

Malaria as Lifesaving Therapy

Vivax malaria was once familiar to doctors not only as a foe, but also as an ally. In the first half of the 20th century, people with tertiary syphilis, the phase of the disease in which *Treponema pallidum* bacteria attack the brain and nervous system, were doomed to a gruesome death: They would become increasingly neurotic and gradually paralyzed. Most were institutionalized, and there was no cure.

So physicians drew on a theory that had gained prominence in the late 19th century—that high fever could help cure a variety of mental illnesses. Austrian psychiatrist Julius Wagner-Jauregg was one of the idea's strongest proponents, but his initial experiments in the 1880s with fever-inducing pathogens and compounds such as tuberculin and salmonella toxin failed. He reasoned that the fevers they induced were not severe enough. In 1917, he tried again when a soldier who had caught malaria while fighting in the Balkans was admitted to his ward. Wagner-Jauregg used the soldier's blood to inoculate nine neurosyphilis patients. Six of them got better.

Soon, malariotherapy was seen as a miracle cure. It became a leading treatment for end-stage syphilis, quickly spreading across Europe and North America. Between 1917 and the rise of penicillin in the 1940s, tens of thousands of syphilis patients were infected with malaria. Different clinics used different parasites, but "after a few costly mistakes" with *Plasmodium falciparum*, a more lethal parasite, "most people settled on vivax," says Nick White, professor of tropical medicine at Mahidol University in Bangkok and the University of Oxford in the United Kingdom.

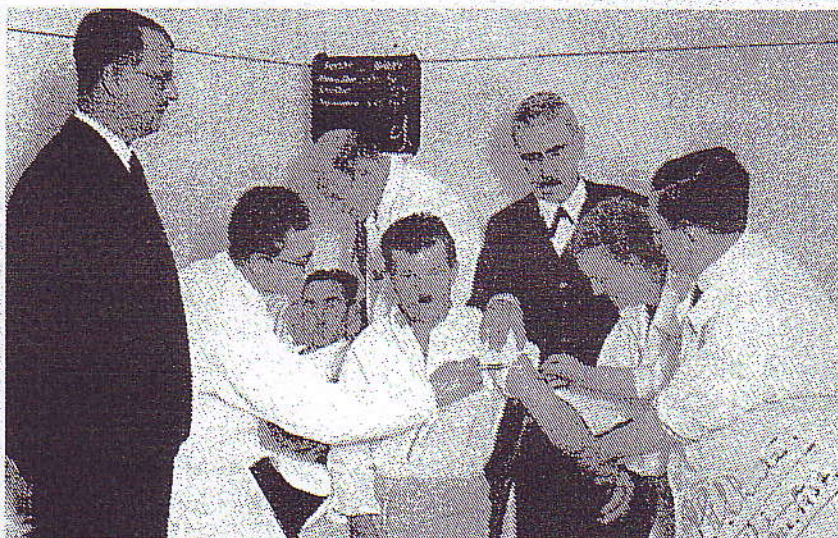
No one is sure exactly how it worked, but the high fevers that resulted seemed to help the patients' immune systems fight off the bacteria. Roughly half recovered enough to resume normal activities; many were able to resume independent lives. In 1927, Wagner-Jauregg won the Nobel Prize

in physiology or medicine for his discovery. (The Austrian's legacy has a darker side as well. He was an advocate of eugenics, and in the 1930s he was a Nazi supporter.)

Because of malariotherapy, "the parasite's biology was investigated in amazing detail," White says. The result was a wealth of information about the disease process and how it differs depending on the strain of *P. vivax*. Those records are gaining some new attention today, as vivax starts to emerge from the shadow of its better-known cousin, falciparum (see main text, p. 684).

But this medicinal use of the parasite is in part to blame for the later neglect of the disease it causes, says Kevin Baird of the Eijkman Oxford Clinical Research Unit in Jakarta. Because doctors used *P. vivax* as a medical treatment, he says, many people assumed that it must be relatively harmless. But Baird says that even at the height of the therapy's use, that reputation was unfounded: Although malariotherapy saved lives, it also killed as many as 15% of the patients who received it, despite close monitoring and treatment of the infection.

—G. V.



Radical treatment. In a 1934 image, Julius Wagner-Jauregg (center, in black suit) watches as blood from a malaria patient (in background on left) is injected into a neurosyphilis patient (center).