



Julius Wagner-Jauregg: pyrotherapy, simultanmethode, and 'racial hygiene'

G Gartlehner^{1,2} • K Stepper¹

¹Department for Evidence-based Medicine and Clinical Epidemiology, Danube University Krems, Dr.-Karl-Dorrek-Straße 30, A-3500 Krems, Austria

²Research Triangle Institute – International Research Triangle Park, NC, 27709, USA

Correspondence: Gerald Gartlehner. Email: gerald.gartlehner@donau-uni.ac.at

DECLARATIONS

Competing interests

None declared

Funding

None

Ethical approval

Not required

Guarantor

GG

Contributorship

Both authors contributed equally to this article

Acknowledgements

None

Additional material for this article is available from the James Lind Library website (www.jameslind.org) where it was first published

Julius Wagner-Jauregg, Nobel Laureate and one of the leading psychiatrists of his time, was born on 7 March 1857, in Wels, Austria. Colleagues described him as a brilliant but extremely difficult person – a man able to think 'outside the box' but who also claimed that 'common principles' did not apply to him – and who lived by the motto 'a man with character needs no principles'.

Wagner-Jauregg's career path was steep and successful. After graduating with a medical degree from the University of Vienna in 1880, he worked at the Institute of Pathology and for four years as an assistant at the Vienna Psychiatric Clinic. During this time, he developed an interest in the therapeutic potential of fever in the treatment of psychotic patients.¹

Pyrotherapy

Since antiquity, claims had been made about the beneficial effects of fever on psychotic symptoms² and Wagner-Jauregg became interested in this topic through observations of his own patients. His article entitled *On the Effect of Feverish Disease on Psychoses* published in 1887 summarized relevant publications on the subject and provided descriptions of his own cases.³ Wagner-Jauregg concluded that fever could cure psychoses and debated in his article whether it was justifiable to infect patients to induce fever as a therapeutic intervention. His first attempt to use such an approach involved inoculating several psychiatric patients with streptococci derived from sufferers of erysipelas, but this did not yield any evidence of useful effects.²

Two years later, in 1889, Wagner-Jauregg was appointed head of the Neuro-Psychiatric Clinic

at the University of Graz, Austria. While there, he discontinued his fever experiments in psychotic illness, and focused instead on researching the effects of iodine on cretinism and goitre. Both conditions were endemic in some of the neighbouring Alpine valleys in Austria, as well as in Switzerland.^{4,5} Wagner-Jauregg's work led to the introduction of iodized salt in the Austrian regions in which goitre was endemic.⁶

In 1893, Wagner-Jauregg returned to Vienna as Professor of Psychiatry and Nervous Diseases, and Director of the Clinic for Psychiatry and Nervous Diseases. He resumed his pyrotherapy experiments there, now using tuberculin to induce fever in psychotic patients. A coincidental finding during his fever experiments was that some of those with progressive paralysis from tertiary syphilis showed signs of improvement.⁷ During 1900 and 1901, Wagner-Jauregg and his assistant, Alexander Pilcz, treated 69 progressive paralysis patients with tuberculin and compared them with 69 untreated cases. Patients were assigned to treatment or control by alternation.⁸ Results showed higher rates of remission in tuberculin-treated than untreated patients. Wagner-Jauregg presented these results in 1909 at the 16th International Medical Congress in Budapest, where his findings were met with great scepticism.²

In 1917, to induce repeated spikes of high fever in patients with progressive paralysis, he inoculated them with blood from patients who were suffering from tertian malaria (usually soldiers who had been fighting in the Balkans). The treatment proved to be very successful and Wagner-Jauregg published a case series in 1918.⁹ In a lecture in 1921, he claimed to have treated more than 150 patients with malaria-therapy.¹⁰ In a study

published in 1926, Wagner-Jauregg reports allocating patients to treatment or control groups using alternation:

*I therefore organized a series of comparative observations by treating, over a specific period, and alternately according to the order of their admission, some patients with progressive paralysis with malaria only, and the others, in addition and later, with Salvarsan, in the previously indicated manner. In the first series there were 32 cases, in the second 33.*¹¹

Malaria-therapy for the treatment of progressive paralysis was rapidly adopted internationally, particularly because quinine was available as an effective cure of malaria. In 1927, Wagner-Jauregg was awarded the Nobel Prize in Medicine for the discovery of the beneficial effect of malaria on progressive paralysis, a fatal disease at that time. Although he retired the following year (in his early 60s), he remained active and published more than 80 papers before his death in 1940. Indeed, his main publication on the work that led to his award of a Nobel Prize was not published until 1931.¹²

Prompted by the induction of pyrotherapy with malaria, others proposed alternative ways of inducing fevers. When a Danish psychiatrist claimed that a new, non-infectious intervention (an intramuscular injection of a mixture of olive oil and sulfur) to induce fever would prove superior to malaria-therapy, Wagner-Jauregg replied that this was pure speculation and that a direct 'head-to-head' comparison in similar patients would be the only method to establish superiority of one treatment over another.¹³

Simultanmethode

These methodological issues were addressed by Wagner-Jauregg in a paper published in 1931:¹⁴

It seems to me that one has not always proceeded very critically and systematically with the introduction of other new methods. First one should demonstrate that the method is effective.

This was demonstrated with tuberculin in the following way: in a sufficiently large number of unselected paralytics, one was treated alternately with tuberculin, the other was left untreated.

He went on to discuss the criteria that should be observed when comparing different approaches to inducing fever:

This approach is no longer acceptable today, for one could not take responsibility for leaving a substantial number of paralytics untreated, in order to test the effectiveness of a new procedure, the more so as a quite effective procedure, malaria treatment, already exists. Optimally, one should therefore compare the new procedure that one wishes to test, with malaria, by treating alternately from a large number of untreated paralytics alternately one with malaria and one with the new procedure. I do not consider it appropriate that a researcher uses one procedure at one place and another [researcher] other patients at another place with another procedure, and that the results be compared afterwards with each other. Simply consider how different the perspectives of cure are according to whether the patients are in an asylum, in a psychiatric clinic, in a general hospital ward, or in a private hospital; furthermore, an important role is played by the selection of the patients to be treated. Furthermore, the results of a treatment can only be reviewed when one has monitored over years the fate of those treated.

Therefore I am of the opinion that one can obtain incontestable (unobjectionable) judgements about the effectiveness of two different kinds of treatment only if a researcher treats the patients selected according to the same principles, alternately according to the one and the other way of treatment, and when the successes (results) are evaluated by the same examiner according to the same principles: and furthermore if the constancy of the successes (results) are re-examined after a sufficiently long time.

Using this approach in the Vienna clinic, treatment with malaria was compared both with Saproviton and with Pyrififer. The number of cases treated with these methods was modest; it amounted to 10 each with [malaria or] Saproviton, and 11 each with [malaria or] Pyrififer. This number seemed, however, to suffice, because none of the 10 Saproviton cases showed any remission, and although the Pyrififer treatment was not ineffective, malaria treatment showed an advantage. Apart from this, both [the new] methods of treatment proved, however, not to be far from safe, despite the fact that they had been promoted precisely because of their [supposed] safety in contrast to the allegedly so

*dangerous malaria cure. I have been surprised that this method of testing therapeutic procedures has not found any imitation at all. But this may be because the child has not hitherto been given a name. I will therefore christen it 'The Simultaneous Method' [Simultanmethode] and use this term henceforth.*¹⁴

By introducing a term in German – *simultanmethode* – for the important methodological principle of unbiased allocation to treatment groups using alternation, Wagner-Jauregg was adding to the earlier introduction of similar terms in English and French.¹⁵

One of Wagner-Jauregg's former assistants reported that Wagner-Jauregg became skeptical about the scientific validity of case series and studies using historical controls during the 1890s. Indeed, he also became skeptical of his own observations and expectations. In the late 1890s, to reduce his own subjective impact on his experiments, he began delegating all experimental treatments to his assistants.¹⁶

'Racial hygiene'

Julius Wagner-Jauregg's important medical achievements are overshadowed, however, by his anti-semitism and his support for the concept of 'racial hygiene'. He was an enthusiastic Nazi, even before the annexation of Austria by Germany in 1938. His attempt to join the National Socialist Party failed, however, because his first wife was Jewish.

Wagner-Jauregg became a strong proponent of 'racial hygiene', an ideology which enjoyed wide popularity throughout Europe at the time. He became the president of the Austrian League for Racial Regeneration and Heredity, and advocated the forced sterilization of people who were mentally ill, criminal, or regarded as genetically inferior.

In Austria today, the names of some streets and medical facilities commemorate the medical achievements of Wagner-Jauregg. He continues to be a controversial figure in history, teetering between brilliance and despicableness.

References

- Whitrow M. Wagner-Jauregg and fever therapy. *Medical Hist* 1990
- Wagner-Jauregg J. Lebenserinnerungen [Memoirs]. In: Schönbauer L, Jantsch M, eds. Vienna:Springer 1950
- Wagner-Jauregg J. Über die Einwirkung fieberhafter Erkrankungen auf Psychosen. [On the effect of febrile disease on psychoses]. *Jahrbuch Psychiat. Neurol.* 1887;7:94–131
- Tröhler U. Towards endocrinology: Theodor Kocher's 1883 account of the unexpected effects of total ablation of the thyroid. *JLL Bulletin: Commentaries on the history of treatment evaluation* 2010. See: www.jameslindlibrary.org (last accessed 12 July 2012)
- Slater SD. The discovery of thyroid replacement therapy. *JLL Bulletin: Commentaries on the history of treatment evaluation* 2010. See: (www.jameslindlibrary.org) (last accessed 12 July 2012)
- Wagner-Jauregg J. Vorbeugung des Kropfes. [Prevention of goitre] *Wiener Medizinische Wochenschrift* 1923;47:2089–2090
- Boeck E. Versuche über die Einwirkung künstlich erzeugten Fiebers bei Psychosen. [Experiments on the effects of intentionally induced fever on psychoses] *Jahrbuch Psychiat. Neurol* 1895;14:199–268
- Pilcz A. Über Heilversuche an Paralytikern [On therapeutic experiments in paralytics]. *Jahrbuch Psychiat. Neurol.* 1905;25:141–67
- Wagner-Jauregg J (Über die Einwirkung der Malaria auf die progressive Paralyse. [On the effect of malaria on progressive paralysis] *Psychiat.-neurol. Wochenschrift* no. 21/22:132–4.1918
- Wagner-Jauregg J. Die Behandlung der progressiven Paralyse und Tabes. [The treatment of progressive paralysis and tabes] *Wiener Medizinische Wochenschrift*, 1921;71 (25):1105–9; (27):1209–15
- Wagner-Jauregg J. Die moderne Therapie der Neurosiphilis. [On modern therapy of neurosyphilis] *Verhandlungen der Deutschen Gesellschaft für Innere Medizin*. [38. Kongress. München: Bergmann, 1926;34–62
- Wagner-Jauregg J. Verhütung und Behandlung der progressiven Paralyse durch Impfmalaria [Prevention and treatment of progressive paralysis by malaria inoculation]. *Handbuch der experimentellen Therapie Ergänzungsband*, Munich, 1931a
- Wagner-Jauregg J. Fieber- und Infektionstherapie von Nerven- und Geisteskrankheiten. [Fever- and infection treatment for neurological and mental illnesses] *Wiener Medizinische Wochenschrift* 1930;20:651–654
- Wagner-Jauregg J. Über die Infektionsbehandlung der progressiven Paralyse. [On infection treatment of progressive paralysis]. *Münchener Medizinische Wochenschrift* 1931;78:4–7
- Chalmers I. Why the 1948 MRC trial of streptomycin used treatment allocation based on random numbers. *JLL Bulletin: Commentaries on the history of treatment evaluation* 2010. See: www.jameslindlibrary.org (last accessed 12 July 2012)
- Kauders O, Julius Wagner von Jauregg. *Wiener Medizinische Wochenschrift* 59:130–2