

December 22, 1964

Dr. W. Charles Cockburn
World Health Organization
Palais des Nations
Geneva, Switzerland

* assigned to write
report for 1965
Assembly

Dear Charles:

It was with keen disappointment that I received notice that the smallpox team^{*} had been constituted by other and I am sure worthy, knowledgeable persons in the smallpox field. We have, as you know, become deeply interested in and committed to major activities in smallpox. In consequence, we have been exploring a number of theoretical and practical considerations, each of which, we feel could have a significant bearing on an overall program. From the standpoint of the Committee, the WHO or yourself, none of these may be of particular consequence. However, I do believe they merit discussion.

1. The basic approaches to eradication. The administrative approach to vaccination in most areas has been based on that employed in malaria. This demands a large manpower reserve with all of the manifold problems involved in quality control. It is a costly and time-consuming approach. Although probably the best means to reach the largest proportion of the population, other methods based on the less costly and more easily controlled approach of mass vaccination (with or without the jet gun) may reach a sufficient proportion of people to tip the balance sufficiently to accomplish the objective of eradication. We suggest that the level of vaccination necessary for eradication may be a function of a relatively few variables subject to analysis and definition. Thus, for example, in a densely crowded area with many susceptibles being constantly added through births and migration, higher levels of vaccination might be required and a more costly approach might be indicated. In less crowded areas with fewer susceptibles being added, the mass approach might be more practicable and as effective at far less cost. In brief, it would seem worthwhile to consider tailoring vaccination programs to the needs of specific areas. Further exploration of this problem, we feel, is clearly needed. If a single, simple approach, modeled on the house-to-house, around-the-block scheme devised for malaria, were to be advocated for every country, I suspect that it might serve as the most significant major administrative hurdle to accomplishing a world eradication program.

2. Need for investigation of the theoretical aspects of eradication. Of particular importance is the need to establish at least one small but knowledgeable group concerned with the theoretical aspects of eradication. Application of the principles implicit in basic epidemic theory and the testing of hypotheses under various field circumstances should provide a good deal of information which could effectively guide a global program. Questions pertaining to the extent and ease of spread of smallpox under varying conditions of community susceptibility could provide substantive information as the need to achieve particular levels of immunization. In this context, there is a real need for a competent, thorough appraisal of the meaning of neutralizing and hemagglutination-inhibiting antibodies in protection. To achieve an adequate understanding of the conditions required for spread of the disease, a more accurate appraisal of immunity status is required than are presently available through a crude reading of the cutaneous response following revaccination. Candidly, and despite the ex cathedra statements of certain "experts" in the field, I suspect that levels of circulating antibody do have a direct correlation with clinical protection. They certainly bear such a relationship in other viral diseases.
3. Need for international surveillance. If a program in international surveillance is to be initiated, I can think of no happier place to begin than with smallpox. Good data regarding smallpox, the characteristics of outbreaks, the cyclical patterns, age distributions, etc. are vital to the program. The simple count of cases in each of the countries is a starting point but not more than this. If a program of good international surveillance for this one disease could be made to operate effectively, international surveillance programs for other diseases could follow logically. In my mind, the evolution of a good, functioning scheme of international surveillance for smallpox could have more important implications than eradication of the disease itself (although I must confess that eradication of even one disease is no mean accomplishment).
4. Need for standardization and adequate testing of vaccine strains It appears as though each country has its own pet strain of vaccinia virus passed and repassed in its own unique fashion. Adequate data regarding safety and potency for even one of these strains cannot be found. Detailed testing of one or a few candidate strains for more general use is sorely needed. In this context, we have heard of and hope soon to test a long neglected strain, until now regarded as a "laboratory curiosity", which may be grown in very high titer in rabbits. One rabbit, in fact, produces as much virus as four calves. Very limited

observations indicate that its potency is very high, probably higher than currently available U.S. strains. Its safety must, of course, be appraised. Whatever the problem of standardization is, I am sure, more vivid in your own experience than in mine.

In brief, I firmly believe that we need to, we must and we can more effectively press global smallpox eradication. The program should not, without considerable consideration, be conducted on the classical pattern employed in malaria eradication. The disease is totally different; the problems are totally different. Effective, imaginative and adaptable central leadership is demanded. I can only hope, in endeavoring to work from this vantage point, that the recommendations to the Assembly are imaginatively conceived, since these recommendations may have a major impact on our own plans and activities.

I hesitate to trouble you with all of this but hope you will understand our primary concern and interest in the Committee's deliberations.

Sometime soon, I must journey to London to work out with Dr. Roberto (now at London School) his plans for next year. I had thought it might be expedient to review with you at an early date our recent data regarding one as opposed to two insertions of smallpox vaccine plus other new data pertaining to responses to smallpox vaccination, complications of vaccination, characteristics of imported cases and outbreaks and recent information pertaining to measles vaccines. This trip can be conveniently adjusted to suit other purposes since I have been declining essentially all engagements for January, February, and early March. I should be most happy to work out whatever arrangements would be most convenient. If I can be of assistance in evolving a sound and realistic report on the global smallpox program, I should be happy to oblige in whatever capacity would be most appropriate.

With every best wish for the New Year.

Sincerely yours,

Donald A. Henderson, M.D.
Chief, Surveillance Section
Epidemiology Branch

bc: Dr. Ruthig
Dr. Langmuir
Dr. Millar