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GENERAL REVIEW OF EPIDEMIOLOGY
OF SMALLPOX

by

Dr. Henry M. Gelfand *

WHO Temporary Adviser

*Epidemiologist, Public Health Services
for Europe, London
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I INTRODUCTION

Smallpox is a disease of potentially worldwide distribution; there are no naturally resistant human populations and no climatic barriers to its spread. In past millenia, its absence from certain areas was due solely to geographic factors which isolated large groups of people from its original homeland, perhaps eastern and southern Asia. Increasing human travel led to its dissemination even to the distant Americas and the islands of the Pacific. During the three or four centuries preceding our own, smallpox was one of the principal causes of death, killing perhaps millions of people every year throughout the world, and disfiguring and blinding millions more.

From the latter part of the nineteenth century and with increasing rapidity during the past two or three decades, the endemic areas for smallpox have dramatically contracted. At the present time only three remain - Southern Asia, Africa South of the Sahara, and parts of South America - and the total number of cases reported during the past ten years has been only about sixty to one hundred thousand per year.

This decline has been due in large part to the utilization of prophylactic vaccination, in organized mass campaigns as well as in a random, unorganized fashion. However, the epidemiologic characteristics of this disease have permitted vaccination to be the effective tool that it is, and have provided opportunities for other measures, both deliberate and incidental, to contribute to this achievement. By virtue of these factors, smallpox, among all of the serious human diseases of worldwide distribution, is the most promising candidate for eradication.

A brief review of these characteristics, together with some additional notes and a comment on the epidemiology of smallpox vaccination, should constitute a basic summary which can serve as the framework for our further discussions this week.

II EPIDEMIOLOGIC CHARACTERISTICS OF SMALLPOX SIGNIFICANT FOR ERADICATION

1. Man is the only known host

Despite some poorly documented reports of the natural concurrence of smallpox in non-human primates, and the confirmed infection of monkeys under laboratory conditions, there is no valid evidence that animals other than man act as hosts in nature

On the other hand, monkeypox is now known as a fatal disease of various primate species, similar in appearance and caused by a poxvirus related to but distinct from variola virus. Some past records of epidemics in monkeys occurring concurrently with smallpox in man may have been caused by this agent, as well as by other unrelated disease agents. No cases have occurred among the human contacts of monkeypox.

Cynomolgous monkeys, more susceptible than the Indian monkeys M. mulatta or M. radiata to variola virus in the laboratory, abound in the forests of South-East Asia. There is no record of "smallpox" in monkeys since elimination of the human disease from this area, nor has there been any unexplained reappearance of the disease that could be attributed to this source.

2. Transmission is man-to-man

There are no arthropod vectors of variola virus such as those which compound the difficulties in the attempt to eradicate malaria.

Environmental contamination does occur, both in the immediate surroundings from droplets of oral secretion and more distantly by means of shed dermal scabs, and indirect man-to-man transmission is possible. This is of relatively minor importance, however, and instances of distant transmission have been sufficiently infrequent as to attract individual attention.

3. Communicability is of a low order

Despite its reputation to the contrary, smallpox is not highly infectious. Close personal contact can almost always be documented between cases and each infected person usually transmits the disease to no more than one to five other persons. Furthermore, within households containing cases, fully susceptible, unvaccinated contacts frequently escape infection. Even more dramatically, household epidemics have been described, in which as many as five generations of transmission have been required to infect all of the susceptibles, despite their continuous presence.

Spread within communities is slowly progressive. An epidemic of eighty-seven cases in a population of 897 in a village in Mali lasted from February through May 1967, and the epidemic of 1964-1965 in the metropolis of Bombay, with over 3000 cases lasted at least nine months. Epidemics in rural areas, spreading from one small village to another, similarly extend over many months; they are connected by tenuous lines of virus transmission, and no more than a small proportion of villages is infected at any one time.

4. Cases are usually readily detected

Eighty to ninety percent of cases are "classical" and are readily identified by laymen acquainted with smallpox. The major difficulty

is with those cases which are most mild (or modified by previous vaccination) or most severe, but only a very small proportion of these should be missed by the reasonably alert physician.

The unusually mild or severe case is the result of personal factors of susceptibility in that individual host, and the disease he transmits to contacts covers the usual spectrum of host reactions, i.e. in which eighty to ninety percent are classical. It is thus unlikely that more than one passage generation of cases would not be clinically recognizable.

5. Subclinical infections are rare

Even if they exist, such cases are probably of no epidemiologic importance since it is most unlikely that they would shed virus.

6. Smallpox is always an acute disease, with a limited period of infectiousness

There is no chronic state, and no recrudescence. A case is not infectious during the incubation period.

Transmission is principally through the respiratory route, by means of virus shed from ruptured lesions of the fragile oral enanthem. Virus has been detected in the mouth by laboratory culture only during the period three to thirteen days after onset of illness. Eighty percent of transmissions occur during the first week of illness, even though unvaccinated susceptibles remain in contact thereafter.

The shed scabs contain virus that may remain viable for years. Infections have certainly resulted from exposure to scabs, probably by inhalation of dust, but for reasons that remain obscure they seem to be infrequent. The demonstration that vaccination scabs contain interferon may provide a clue.

7. The incubation period is 11 to 14 days in the great majority of instances

There is probably an epidemiologic ideal - not so short that many generations of cases can occur before detection (as in influenza) and not so long as to complicate the tracing of contacts (as in infectious hepatitis).

The extreme limits of documented incubation periods are 8 and 17 days, but these extremes are rarities.

8. Immunity following smallpox is solid

Reinfection with recurrence of disease is rare, and each recovered patient becomes yet another block to subsequent transmission.

9. There is, antigenically, only one smallpox virus

The three "types" - V. major, V. minor, and V. intermedius differ significantly only in pathogenicity and in the spectrum of disease severity that they produce. The unvaccinated case fatality rate of disease caused by V. major is about 40%, that by V. minor is 1% and that by V. intermedius is 5 to 10%.

Individual cases cannot be distinguished, and cross protection is virtually complete.

10. There is no direct socio-economic association with smallpox transmission

This is not a disease of poor nutrition or of unhygienic living per se. It is related only to the degree of person-to-person intimacy, and, to the extent that household crowding is characteristic of poverty, the incidence is often, though not always, higher among the poor. The royal families of Europe and of India suffered cruelly from smallpox and at least one ancient Egyptian pharaoh is believed to have died from it.

The most striking socio-economic association with smallpox is related to differences in vaccination history.

11. Smallpox "burns itself out" in small communities

The accumulation of specific immunes combined with the need for close contact prevent the long-continued presence of the disease in small population groups. The perpetuation of transmission is dependent upon the continued movement of cases to new communities.

12. Incidence of the disease is markedly affected by seasonal changes

In both India and Nigeria, for example, peak incidence is during the first few months of the year, and it declines to very low levels just before the onset of the dry season. The direct effect of the weather, particularly relative and absolute humidity, has been suggested as the reason for this, but the indirect effect of weather on social activities and population movement is probably more important.

From the point of view of epidemiologic surveillance and disease control, the great significance of this phenomenon lies in the existence of a period of time during which the reservoir of infection is markedly limited.

13. Smallpox occurs in a cyclic pattern in endemic areas

Epidemics usually have recurred at 5 to 10 year intervals, suggesting that there is an epidemic threshold.

III SOME ADDITIONAL FEATURES OF SMALLPOX EPIDEMIOLOGY WHICH AFFECT THE PATTERN OF DISEASE

1. Age

There are no intrinsic differences in susceptibility to smallpox infection on the basis of age. The only partial exception is the passive protection conferred on an infant born of a mother who had been

vaccinated or who had had smallpox, and it lasts for up to about six months.

Exposure, however, does vary with age. Young children are often more intimately exposed within the household than are other age groups, and consequently may have higher secondary attack rates.

After infection, the severity of disease varies markedly with age. Infants often suffer from the more severe forms and have high case fatality rates, but this is particularly notable among elderly adults, and over half of the unvaccinated cases may be expected to die.

The most important determinant of differences in age-specific attack rates is previous history of vaccination or of smallpox itself. When the disease is introduced into communities which have never been vaccinated, or not for many years, all ages are attacked about equally - or up to a maximum age which defines the last major vaccination campaign or the last epidemic. Where smallpox is regularly endemic and vaccination has been only a casual practice, smallpox is a pediatric disease. Where vaccination has long been a general but incomplete programme, smallpox epidemics involve principally unvaccinated children and vaccinated adults with waning immunity.

2. Sex

As with age, there are no intrinsic sex differences in susceptibility to infection, and differences in exposure are related to the intimacy of personal association within the household. Among adults, unvaccinated women usually have higher secondary attack rates than do men because they are more likely to attend those first attacked.

After infection, pregnancy greatly increases the probability of severe disease and the hazard of death. Over 50 percent of unvaccinated pregnant women with smallpox will die.

Again as with age, variations from the expected 1 : 1 ratio of male to female cases are due principally to differences in vaccination history. In societies where women and girls are unwilling or unable to present themselves for vaccination, outbreaks of disease are characterized by an excess of female cases. Conversely, when men and boys may be missed by vaccination teams because they are inaccessible for occupational reasons, male cases will predominate.

3. Transmission patterns

Smallpox is transmitted from household to household and from community to community by the movement of infectious cases or of infected, incubating contacts of cases. Patterns of travel thus play a large role in shaping patterns of dissemination, and these vary among different societies. Children of school-going age are a very mobile group and are often responsible for transmission within a community. Between communities, group movements - as of nomads, seasonal migrants, and pilgrims - may be of great importance. The ebb and flow of rural people to urban centers for **temporary** work or for marketing and trade may serve to perpetuate endemic smallpox or to introduce the disease to usually untouched areas. The itinerant tradesman or the customary pattern of family reunion for religious or social purposes may be all-important. Closely integrated minority groups, particularly if they reject or otherwise avoid vaccination, may be involved in a narrow but remarkably effective stream of transmission.

The hospital has been prominent as a focus of infection for introduced smallpox, and it also plays an important role in endemic areas. The undiagnosed or carelessly isolated patient, and his clothing and bedding, is a fertile source of infection. For obvious reasons, the case hidden at home is even more dangerous. If the patient dies, the disposal of his body and his close personal effects may be an occasion for wider exposure to susceptibles than he was while still alive.

IV SOME EPIDEMIOLOGIC EFFECTS OF SMALLPOX VACCINATION

As a climax to the epidemiologic vulnerability of smallpox, we have a highly effective vaccine. Its effectiveness in protecting the vaccinee from acquiring disease will be discussed in another session, and will not be detailed further here. It has other effects in addition, however, and despite the fact that cases certainly do occur among vaccinees, it is probable that the transmission of smallpox cannot be sustained in a vaccinated population without an unvaccinated reservoir of susceptibles.

1. Effect of prior vaccination on clinical severity of disease

That vaccinated cases of smallpox are generally milder than unvaccinated cases has long been recognized. In a study involving almost 7 000 consecutive cases of smallpox in Madras, Dr. A.R. Rao has now demonstrated this quantitatively. The case fatality rate among all those with a history of vaccination at some time in the past was six percent; among the unvaccinated it was thirty-five percent. Of greater importance epidemiologically (see Part IV para. 2) was the finding that the proportion of the mildest or "modified" cases was only one percent among unvaccinated cases, whereas it was twenty-five percent among those vaccinated once, and forty percent among those who

had been revaccinated.

2. Effect of clinical severity of case on contact rate

In a related study of intrafamilial transmission of smallpox in households with a primary case, Dr. Rao was also able to show the relative infectiousness of vaccinated and unvaccinated cases of differing clinical type. The secondary attack rate of "ordinary" (i.e. "classical") cases was 4.5 percent. among "modified" cases it was 1.7%. Even within the same clinical variety ("ordinary"), previous vaccination affected the percentage of contacts who contracted disease. from unvaccinated index cases the secondary attack rate was 6.1% but from vaccinated cases it was only 2.2%. It thus appears that the case of smallpox who had previously been vaccinated is a relatively poor source of infection, as a result of the smaller number of lesions present in the mouth.

On the other hand, it should be noted that the not-very-sick, ambulatory case represents an especial danger as a transmitting agent of smallpox. Although an inefficient vector, he may not realize that he has smallpox, nor be recognized by others as having it, and he may travel far, to introduce the disease into a non-infected area.