Dangerous Liaisons – Malaria, Psychiatrists, and Tropical Medicine physicians in England in the early 1920s

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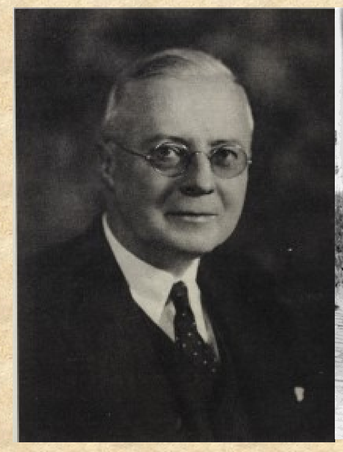
Introduction Wagner-Jauregg developed malarial therapy for general paralysis in Vienna during the First World War (FWW). How did psychiatrists in England implement this unusual treatment?

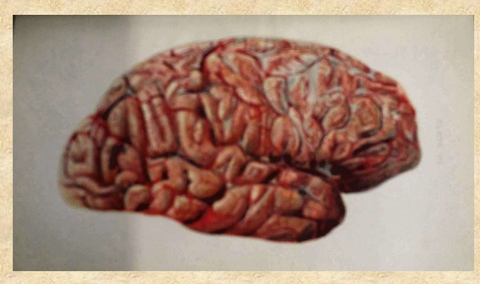


Professor Warrington Yorke
www.royalsocietypublishing.org

Dr A.R. Grant standing right
The Museum of Lancashire

Background: The first patients in England were inoculated with malaria in July 1922 at the Liverpool School of Tropical Medicine (LSTM) - a collaboration between Dr Alastair Robertson Grant, Deputy Medical superintendent at Whittingham asylum near Preston, Lancashire, and Professors Warrington Yorke and JWW Stephens at LSTM.

General paralysis accounted for a high proportion of admissions to mental hospitals in England in the early 20th century. Thought to be related to neurosyphilis, it was a progressive neuro-psychiatric disorder that almost invariably had a fatal outcome. No effective treatments were then available



Artist's impression of the appearance of the brain of a patient with GPI. It shows two major features of brain involvement in syphilis, vascularisation, causing the reddish appearance, and loss of frontal lobe tissue (to the right). From Maurice Craig, Psychological Medicine, 3rd Edition, London, J&A Churchill 1917.

Although there were no major advances in treatment before 1917, the detection of spirochaetes in the brain advanced understanding of the cause of GPI.

Methods: Historical research based on Journal articles and the MD thesis of Dr Alastair Robertson Grant. Retrospectively, 50 patients at Whittingham asylum underwent active malarial treatment and 6 received a comparator (phlogetan) in1922-23. Following Grant's descriptions of outcomes, patients were allocated to two groups, 'recovered' or 'remitted or died'. Fisher's exact test statistics were calculated using www.socscistatistics.com

Results Warrington Yorke served in the Royal Army Medical Corps (RAMC) in Malta before returning to LSTM in 1916 where he carried out important research on anti-malarial agents. Grant served in the Middle East with the RAMC in 1918-19, and it is improbable that he did not gain experience of treating servicemen with malaria.

- Nevertheless, a source of malarial parasites had to be found near Preston. LSTM had become a major wartime centre for research into malaria and anti-malarial chemotherapy, and was within easy reach by railway.
- Grant described a series of 50 patients with GPI who underwent malarial therapy in his MD thesis. Patients from Whittingham were transferred to Liverpool where they were inoculated with venous blood from a patient with benign tertian malaria. Yorke studied the effects of antimalarials in early malaria in the same patient group.
- Grant observed that 7 of his patients had 'recovered', several having been discharged 'in a state of complete remission', whereas 43 had 'remitted', or died. He concluded that *'General paralysis is at present best treated by malarial therapy … Caution, however, is necessary in interpreting results as remissions are by no means unknown in general paralysis, and, in addition, there is, perhaps, a natural tendency to unconsciously over-estimate the value of one's own results'.*
- Retrospective statistical comparison of his results with malarial therapy against a small earlier series of patients he had treated with the non-specific pyretic agent, phlogetan, (1 recovered, 5 remitted or death), unfortunately suggests that there had been no benefit for treatment with malaria (Fisher's exact test statistic, 1, *not* significant at $p < .05$).

Phlogetan versus Malarial Therapy, based on Grant's observations

	Recovery	Partial remission or death	***Marginal Row Totals***
Phlogetan	1	5	6
Malarial **therapy**	7	43	50
Marginal Column Totals	8	48	56 (Grand Total)

The Fisher exact test statistic value is 1. The result is *not* significant at $p < .05$.

Conclusions: The contemporary ethical and legal frameworks of the 1920s allowed the introduction into widespread use of a psychiatric treatment, considered highly effective until the 1950s, that would now be considered highly contentious. The early development of malarial therapy in England provides an unusual historical paradigm offering opportunity for reflection on the vulnerability of people lacking mental capacity, and the efficacy and safety of psychiatric treatments today. Liaison between psychiatrists and physicians is again of increased importance with recognition of the impacts of Covid-19 on mental health care.

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Acknowledgements: I am very grateful to Jan Smith of the Sir Duncan Rice Library at the University of Aberdeen for access to Dr Grant's MD Thesis, to the Museum of Lancashire for the group photograph of Army officers, and to Fiona Watson at RCPsych Library for assistance in accessing JNMD.

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