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Modeling Potential Responses to Smallpox as a Bioterrorist Weapon

Appendix I: A Mathematical Review of the Transmission of Smallpox

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The mathematical model we described requires the researcher to preset the average number of disease-susceptible persons infected by an infectious patient (i.e., the rate of transmission). To obtain historical data describing the average number of persons infected per infectious person, we examined the literature for data regarding the rate of transmission. Since there are already a number of excellent reviews of smallpox epidemiology (1-3), we reviewed and reported only papers in which transmission rate was specifically measured or sufficient data were provided for it to be calculated.

Methods

We reviewed both published and unpublished papers, books, and reports to compile a set of tables containing data related to the rate of transmission of smallpox. We did not use computerized medical literature databases as the primary means to identify reports and papers because such databases typically do not catalog published papers before 1950, when smallpox was common. Further, such databases do not typically catalog unpublished reports and papers with limited distribution. This last limitation excludes many reports written by epidemiologists working for the World Health Organization (WHO) and other public health organizations during the smallpox eradication program.

We considered data that used at least one of three possible methods to measure rate of transmission: using a mathematical formula to derive the transmission rate from data describing the percentage of susceptible persons that must be vaccinated to eradicate the disease (i.e., stop transmission); examining data regarding the attack rate among susceptible persons for a given period; and evaluating data reporting the number of persons directly infected by an infectious person. These methods progress from the most indirect to the most direct. The data produced by the methods, therefore, may progress from the least to the most exact measurement of the rate of transmission of smallpox.

Review of the Data

Rate of Transmission as Measured by Percentage of Population Vaccinated Needed for Eradication

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The larger the percentage of a susceptible population that must be vaccinated to eradicate a disease, the relatively more infectious the disease. Anderson and May (4) present the following equation for calculating the critical or minimal proportion of a population that must be immunized for eradication to be achieved:

$p_c = 1 - (1/R_o)$

where p_c is the critical proportion and R_o is the basic reproductive rate of a parasite. R_o is essentially the average number of offspring that a parasite (a term that includes macro- and microparasites) can produce. For a parasite to continue to survive, $R_o > 1$. For a microparasite such as the variola virus that causes smallpox, R_o is more precisely defined as the average number of secondary infections produced when one infectious individual is introduced into a population of susceptible hosts (4).

Using the above equation and data from a variety of sources, Anderson and May presented estimates of the critical value p_c for 10 diseases (Table 1). However, exactly how the value of p_c for smallpox was calculated is unclear because the lack of published mathematical models describing the spread of smallpox has resulted in a lack of readily available published estimates of the value of R_o for smallpox. The upper estimate of 80% of the susceptible population that must be vaccinated to eradicate smallpox (Table 1) may have come from a WHO recommendation published in 1967 (1,5). The mathematical reasoning behind such a recommendation is not clear. History showed that actually vaccinating 80% of susceptible persons does not necessarily cause smallpox to disappear from a population. In Asia, particularly India, even when apparently80% of the population was vaccinated, outbreaks still occurred (2). One reason why vaccinating 80% of the population may not have halted the spread of smallpox is that the value of R_o for smallpox, and thus p_c, may vary with density of susceptible populations (4,6).

Table 1. Estimates of the critical percentage of susceptible persons that must be vaccinated to eradicate a given disease from a population

Disease	Critical percentage of susceptible persons that must be vaccinated to eradicate a disease (% of susceptible persons)
Measles	90-95
Pertussis	90-95
Fifth[a]	90-95
Chickenpox	85-90
Mumps	85-90
Rubella	82-87
Poliomyelitis	82-87
Diptheria	82-87
Scarlet fever	82-87
Smallpox	70-80

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[a]Fifth disease is caused by human parvovirus infection.
Adapted from Anderson and May (4), p. 88.

The failure to stop smallpox transmission when 80% of the population was vaccinated against the virus led to a 1964 WHO expert committee recommendation that the goal of the smallpox eradication campaign must be to vaccinate 100% of the population (7); however, that goal was difficult if not impossible to achieve in India. In 1973, the strategy was changed, with emphasis on surveillance to detect and then contain outbreaks of smallpox. This strategy and its variants worked so well that by 1977 India was officially declared free of smallpox (7).

There have also been recorded instances when smallpox disappeared even though <80% of the population was vaccinated. For example, in 1968, Sierra Leone had the highest incidence of smallpox in the world; yet the disease disappeared in 1969 when only 66% of the population had been vaccinated (8). Similarly, smallpox disappeared in Mali when only 51% of the population was vaccinated (8). In these and other West African countries, one reason that smallpox disappeared without ≥80% of the susceptible population being immunized is that the eradication program shifted to a policy of focusing on controlling outbreaks. Each outbreak was promptly investigated, and all the susceptible population surrounding the reported case(s) was vaccinated (i.e., a "ring" vaccination policy) (8).

Rate of Transmission as Measured by Attack Rates among Susceptible Populations

Data collected from an outbreak of smallpox in Sheffield, England, >100 years ago can be used to demonstrate both the attack rate of smallpox and the risk factors associated with infection (Table 2). The investigators found that persons with a history of vaccination or immunity (generally defined as having a visible vaccination scar or a history of a clinical case of smallpox) had attack rates 60% to 96% lower than those of persons without a history of vaccination (Table 2).

The attack rates among the unvaccinated "general population" are approximately 87% lower than those among the unvaccinated who lived in the same house as a person with a previously confirmed case. In other words, the most susceptible population was unvaccinated persons who lived in close proximity to a smallpox patient. [1] From Table 2, we can conclude that smallpox in Sheffield was not readily spread among the general population by brief, casual encounters, such as walking down the street beside an ill person or briefly being in the same shop or business. Rather, smallpox was primarily spread among persons living in the same house as a smallpox patient. One can only guess how crowded the average living conditions were in the industrial town of Sheffield in the late Victorian era.

Table 2. Attack rates of smallpox among the general population and those living in houses with a case(s) of smallpox, Sheffield, England, 1887-88

Population and age group	Attack rates (%)

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General population	Vaccinated	Unvaccinated
All ages	1.6	7.5
<10 years of age	0.5	7.8
≥10 years of age	1.9	7.3
Living in house with a patient		
All ages	23.3	58.6
<10 years of age	7.9	67.6
≥10 years of age	28.3	53.6

From 1898 Report of Royal Commission on Vaccination (9), p. 133-6.

Data concerning attack rates were also gathered from cities and villages around the world during the smallpox eradication campaign during the 1960s (Table 3). From the data we conclude that a susceptible person living in the same house as a smallpox patient had a notably higher risk of contracting smallpox than a member of the "total population." Thus, the conclusions drawn from Table 3 are similar to those from Table 2.

Table 3. Attack rates of smallpox among the general population and those living in houses with a smallpox patient(s)

		Attack rates (%)			
Site	Year	total population	susceptible persons in house	nonsusceptible persons in house[a]	Ref.
Bengal, Bangladesh[b]	1967	0.2-0.5[c]	36	12	10-12
Campo Alegre, Brazil	1968-69	27	79	2	13
Gerere hamlet, Nigeria[d]	1968	30	52	2	14
Pirapitinga, Brazil	1969	25	65	0	13
Nellore district, Andrapradesh, India[e]	1969	5.3-23	40	8.5	15
Madras, India	1968	n/a[f]	20	2	16
Rural Afghanistan	1969	n/a[g]	50	0	17
Punjab Province, West Pakistan	1968-70	n/a[g]	70[h]	5[h]	18
Brazil[i]	1969	n/a[g]	69	3	19
Utinga City, Brazil	1969[j]	12	68	3.5	20

[a]Nonsusceptible persons include those with evidence of vaccination (e.g., scar) or history of a clinical case of smallpox, who thus were naturally immunized.
[b]Known as East Pakistan when the data were collected (10).
[c]The attack rate depended on population density, with the lowest attack rates in villages with

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baris (a group of patrilineally related families) described as "scattered" and the highest rates in villages with baris described as "compact" (10).
[d]The source (14) did not analyze the village population by household, and thus the result presented is the average for all susceptible persons throughout the village. However, the total population of the village at the time of the outbreak was 203.
[e]This reference documented outbreaks in seven small villages (15). The results are the range of attack rates measured in the villages.
[f]The source did not provide an estimate of the total population where the outbreaks occurred but did note that in the city of Madras 3,000 to 4,000 cases occurred annually until the Smallpox Eradication Programme began in 1963. Subsequently, 725, 75, 38, and 25 cases were reported in 1965, 1966, 1967, and the first half of 1968, respectively.
[g]These studies did not provide a denominator that would permit total population attack rates to be calculated.
[h]The source did not identify individual cases in individual houses, but calculated the average secondary attack rate among vaccinated and unvaccinated "family contacts" of index cases.
[i]The source reports data from 33 outbreaks in five provinces in Brazil, with 27 outbreaks in rural areas and six in urban areas.
[j]The data refer to cases only in Utinga city. Additional cases occurred in the surrounding municipality (20).

Rate of Transmission as Measured by the Number of Persons Infected by an Infectious Person

Using data from a number of different outbreaks around the world during the 1960s and early 1970s, we estimated the number of persons directly infected by an infectious person (Table 4). Most reports cited had an average of <2 persons infected per infectious person (Table 4), but there was a wide range in numbers. In all outbreaks, some infected persons apparently did not transmit a symptomatic case of smallpox to another person. The upper estimates of number infected per infectious person vary widely, from 38 in Yugoslavia (27) to 1 in West Bromwich, United Kingdom (29). The average numbers of persons infected per infectious person range from 0 to 8, with most outbreaks recording an average of <1 person infected per infectious person (Table 4).

Table 4. Number of persons directly infected by an infectious case of smallpox

Site	Year and duration of outbreak	Total no. of cases[a]	No. infected per infectious person		Ref.
			Range	Mean	
Erode, Tamil Nadu, India	1969; 2.5 months	6	0 - 3	1	21
Visalur, Tamil Nadu, India	1969; 1 month	1	0	0	21
Bengal, East Pakistan[b]	1967;	20[c]	0-2.3	0.8	10

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Campo Alegre, Brazil	12 months 1968-69;	74	n/a[d]	2.1	13
Gerere hamlet, Nigeria	10 months 1968;	12[e]	n/a[e]	2[e]	14
Kathmandu Valley, Nepal	4 months 1966-67: various	47	0-7[f]	2.75	22
Chingleput district, Madras, India	1968	47[g]	0-?[g]	0[g]	16
Madras, India	1968	25	0-4	0.48	23
Bawku district, Ghana	1967	66	0-11	0.9	24
Punjab District, West Pakistan	1968-70	138[h]	n/a[h]	1.2[h]	18
Loralai District Pakistan	1971	23	0-9	2[i]	25
Botswana	1973	30	0-3	0.78	26
Yugoslavia	1972	175	0-38[j]	8-11[j]	27
Meschede Hospital, Germany	1970	20	0-17	0.95[k]	28
London, UK	1961	3	0-2	0.66	29
West Bromwich, UK	1961	2	0-1	0.5	29
Bradford, UK	1961	14	0-10	0.9	29
Birmingham, UK	1962	1	0	0	29
Cardiff, UK	1962	47	0-18	0.97	29
Toffo-Gare, Dahomey	1967	28	0-4	0.93	30

[a]Total number of cases includes the index patients who spread the disease to others.
[b]East Pakistan is now called Bangladesh.
[c]In the area studied, for the time reported, there were 119 cases in 30 outbreaks. However, data regarding the number of "introducers" and the number of first-generation cases associated with those introducers were limited to 20 cases (11 introducers, 9 first-generation cases).
[d]The source (13) provided only the total number of primary or coprimary cases and total number of secondary cases. Thus, only an average number of cases per infectious person can be calculated.
[e]The total number of reported cases was 62. However, the reported average was calculated from a subset of 12 cases in a single compound of 24 people who lived in the village where the outbreak occurred. The source (14) reported the total number of generations (6) and the total number of cases in the compound, but not the actual cases per generation.
[f]Although the source reported 13 outbreaks resulting in 47 cases, the source of infection could be traced in only four outbreaks. Further, the source did not report generations, only "subsequent cases," which may be a single generation or more. Thus, the upper range of 7 cases per infectious case may be an overestimate.
[g]The source reported 47 cases but only specifically identified transmission (who infected whom) of one patient admitted to an infectious disease hospital in Madras. This patient, despite being sick at home for nearly 8 days, did not infect anyone else.
[h]The source did not specify the number of index cases, although the authors reported data for 47

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outbreaks, resulting in 70 first-generation and 21 second-generation cases. Our assumption that there was a single index case per outbreak maximizes the calculated average transmission rate.
[i]The source reported that four second-generation cases infected eight third-generation cases. However, among these cases, the authors did not describe who infected whom. Therefore, the average was calculated by assuming that just one of the second-generation cases infected all eight third-generation cases. This assumption maximizes the calculated average transmission rate.
[j]This is a weighted average, based on the report of 11 first-generation cases, 140 second-generation cases, and 23 third-generation cases. Thus, the average first to second generation was 13 cases per infectious person, and the average second to third generation was 0.2 cases per infectious person. However, since one first-generation case caused 38 second-generation cases (reputedly the largest reported number of infections known to have been caused by a single patient) and another first generation caused 16 second-generation cases, there must have been a number of first- and second-generation cases that did not infect any others. Removing these two first-generation cases and the second-generation case attributed to them, the weighted average becomes 8 (11 first generation, 86 second generation, and 23 third generation).
[k]Although one patient infected 17 others, only two other patients infected one case each. The other 17 patients did not transmit smallpox to others.

Since transmission was eventually halted in all the outbreaks (Table 4), most outbreaks have an average transmission rate for the entire outbreak of <1 person infected per infectious person. A more detailed examination of the data from six of the outbreaks is presented in the Figure, which presents the frequency of persons infected per infectious person over time (generation of disease). The average rate of transmission per generation ranges from 0.47 persons infected per infectious person (third to fourth generation) to 1.48 (index cases to first generation) (Figure). The overall rate of transmission in the six outbreaks was 0.47. In any given generation, there is a wide range in the number of persons infected per infectious person, ranging from zero (occurring in all generations) to as high as 11 or even 18 (the latter occurring in the graph depicting transmission from the fourth to fifth generation).

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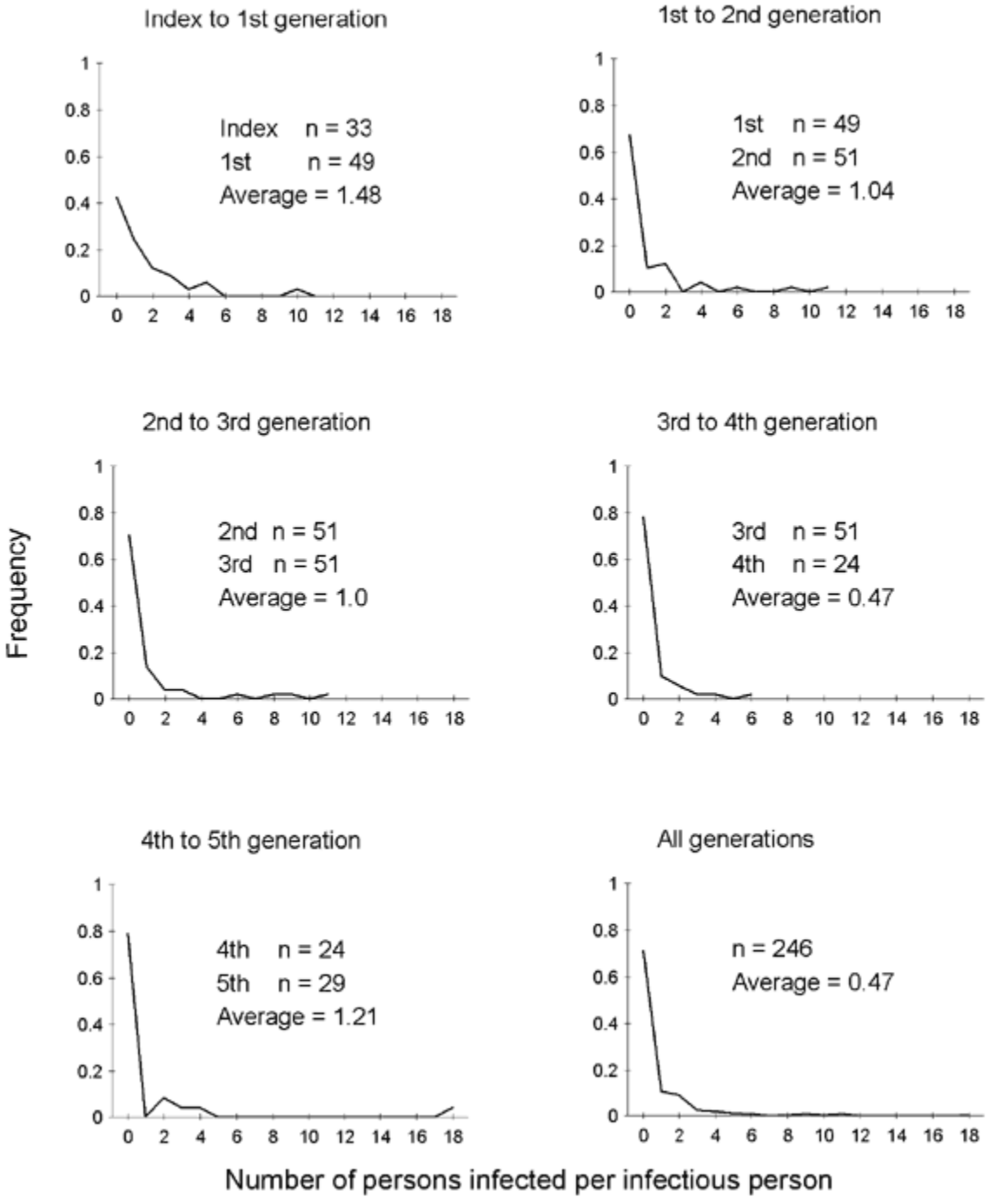

Figure. Frequency, by generation of disease, of the number of persons infected with smallpox by an infectious person. Average refers to the mean number of persons infected. Not all sources reported five generations of disease. In some instances, the reported outbreak was contained or died out before the fifth generation (23-26,29,30).

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Further evidence of the relative difficulty for one person to infect (i.e., explaining low transmission rates) is found in data representing the contacts of the last case of naturally occurring smallpox on earth (31; Table 5). The contacts are persons who visited the patient at his home when he first developed a fever (prodromal stage), who had contact with him after he was admitted to a hospital (but before he developed a rash), and who visited him at his home after he was initially discharged (with a rash) with a diagnosis of chickenpox. Of the 161 persons who had contact with him, at least 12 unvaccinated persons had "face-to-face" contact yet did not subsequently become ill with clinical cases of smallpox.

More evidence that sustained close contact is typically needed for transmission is provided by data from the 1972 Yugoslavian outbreak, in which 84 of 175 patients contracted the disease while in the hospital with a smallpox patient (27). One patient, who spent time in three different hospitals, infected 38 people, probably a record number directly infected by a single person. Close, sustained contact in a hospital, probably through a connected ventilation system, also permitted one patient in Meschede Hospital, Germany, to directly infect 17 others (28).

Table 5. Number, type of exposure, and vaccination status of possible contacts of the last recorded human smallpox case in the world[a]

	No. of persons exposed, by type of exposure		
Vaccination status at exposure	Face-to-face	Incidental	Total
Within past 3 years	58	62	120
>3 years previously	21	8	41
Unvaccinated	12		
Totals	91	70	161

[a]Ali Maow Maalin was the last human on earth to have been diagnosed, in October 1977, with a naturally occurring case of smallpox. Although he had numerous contacts with both vaccinated and unvaccinated persons, none of the contacts had overt, clinical smallpox (31).

Conclusions

Although smallpox cases were recorded throughout human history until its eradication in the 1970s, remarkably few data are available that allow us to calculate the transmission rate of smallpox. Understanding the possible transmission rate of smallpox after a deliberate release of the virus is crucial to developing estimates of impact suitable for policy planning purposes. We therefore evaluated data that potentially measured the rate of transmission by three possible methods.

The first, and possibly most indirect, method was to examine estimates of vaccination coverage needed to eradicate smallpox. We found, however, that the available data do not contain sufficient information regarding the transmission rate of smallpox suitable for modeling an

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outbreak. Experiences from the field appear to differ distinctly from theoretical estimates. These differences stand in contrast to the experience gained from the use of vaccines to control rubella and measles. For these diseases, vaccination levels must be >90% for disease to be eliminated (32,33; Table 1). The overall conclusion from the data regarding estimates of vaccination coverage needed to eradicate smallpox is that the epidemiology of smallpox differs notably from that of other infectious diseases (1,34; Table 1).

The second method of measuring rate of transmission was to consider data relating to the attack rates. We noted, however, that attack rate can vary by time, population, and residence of a susceptible person in the same house as an infectious person (Tables 2, 3). We therefore conclude that the use of attack rates derived by simply dividing the number of cases of smallpox by the total population can often be an inadequate measure of the rate of transmission of smallpox. In the report describing the Sheffield data (Table 2), average attack rates range from 1.9% (Sheffield, 1887-88) to as low as 0.2% (Leicester, 1892-93) (9). Attack rates may differ for a variety of reasons, including prior exposure to smallpox and previous vaccination. The level of prior vaccination and naturally acquired immunity differed from town to town. In Leicester, for example, only 50%-60% of the population had been vaccinated at the time of the outbreak (1892) (9). Thus, in considering attack rates as a measure of rate of transmission, it is important to define both the population of susceptible persons and their degree of contact with an infectious person (e.g., whether they live in the same house as an infectious person). Clearly, not all susceptible persons are at equal risk. This requirement makes it very difficult to use existing data regarding attack rates to calculate an average rate of transmission.

Given the problems associated with the first two methods of calculating a transmission rate, we must therefore rely on data that directly measure the number of persons infected per infectious person. In almost any situation, there is likely to be a wide range in the numbers infected per infectious person (Tables 4,5; Figure). The reason for such variability is that, despite the fact that smallpox can be transmitted by aerosolized particles (1), it is not as easily transmissible as, for example, measles (Table 1). Some form of sustained face-to-face contact is needed to ensure transmission (Table 5). If such close contact is a typical (but not necessarily sole) requirement for transmission, then the data in Tables 2 and 3 can be readily explained.

Despite strong evidence that one person can infect many others, available data suggest that the average rate of transmission is <2 persons infected per infectious person (Table 4; Figure). Given the large percentage of the population in the United States that is now susceptible (i.e., never exposed to or vaccinated against smallpox), the average transmission rate following a deliberate release of smallpox might be >2. Unfortunately, the probability that the average transmission rate will be >2 cannot be demonstrated reliably. Thus, in our model, we examine the impact of three rates of transmission: 2, 3, and 5 persons infected per infectious. Our data suggest that the lowest rate (2 persons infected per infectious person) is the most accurate representation of previous transmission rates.

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References

1. Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. Smallpox and its eradication. Geneva: World Health Organization; 1988.
2. Rao AR. Smallpox. Bombay: The Kothari Book Depot, 1972.
3. Dixon CW. Smallpox. London: Churchill; 1962.
4. Anderson RM, May RM. Infectious diseases of humans: dynamics and control. New York: Oxford University Press; 1991.
5. Henderson DA. Smallpox eradication. Proc R Soc Lond B Biol Sci 1977;68:83-97.
6. Arita I, Wickett J, Fenner F. Impact of population density on immunization programmes. J Hyg Camb 1986;96:459-66.
7. Basu RN, Jezek Z, Ward NA. The eradication of smallpox from India. New Delhi: World Health Organization, South-east Asia Regional Office; 1979.
8. Foege WH, Millar JD, Lane JM. Selective epidemiologic control in smallpox eradication. Am J Epidemiol 1971;94:311-5.
9. Royal Commission on Vaccination. A report on vaccination and its results, based on evidence taken by the Royal Commission during the years 1889-1897. Vol 1. The text of the commission report. London: New Sydenham Society; 1898.
10. Thomas DB, Arita I, McCormack WM, Khan MM, Islam S, Mack TM. Endemic smallpox in rural East Pakistan. II. Intravillage transmission and infectiousness. Geneva: World Health Organization (WHO/SE/71.25); 1971.
11. Thomas DB, McCormack WM, Arita I, Khan M, Islam S, Mack TM. Endemic smallpox in a rural area. Geneva: World Health Organization (WHO/SE/69.11); 1969.
12. Thomas DB, McCormack WM, Arita I, Khan MM, Islam S, Mack TM. Endemic smallpox in rural east Pakistan: I. Methodology, clinical and epidemiological characteristics of cases, and intervillage transmission. Geneva: World Health Organization (WHO/SE/71.24); 1971.
13. Arnt N, Morris L. Epidemiological characteristics of smallpox outbreaks in two small Brazilian villages. Geneva: World Health Organization (WHO/SE/70.22); 1970.
14. Pifer J, Adeoye CL. Characteristics of an epidemic of smallpox: Gerere hamlet, Nigeria, 1968. Geneva: World Health Organization (WHO/SE/68.5); 1968.
15. Rao AR, Paramasivam TV, Kamalakshi S, Parasuraman AR, Shantha M. A short report of epidemiological investigations of smallpox outbreaks in 1969 in a few villages of Nellore district of Andrapradesh, India. Geneva; World Health Organization (WHO/SE/70.17); 1970.
16. Rao AR. An outbreak of smallpox in Chingleput district, Madras. Geneva: World Health Organization (WHO/SE/68.6); 1968.
17. Rangaraj AG. An outbreak of smallpox in a village in Afghanistan. Geneva: World Health Organization (WHO/SE/69.9); 1969.
18. Heiner GG, Fatima N, McGrumb FR. A study of intrafamilial transmission of smallpox. Am J Epidemiol, 1971;94:316-326.
19. de Quadros CCA, Morris L, da Costa EA, Arnt N, Tigre CH. Epidemiology of variola minor in Brazil: A study of 33 outbreaks. Geneva: World Health Organization (WHO/SE/71.32); 1971.

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Article Type: Research; Volume: 7; Issue: 6; Year: 2001; Article ID: 01-0607
DOI: 10.321/eid0706.0607; TOC Head: Research

20. de Costa EA, Morris L. Smallpox epidemic in a Brazilian community. Geneva: World Health Organization (WHO/SE/74.64); 1974.
21. Rao AR. A short report on the epidemiological findings of smallpox outbreaks in the state of Tamil Nadu, July 1968--June 1969. Geneva: World Health Organization (WHO/SE/70.19); 1970.
22. Singh S. Some aspects of the epidemiology of smallpox in Nepal. Geneva: World Health Organization (WHO/SE/69.10); 1969.
23. Rao AR. A short report on epidemiological findings of smallpox outbreaks in the city of Madras. Geneva: World Health Organization (WHO/SE/68.7); 1968.
24. de Sario V. Field investigation of an outbreak of smallpox at Bawku, Ghana: May-October, 1967. Geneva: World Health Organization (WHO/SE/69.24); 1969.
25. Suleimanov GD, Mandokhel KK. Smallpox transmission on a bus. Geneva: World Health Organization (WHO/SE/72.41); 1972.
26. Presthus GT, Sibiya JB. A persistent focus of smallpox in Botswana. Geneva: World Health Organization (WHO/SE/74.89); 1974.
27. Litvinjenko S, Arsic B, Borjanovic S. Epidemiologic aspects of smallpox in Yugoslavia in 1972. Geneva: World Health Organization (WHO/SE/73.57); 1973.
28. Wehrle PF, Posch J, Richter KH, Henderson DA. An airborne outbreak of smallpox in a German hospital and its significance with respect to other recent outbreaks in Europe. Bull World Health Organ 1970;43:669-79.
29. Great Britain Ministry of Health. Smallpox, 1961-62. Reports on public health and medical subjects, No. 109. London: Her Majesty's Stationery Office; 1963.
30. Henderson DA, Yekpe M. Smallpox transmission in southern Dahomey: a study of a village outbreak. Am J Epidemiol 1969;90:423-8.
31. Smallpox Eradication Unit (WHO, Geneva). A smallpox outbreak in Merka town, Somalia. Geneva: World Health Organization (WHO/SE/78.123); 1978.
32. Anderson RM, May RM. Vaccination against rubella and measles: quantitative investigations of different policies. J Hyg Camb 1983;90:259-325.
33. Cliff AD, Haggett P. Statistical modeling of measles and influenza outbreaks. Stat Methods Med Res 1993;2:43-73.
34. Henderson DA. Principles and lessons from the smallpox eradication programme. Bull World Health Organ 1987;65:535-46.

1. The data in Table 2 indicate some age-specific risk, both among the vaccinated and unvaccinated. However, the risk does not appear to have a consistent pattern. For example, among those with a history of vaccination living in a house with a smallpox patient, those >10 years of age had a higher attack rate than those <10 years of age. Yet, among the unvaccinated, those <10 years of age had a higher attack rate than those >10 years of age. This relationship between vaccination status, age, and attack rate is repeated in the general population.

Selected Sources

- Anderson RM. Transmission dynamics and control of infectious disease agents. In: Anderson RM, May RM, editors. Population biology of infectious diseases. Berlin: Springer-Verlag; 1982. p. 149-77.

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Article Type: Research; Volume: 7; Issue: 6; Year: 2001; Article ID: 01-0607
DOI: 10.321/eid0706.0607; TOC Head: Research

- Anderson RM, May RM. Population biology of infectious diseases: Part I. Nature 1979;280:361-7.
- Anderson RM, May RM. Population biology of infectious diseases: Part II. Nature 1979;280:455-61.
- Anderson RM, May RM. Directly transmitted infectious diseases: control by vaccination. Science 1982;215:1053-60.
- Aron JL, May RM. The population dynamics of malaria. In: Anderson RM, editor. The population dynamics of infectious diseases: theory and application. London: Chapman and Hall; 1982.
- Bartlett MS. Measles periodicity and community size. J Royal Stat Soc Series A 1957;120:48-60.
- Bardi J. Aftermath of a hypothetical smallpox disaster. Emerg Infect Dis 1999;5:547-51.
- Bartlett MS. Critical community size for measles in the United States. J Royal Stat Soc Series A 1960;123:37-44.
- Christie AR. Infectious diseases: epidemiology and clinical practice. 3rd ed. New York: Churchill Livingstone; 1980.
- Cliff AD, Haggett P. Statistical modeling of measles and influenza outbreaks. Stat Methods Med Res 1993;2:43-73.
- Deria A, Jezek Z, Foster S. Outbreak containment in the Somalia smallpox eradication programme. Geneva: World Health Organization (WHO/SE/78.104); 1978.
- Frauenthal JC. Smallpox: When should routine vaccination be discontinued? The UMAP Expository Monograph Series. Boston: Birkhäuser; 1981.
- Glokpor GF, Agle AN. Epidemiological investigations--Smallpox Eradication Programme in Togo: 1969. Geneva: World Health Organization (WHO/SE/70.21); 1970.
- Henderson DA. Smallpox: Clinical and epidemiological features. Emerg Infect Dis 1999;5:537-9.
- Henderson DA. The looming threat of bioterrorism. Science 1999;283:1279-82.
- Henderson DA, Inglesby TV, Bartlett JG, Ascher MS, Eitzen E, Jahrling EP, et al. Smallpox as a biological weapon: Medical and public health management. JAMA 1999;281:2127-37.
- Kaufmann AF, Meltzer MI, Schmid GP. The economic impact of a bioterrorist attack: Are prevention and postattack intervention programs justifiable? Emerg Infect Dis 1997;3:83-94.
- Mack TM. Smallpox in Europe, 1950-1971. J Infect Dis 1972;125:161-9.
- O'Toole T. Smallpox: An attack scenario. Emerg Infect Dis 1999;5:540-6.
- Pattanayak S, Sehgal PN, Raghavan NGS. Outbreaks of smallpox during 1968 in some villages of Jaipur district, Rajasthan. Geneva: World Health Organization (WHO/SE/70.20); 1970.
- Smith ADM. Epidemiological patterns in directly transmitted human infections. In: Croll NA, Cross JH, editors. Human ecology and infectious diseases. New York: Academic Press; 1983. p. 333-51.
- Statistical abstracts of the United States: 1999. 119th ed. Washington: U.S. Bureau of the Census; 1999.

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