Comments on Leprosy Vaccination

TO THE EDITOR:

As Eleanor Storrs observed the abundance of *Mycobacterium leprae* in infected armadillos, a glimmer of hope resurrected the project of a vaccination against leprosy. With time, diligence and funds, masses of *M. leprae* would be accumulated, a vaccine would be readied for worldwide vaccination—the road to control and eradication, as in the case of smallpox, polio or typhoid.

Talents were recruited into a task force. Hard work in the workshops materialized the *sine qua non* of vaccination: armadillo colonies producing masses of leprosy bacilli and a perfect technique to separate bacilli from host components. Now, with close to a ton of infected livers, spleens, lepromas and purified *M. leprae* masses, are we ready to vaccinate?

This writer takes the liberty of reiterating the opinion previously expressed in written and spoken words, risking to look like the devil in holy water. Many of us watched with scepticism the feverish labors for vaccination; nobody expressed his/her view on paper. Is it not time to raise questions and ask for an open debate?

The vaccination project has already consumed a fortune. This is just a drop in the sea compared to the financing of worldwide vaccination. But is not all the gold on earth worth successful vaccination? Before predicting such success, a simple question arises: Is it feasible? Whom and how shall we vaccinate, who will do it, and who will pick up the bill?

First of all, based on the observation that in even the most highly endemic areas leprosy rarely affects more than 5% of the population, about 95% of the world's population does not need vaccination. Half of the remaining 5% live in nonendemic areas and would never be expected to encounter *M. leprae*. Thus, there remains 2.5% in need of vaccination. Let us put this into practice.

A biosphere of 10 million people in an endemic area is our hypothetical target; 250,000 of them—the 2.5%—need vaccination. No problem! We have the vaccine, technicians, equipment, and the funds to finance the venture. So far it does not need a gold mine. What it does require is a bottomless purse to select the 2.5% out of the 10 million subjects. Let us assume that we can identify them on the basis of a negative lepromin reaction. Ten million people must be examined, tested, registered, and all have to be seen again in 3 weeks' time for the lepromin test results to be observed and interpreted. Imagine 10 million lepromin tests and reading the Mitsuda reactions in 3 weeks' time, with names and addresses, identification of a populace in constant movement, not to mention inborn resistance to such a carnival. But our task force will do it. That is what task forces are for; the 2.5% of the 10 million will be computerized. Or should we stop half way and vaccinate only certain age groups, just to regret it later?

Another variation might be to forget about the selection of susceptible "nonreactors" and vaccinate all 10 million. Oh, yes, and then vaccinate and revaccinate the other 4,000 million. A simple calculation shows that for such a project we need all the armadillos of the planet. The clever beasts do not breed in captivity. When leprosy is under control, armadillos will be an extinct species—a task for Greenpeace.

Now, the devil in the holy water asks a simple question: Why vaccinate? The 2.5%-susceptible population is already vaccinated. Do they not live in endemic areas where dust and droplets, scratches and kisses vaccinate and revaccinate them day after day? How is it they are still Mitsuda negative after all of this daily, highly powerful, natural vaccination with dead and live leprosy bacilli?

What does the vaccinator expect from one more shot? A life-long exposure to the live vaccine transmitted from a relative or neighbor by "close prolonged contact" did not convert the Mitsuda reaction. What nonexisting evidence can one offer that our vaccine will provide better immunity compared to the live vaccine given free of charge by the contacts? Are we not losing time and funds, and raising false hopes? Is the lepromatous leprosy patient not vaccinated with virulent bacilli from head to toe and, if multidrug therapy does not solve the problem, will he not be a burned out case,

still immune deficient? So long as these questions remain unanswered, vaccination is a shot in the dark.

A task force proposes a BCG coupled *M. leprae* vaccine to immunize the exposed susceptible population. Argument: *M. leprae* serves as an immunogenic antigen and BCG as a booster of deficient cell-mediated immunity. BCG vaccination against leprosy was the hope of the 1960s. The World Health Organization trial provided very important data on vaccination, epidemiology, clinical forms and aspects, and lepromin reactivity. Despite perfect planning and expert execution, the trial clearly showed that BCG provided a very modest level of protection. With the best of intentions and a top scientist at the helm, the BCG vaccination was tested in endemic and highly endemic geographical locations. The result was clear: "BCG vaccination is not likely to be an important solution for leprosy control."

Again, those vaccinated with BCG were also exposed to live *M. leprae* from dust and droplets, scratches and kisses of the bacilliferous cases in the highly endemic and in the less-endemic areas. Indeed, the vaccination with BCG was actually BCG plus *M. leprae* vaccination; BCG was provided by the vaccinators, *M. leprae* through the involuntary sure contact with *M. leprae* cells. And it did not work. So what can we expect from the repetition of the gigantic aborted experiment of the 1960s, with the insignificant difference that in addition to BCG *M. leprae* was provided by the environment in the 1960s and by the Armadillo Bank in the 1980s. Are the results of the 1960s not a lesson for the 1980s? In addition to this argument, it is a fact that BCG did not control tuberculosis; multidrug therapy does.

Then, just as the Armadillo *M. leprae* Bank became rich, appeared the leprosy-derived mycobacteria in *M. leprae* infected tissues. Even if these secondary, opportunistic mycobacteria are present only in small numbers, they are there in most if not all of the *M. leprae*-infected tissues of the Bank. One wonders how many cells labeled *M. leprae* are actually leprosy-derived mycobacteria. They will be an integral part of the vaccine. Perhaps they are also an integral part of the disease. We can now produce highly purified *M. leprae* masses free of host components, but not free of the leprosy-derived mycobacteria. These are difficult to detect because of their small number, not necessarily all viable cells, and hard to cultivate because of well-documented specific growth requirements. For these reasons, the leprosy-derived mycobacteria will remain mostly undetected in *M. leprae* suspensions used as a prospective vaccine. The Bank is certainly not free of leprosy-derived mycobacteria, thus adding further complications to the vaccination trial.

What then if not vaccination? This writer believes in chemical control of leprosy rather than vaccination. If the source of infection is reduced or eliminated by efficient multidrug therapy, coupled with efficient use of soap, shoes and brooms; with the demystification of leprosy; with socioeconomic justice in the leprosy belt, fighting ignorance, filth, poverty and prejudice with kindness rather than with cold, computerized bureaucracy: this package is worth a thousand vaccines. Priority must be given in every instance to the elimination of the source of infection. Our present multidrug therapy, if efficiently instituted, is a promise, but not enough for leprosy control. Increasingly potent new antileprosy drugs are urgently needed. While fully appreciating the high potency of rifampin and the promise of the new fluoroquinolones, we must find drugs as potent as penicillin against syphilis. And such ultra drugs will be in the making only if the appropriate pharmacological model—the *in vitro* culture of *M. leprae*—is available in the workshops of pharmacologists.

This exercise is not intended to compete with Lord Byron in wit, cynicism and sarcasm. The style might help present this sad chapter as not too boring reading and provoke some helpful comments in directing the train onto the right track. I label vaccination a Methuselah project because, if forcefully pursued, it will take a quarter of a century or more to recognize it as an error, *non sine lacrimis*. Sealing these pages in a bottle and committing them to the sea off Cape Horn would be a betrayal of my convictions.

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