

Note: Chygin .03/yr. (7)
Spox 1838 U.S. more deaths in
London than cholera 1832
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Presentation to the American Epidemiological Society - Dr D. A. Henderson

In 1967, just over two years ago, a ten year programme for global smallpox eradication was launched by the World Health Assembly. The concept of such a programme had been actively incubating since the mid 1950's when eradicationists were dreaming most vividly of the global extinction of a variety of diseases. Any semblance of activity, however, was submerged by the malaria eradication tidal wave which commenced in 1955. For example, only 3 years ago more than 100 persons were occupied with malaria at WHO Headquarters and Regional Offices alone - one Medical Officer dealt with smallpox.

Smallpox indeed was a poor cousin. As the dreams of the malaria eradicationists faded in the harsh light of experience, there was little enthusiasm for launching yet another eradication effort. If it failed it could not fail to seriously damage the reputation of the World Health Organization. There were a few, however, who insisted that smallpox was a sufficient problem to warrant an eradication effort. ~~They pointed out that the two diseases were totally dissimilar and the prospects for success very different.~~ While failure could have serious repercussions, a successful effort could bring renewed vigour and respect to what sometimes seemed to be a tiring, middle-aged WHO. The Soviet Union, long a protagonist for such a programme, was joined by the United States in spearheading the proposal - the Assembly with surprising enthusiasm concurred - and in January 1967, the programme began.

At the inception, the prevalent mood was scarcely one of optimism. The Assembly provided only \$3 million per year to assist in ~~financing~~ programmes in approximately 50 countries - obviously substantial additional help would be required from other ~~international sources and the countries themselves~~. There was a legacy of disillusionment and despondency with malaria eradication in particular and with the concept of eradication in general. Surprisingly prevalent was the view that "an eradication programme is an eradication programme" - that, except in lesser detail, the strategy and techniques employed in the malaria programme would be applied in the smallpox programme and that the problems and failures would be little different.

Even today, the apparent public health sophisticates do not fully comprehend that we are dealing with two totally different diseases with little in common either ecologically or epidemiologically.

At the inception of the programme, it was encouraging to note that a considerable number of countries had become free of the disease during the preceeding 10 to 15 years. In 1950 (1) the first year for which we have reasonable data, smallpox was prevalent in most parts of the world except Europe, North America and Oceania. By 1966 (2), not only was the overall incidence less but a number of countries with very limited health facilities had become free of the disease - e.g. countries in Central America, the Middle-East, Laos, Cambodia, Vietnam and Malaysia. Many had accomplished this by indiraction, ~~if you will~~, while conducting routine vaccination programmes for control purposes. This alone was tangible evidence that eradication was ^afeasible proposition even in economically impoverished areas.

It was also apparent that every endemic country vaccinated every year a sizeable proportion of its population simply as a control measure. This was done not as a blind adherence to public health practice of a colonial era, but because of practical political, if not public health necessity. It is sometimes forgotten that such diseases as tuberculosis, yellow fever, cholera, malaria or leprosy are comparatively minor problems contrasted to smallpox which, as variola major, kills 30 to 40% of those contracting infection. Moot testimony that the people themselves recognize its seriousness is the existence of smallpox idols and religious cults, both in Africa (3) and Asia (4) - no other disease, to my knowledge, has been accorded so prominent a place in the social structure.

At the inception of the programme, we found, that not less than 80% and perhaps as many as 90% of the vaccinations were being performed with liquid vaccine whose stability is negligible in the tropics or with freeze-dried vaccine whose original potency was abominable.

We felt that if we could assure that potent vaccine was employed for routine vaccinations, this of itself should have an impact on disease incidence. Initially most of our efforts were devoted towards assuring such a supply. Connaught Laboratories in Canada agreed to provide consultation, assistance and vaccine testing for the laboratories in the Americas and a panel of competent vaccine

producers was recruited to assist in other areas. The Rijks Institute in the Netherlands agreed to test vaccines for us and, finally, a special group was convened to prepare a Manual on Vaccine Production. Gradually, we managed to stop distribution of liquid vaccine and, by testing freeze-dried vaccines produced at various laboratories, either put them out of business or demonstrated that consultant help was required. Donations of vaccine were solicited. The USA provided approximately 40 million doses for West Africa; the Soviet Union 140 million doses and some 15 other countries contributed about 10 million doses annually. At present, more than 95% of vaccine employed in the endemic countries is freeze-dried and meets ~~the high~~ WHO potency standards.

Vaccination techniques were a second problem. The scratch technique was the one most readily taught and most extensively used. Take rates in the field, however, were often 10 to 15% lower than those induced by good multiple pressure technique. Unfortunately, the multiple pressure technique was taught only with difficulty and performance was generally poor. The jet injectors provided a first solution to the problem - take rates were good, less vaccine was used and large numbers of vaccinations could be performed rapidly - if people could be assembled at collecting points and if the machines could be kept operating. Jet injectors were introduced for use in West Africa, Brazil and the Congo and, when given ample tender, loving care, proved successful. In many areas, however, populations are disperse or more difficult to assemble and maintenance of the guns is less certain. Some other approach was needed.

The bifurcated needle (5), developed by Wyeth, was considered and we elected to try the technique of multiple puncture vaccination. The needle was simply dipped into the vaccine - approximately .02 ml. of vaccine was held between the points. With 15 rapid strokes, vaccination was accomplished. Cleansing of the arm, I should note, was also abandoned. Studies showed that the takes were at least as good as with the multiple pressure method. The technique could be easily taught, and it was rapid. In Tanzania, for example, vaccinators average between 400 and 500 vaccinations per day. The proportion of vaccination takes has been found to be related to the vigour with which the needle is applied. The fabled fear that, if blood were drawn, the virus would be washed out - turned out on examination to be - fable. The vaccinators are instructed to vaccinate in such a way that a trace of blood is seen at the site.

The needles use 1/4 to 1/5 as much vaccine as is consumed by ordinary methods - thus easing our vaccine supply problem. Although considered disposable in the USA, our budget required that they be used at least 4 or 5 times - 350 million needles per year was more than we could afford. To our amazement we found that even after 200 vaccinations, the needles performed well. The Wyeth Company agreed to waive patent costs and we were in business. By the end of this year, more than 90% of all vaccinations in endemic countries will be performed with either the gun or the bifurcated needle, two instruments not in field use three years before.

The strategy of vaccination programmes had next to be considered. In the past, vaccination programmes had been directed towards the total coverage of the population without emphasis on any group or segment. Usually plans were made to revaccinate the entire population every 3 to 5 years, in order to maintain immunity. Not the slightest attention was paid to the pattern of occurrence of smallpox by age, sex, locale or vaccination status. To us, it seemed ~~un~~ sensible to determine in which groups cases were occurring and to emphasize vaccination in these groups specifically. Data of this type are ~~only~~ gradually becoming available but with these has come a shift in emphasis of programmes. In Asia, Eastern Africa and Brazil, we find that between 70 and 90% of cases occur among those less than 15 years of age (6). This group constitutes between 40 and 45% of the population. Surveys of vaccination status in these areas indicate that ~~this~~ may be partly explained, by the higher proportion of adults who have, at some time, been vaccinated successfully.

In most programmes, we are, therefore, placing a greater emphasis on vaccination of those under 15 years of age. This often simplifies the logistics for, in many instances, adults are less accessible and not infrequently more resistant to being vaccinated. The exception to this rule is the urban area where ~~it has been found that~~ migratory populations ~~many of whom are ill~~ serve as reservoirs of disease and introduce the disease to surrounding rural areas on returning home. Further, between 85 and 95% of cases occur among those with no vaccination scar (7). Because of the comparative rarity of cases

among those previously vaccinated, assessment procedures to measure the success of the programme are now directed towards determining the proportion of persons with a vaccination scar, irrespective of when vaccination was performed and whether or not revaccination has been carried out. This tacitly ascribes to primary vaccination a higher degree of immunity than is in fact, probable. That few cases occur among those with a scar of primary vaccination could reflect the fact that these same persons have been revaccinated one or more times. It is our sense, however, that in most areas, revaccination, particularly of adults, has been infrequent. When performed, the vaccines used have been of such doubtful potency that little response could be expected. Interesting is a study of secondary attack rates in households conducted recently in Madras by Rao (8). Among unvaccinated contacts, 36% contracted the disease, while among persons who had ever been previously vaccinated, the rate was only 1.2%. Although attack rates among the previously vaccinated are somewhat higher in the older age groups, they do not approach the rates among the unvaccinated.

A further justification for the emphasis on reaching those never previously vaccinated is provided in studies both by Rao and by Mack. Both found that the vaccinated individual who does contract smallpox transmits the disease with less frequency than the unvaccinated person and so is less important epidemiologically.

But regarding this vaccination phase of the eradication effort, I shall say little more for it is principally an organizational and logistical problem, although the problems come in all shapes and sizes. Recently, for example, substantial quantities of vaccine from Mainland China showed up in an East African country complete with instructions for use and quotations from Chairman Mao who apparently inspired its production. Its use was withheld pending tests. In Tanzania, one of the senior vaccinators vanished one night. On search the following day all that could be found was his vaccinators certificate and a fragment of bone recognized as a piece of cranium. The problem - hyenas who savoured vaccinators but not vaccinators' certificates. In Nepal, there are some gun-toting fiercely independent types who sometimes

are a bit reluctant to be vaccinated - ^{to} more vaccinators gone. The problems are many and varied to say the least - but rarely dull.

In the broader strategy of the vaccination programme we have been guided in its execution by Sutton's law - our efforts preferentially being focused on vaccination in countries and areas where the disease is extant. At the same time, we endeavour to terminate outbreaks, as rapidly as possible, when the disease is introduced into non-endemic areas. In execution, no two programmes are identical for in each country, we have endeavoured to strengthen and to build on existing programmes of vaccination rather than in each instance to impose a new rigidly formed structure.

With potent vaccine and better vaccination devices, the vaccination component of the programme is clearly on a sounder footing. In passing, I might note that, 27 countries are presently defined as endemic (C). These countries account for ^{all but 0.5 of 1%} ~~more than 99.5%~~ of all smallpox cases. Formal programmes have begun in 25 - only two are doing nothing - Southern Rhodesia which records so few cases that it may be mislabelled as "endemic" and Ethiopia. Approximately 200 million of the one billion inhabitants in these endemic areas were vaccinated last year.

Although systematic vaccination ~~is~~ a necessary component of the eradication effort, we feel that ~~the~~ ^{our} ultimate success or failure ~~of the eradication effort~~ will depend upon our ability to develop effective surveillance programmes. While vaccination of perhaps 85% or 90% or 95% of the population, depending on density, should interrupt transmission, such a thorough coverage is essentially unattainable in practice in most areas. Each proportionate increase in coverage requires a logarithmic increase in expense and organization. To reduce the cost of programmes and to increase the chances of success, a simultaneous attack on the disease is being mounted through surveillance-containment activities. While erecting a partial barrier to transmission through vaccination, the chain of transmission of the disease is being attacked specifically. In smallpox, for a number of reasons, this approach is more feasible than for virtually any other disease.

Identification of cases is comparatively simple. In smallpox, a distinctive rash is produced which is readily identifiable in at least 80% of cases. Laboratory confirmation is unnecessary in the majority. The rash is most dense over the face and hands, the unclothed portions of the body; persons

with subclinical infections are rare and are of little importance since they do not appear to transmit infection to others. In addition, in Asian countries, 75% of the survivors are left with disfiguring facial scars. Thus, not only is it possible to determine if the disease is present in an area but it is possible, at least in Asia and some parts of Africa, to know whether in past years, it has or has not been present in any particular area.

Given a case of the disease, we can assume that the individual has been in contact with someone equally obviously infected for, as you know, smallpox is transmitted solely from man to man - there are no animal or insect reservoirs. Parenthetically, I might note, recalling the past experiences in malaria and yellow fever, we have fostered a number of studies dealing with a possible smallpox reservoir in monkeys. Thus far, every study undertaken has more certainly denied this possibility.

The chain of transmission is thus sustained only by an infected person with clinically apparent disease infecting a second person and so on. The pace of transmission is limited by the fact that the infected individual is capable of transmitting the virus only from the time of emergence of the first lesions until the scabs have separated. There is no carrier state. Since a period of two to four weeks must elapse between each generation of cases, simple arithmetic indicates that the most tenuous sustained chain of transmission in a country requires that 15 to 25 definitive clinical cases of smallpox occur each year. Considering ~~that~~ transmission is never so efficient, ~~thus~~ it is probable that a country would need to experience at least 200 cases per year to sustain endemic disease. It may be noted, ~~that only~~ 10 of the 27 presently endemic countries should account for this number of cases in 1969 even when under-reporting is taken into account.

A second feature of the disease which is important to the eradication effort is the fact that smallpox is less easily transmitted from person to person than many of the other exanthemata. Close contact normally appears to be required such as one might experience in the household, school or hospital. Data from many outbreaks might be cited in illustration - four are illustrated here (10), Sweden and Abakaliki, Nigeria, in which immunity levels were comparatively good and Kuwait and the United Kingdom where they were poor. Few cases contracted infection outside of the home of the infected person or the hospital.

Similar observations have been made by Rao who found that even in densely crowded areas of Madras, transmission infrequently occurred outside of the home of the infected person - even in areas where houses were distinguished as such only by partial walls. This feature of smallpox simplifies greatly the identification of spread of the infection and, of course, the containment of outbreaks. This is not to say that transmission never occurs through contact in markets or on public transportation, ~~the usual major concerns of public health officials~~. It is only to say that it is infrequent. In part, this may be explained by an apparent need for closer contact than is normally afforded in this environment. You will also recall, however, that the infected individual is usually acutely ill in the initial phases of the disease and frequently does not want to leave his bed. Likewise, it is during the initial stages of illness that the patient, in addition to being most symptomatic, is also most infectious. As he recovers, as scabs begin to form, his capability to transmit infection appears to wane. ^{Although transmission in public places is common} However, we had one notorious case in Nepal in which a severely ill patient in the pustular stage of the disease did take a two hour ^{trip} journey by bus from one city to another. The bus was crowded, as buses often are in Asia. Only one secondary case could be found ~~Despite~~ intensive search. This case was in the man who sat next to the patient and who recalled the episode with considerable ^{wealth} ~~wealth~~ because his clothing had been so badly soiled with pustular material.

The disease itself thus spreads with difficulty under usual circumstances. Not more than a few persons become infected from the index case. Examination of several outbreaks in both endemic and non-endemic areas reveals that the average is, at most, between 2 and 3 secondary cases for each primary case. ~~(This excludes consideration of hospitals which may be the site of much wider dissemination).~~

With a disease which normally requires close contact for transmission and in which the index case infects comparatively few others, one might suppose that in larger geographic areas, smallpox would occur essentially as ~~concentrated~~ clusters of cases rather than as a diffusely distributed disease. And, indeed, this is so. Dr Mack and his associates intensively studied smallpox occurrence in a rural district of West Pakistan over the course of a year. The population of one million persons lived in 1700 villages. During the year, 898 cases were discovered of which only 20% were officially reported.

Even when the officially reported cases are employed to calculate the incidence rate, this District ranks among the most highly endemic in the world. Despite the fact that smallpox incidence was high, only 160 or 10% of all villages experienced cases of the disease at any time during the year. During the several months when smallpox was at a seasonal low, less than 1% of the villages were affected. Studies in Haryana State in India have revealed similar findings and less precise observations in other parts of the world substantiate these studies. The implications of these observations are, of course, considerable. One is not concerned with combatting smallpox distributed over extensive geographic areas but rather in limited focal clusters. Active containment measures, vaccination and, where possible, isolation, can be highly effective in rapidly reducing disease incidence even in heavily endemic areas.

Every effort is now being made to create surveillance-containment teams (fire-fighting teams) in every country at National, State and sometimes District level. Such units are now active throughout West Africa, Brazil, Indonesia, Afghanistan and Nepal. We hope to see such units in place in all countries by early next year.

For these teams to be fully effective, reporting of cases must be improved. A number of steps of an administrative nature have been taken in this direction. Additionally to assist in the detection and diagnosis of cases, we have taken some 4000 pictures of smallpox and chickenpox in African patients. A full colour poster is in preparation along with ~~the~~ slide series for teaching purposes. In May, a similar photographic mission will obtain pictures of Asian patients. A manual on laboratory diagnosis has been produced and requisite reagents obtained ~~in preparation for the development of an~~ international network of diagnostic laboratories. And - finally - every two weeks, a summary of the status of smallpox and progress in the ~~smallpox~~ programme is published in the Weekly Epidemiological Record.

I might mention, lastly, the implications with respect to maintenance of a smallpox-free status. There are a number of smallpox-free countries in South-east Asia which are geographically proximate to the endemic areas, but which have experienced no more than an occasional importation for 10

years or more. Heretofore it has been assumed that their excellent vaccination status accounted for this. Data from several recent surveys cast doubt on this point (11). The surveys illustrated were not country-wide. If anything, they probably overstate the immunity level for the country as a whole. In Ceylon, the data were obtained from children attending an out-patient clinic in Colombo; in Laos, the survey was in a District near the capital; in Australia, in Sydney. Despite an obvious favourable bias, there is a remarkably poor level of immunity in each of these areas contrasted to levels in three areas in Indonesia, Pakistan and India in which smallpox rates presently are among the highest in the world. Obviously, population immunity has not served to protect these countries. As we have studied the pattern of smallpox spread during the past two years, it has been interesting to note that although smallpox is sometimes transmitted from country to country when they are geographically contiguous, introductions from more distant areas are really quite uncommon. Ceylon, Thailand and Australia are all buffered by smallpox-free countries or by water. Ceylon has experienced an occasional smallpox introduction but effective containment measures, quickly applied, have prevented the disease from becoming reestablished. The moral of the story would appear to be that for most countries the costs of maintaining smallpox control are greater than to maintain a smallpox-free status.

Such is the strategy and such is, in brief, a resumé of some of the epidemiological considerations which have led to this approach and a rationale as to why we feel this programme bears promise for the future and for meeting the 10 year target demanded by the Assembly.

The objective of the programme is "0" cases of smallpox and so our efforts we measure primarily by our progress in reaching this goal.

A brief overview as to progress to date would seem appropriate:

Total cases	12
West Africa	13
Brazil	14
East Africa	15
Asia	16

As a Langmurian disciple, I feel it would be wrong to leave the subject of progress at this point without at least a few confident predictions regarding eradication

Areas

West Africa	1969
Brazil	1970
East Africa	1972
Indonesia	1972
Asia (timidly - do have to deal with India)	1975

In 1961, John Kennedy said we shall land a man on the moon by the end of this decade - remarkably the programme is on schedule. In 1966, the World Health Assembly said we shall have no more smallpox in 10 years, - after 2 years we are still on schedule - but to the taxpayer, it might be added that we have not yet gone to the Assembly to request more money. Assistance has come from all quarters and what normally might have been international frictions have been amicable relationships. Of the 52 WHO staff working on the programme, we have an extraordinary conglomerate of Russians, Iranians, Peruvians, Americans, Brazilians, etc. in all some 31 nationalities. Bilateral aid has flowed in in large amounts from the USA and the USSR, Belgium, Japan, Netherlands, Argentina, Brazil and a dozen or more other countries - most recently and surprisingly, Mainland China. In Afghanistan, we have a Burmese nurse and a Soviet technician supervising U.S. Peace Corps girls administering Soviet vaccine. ~~In the Assembly, at present, our most articulate supporters are the Soviet Union, the African countries and Australia.~~ The League of Red Cross Societies has decreed the programme to be one of its primary areas of assistance. In Nigeria, the International Red Cross is conducting a massive smallpox vaccination programme inside Biafra while the US supported bilateral programme vaccinates in the Federal area.

Chapman's comment 1967

To say that there have been a few problems in endeavouring to keep this conglomerate moving and ~~moving~~ ^{pointed} in the right direction would be to understate the case but moving they ~~are~~ and usually in the right direction. If we can truly mobilize a global effort for a task such as this and carry it through to a successful conclusion, I am sure that we will have learned a bit which

may be applicable in the evolution of other projects and other relationships internationally. One point, however, is abundantly clear - epidemiology has been key to the development of this programme and, in the future, is expected to play an even greater role for with it, we may succeed - without it, we will certainly fail.