Epidemiology of variola minor in Brazil based on a study of 33 outbreaks[*]

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Surveillance-containment units were established in 1969 in four States of Brazil as part of the national smallpox eradication programme. Their responsibilities included both the investigation of reported cases and the control of outbreaks, and the further extension and development of the reporting network. Altogether, 33 outbreaks of smallpox were investigated in detail, all in endemic areas not yet reached by the attack phase of the eradication programme. Official reports of 27 cases led to the discovery of an additional 1 465 cases, suggesting that reporting was not more than 2 % complete in endemic areas. The total of 1 492 cases in 33 outbreaks occurred in 493 households comprising a study population of 3 088 persons : three-quarters of the cases were in children under 15 years of age. Only 5 % were in individuals aged 30 years or more. The case-fatality ratio was 0.8 %. The overall attack rate among unvaccinated persons (76.2 %) was 23 times that among vaccinated persons (3.3 %). Age-specific vaccine effectiveness ratios ranged from 94 % to 100 % with an overall reduction in expected cases among the vaccinated of 95 %. There was no evidence to suggest waning of immunity among persons who had been successfully vaccinated. There was an inverse relationship between susceptibility and age since a greater proportion of adults had already had smallpox or a successful vaccination ; 97 % of pre-school-age children and 82 % of school-age children had no history of smallpox and no vaccination scar. In all 33 outbreaks, more than 60 % of unvaccinated persons became ill ; in 5 outbreaks the attack rate for unvaccinated persons was greater than 90 %.

The National Brazilian Smallpox Eradication Campaign (Campanha de Erradicação da Varíola; CEV) was established by the Ministry of Health of

Brazil in August 1966. Vaccination programmes were first strengthened or initiated in the north-eastern states of Brazil; then, as programmes were completed, field operations were progressively extended to the more populous south-eastern and southern states.

Field training and the organization of the systematic vaccination programme were the principal activities during 1968. In 1969, greater emphasis was placed on surveillance activities and epidemiological investigation. Smallpox surveillance–containment units were established early in 1969 in the States of Bahia, Minas Gerais, and Paraná. Physicians from the Special Public Health Service (Fundação Serviço Especial de Sáude Pública; FSESP) were assigned to the smallpox programme to assume responsibility for these activities. In late 1969, another surveillance–containment unit was established in the State of Rio Grande do Sul.

The responsibilities of these units included both the investigation of reported cases, the control of outbreaks, and the extension and development of

the reporting network. In the 10 months from March to December 1969, 33 outbreaks of smallpox were investigated in detail—namely, 17 in Paraná, 7 in Bahia, 5 in Minas Gerais, 3 in Rio Grande do Sul, and 1 in the State of São Paulo. The data collected during these investigations provided important epidemiological information on smallpox in Brazil not previously available.

METHODS

Data on reported cases of smallpox were collected on a national smallpox case record form. A preliminary report requested such epidemiological information as age, sex, residence of patient, date of onset of illness, and outcome of illness. A supplementary epidemiological form for field investigations requested information about vaccination history, history of contact with possible cases, information on travel within the 3 weeks prior to the onset of illness, laboratory findings, and the age, sex, vaccination status, and smallpox history of each household contact. A " vaccinated person " was defined as anyone with a vaccination scar.

The 33 outbreaks occurred in 33 localities in 29 *municípios* (counties); there were 27 in rural areas and 6 in urban areas. An outbreak was defined as the occurrence of smallpox cases in 2 or more epidemiologically related households in a locality. In 32 outbreaks, every household in the locality was visited and the occupants in the affected households were interviewed; in 1 outbreak, every other household was visited.

Altogether, 19 of the 33 outbreaks were discovered by investigating officially reported cases: 15 (45.5%) through normal health department reporting channels and 4 (12.1%) through civil authorities. Careful investigation of these 19 outbreaks led to the discovery of the 14 (42.4%) additional outbreaks. All outbreaks studied were in endemic areas not yet reached by the attack phase of the systematic vaccination programme.

RESULTS

Study population

In the 19 reported outbreaks, 27 cases of smallpox were officially notified. Careful investigation of these cases, as well as those in the outbreaks subsequently discovered, revealed an additional 1 465 cases of smallpox, suggesting that reporting was not more than 2% complete in endemic areas of Brazil.

The outbreaks in most instances had been in progress for several months. The minimum time delay between the occurrence of the first case and the date of reporting was 32 days. One outbreak totalling 77 cases had been in progress for 8 months before the one, and only, case requiring hospitalization was reported. Although control measures were taken during each investigation, the outbreaks had usually reached, or passed, their peak by the time these measures were instituted. In some instances, the outbreaks had already terminated spontaneously with periods of 15–30 days between the onset of the last identified case and the date of investigation.

There was an average of 45 cases in each outbreak, with a range of 25–246 cases in the 6 urban outbreaks and 12–85 cases in the 27 rural outbreaks. The total of 1 492 cases occurred in 493 households, comprising 3 088 persons.

Smallpox attack rate

Of the 3 088 persons in the affected households, 638 (21%) had a history of a previous smallpox illness (Table 1). Among the remaining 2 450 persons, 1 492 cases of smallpox were recorded. There were no cases among persons with a history of smallpox. Three-quarters of the cases were in children under 15 years of age, and only 5% were in individuals aged 30 years or more.

Of the 1 492 who became ill, only 17 had a vaccination scar. The overall attack rate for the unvaccinated (76.2%) was 23 times greater than the rate (3.3%) among those vaccinated at any time prior to this study. For unvaccinated persons, the age-specific attack rate was highest in the school-age group (5–14 years), although there was no significant difference between attack rates for all age groups under 30 years.

The effectiveness of smallpox vaccine was assessed for each age group. Attack rates for the unvaccinated persons were calculated, and from these rates the expected number of cases in the vaccinated population was obtained. The effectiveness ratios were estimated to be between 94% and 100% for the different age groups, with an overall reduction in cases among vaccinated persons of 95%.

Among patients who had previously been vaccinated, the interval between vaccination and onset of illness was less than 6 years in 7 cases and more than 15 years in 5 cases (Table 2). There was no evidence to suggest waning of immunity among persons who had been successfully vaccinated (on the evidence of a vaccination scar).

Table 1. Percentage smallpox attack rates by age and vaccination status

Age group (years)	Population under study	History of smallpox	Previously vaccinated			Unvaccinated			Vaccine effectiveness ratio (%)
			Total	No. of cases	Attack rate	Total	No. of cases	Attack rate	
0–4	556	2	16	0	0.0	538	408	75.8	100.0
5–14	1 064	62	134	6	4.5	868	723	83.3	94.6
15–29	738	194	160	7	4.4	384	280	72.9	94.0
⩾ 30	730	380	203	4	2.0	147	64	43.5	95.4
total	3 088	638	513	17	3.3	1 937	1 475	76.2	95.7 [a]

[a] Age-adjusted effectiveness ratio for total = 94.8 %.

Table 2. Interval between vaccination and onset; vaccinated cases

Interval (years)	No. of cases
< 3	3
3–5	4
6–8	3
9–14	2
⩾ 15	5
total	17

Mortality

Death occurred in 12 of the 1 492 cases; i.e., the case–fatality ratio was 0.8%. All patients who died were unvaccinated and the interval between the onset of illness and death ranged from 2 to 13 days. Six of the victims were less than a year old; 3 of them were less than a month old and were born of mothers already infected with smallpox. Of the other 6 patients who died, 5 were females between the ages of 16 and 22 years, 2 of whom were known to be pregnant at the time of infection.

Past smallpox and immunity in the affected households

In both urban and rural areas, the proportion of persons with a history of previous smallpox increases with age (Table 3). Overall, 21.8% and 19.8% of the residents of affected households in urban and rural areas, respectively, had a history of smallpox. Approximately half the adults aged 30 years or more in both areas stated that they had had smallpox.

Only 2 children less than 5 years of age had a history of smallpox, suggesting that smallpox had been absent for at least 5 years in most localities. In most of the 27 rural localities, smallpox had been absent for 10 years or more.

Altogether, 21% of the residents of affected households in the 6 urban areas, but only 13% in the rural areas, had been successfully vaccinated. Very few pre-school-age children, only 1.3% in the rural areas, had been vaccinated.

Since the effectiveness of vaccination in preventing the disease is well above 90%, those individuals with no history of smallpox and no vaccination scar should be considered as the truly susceptible population. Two-thirds of the residents in affected households in the rural outbreaks were susceptible to smallpox at the time the outbreak began. In the urban areas, 58% of the household residents were susceptible.

In all but 3 of the 33 outbreaks, at least 50% of the residents in affected households were susceptible. In 32 of the 33 outbreaks, more than half of the school-age children were considered susceptible and, in fact, in 24 outbreaks, more than 80% were susceptible. In 30 outbreaks, more than 90% of the pre-school-age children were susceptible; in 24 outbreaks, all children were susceptible.

As previously noted, the outbreaks in most instances had been in progress for several months when investigation and control measures were undertaken. Between the onset of the outbreak and the time of investigation, there was ample time for most, if not all, household residents to have been exposed to the first case in their respective households before control measures were taken. In 28 of the 33 outbreaks, over two-thirds of the susceptible household

Table 3. Susceptibility of residents in affected households by age group and by urban and rural area *

Age group (years)	Population under study	History of smallpox		Vaccination scar		No history of smallpox and no vaccination scar	
		No.	%	No.	%	No.	%
Urban outbreaks							
0–4	238	1	0.4	12	5.0	225	94.5
5–14	488	46	9.4	80	16.4	362	74.2
15–29	322	92	28.6	85	26.4	145	45.0
⩾ 30	335	162	48.4	109	32.5	64	19.1
total	1 383	301	21.8	286	20.7	796	57.6
Rural outbreaks							
0–4	318	1	0.3	4	1.3	313	98.4
5–14	576	16	2.8	54	9.4	506	87.8
15–29	416	102	24.5	75	18.0	239	57.5
⩾ 30	395	218	55.2	94	23.8	83	21.0
total	1 705	337	19.8	227	13.3	1 141	66.9

* Status at time outbreak was introduced into the affected locality.

residents contracted smallpox, and in 5 of the 28 outbreaks, the attack rate for susceptible persons was greater than 90%. The attack rate for susceptibles in the 5 other outbreaks ranged from 60% to 65%.

Among affected households, the average size was 6.3 persons and the mean number of cases per affected household was 3.0 (Table 4). Half of the 493 affected households had only 1 or 2 cases, but 2 households had as many as 12 cases each.

Secondary attack rates in the rural outbreaks

The 27 outbreaks in rural areas affected a total of 272 households. In all but 17 households, it was possible to determine the primary (or co-primary) case(s) in each household as an indication of the age group most likely to introduce the disease. With the determination of index cases, secondary attack rates could be calculated for remaining household contacts. Another 7 households were eliminated from this analysis as the introduction and spread of disease were due to variolization and 2 additional households were deleted since the primary case was the only resident of the household.

In 246 households with 1 533 residents, 349 primary or co-primary cases were identified. Three-quarters (75.2%) of the households had 1 index case

and the introduction of disease in the other quarter was due to 2 or more co-primary cases. Among the 1 184 household contacts of primary cases, 473 secondary cases occurred.

Table 4. Distribution of cases of smallpox by number of cases per affected household

No. of cases per household [a]	Affected households	
	No.	%
1	141	28.6
2	103	20.9
3	79	16.0
4	64	13.0
5	46	9.3
6	27	5.5
7	16	3.3
8	13	2.6
⩾ 9	4	0.8
total	493	100.0

[a] Average household size = 6.3; average no. of cases per household = 3.0.

Table 5. Primary cases and secondary attack rate by immunity status in 27 rural outbreaks of smallpox in Brazil in 1969

Immunity status	Total no. of residents	Primary or co-primary cases	Household contacts	Secondary cases	Secondary attack rate (%)
history of smallpox	306	0	306	0	0.0
vaccination scar	206	2	204	7	3.4
no vaccination scar	1021	347	674	466	69.1

Table 6. Secondary attack rates among unvaccinated household contacts by age group in 27 rural outbreaks of smallpox in Brazil in 1969

Age group (years)	Population under study	Primary or co-primary cases	Primary attack rate (%)	Household contacts	Secondary cases	Secondary attack rates (%)
0–4	275	63	22.9	212	151	71.2
5–14	450	174	38.7	276	219	79.3
15–29	227	91	40.1	136	85	62.5
⩾30	69	19	27.5	50	11	22.0
total	1 021	347	34.0	674	466	69.1

The distribution of primary cases and secondary attack rates by immunity status are presented in Table 5. There were no cases among individuals with a history of smallpox. All but 2 of the 349 primary cases were unvaccinated. The secondary attack rate was 69.1 % in persons with no vaccination scar, compared with 3.4% in persons with a vaccination scar.

The unvaccinated residents are shown in Table 6 by age group. Although the greatest number of primary cases were among children aged 5–14 years, there was no difference in primary attack rates between the 5–14 years and the 15–29 years age groups. The proportion of older adults (⩾30 years) introducing disease into the household was 27.5% while 22.9% of the pre-school-age children (0–4 years) were index cases.

Secondary attack rates ranged from 62% to 79% in all age groups up to 30 years. Approximately 8 of every 10 contacts aged 5–14 years acquired smallpox once the infection was introduced into the household. Although least likely to introduce disease into the household, the 0–4 years age group suffered the second highest secondary attack rate.

Origin of outbreaks

The age and sex of the first patient in each outbreak could be identified with certainty in 25 of the 33 outbreaks; 16 were under 15 years of age, and 9 were adults—5 males and 4 females. Based on the distribution of the general population, no one group accounted for a disproportionate number of source cases.

Two-thirds of the source patients were temporarily absent from their home village when infected, while the other third was moving from one locality to another with their families. In only 1 case was the initial infection acquired in a large city. Slightly more than half the introductions into rural areas came from urban areas with a population of less than 25 000. The remaining introductions came from other rural areas.

DISCUSSION

The suggestion that reporting has not been more than 2% complete in endemic areas of Brazil is startling, and represents much less complete reporting than has been observed in a number of other

countries. It should be noted, however, that only variola minor infections are present in Brazil, and many persons are not sufficiently ill to require medical attention. The case–fatality ratio of less than 1 % is an epidemiological indication of variola minor. In addition, laboratory studies have indicated that variola minor has been the only form of variola present in Brazil in recent years (Briceno Rossi, 1963; Downie et al., 1963; Noble & Salles-Gomes, 1968).

The extent to which infection can spread in households (or villages) when control measures are not promptly undertaken is illustrated by the very high attack rates for the susceptible population. At least 60 % of the unvaccinated residents in affected households contracted smallpox in all 33 outbreaks and the overall attack rate for this group was 76.2 %.

The considerable protection afforded by vaccination is apparent. The overall vaccine effectiveness ratio of 94.8 % compares favourably with the 90 % effectiveness ratio reported in East Pakistan (Thomas et al., 1969). However, in East Pakistan, the age-specific effectiveness ratio for adults (25 years of age and over) fell to 74 %, and for vaccinated persons, age-specific attack rates increased progressively with age, suggesting a waning of immunity. In contrast, the effectiveness ratio for adults in Brazil (30 years of age and over) was 95.4 %, and attack rates for vaccinated persons did not increase with age. Very few of those who had a vaccination scar had ever been revaccinated, so the estimate of the effectiveness of vaccination essentially represents that of primary vaccination. Although there may be some error of bias owing to the small proportion of persons who had been successfully revaccinated, primary smallpox vaccination appears to give considerable protection against variola minor. The protection is not only effective but also durable. It must be noted, also, that the effectiveness of smallpox vaccine in preventing smallpox is being assessed here under the most taxing conditions—i.e., continuous intimate household contact.

Rao et al. (1968) observed that the transmission rate for smallpox increased with an increase in the size of the family to a limit of 6–9, beyond which the transmission rate decreased. The average household in our study consisted of 6.3 persons. In a detailed study of smallpox transmission in two small Brazilian villages, the average size of households with smallpox was 6.1 persons; in households without smallpox it was only 3.4 persons (Arnt & Morris, 1971).

Although large urban areas reportedly play a disproportionate role in generating smallpox outbreaks in rural areas in Asia (Rao et al., 1968; Thomas et al., 1969),[1] this was not found to be true in Brazil, where only one of the outbreaks could be attributed to the introduction of infection from a large city. In rural outbreaks, the index or primary case(s) in the household was most likely to be a school-age child (5–14 years) or a young adult (15–29 years); clearly, these are the most mobile age groups. Although least likely to introduce disease into the household, the 0–4 year age group suffered a secondary attack rate second only to the school-age group. In all, 58 % of the members of affected households in the urban outbreaks, and 67 % in the rural outbreaks, were considered susceptible. Considering that 87 % of the children less than 15 years of age had never had smallpox and had never been vaccinated successfully, it is not surprising that the great majority (two-thirds) of cases occurred in this age group. In most of the 33 localities studied, there had been neither a smallpox outbreak nor a mass smallpox vaccination campaign in 15 years. Therefore, the current national smallpox eradication programme in Brazil is correctly emphasizing the vaccination of pre-school- and school-age children, especially those who do not attend school, in its systematic vaccination programme. This latter point is particularly important since it has been shown in Pakistan that the attack rate for school-age children not attending school is 6 times higher than the attack rate for children attending school.[2]

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RÉSUMÉ

ÉPIDÉMIOLOGIE DE LA VARIOLE MINEURE AU BRÉSIL D'APRÈS LES DONNÉES RECUEILLIES LORS DE L'ÉTUDE DE 33 FOYERS ÉPIDÉMIQUES

En 1969, dans le cadre du programme national d'éradication de la variole, des unités de surveillance et d'endiguement ont été constituées dans quatre Etats du Brésil. Elles avaient pour tâches d'enquêter sur les cas déclarés, de lutter contre les poussées épidémiques et de veiller au développement et à l'amélioration du réseau de notification.

De mars à décembre 1969, on a étudié en détail 33 épidémies de variole, toutes survenues dans des zones d'endémicité non encore touchées par la phase d'attaque du programme d'éradication. Les rapports officiels, qui faisaient état de 27 cas, ont conduit à la découverte de 1465 cas supplémentaires, ce qui laisse supposer que dans les régions d'endémicité la notification ne porte guère sur plus de 2 % des cas réellement existants.

Les 1492 cas dénombrés lors de ces poussées épidémiques sont apparus dans 493 familles comptant au total 3088 personnes. Les trois quarts des malades étaient des enfants de moins de 15 ans et 5 % seulement des sujets âgés de 30 ans ou plus. Le taux de létalité a été de 0,8 %. La morbidité globale a été 23 fois plus élevée parmi les sujets non vaccinés (76,2 %) que parmi les sujets vaccinés (3,3 %). Le taux de protection conféré par la vaccination, variant selon l'âge de 94 à 100 %, a atteint en moyenne 95,7 %. On n'a constaté aucun signe d'un affaiblissement de l'immunité chez les personnes vaccinées précédemment avec succès.

La relation inverse entre l'âge et la réceptivité à la variole s'explique par le fait que de nombreux adultes avaient déjà contracté la maladie ou subi la vaccination avec succès: chez 97 % des enfants d'âge préscolaire et 82 % des écoliers, on ne relevait aucun antécédent de variole et les cicatrices de vaccination étaient absentes. Chez les sujets non vaccinés, le taux de morbidité a été de plus de 60 % pour l'ensemble des 33 poussées épidémiques; dans 5 d'entre elles, il a dépassé 90 %.

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