



EPIDEMIOLOGY OF VARIOLA MINOR IN
BRAZIL: A STUDY OF 33 OUTBREAKS¹

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by

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SYNOPSIS

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 outbreak control, and the further extension and development of the reporting network. Thirty-three 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 1465 cases suggesting that reporting was not more than two per cent. complete in endemic areas of Brazil. The total of 1492 cases in 33 outbreaks occurred in 493 households comprising a study population of 3088 individuals. Three-quarters of cases were in children under 15 years of age. Only five per cent. were in individuals 30 years of age or older. The case fatality ratio was 0.8 per cent. The overall attack rate among the unvaccinated (76.2 per cent.) was 23 times greater than the rate among the vaccinated (3.3 per cent.). Age-specific vaccine effectiveness ratios ranged from 94 to 100 per cent. with an overall reduction in expected cases among the vaccinated of 95 per cent. 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 as a greater proportion of adults had already had smallpox or a successful vaccination. Fully 97 per cent. of pre-school-age children and 82 per cent. of school-age children had no history of smallpox and no vaccination scar. In all 33 outbreaks, more than 60 per cent. of the unvaccinated became ill; in five outbreaks, the attack rate for unvaccinated individuals was greater than 90 per cent.

INTRODUCTION

The National Brazilian Smallpox Eradication Campaign (Campanha de Erradicacao da Variola) was established by the Ministry of Health in August 1966. Vaccination programmes were first strengthened or initiated in the north-eastern states of Brazil. As programmes were completed in the north-eastern states, field operations were progressively extended to the more populous south-eastern and southern states.

Field training and organization of the systematic vaccination programme were the principal activities through 1968. In 1969, greater emphasis was placed on surveillance activities and epidemic investigation. Smallpox surveillance-containment units were established in early 1969 in the States of Bahia, Minas Gerais and Parana. Physicians from the Special Public Health Service (Fundacao Servico Especial da Saude Publica - 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.

Their responsibilities included both the investigation of reported cases and outbreak control and the further extension and development of the reporting network. In the 10 months from March to December 1969, 33 outbreaks of smallpox were investigated in detail - 17 in Parana, 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. These data are summarized in this report.

METHODS

Data on reported cases of smallpox are collected on a national smallpox case record form. A preliminary report requests such epidemiological information as age, sex, and residence of patient, date of onset of illness, and outcome of illness. A supplementary epidemiological form is utilized for field investigation, which requests information regarding vaccination history, history of contact with possible cases, information on travel within three weeks prior to 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 municipios (counties); there were 27 in rural areas and six in urban areas. An outbreak was so defined when smallpox cases occurred in two 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 one outbreak, every other household was visited. Nineteen of the 33 outbreaks were discovered through investigation of officially reported cases (Table 1): 15 through normal health department reporting channels and four through civil authorities. Careful investigation of these 19 outbreaks led to the discovery of the 14 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 had been officially notified. Careful investigation of these cases as well as those in the outbreaks subsequently discovered, revealed an additional 1465 cases of smallpox, suggesting that reporting was not more than two per cent. complete in endemic areas of Brazil.

The outbreaks in most instances had been in progress for several months. The minimum time period between onset of the first case and date of report was 32 days. One outbreak totalling 77 cases had been in progress for eight 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 to 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 to 246 cases in the six urban outbreaks and 12 to 85 cases in the 27 rural outbreaks. The total of 1492 cases occurred in 493 households comprising 3088 individuals.

Smallpox attack rate - Of the 3088 persons in the affected households, 638 (21 per cent.) had a history of a previous smallpox illness (Table 2). Among the remaining 2450 individuals, there were 1492 cases of smallpox recorded. There were no cases in persons with a history of smallpox. Three-quarters of the cases were in children under 15 years of age. Only five per cent. were in individuals 30 years of age or older. Of the 1492 who became ill, only 17 had a vaccination scar. The overall attack rate for the unvaccinated (76.2 per cent.) was 23

times greater than the rate (3.3 per cent.) among those vaccinated at any time prior to this study. For the unvaccinated, the age specific attack rate was highest in the school-age group (5-14 years), although there is no significant difference between attack rates for all age-groups under 30 years of age.

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

Among cases who had previously been vaccinated, the interval between vaccination and onset of illness was less than six years in seven cases and more than 15 years in five cases (Table 3). There was no evidence to suggest waning of immunity among persons who had been successfully vaccinated, as evidenced by a vaccination scar.

Mortality - Death occurred in 12 of the 1492 cases: a case-fatality ratio of 0.8 per cent. All patients who died were unvaccinated and the interval between onset of illness and death ranged from 2 to 13 days. Six of the victims were less than a year of age; three of these were less than a month of age, born of mothers who were already infected with smallpox. Five of the other six deaths were in females between the ages of 16 and 22, two of whom were known to be pregnant at the time of infection.

Past smallpox and immunity in the households affected - In both urban and rural areas the proportion with a history of previous smallpox increases with age (Table 4). Overall, 21.8 and 19.8 per cent. of the residents of affected households in urban and rural areas, respectively, gave a history of having had smallpox. Approximately half the adults 30 years of age or over in both areas stated that they had had smallpox.

There were only two children less than five years of age with a history of smallpox, suggesting that smallpox had been absent for at least five years in most localities. In most of the 27 rural localities, smallpox had been absent for 10 years or more.

Twenty-one per cent. of the residents of affected households in the six urban areas had had a successful vaccination, but only 13 per cent. in the rural areas had. Very few pre-school children had been vaccinated - only 1.3 per cent. in the rural areas.

Since the effectiveness of vaccination in preventing the disease is well above 90 per cent., those individuals with no history of smallpox and no vaccination scar should be considered the truly susceptible population under study. 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 per cent. of the household residents were susceptible.

In all but three of the 33 outbreaks, at least 50 per cent. 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 per cent. were susceptible. In 30 outbreaks, more than 90 per cent. of the pre-school age children were susceptible; in 24 outbreaks all (100 per cent.) 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 household before control measures were taken. In 28 of the 33 outbreaks, over two-thirds of the susceptible household residents contracted smallpox, and in five of the 28 outbreaks, the attack rate

for susceptibles was greater than 90 per cent. The attack rate for susceptibles in the other five outbreaks ranged from 60 to 65 per cent.

Among affected households, the average size was 6.3 persons and the mean number of cases per affected household was 3.0 (Table 5). Half of the 493 affected households had only one or two cases, but two 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 seven households were eliminated from this analysis as the introduction and spread of disease was due to variolization and an additional two households were deleted as the primary case was the only resident of the household.

In 246 households with 1533 residents, 349 primary or co-primary cases were identified. Three-quarters (75.2 per cent.) of the households had one index case and introduction of disease in the other quarter was due to two or more co-primary cases. Among the 1184 household contacts of primary cases, 473 secondary cases occurred.

The distribution of primary cases and secondary attack rates by immunity status are presented in Table 6. There were no cases among individuals with a history of smallpox. All but two of the 349 primary cases were unvaccinated. The secondary attack rate was 69.1 per cent. in persons with no vaccination scar, as compared to 3.4 per cent. in persons with a vaccination scar.

The unvaccinated residents are shown in Table 7 by age-group. Although the greatest number of primary cases were children between five and 14 years of age, there was no difference in primary attack rates between those five to 14 and 15 to 29 years of age. The proportion of older adults (30+ years) introducing disease into the household was 27.5 per cent, while 22.9 per cent. of the pre-school children (0-4 years) were index cases.

Secondary attack rates ranged from 62 to 79 per cent. in the age-groups to 30 years of age. Approximately eight of every 10 contacts from five to 14 years of age acquired smallpox once introduced into the household. Although least likely to introduce disease into the household, the 0-4 year age-group suffered the second highest secondary attack rate.

Origin of the outbreaks - The age and sex of the first case in each outbreak could be identified with certainty in 25 of the 33 outbreaks. Sixteen were under 15 years of age, and nine were adults - five males and four 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 cases were temporarily absent from their home village when infected, while the other third were moving from one locality to another with their families. In only one case was the initial infection acquired in a large city. Slightly more than half of the introductions into rural areas came from urban areas with less than 25 000 population. The remaining introductions came from other rural areas.

DISCUSSION

The suggestion that reporting has not been more than two per cent. complete in endemic areas of Brazil is a startling figure. This 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 one per cent. 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, 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 per cent. of the unvaccinated residents in affected households contracted smallpox in all 33 outbreaks and the overall attack rate for this group was 76.2 per cent.

The considerable protection afforded by vaccination is apparent. The overall vaccine effectiveness ratio of 94.8 per cent. compares favourably with the 90 per cent. effectiveness ratio reported in East Pakistan (Thomas et al., 1969). However, in East Pakistan, the age-specific effectiveness ratio for adults (25 years and over) fell to 74 per cent., 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 and over) was 95.4 per cent., and attack rates for the vaccinated did not increase with age. Very few of those who had a vaccination scar had ever been revaccinated, so the estimate of vaccine efficacy essentially represents the effectiveness of primary vaccination. Although there may be some error of bias due to the small proportion who had been successfully revaccinated, primary smallpox vaccination appears to give considerable protection against variola minor that is not only effective but also durable. It must be noted, also, that the efficacy of smallpox vaccine in preventing smallpox is being measured here under the most taxing conditions - continuous intimate household contact. Rao (1968) has observed that the transmission rate for smallpox increased with the increase in the size of the family to a limit of six to nine, beyond which the transmission rate decreases. 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, compared to only 3.4 in households without smallpox (Arnt & Morris, 1971).

Although large urban areas reportedly play a disproportionate role in generating smallpox outbreaks in rural areas in Asia (4-5, 7) this was not found to be true in Brazil, where only one of the outbreaks could be attributed to introduction 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) or a young adult (15-29), clearly 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.

Fifty-eight per cent. of the members of affected households in the urban outbreaks were considered susceptible, and 67 per cent. in the rural outbreaks. Considering that 87 per cent. 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 neither been 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 six times higher than the attack rate for children attending school (Heiner et al., 1969).

SUMMARY

Surveillance-containment units were established in 1969 in four states of Brazil as part of the national smallpox eradication programme. Their responsibilities included investigation of reported cases, outbreak control, and extension and development of the reporting network.

Thirty-three smallpox outbreaks were investigated in detail; all were in endemic areas not yet reached by the attack phase of the eradication programme. Official reports of 27 cases led to the discovery of 1465 more cases, suggesting that reporting was not more than two per cent. complete in endemic areas of Brazil. The 1492 cases in the 33 outbreaks occurred in 493 households comprising 3088 individuals.

Three-quarters of the cases were in children under 15 years of age. Only five per cent. were in individuals 30 years of age or older. The attack rate for the unvaccinated (76.2 per cent.) was 23 times greater than the rate for the vaccinated (3.3 per cent.). The case-fatality ratio was 0.8 per cent. Age-specific vaccine effectiveness ratios ranged from 94 to 100 per cent., with an overall reduction in expected cases among the vaccination of 95 per cent. There was no evidence to suggest waning of immunity in persons who had ever been successfully vaccinated.

There was an inverse relationship between susceptibility and age, because a greater proportion of adults had already had smallpox or a successful vaccination. Fully 97 per cent. of pre-school-age children and 82 per cent. of school-age children had no history of smallpox and no vaccination scar. In all 33 outbreaks at least 60 per cent. of the unvaccinated became ill; in five outbreaks, the attack rate for unvaccinated individuals was more than 90 per cent.

REFERENCES

1. Arnt, N. & Morris, L., Smallpox outbreaks in two Brazilian villages: an epidemiological study, Amer. J. Epid. (Submitted for publication)
2. Briceno Rossi, A. L. (1963) Bol. Ofic. sanit. panamer., 24, 419-423
3. Downie, A. W., Dumbell, K. R., Ayrosa Galvao, P. A. & Zatz, I. (1963) Trop. geogr. Med., 15, 25-28
4. Heiner, G. G., Fatima, N. & Ali, A. (1969) WHO Smallpox Eradication Unit Technical Report 69, 13, Geneva
5. Noble, J. & Salles-Gomes, L. F. (1968) A laboratory study of Brazilian smallpox. Presented at the Seminar on Laboratory Diagnosis of Smallpox in the Americas, Instituto Oswaldo Cruz, Rio de Janeiro, Brazil
6. Rao, A. R., Jacob, E. S., Kamalakshi, S., Appaswamy, S. & Bradbury (1968) Indian J. med. Res., 56, 1826-1854
7. Thomas, D. B., McCormack, W. M., Khan, M., Islam, M. S. & Mack, T. M. (1969) WHO Wkly epidem. Rec., 44 (51/52), 669-676

TABLE 1. SOURCE OF REPORT, 33 SMALLPOX
OUTBREAKS, BRAZIL, 1969

Source of report	Urban	Rural	Total	Per cent. of total
Health department	1	14	15	45.5
Civil authority	0	4	4	12.1
Investigation of other case or outbreak	5	9	14	42.2
Total	6	27	33	100.0

TABLE 2. SMALLPOX ATTACK RATES (%) BY AGE AND VACCINATION STATUS

Age group	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*

* Age-adjusted effectiveness ratio for total - 94.8%

TABLE 3. INTERVAL BETWEEN VACCINATION AND ONSET - VACCINATED CASES

Interval (years)	No. of cases
Less than 3	3
3-5	4
6-8	3
9-14	2
15+	5
TOTAL	17

TABLE 4. SUSCEPTIBILITY OF RESIDENTS IN AFFECTED HOUSEHOLDS
BY AGE GROUP AND BY URBAN AND RURAL AREA*

Age group	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

TABLE 5. DISTRIBUTION OF CASES BY NUMBER OF CASES
PER AFFECTED HOUSEHOLD¹

No. of cases per household ²	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

¹ Average household size 6.3

² Average No. of cases per household 3.0

TABLE 6. PRIMARY CASES AND SECONDARY ATTACK RATE BY IMMUNITY STATUS
27 RURAL OUTBREAKS - BRAZIL, 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	1 021	347	674	466	69.1

TABLE 7. SECONDARY ATTACK RATES AMONG UNVACCINATED HOUSEHOLD CONTACTS
BY AGE GROUP, 27 RURAL OUTBREAKS, BRAZIL 1969

Age group	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