

THE BIOLOGISTS' FORUM

Murder, Malaria and Me

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Nathan Leopold was the most notorious murderer I ever met. He was one of the most notorious murderers of the present century. Indeed, he and his partner, Richard Loeb, were easily the most notorious murderers of the notoriously murderous 1920s. The notoriety of these men derived not only from their "thrill killing" of a harmless young boy but also from the fact that they were defended in court by the great Clarence Darrow; one could hardly find a more sensational combination.

Actually, Nathan Leopold was the **only** murderer I ever met (so far as I know). I met him first in Puerto Rico and later in Washington, D.C., and I would not have met him at all had it not been for parasites. In 1966, I was attending a conference in Puerto Rico because of my interest in parasites and Leopold was there because of **his** interest in parasites. He had been sentenced to "life plus 99 years". Parole had been denied repeatedly and so horrible was his crime that it seemed likely that he would never be released. It is believed that a major factor in his eventual parole, after 33 years in jail, was his participation in a volunteer research program—a program in which prisoners allowed themselves to be used as guinea pigs for testing experimental antimalarial drugs. There is some doubt as to how heroic, or even how useful, Leopold's contribution was but there is no doubt that participation in the malaria project was a good thing to have on one's resume when being considered for parole. In any case, it was Leopold's parole that got him to Puerto Rico where he lived out the remaining years of his life. What got him to the conference in San Juan and later to Washington, D.C., was that his post-prison activities included research on parasitic diseases.

The malaria program had been Leopold's introduction to parasitology. During World War II, the development of antimalarial drugs was of tremendous importance. It still is, even though very few people are trying to do it, but then the need was particularly acute because the chief sources of quinine were cut off from the Allies. Ducks and chickens were OK for testing chemicals against avian malaria; monkeys were OK for tests against simian malaria; but there came a time when drugs for people had to be tested in people. Fortunately, there were

people in the United States who had malaria and needed to be treated. Unfortunately, they were in mental hospitals, suffering from advanced syphilis. They had been given malaria (*Plasmodium vivax*) as a means of inducing fever high enough to kill spirochetes in their central nervous system—not exactly “normal” human subjects and not in abundant supply. Some of them were given test compounds instead of the usual quinine but another source of experimental subjects was clearly needed. That is where the prisoners came in handy.

Ethical views on prisoner experimentation have changed since those days and are not considered here. The United States antimalarial drug testing program was organized by the Public Health Service and the National Institutes of Health in cooperation with the prison authorities. It was conducted with a high level of scientific expertise and with what appears to have been a high level of respect for the prisoners (given the acceptance of such experimentation in the first place). Tests were conducted at federal penitentiaries in Atlanta, Georgia, and Seagoville, Texas, and Statesville, Illinois. Prisoners who volunteered for the program were infected with malaria parasites (*P. vivax*) either by mosquito bite or by blood inoculation. They were then used as test subjects for evaluating various candidate compounds—including two that became important antimalarials, chloroquine and primaquine. The program continued for four years after the end of World War II and had just been phased out when it was hurriedly reactivated upon the outbreak of hostilities in Korea (some studies, mainly on the biology of exotic malaria species in prisoner volunteers, continued into the 1960s).

Leopold was involved in the Statesville malaria project which began just as World War II was ending. He served at various times as lab technician, clerical worker and malaria test subject. It is tempting for us to assume that his motivations were ones of humanitarian concern and personal atonement and it was tempting for Leopold to present them in that light—at least prior to his parole. However, much of what he did in his long prison career was the product of boredom and intellectual restlessness (he admitted as much) and there are hints that his personal behavior made him a nuisance in the malaria program. That may be true but it does not give us any reason to doubt his own account of long hours at the microscope, long days of clerical and supervisory duties and painful first-hand experience of acute malaria. Whatever other benefits he may have received, he had the satisfaction of being one of the first humans to be treated with the new 8-aminoquinolines. These were the first drugs to give radical cure of malaria and one of them, primaquin, continues to be of great importance in the treatment of malaria.

Nathan Leopold was paroled in the late 1950s and despite flagrant disregard of parole regulations, became free in 1963. Before his death in 1971, he held a variety of jobs and in one of them, he became

involved in parasitological research of a different kind. Several important worm parasites, protozoan parasites and bacterial pathogens are transmitted through fecal contamination of the environment and such diseases were longstanding problems among the poor people of Puerto Rico. (One of the main streets of San Juan, Avenida Ashford, is named after a hookworm pioneer.) Leopold, when he was an employee of the Puerto Rico Department of Health, tried to find out how much fecal contamination there really was. It was easy to see the danger inherent in badly made privies, misused privies, and the lack of privies or running water. But is disease transmission confined to the immediate sites of defecation or is it pervasive? Do young children who have no toilets and no running water spread infinitesimally small traces of fecal contamination throughout their dwellings? How could one tell? Leopold had a neat approach to the problem. If people would swallow a non-absorbed fluorescent dye, the dye should eventually be present on fecally contaminated surfaces and could be detected by means of an ultraviolet lamp. He swallowed some dye himself and felt confident that it was safe to use in the way he intended (nowadays it would be unthinkable to do the work with such limited safety data). He carried out trials in a number of homes and his results suggested that the method was indeed useful (and that traces of fecal contamination were ubiquitous). The method was not adopted by other workers—probably because of the ethical and regulatory problems associated with it. It does not seem to have been published formally, but Leopold and a colleague presented their findings at national parasitology and tropical medicine conferences.

It was about this work that I spoke to Nathan Leopold at a Washington conference. We were in the midst of a noisy reception in one of the big hotels and he suggested that perhaps we might find a quieter spot for a chat. We adjourned to the mezzanine where we sat on a couch and enjoyed a thoroughly good chat about his work. I don't know if he knew that I knew that he was **that** Leopold, not just any old Leopold. We did not talk about his past. He was impeccably dressed in a business suit; he was portly; he was friendly; and of course, he was articulate and knowledgeable (after all he had caused a sensation by graduating from the University of Chicago at the age of 18!). I must confess that my knowledge of his more celebrated past exploits gave the conversation an added piquancy. To really escape the hustle and bustle of the hotel, Leopold might well have suggested that we go for a quiet stroll in the park. I suppose that would have conjured up images of a boy's body being stuffed into a culvert in the woods near his home and I sometimes wonder what my response would have been.