath psychiatrist Henry Rollin (1911-2014) did an excellent job in highlighting the significance of the laboratory and the hospital at which he had worked between 1948 and 1975.[45] However, his predecessors had also been very good at privileging their own role to the detriment and exclusion of all other researchers and centres. One way that they achieved this was to exclude mention of other British hospitals involved in malariotherapy in the research papers and reports that came from London. Writing in 1927, two years after the founding of the Horton Laboratory, William Drew Nicol made no mention of the preceding work conducted in the North West and other regions.[46] With the possible exception of the psychiatrist and historian Julie Hurn's doctoral thesis, most historical accounts have not explored the accounts of other English psychiatric hospitals at the lead of malariotherapy like Whittingham.[47]

The person primarily responsible for the foundation and initial rise of Horton was the same SP James who had speculated that the early deaths caused by malariotherapy in Britain might be due to a particularly virulent strain of malaria and was responsible for the guidelines sent in a Board of Control circular to all asylum superintendents.[48] Hurn suggests that in the face of growing public and professional anxiety about psychiatric hospitals' experiments in malariotherapy exacerbating endemic malaria, it was James's concerns and solutions which led the Ministry of Health and the Board of Control to establish the Horton Treatment Centre:

> If it were desired to essay the treatment experimentally in England it could only be done in an Institution where the Ministry or other responsible Government Department could control the arrangements for the diagnosis of syphilis and for otherwise safeguarding the interests of the patients who act both as the subjects of treatment and as carriers of the particular strain of malaria parasites.[49]

In 1924, there was still no approved national protocol for inoculating the malarial parasite into those affected by GPI. Some hospitals preferred direct infection with infected blood, others used mosquitoes for the task which required careful husbandry. Both methods carried risk to civilian populations near to the hospitals.

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[45] Rollin HR. The Horton Malaria Laboratory, Epsom, Surrey (1925-1975). *Journal of Medical Biography*. 1994; 2(2): 94-97; Bluglass R. Dr Henry Rollin MD. *Psychiatric Bulletin.* 2014; 38(3): 141-142.

[46] Nicol WD. The Care and Management of Induced Malaria. *Journal of Mental Science*. 1927; 73(301): 209-217.

[47] Hurn JD. *The History of General Paralysis of the Insane in Britain*, *1830-1950*. Doctoral thesis. University of London. 1998.

[48] Dickinson O (Secretary to the Board of Control of England and Wales). Circular letter to Medical Superintendents of County and Borough Mental Hospitals and Registered Hospitals in England and Wales concerning the Malarial Treatment of General Paralysis, 27 Feb 1924. Reprinted in: The Board of Control, 1924 (Note 41).

[49] Hurn. *The History of General Paralysis,* 1998 (Note 47). p.207.

Though a tropical medicine physician rather than a psychiatrist, James had worked nearby at the Manor War Hospital, another of the Epsom cluster, a group of five large psychiatric hospitals originally built to the west of Epsom by the London County Council. They had been requisitioned over the FWW for military casualties but were slowly returning to use as psychiatric hospitals.[50] The site was large enough to boast its own railway, power station and cemetery. James suggested that it might be possible to develop a national centre to breed mosquitoes safely for local and national use. He thought that Horton Hospital, at that time a women's psychiatric hospital, would be ideal for the purpose.[51] The existing railway line could act as a distribution network for the infected mosquitos.

At a meeting between the London County Council, the Ministry of Health, the Board of Control and the London Mental Hospitals Committee in the summer of 1924, agreement was reached to follow James's plan.[52] By 1925, the hospital had taken over the care of the majority of London women with suspected GPI and a fourteen-bed isolation unit was converted to house those being treated with malaria. It was designed to keep local mosquitoes out, as much as preventing the escape of the farmed mosquitoes. The Ministry of Health provided the majority of funding for an on-site laboratory and 'insectarium' from which to propagate the mosquito swarm. James, an advisor on tropical diseases to the Ministry of Health, became its first director.

James remained the director and then medical superintendent at Horton Malaria Laboratory (initially 'C' block) for over ten years, until he joined the Molteno Institute in Cambridge. Perhaps unsurprisingly given James's specialty, Horton Hospital became a centre for tropical medicine research into malaria rather than research into the treatment of GPI. Horton became internationally famous as the originator of the Madagascar 'M.' strain of *P. vivax* that was safer for use in humans.[53] Researchers from across the world visited to learn their methods. Apart from establishing the best conditions to practically breed and disseminate the mosquitos and malaria parasite, both nationally and internationally, the laboratory made several important discoveries and tested new anti-malarial drugs.[54]

That is not to say that the GPI treatment programme had stopped; indeed, the lab provided the parasite for the entire country. It is estimated that Horton provided the infective material for the treatment of around 10,000 cases of GPI.[55] It was just that there was no formal research programme there until 1937. See Figure 3 for an illustration of patient treatment.

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[50] Arnould K. *The Epsom Cluster: Voices from Europe's Largest Psychiatric Hospital Complex*. Stroud, UK: Amberley; 2019; Lost Hospitals of London – The 'Epsom Cluster'. https://ezitis.myzen.co.uk/briefhistoryepsom.html (accessed 24 Nov 2025).

[51] Hurn. *The History of General Paralysis,* 1998 (Note 47). p.209.

[52] Hurn. *The History of General Paralysis,* 1998 (Note 47). p.209.

[53] Anon. Malaria-Therapy by Means of Infected Mosquitos. *Nature.* 1938; 142: 390.

[54] Anon. A Malarial Treatment Centre. *British Medical Journal.* 1937; 1: 1081; Quick. Once Bitten, 2023 (Note 6). p.85-92.

[55] Rollin. The Horton Malaria Laboratory, 1994 (Note 45).

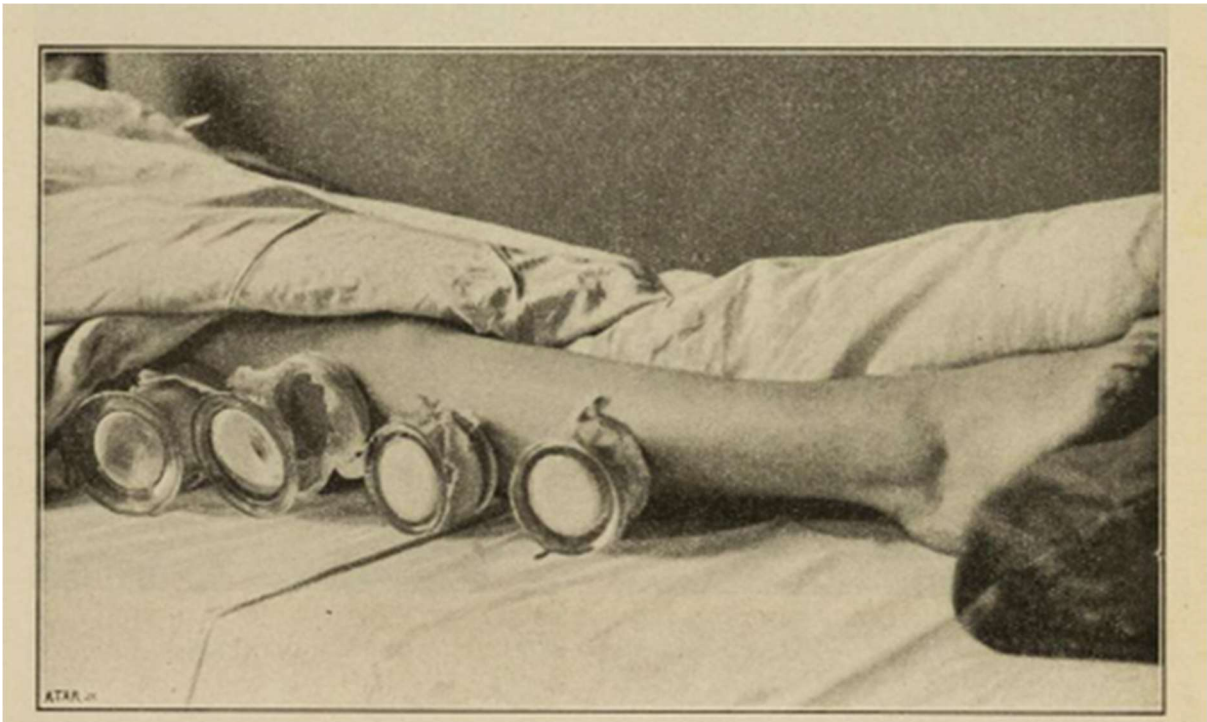

Figure 13. — MOSQUITOES BITING THE PATIENT.

Figure 3. Illustration of mental hospital patient infection using mosquitoes. From: League of Nations. *Principles and Methods of Antimalarial Measures in Europe: Second General Report of the Malarial Commission.* Geneva: League of Nations; 1927. p.44.

Fortunately, there were other researchers who did investigate the treatment. In 1931 W Alex Caldwell (dates unknown), the Officer-in-Charge of General Paralysis at the Central Pathological Laboratory of the London County Mental Hospitals, published a report on the results of treatment of 579 cases in London County Council Hospitals.[56] As with previous reports he found that about 30% of those treated had achieved a 'good remission' and of the remarkable 165 patients who were discharged from hospital, 73% were still working when followed up as out-patients. If evidence was required for the effectiveness of the treatment then this seemed to be it.

Recent commentators have been less convinced of malariotherapy's positive effects. For example, the sociologist and historian Andrew Scull finds the effectiveness of malariotherapy 'not proven'. He points to the potential confounding effects of misdiagnosis of GPI and the known occurrence of early spontaneous remissions, the variability of responses to the treatment and its high mortality and morbidity, the lack of well-defined measures of patient improvement and reporting bias from clinicians

[56] Nicol WD. Review of: Caldwell WA. *General Paralysis: Report of 579 Cases Treated by Malaria in the London County Mental Hospitals*. London: London County Council, 1931. No. 2821. *Journal of Mental Science*. 1932; 78(323): 946.

evaluating their own patients' responses to treatment (to which might be added a further source of possible bias from the non-publication of poor outcomes).[57]

Nevertheless, clinicians in Britain at the time appear to have been aware of many of the issues raised. WD Nicol, who became the Medical Superintendent at Horton, presented the results of treatment of 200 female patients admitted to the ward 'set apart' for malariotherapy at the hospital. In a complex paper, Nicol compared the outcomes of the Horton patients with the results of treatment at five other centres in London, Hamburg, Vienna, New York and Paris. He discussed the importance of reliable clinical diagnosis of general paralysis and the potential pitfalls of reliance on the available serological tests, including the Wassermann reaction, before examining the relationship of patient related factors and treatment related factors to response to treatment, including variation due to age, duration of symptoms and the recognised psychiatric sub-types of GPI, and that due to the specific species of malaria employed, and the duration of fever and height of the pyrexia attained.[58]

Mortality was high, ranging from 14% to 27% across the six centres, the variation being attributed to differences in the length of time patients had been 'observed' untreated in hospital and the severity of the induced malarial infection. Nicol noted that: 'Risks, however, must be taken in treating a disease which, if untreated, proves fatal'.[59] Reportedly, mortality fell after quinine was introduced to 'save' patients at the height of malarial paroxysms. More encouraging were observations made over several years of follow-up that 35 (17.5%) of the Horton patients experienced what is said to have been a 'good remission'. Nicol described the progress of his female patients thus: 'The majority of the discharged patients are carrying out domestic duties in their homes. A few of the single women have returned to their former occupations.'. Clinicians were familiar with patients who showed spontaneous improvement prior to the era of malariotherapy, but sustained remissions of such a nature were seen only infrequently.

After the Board of Control introduced restrictions on the use of the inoculation technique in 1924 the laboratory at Whittingham found itself side-lined. Having previously supplied hospitals across Britain with infective material for inoculation, the artificially induced W. strain, Whittingham's role would be taken over by the central laboratory at Horton which could supply live infected mosquitoes. Grant and Silverston had described a method of maintaining refrigerated serum samples in an infective state for up to 72 hours with which,

> … we have enabled other hospitals in the country to commence and make observations on this form of treatment. The W. strain in this way has been of service in the following general and mental hospitals: Leavesden, Exeter, Cardiff, Shrewsbury, Birmingham, Bradford, Cheddleton, Morningside, Cheadle Royal, York, Sunderland, and the Liverpool School of Tropical Medicine.[60]

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[57] Scull A. *Desperate Remedies: Psychiatry and the Mysteries of Mental Illness*. London: Allen Lane; 2022. p.92-109.

[58] Nicol WD. A Review of Seven Years' Malarial Therapy in General Paralysis. *Journal of Mental Science*. 1932; 78(323): 843–866.

[59] Nicol. A Review, 1932 (Note 58). p.858.

[60] Grant, Silverston. The Whittingham (W.) Strain, 1926 (Note 31). p.347.

Until the establishment of Horton, they had been responsible for the direct subcutaneous inoculation of over 150 cases of GPI over three and a half years.

Consent and ethical considerations

Before modern ethical and research frameworks, the ethics of giving a potentially fatal infection to a patient to cure another disease did not seem to concern those responsible. Patients in county asylums in Britain such as Whittingham were legally detained and had little personal autonomy. In addition, GPI carried a progressive and grave prognosis and was thought to be readily diagnosed with little room for error. In an era before randomised trials, psychiatrists were enthusiastic in their early case reports of good responses to malariotherapy, notwithstanding the difficulty of devising a control arm for malarial fever, and the absence of an effective alternative treatment.

When the medical historian William Bynum reviewed the experimental development of malariotherapy, he concluded that Wagner-Jauregg's research methods should be judged by the standards of the time, although they may appear crude by present standards.[61] The capacity of patients suffering from later stages of GPI to consent in modern terms to the treatment cannot be assumed, but it seems likely that, at the time, they were not asked.

Hurn notes variable practice between doctors and institutions in the early days of the therapy with only relatives or friends being consulted, if anyone at all was consulted. Amongst clinicians, malariotherapy was soon taken to be a routine treatment. For example, RD Clarke, the medical superintendent at Whittingham, wrote: 'To begin with consent was always asked of relatives and almost always readily given – latterly I have not considered this necessary as malaria treatment at present may be said to be the usual and recognised treatment for GPI on the Continent at any rate'.[62]

In a retrospective ethical review of American practice, the authors concluded that consent would not have been required for a routine and recognised treatment.[63]

Conclusions

The idea that malaria might be a treatment for major mental illness is surprising and counter-intuitive despite the longstanding observation of improvements in physical illnesses with pyrexia. The mechanism of action remains unknown but the question became less relevant after the beginning of the antibiotic era. However, malariotherapy marked an important stage in the physical and organic 'turn' in psychiatric treatment, challenging the Victorian conceptions of mental illnesses being physical and mostly hereditary but static and incurable conditions.

The primacy of Horton in the history of British malaria research and malariotherapy is understandable. However, this account sheds light on the important role of the

[61] Bynum W. Experimenting with fire: giving malaria. *Lancet*. 2010, 376(9752), 1534–35.
[62] Hurn. *The History of General Paralysis,* 1998 (Note 47).
[63] Weijer C, Goldsand G, Emanuel EJ. Protecting communities in research: current guidelines and limits of extrapolation. *Nature Genetics*. 1999; 23(3): 275–280.

collaboration between Whittingham Hospital and the LSTM in the early years of this novel treatment. That the initial innovation and enthusiasm away from the English metropolitan centre has been little commented on may suggest a London bias against the provincial hospitals, from both the journal editors of the time and later medical historians.

Despite the many reports of the outcomes of malariotherapy it remains difficult to determine how effective the treatment was in reality.[64] Most of the reported studies were carried out prior to the development of modern clinical trial methodologies and research ethics, and before the introduction of medical statistics. Scull reminds us that, in retrospect, Wagner-Jauregg's results of treatment of his initial nine patients provided a dubious basis even for further investigation of malariotherapy.[65] However, two recent analyses of historical data find that the overall survival of patients who received malariotherapy was not reduced and patients who received treatment may even have lived longer.[66] [67] These authors employed statistical approaches that were not available at the time.

The researchers of the period pointed to many patients who showed good improvement overall and others who showed less marked improvement. It is nevertheless difficult to equate the historical observations of improvement in some patients to the measurable improvements in health-related quality of life that would be looked for today. Further statistical exploration of the historically reported data, particularly utilising modern techniques of systematic review and meta-analysis, might help to resolve some of the questions that are still unanswered around the effectiveness, or otherwise, of a treatment that remains controversial.

Despite the belief of clinicians that they were offering routine treatment, malariotherapy treatment in Britain was considered experimental by the Board of Control who were responsible for the patient group.[68] Additional investigations and treatments that were performed to assess patients' responses to new anti-malarial drugs or to investigate the pathological processes in malarial infection did constitute research activity requiring consent. Commentators pointing to the wider and indirect benefits from malariotherapy of greater understanding of malarial infection and its treatments nevertheless raise ethical dilemmas over the morality of gains from research with an unclear ethical basis. The history of malariotherapy warns us today to maintain the highest integrity in research methodology and ethics in human experimentation.

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[64] Braslow J. The Influence of a Biological Therapy, 1996 (Note 4). See Figure 2, p.589.
[65] Scull, *Desperate Remedies*. 2022 (Note 57). p.96.
[66] Ouwens IMD, Lens CE, Fiolet ATL, Ott A, Koehler PJ, Kager PA, Verhoeven WMA. Malaria Fever Therapy for General Paralysis of the Insane: A Historical Cohort Study. *European Neurol*ogy. 2017; 78(1-2): 56-62. See Figure 2. Survival after admission (Kaplan-Meier) per treatment category. p.59.
[67] Hilton C. *Petty Tyranny and Soulless Discipline? Patients, policy and practice in public mental hospitals in England, 1918-1930*. London: UCL Press; 2025. See Table 4.2. Malaria treatment 1922-24 and its outcome in 1927. p.133.
[68] Snounou G., Pérignon J-L. (2013). Malariotherapy – Insanity at the Service of Malariology. *Advances in Parasitology*. 2013; 81: 223-255.

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