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SCHOOL OF PUBLIC HEALTH

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BERKELEY, CALIFORNIA 94720

March 10, 1970

Professor Joshua Lederberg
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Dear Dr. Lederberg:

Please excuse my tardy answer to your request about smallpox and vaccination. Your letter was sent to Atlanta, but I have recently moved out here to California and the letter took some time to track me down. Enclosed please find two copies of the recent "New England Journal of Medicine" papers, plus a copy of an as yet unpublished paper which will be appearing shortly in the "Journal of the American Medical Association". At the risk of boring you somewhat, I would like to respond to some of your points in detail. Those of us who are on the outside end of controversy seldom get an opportunity to "convert" a man of your stature.

First, you state "a deterioration in our standards of community protection would expose the entire population to eventual risks of utmost gravity." This assumes that our public health establishment would simply sit by and watch with dismay the progress of a smallpox epidemic on our soil. In fact, smallpox is a highly visible and, in classic cases, an easily diagnosable disease. Our health authorities would immediately isolate and vaccinate contacts of cases, and shortly terminate any importation epidemic of smallpox, even in a fully susceptible population.

Second, "new vaccines are being introduced that show some promise of having even lower rates of side effects." The recent cutback on research funds, plus the lack of glamor in the smallpox field mean that only two groups are working with the CV1-78 vaccinia strain. First is Professor Kempe's group in Colorado, and second is Dr. Neff's group at Johns Hopkins. Neither of these are doing a great deal of basic work with this strain. With a death rate of only 1 per million primary vaccinees, a massive field trial would have to be mounted to show differential safety of these two virus strains. Such a trial would be administratively and practically unfeasible. Also, the amount of smallpox in the world, even in India, is now so low that a field trial to demonstrate the effectiveness of such a vaccine against smallpox would be essentially impossible.

I am neither a geneticist nor a virologist, but I can say something about the various strains of vaccinia virus. There are several strains

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of vaccinia, which in the laboratory apparently breed true. These can be distinguished by simple morphological and growth characteristics. Strains which have been used in Holland and Scandanavia apparently cause a much higher rate of post-vaccinial encephalitis than does the New York City Board of Health strain which we use in this country. There are strains which, in the laboratory, have been found to be particularly neuro-tropic for laboratory animals. However, as far as we know the vaccines we use in this country are genetically homogeneous, and the rare case of post-vaccinial encephalitis is due to some host-factor (as yet unknown) rather than a virus mutation. The CV1-78 was "bred" by serial passage on chick embryos at relatively low temperatures.

The reduction of non-lethal vaccination complications by case selection probably cannot change our current complications rates significantly. There is no known identifyable host factor which predisposes to post-vaccinial encephalitis, generalized vaccinia, accidental implantation, or erythema multiforme. The stricture against vaccinating children with eczema has been in existence for many years. Further publicity about the eczema problems may not reduce the number of eczemitus children accidentally vaccinated. More important, all of the deaths due to eczema vaccinatum in the last ten years have occurred in children who have not been vaccinated themselves, but whose siblings or parents were vaccinated and transmitted the virus to them. The Public Health Service and the American Academy of Pediatrics have said for some years that siblings or parents of children with eczema should not be vaccinated. Apparently however, many physicians simply don't take the time to carefully inquire about this situation. The children with leukemia and agammaglobulinemia who get vaccination complications are generally undiagnosed until vaccination. Therefore it is the adverse reaction to vaccination which leads to diagnostic investigation. It is not feasible to require a careful work up to rule out such diseases before children are routinely immunized.

But to me, all of these points are tangential to the real issue. We know that our current policy, while causing some unfortunate side effects, is not effective in producing a solidly immune population. Nearly fifty percent of the population is completely unprotected, and only some twenty to twenty five percent are well protected. The reason why we have not had smallpox in the last twenty years is luck and our restrictive immigration policy, plus vaccination of travellers. If we were to have an importation today, we would act exactly as if the population were totally unimmunized. That is, we would vigorously hunt down, vaccinate, and place under surveillance all possible contacts, while alerting the medical community to give us early reporting of suspect cases. In European hands, such techniques have limited most importation outbreaks to a small number (a dozen or so) cases.

Finally, please rest assured that my colleagues and I are not "anti-vaccinators". Quite the contrary, we have been instrumental in the eradication of smallpox in West and West-central Africa, having given over 120 million vaccinations in our program. I strongly believe that vaccination should be pursued vigorously wherever there is smallpox or a reasonable risk of smallpox importation. When smallpox is gone, then one must weigh the relative risk of routine vaccination, and try to assess how quickly the health structure could detect and eliminate an epidemic if it occurs. When we weigh these risks, we believe that in the United States at this time routine vaccination is a greater hazard than is smallpox itself. We certainly don't advocate this policy for nations in Africa, even those which have not had smallpox in recent years, nor would we necessarily advocate this policy if smallpox once again became established in Mexico and/or Canada.

Thank you for your patience in reading this long letter. I hope I've helped clarify some of the issues.

Sincerely yours,

J. Michael Lane, M.D.
Associate Professor in Epidemiology

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