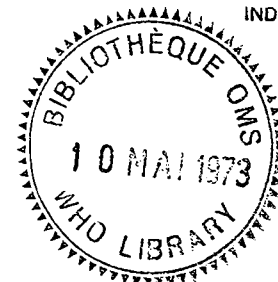




THE STATUS OF SMALLPOX VACCINATION
A BRIEF FOR DISCONTINUING ROUTINE VACCINATION^a

by

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On 1 October 1971, the Surgeon General of the United States Public Health Service officially accepted the report of his Advisory Committee on Immunization Practices¹ that had recommended -

" ... The practice of routine smallpox vaccination is no longer indicated in this country".

This decision culminated a period of intensive study and debate of the issue during the preceding decade. Thus, it was a deliberate action, although an abrupt reversal of one of the most traditional and presumably well-founded epidemiological doctrines in worldwide public health practice. As an active litigant in this issue and as a relatively recent but enthusiastic convert to the new policy, I welcome the opportunity to review the history of this controversy and expound the epidemiological evidence upon which the new policy was based. The epidemics in Yugoslavia and Bengal which developed subsequent to the new policy have provided a prompt and serious challenge to its validity, but not in my opinion a sufficient basis for changing it.

Smallpox was endemic in the United States until the early 1940s when it began to disappear apparently spontaneously. By 1950, it had gone altogether. The reasons for its demise are presumably related to the advancing standard of living, the generally improved medical and preventive health services and the steady waning of the anti-vaccination movement which had been so active, particularly in the mid-west. Certainly, there had been no systematic programme comparable to the present Global Eradication Programme of the World Health Organization (WHO). But, routine vaccination at or about one year of age and compulsory vaccination on entry to school became increasingly widely accepted practices in most parts of the country. The basic "herd immunity" thus provided was considered by most of us in the medical and health professions to be the foundation upon which effective smallpox control must be based.

In 1962, Dick^{2,3} in Great Britain and in 1965 Kempe⁴ in the United States challenged the doctrine that such routine vaccination of infants and children was essential. They argued that the "herd immunity" presumably achieved by this practice was of doubtful, if any, effect and that the continuing and cumulative human costs in the form of severe and fatal vaccine reactions greatly exceeded the risks of the disease. These views were considered rank heresy at the time as revealed in the public discussion of Dr Kempe's paper at the American Pediatric Society⁴. I personally was an articulate critic. Within less than a decade, however, the arguments so cogently marshalled by Dick³ became accepted as national policy in both Britain and the United States of America.

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During this decade, repeated studies were made to quantitate the extent and severity of vaccine reactions. Many American epidemiologists participated in field investigations and intensive control programmes in collaboration with the WHO Global Eradication Programme. A large body of data was accumulated for inclusion in the cost-benefit equation which determined the policy decision.

THE HUMAN COSTS OF VACCINATION

Fifty or more years ago, the human costs of vaccination were high but the risk of the disease was much higher. With improved standards of vaccine manufacture and simplified techniques of vaccination, the incidence of severe reactions had declined. A finite residuum, however, persists. In a comprehensive study of vaccine complications in the United States of America in 1968, Lane and his colleagues⁵ identified 16 cases of postvaccinial encephalitis with four deaths. All but one of these occurred in children under 10 years of age. There were 11 cases of vaccinia necrosum with four deaths distributed approximately equally among children and adults. Eczema vaccinatum was identified 126 times with one death and generalized vaccinia 143 times with no deaths.

Summarizing the several studies over the past decade, Neff⁶ concludes, "there are probably 5 to 10 deaths, 200 hospitalized cases and several thousand minor complications a year caused directly by smallpox vaccination". Relating these estimates to the five to six million primary vaccinations and eight to nine million revaccinations performed annually, incidence rates for deaths range from one to two per million primary vaccinations and for severe reactions from 10 to 15 per million total vaccinations.

The risk of encephalitis has been found, both in this country and in Great Britain to be higher under one year of age than at older ages. No substantiation could be found for the widely held belief that vaccine reactions increased in frequency and severity among adults.

This recent experience reveals that the residual human costs of routine smallpox vaccination are sufficiently important to receive serious consideration.

THE RISKS OF THE DISEASE

Quantification of the present risks of the disease in this country and projections of these risks into the future present difficult problems because no outbreaks of smallpox have occurred here since 1949. As long as smallpox exists anywhere in the world, however, a small but finite risk of importation persists. An estimate of this risk must be made by epidemiological inference based on the status of smallpox in the world and the character of recent smallpox outbreaks that have occurred in non-endemic areas that are as reasonably comparable to the United States of America as can be identified.

The world incidence of smallpox

In 1945, as recently summarized by Foege, Foster & Goldstein⁷ the majority of the world's population lived in smallpox endemic areas. The disease receded progressively but in 1967, when the WHO embarked upon its Global Eradication Programme, smallpox still appeared to be an entrenched endemic disease in Brazil, in Sub-Sahara Africa, on the Indian Pakistan Sub-Continent and in Indonesia. Approximately 100 000 cases were annually recorded by the WHO but reporting was known to be grossly deficient.

The initial strategy of eradication was to achieve effective mass vaccination of all age groups in the endemic countries.⁸ The tactics were to improve and strengthen the existing health programme by insuring adequate supplies of potent heat stable freeze-dried vaccine and to introduce simplified and far more acceptable methods of vaccination, namely, the jet injector and the bifurcated needle. The need for surveillance was recognized as an essential supporting feature to measure progress, set priorities and provide a continuing audit.

It soon became apparent, however, as emphasized by Henderson⁹ that mass vaccination alone was an insufficient control measure. As high a proportion as 95% of a population, as in Central Java, could be reached with vaccine and yet smallpox could continue to spread among the remaining 5%. The employment of mobile surveillance teams to seek out individual cases, search for their sources, identify their contacts and direct selective ring vaccination was found to be the most effective measure and essential to the elimination of foci of infection. Thus, a responsive and imaginative surveillance programme became the key factor in achieving eradication of the disease.

The Eradication Programme has been conspicuously successful. By October 1971, the date of the Surgeon General's policy statement, smallpox had been eliminated from West and Central Africa and was rapidly disappearing in Brazil and in Indonesia where well-staffed programmes were active and efficient in their pursuit of the last cases. Successful programmes were also under way in East Pakistan, India, and Afghanistan. Ethiopia and Sudan remained problem areas but plans to mount programmes were progressing well. The trend of world incidence was sharply downward in spite of markedly improved reporting. The disease was clearly being confined to a few residual focal areas and these seemed amenable to elimination.

Thus, the risk of importation of infection into the United States of America, which was low enough in the 1950s that no importations occurred, had declined further by the mid-1960s when the WHO Programme was begun. The risk must have declined even further by 1971 and the trend seemed to be downward. This optimistic epidemiological inference was an important factor influencing the policy decision.

The character of outbreaks

Mack¹⁰ has identified and analysed 49 importations of smallpox into Europe from 1950 to 1971. Of these, 45 were variola major and involved 640 indigenous cases with 109 deaths. Four outbreaks were variola minor with 256 cases and no deaths. Thirteen of the importations resulted in no transmission.

The epidemiological pattern of the outbreaks was remarkably consistent and similar to the two outbreaks that had occurred in the United States of America in Seattle in 1946 and in New York City in 1947. The patients who imported the infection were recent arrivals from areas of high incidence (annual rates exceeding three per 100 000) in Asia, Africa or South America. Fewer than half of these showed symptoms on arrival. Most had "valid" certificates of vaccination or revaccination. The patients were usually misdiagnosed, often for understandable reasons such as the existence of concurrent serious disease such as malaria, or the absence of a typical rash. Such patients were admitted to a general hospital sometimes on an open ward. Only when the first generation of indigenous cases appeared among members of the hospital staff or patients would the true diagnosis become appreciated.

Subsequent cases occurred in very large measure among close and readily identifiable contacts. Of the 680 cases of variola major, 359 resulted from contact within a medical setting, 51 comprised members of other occupational groups such as laundry or mortuary workers, or members of a ship's crew. Of the remaining 270 cases, most were family or other direct face-to-face contacts. Only 44 were classified as unpredictable in that no specific history of contact was demonstrated. It was the general consensus that most of these unaccounted cases represented failure to conduct adequate contact histories, or the purposeful suppression of such a history in order to avoid quarantine, rather than long range or airborne spread of infection.

Certain limited exceptions to this interpretation were recorded by Wehrle et al.¹¹ In Monschau, West Germany in 1961 a hospitalized second generation case infected 19 other persons. Nine of these were face-to-face contacts but 10 developed among seven patients, two members of the medical staff and a carpenter in a neighbouring ward at the end of a common corridor. In 1970, a single patient admitted to an isolation ward in Meschede, Germany, with a presumptive diagnosis of typhoid fever infected 17 other patients in the hospital who had no face-to-face

contact with him. The implications are evident of airborne transmission of infection over considerable distances within an enclosed building. It should be noted, however, that in both instances the source case had a severe hacking cough and presumably was capable of producing highly infective aerosols. It should also be emphasized that both epidemics were promptly contained. Spread beyond the hospital setting was minimal.

Notable in the European experience was the concentration of cases among adults. Less than 15% of cases of variola major were among children under 10 years of age. These were either acquired by exposure within hospitals or in the home from hospital-acquired cases. Spread through schools or nurseries or among childhood playmates was conspicuously infrequent. Three-fourths of the adults gave a history of vaccination usually 10 to 20 or more years previously and 20% of the children had also been vaccinated.

In many of the European outbreaks, public hysteria, either spontaneous or sometimes provoked, forced widespread mass vaccination programmes with all of the inherent disadvantages known to be associated therewith. A similar officially sponsored mass campaign was launched in the New York City outbreak in 1947. Sober review fails to indicate that such heroic shotgun approaches were necessary.

It may be concluded from these critical evaluations of the European experience that imported smallpox is not usually a highly infectious disease but rather that it spreads slowly in localized areas. Once recognized, the 12-day incubation period provides a considerable amount of time for the alert health authority to contain the outbreak by case investigation, identification and quarantine of contacts, and selective ring vaccination among those exposed. Even when the rare dangerous spreader causes cases by the airborne route, containment is still possible with these conservative measures.

The routine vaccination of infants and children does not contribute effectively to herd immunity. In developed countries the disease clearly does not spread among such groups but rather among adults whose immunity has substantially, if not completely waned.

THE REVISED POLICY

The Advisory Committee's recommendations were based on the careful weighing of the continuing and cumulative human costs of routine vaccination against the evidently small and decreasing risk of the disease. The revised policy emphasizes the prevention of importation and the containment of any outbreak if an importation happens.

The specific recommendations are:¹

- (a) the effective vaccination of all travellers to or from countries where smallpox exists;
- (b) the adequate immunization of all persons involved in health services;
- (c) the maintenance of an alert surveillance programme;
- (d) the full support of the Global Smallpox Eradication Programme. This programme is now in effect. The screening of travellers entering the country has been made much simpler and more selective because so few have been in endemic countries. The surveillance system in each state health department, backstopped by the epidemiological and laboratory diagnostic services of CDC, has never been as alert or staffed with as many experienced professional personnel. The Global Eradication Programme is being pursued intensively.

The weakest link in the programme is the vaccination of health personnel, specifically hospital workers of all types. The seriousness of this vulnerability is not as widely appreciated as it should be. It is perhaps inevitable that one or more importations of smallpox

may have to occur with intrahospital spread resulting in malpractice suits before hospital administrators and medical staffs recognize their clear legal responsibility to maintain their immunity at a high level.

The possibility of such importations, while small, must be recognized. If one, or even several, occur, it would not negate the validity of the new policy. Only if importations lead to uncontrolled spread, primarily among infants and schoolchildren, should a return to routine vaccination of such groups be seriously considered. The Surgeon General's Advisory Committee did not believe that such an eventuality was sufficiently possible to justify the present high costs of routine vaccination.

SUBSEQUENT DEVELOPMENTS

These recommendations, formulated in consultation with representatives of the Ministries of Health of Canada and the United Kingdom, were promptly approved by the Committee on Infectious Diseases of the American Academy of Pediatrics (the Red Book Committee) and the Association of State and Territorial Health Officers during the fall of 1971. Since that time a number of anticipated as well as surprising events have taken place. These warrant careful review of the validity of the revised policy.

General acceptance of the new policy has been prompt and almost complete. All states but two have modified their laws, sanitary codes, or regulations or declared their intent to do so. The distribution of smallpox vaccine has been reduced by about two-thirds. The requests for Vaccine Immune Globin for the treatment or prophylaxis of complications has fallen to less than 25% of previous demand. Only a few voices of protest have been raised in the professional press.¹²

On the world scene, smallpox disappeared from Brazil, last known case in April 1971; and from Indonesia, last known case in January 1972. The reported world incidence, however, has increased. From a low of 30 812 cases in 1970, the total rose to 51 834 in 1971. This increase was due primarily to the successful expansion of major control programmes in Ethiopia and Sudan with extensive vaccination, case finding and reporting. More than 50% of the total cases reported in 1971 emanated from these two countries. This increase, therefore, was an artifact of progress toward the goal of eradication of the disease from this last endemic focus on the African continent.¹³

The world incidence further increased in 1972 when an estimated total of 64 000 cases was reported. This resulted primarily from sharp increases in Bangladesh and in Central India following the repatriation of refugees of the Indo-Pakistan Conflict. Intensified control programmes are in progress, but South Asia remains the largest focus of endemic smallpox in the world.¹⁴

The most severe challenge of the new policy was the outbreak of variola major in Yugoslavia in March and April 1972. It involved 176 cases with 36 deaths. The outbreak centred in the autonomous province of Kosovo which adjoins the Albanian border. The infection was most probably introduced by a Moslem pilgrim who, while returning from Mecca by bus, stopped in Baghdad where an unreported outbreak of smallpox was in progress.

The first indigenous generation comprised 11 cases, all spread by community contact in Kosovo and nearby communities. The second indigenous generation included 142 cases mostly in Kosovo but also in two hospital centred foci in Cacak and Belgrade where a patient with confluent smallpox was sent with the mistaken diagnosis of acute penicillin reaction.

The third, and last, generation of cases was limited to 23 cases, all but one of which developed among known contacts in quarantine. The outbreak led to an essentially nation-wide mass vaccination programme begun in the middle of the second generation when the extent of the outbreak was first appreciated. The resort to mass vaccination was understandable in view

of the many ethnic, religious, political and communication problems involved, but had more complete surveillance data been available more promptly, it seems reasonable that effective containment could have been achieved by more selective vaccination.^{15,16}

These developments subsequent to the adoption of the new policy warrant careful reconsideration of the wisdom of the change. The crucial question is whether the estimate of the risk of importation of the disease was in error. Certainly the increased incidence of smallpox in Ethiopia and Sudan cannot be a cause of worry. The increase in India and Bangladesh is a disappointment but an anticipated result of war. No exportations of smallpox from this traditionally highly endemic area have been reported. Prospects for renewed progress in the area are excellent.

The Yugoslavian outbreak was the first one to occur in that country since 1930 and the most severe outbreak in Europe since the end of World War II. In spite of its extent, only one exported case occurred in a worker returning to Hanover, Germany. No further spread resulted.

This outbreak vividly reinforces the fact that as long as smallpox exists anywhere in the world, no other spot is free of risk of the disease. This one extraordinary outbreak must not be weighed alone, but rather with the 49 other outbreaks in Europe during the past 20 years, it should be balanced with the 100 to 200 estimated vaccine deaths and 4000 hospitalized cases of vaccine complications that have occurred during the past 20 years in the United States of America.

In my judgement, only if repeated outbreaks of variola major occur in this country and turn out to be far more formidable to control than can be expected from the total European experience, would there be a valid basis for reconsidering the policy of routine vaccination. In this remote eventuality, routine vaccination not only in children but routine revaccination of adults, as emphasized by Dick,² would be necessary.

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