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EPIDEMIOLOGICAL INVESTIGATION OF A SMALLPOX OUTBREAK IN A CITY REPORTED TO BE 100% VACCINATED[a]

by

Leo Morris, M.P.H.[b]
A. Vera Martinez, M.D.[c]
José Oswaldo da Silva, M.D.[d]

Introduction

During the last week of July 1967, 21 cases of suspect smallpox in the city of Branquinhas, Alagoas State, were reported to the Smallpox Eradication Campaign by the Smallpox Surveillance Unit in the Alagoas State Health Department. This was disturbing news since during the attack phase of the Campaign in March, the number of vaccinations performed in this city and municipio exceeded the population of the area. There appeared to be four possible explanations to account for this report:

1. The cases reported actually represented chickenpox or another disease similating smallpox.

2. If smallpox, the individuals in question had migrated to Branquinhas since March and represented a pocket of unvaccinated persons with the municipio.

3. If smallpox, and the cases in question, had resided in Branquinhas during March, the vaccine applied was not potent or the vaccination technique was very poor.

4. The proportion of the population supposedly vaccinated was substantially less than supposed either because of faulty population estimates or overreporting, on the part of the team, as to the number of vaccinations performed.

Investigations were undertaken between 4 and 10 August to determine the cause of the outbreak. The results are presented in this paper.

Background

The Brazilian Smallpox Eradication Campaign initiated its field activities in November 1966, in the north-eastern State of Alagoas. Between November 1966 and April 1967, 1 262 975 persons were registered as having been vaccinated. This represents 91.5% of the estimated 1 381 000 residents of the State.

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[a] From the Campanha de Erradicação da Variola (CEV), Ministry of Health, Rio de Janeiro, Brazil.

[b] Statistical Consultant, World Health Organization, CEV, Brazil.

[c] Medical Officer, World Health Organization, CEV, Brazil.

[d] Superintendent, CEV, Brazil.

The Municipio of Branquinhas is 62 kilometres north-west of the Capital. The estimated population of the Municipio of Branquinhas is 6317 of which 1435 are considered to live in the urban area (Branquinhas City) and 4882 in rural areas.

Vaccination team no. 5 worked in the Municipio of Branquinhas during the six day period, 8 to 13 March. The number of vaccinations tallied by day and by area are listed:

Day	Area *	No. of vaccinations
March 8	Urban	1 373
March 9	Urban (follow-up)	105
March 9	Rural	1 478
March 10	Rural	1 347
March 11	Rural	373
March 12	Urban (Market day)	739
March 13	Rural	1 143

*Urban area is synonymous with the city of Branquinhas.

The number of persons vaccinated by age group is shown below:

Age group	No. vaccinated	Estimated population
3 months - 4	941)	2 556
5 - 14	1 997)	
15 - 29	1 923)	3 761
30 - 49	1 189)	
50 and over	508)	
TOTAL	6 558	6 317

The number of vaccinations tallied is slightly greater than the estimated population This is understandable in a mass programme, especially in this instance when more than 10% of the vaccinations were performed during the feira (market day) on 12 March. This weekly feira is known to attract people from the rural areas of neighbouring municipios. Excluding vaccinations performed during the feira, the number of vaccinations performed in the urban and rural areas approximately equalled the estimated population in the urban and rural areas, respectively. Although population estimates in many countries are often recognized to be in error, subsequent survey data in this community revealed, in fact, that the actual population was not more than 5% higher than the estimates.

Previous smallpox incidence - Alagoas State

The number of cases of smallpox notified in Alagoas is presented below for the years 1956 to 1966. Cases have been reported as from the Capital or from the "Interior", i.e. other areas in the State.

NOTIFIED CASES OF SMALLPOX, ALAGOAS, 1956-1966

Year	Capital	Interior	Total
1956	104	452	556
1957	48	275	323
1958	23	33	56
1959	11	93	104
1960	62	41	103
1961	80	36	116
1962	138	55	193
1963	152	36	188
1964	15	4	19
1965	5	8	13
1966	8	-	8

Between 1961 and 1966, 17 deaths due to smallpox were reported. Of the 17 deaths, 16 were residents of Maceió, the capital. During this same time period, 398 cases were recorded in Maceio resulting in a case fatality ratio of 4.3%. This ratio is somewhat higher than the usual 1% case fatality ration recorded in Brazil and undoubtedly reflects underreporting of clinically mild illness.

Epidemiological investigation

Following the notification of suspect smallpox in Branquinhas, two of the authors travelled to the area with Dr L.T. Cavalcante, Chief of the Small Surveillance Unit in Alagoas. The suspect cases were confirmed clinically and specimens from five cases were collected for laboratory examination. (Smallpox virus was subsequently recovered from all five specimens).[a] Epidemiological investigation forms were completed for all cases.

During the investigation, 34 additional cases of smallpox were documented of which four had occurred in January and February of 1967. This was in addition to the 21 cases already reported. The four cases in January and February apparently had no connexion with the present outbreak and will not be further considered. The remaining 51 cases, 39 in Branquinhas, 7 in Fazenda Churega (12 kilometres north of Branquinhas), and five in adjacent rural areas, occurred between 10 June and 22 August. Cases by week of onset are shown in Figure 1.

All but one case in the Branquinhas outbreak was under 30 years of age. As shown below, seven cases were under one year of age, including the only death, a seven month old child.

SMALLPOX CASES BY AGE-GROUP AND SEX
BRANQUINHAS OUTBREAK, BRAZIL

Age-group	Male	Female	Total
Under 1	4	3	7
1-4	6	5	11
5-14	8	11	19
15-29	5	8	13
30-44	0	1	1
45 and over	0	0	0
TOTAL	23	28	51

[a] Virological studies performed by the Adolfo Lutz Institute, São Paulo.

Of the 51 cases, one a 14 year old boy, had been vaccinated prior to March. One additional patient had been succesfully vaccinated during the campaign in March. An additional case was vaccinated for the first time on 29 July, five days before the onset of illness, and thus quite clearly after the time of exposure.

The origin of the epidemic is unclear as none of the initial cases had travelled outside of Branquinhas during the three weeks prior to illness. The outbreak spread from Branquinhas City to Fazenda Churega and the rural area. The first case which occurred in Fazenda Churega was a 26 year old female who had gone to Branquinhas during the last week in June. This patient had onset of illness on 12 July. Six subsequent cases occurred in her household and among playmates of her children. The five cases in the rural area occurred near the termination of the outbreak and are believed to have been infected in Branquinhas.

All patients had resided in Branquinhas Municipio since March and should have been vaccinated by the vaccination team during the campaign. Only one, however, had been vaccinated. The outbreak therefore could not be attributed to recently arrived migrants to the area and for these cases, the fault could not be attributed to use of impotent vaccine or faulty vaccination technique.

Control procedures

The Smallpox Surveillance Unit of the Alagoas State Health Department sent vaccinators to Branquinhas on 22 July when notification of an outbreak was first received. The vaccinators proceeded to revaccinate the city house-to-house, and by 8 August, had vaccinated 1460 persons. In addition to this, 368 persons were vaccinated by jet injection on 6 August, during the weekly feira. The age distribution of the 1828 persons vaccinated was as follows:

Age-group (years)	No. vaccinated	Per cent.
0-4	242	13.2
5-14	614	33.6
15-29	602	32.9
30-49	266	14.6
50 and over	104	5.7
Total	1 828	100.0

During the three day period from 6 to 8 August, 3345 persons in the city of Murici (12 kilometres south of Branquinhas) were also vaccinated by jet injection. Vaccinations were performed in the schools and a vaccination post was set up in the town square in front of the church where a three day religious festival was being held.

In addition, 95 persons in Fazenda Churega were vaccinated. Beginning on 11 August, vaccinations were also carried out in the rural area of Branquinhas.

Survey to determine vaccination coverage

Since the other aspects of the investigation disclosed no evident explanation for the outbreak, it seemed most likely that a smaller proportion of the population than reported had been vaccinated in March by the vaccination team. Accordingly, plans were made to conduct household surveys in Branquinahs City, in Fazenda Churega and in Usino Campo Verde, an adjacent area in close contact with Branquinhas but where no cases had been detected (see Annex). One of the authors and a vaccinator carried out these surveys during a three day period. In each household surveyed, a list of the household members was prepared and it was determined by query whether or not each had been vaccinated during the campaign. Their duration of residence in the communtiy was also ascertained.

Details regarding the household surveys are presented below:

	Branquinhas City	Usino Campo Verde	Fazenda Churega
No. of households	340	64	19
No. of houses in sample	114	32	19
Vacant households	4	1	1
Interviews not completed	9	3	0
No. of interviews completed	101	28	18
Households not eligible* for vaccination in March	15	1	0
No. of households eligible for vaccination in March	86	27	18

* These persons and/or households not living in Branquinhas in March at the time of the campaign and infants less than three months of age at the time of the campaign were considered "not eligible" for vaccination.

As shown below, only 49% of those resident in Branquinhas City in March were vaccinated by the vaccination team. A better although still unsatisfactory coverage was noted in Usino Campo Verde, while in Fazenda Churega, none had been vaccinated.

	No. of eligible persons in survey	No. vaccinated in March	%	95% confidence limits
Branquinhas City	379	184	48.6	42-55%
Usino Campo Verde	166	124	74.7	65-84%
Fazenda Churega	95	0	0.0	-

In Branquinhas City, only 26% of the pre-school age-group had been vaccinated, a figure significantly below the overall coverage of 49%. As expected, the school age population was the best vaccinated group.

Age-group (years)	No. of persons		Per cent. vaccinated
	Total	Vaccinated	
3 months - 4	54	14	25.9
5-14	120	78	65.0
15-29	101	48	47.5
30 and over	104	44	42.3
TOTAL	379	184	48.6

A better coverage was obtained in Usino Campo Verde where 75% of the population was vaccinated. There was less variation in the coverage of the different age-groups when compared to Branquinhas.

Age-group (years)	No. of persons		Per cent. vaccinated
	Total	Vaccinated	
3 months - 4	30	23	76.7
5-14	61	52	85.2
15-29	40	28	70.0
30 and over	35	21	60.0
TOTAL	166	124	74.7

As in Branquinhas city, the captive school-age population was the best vaccinated group.

In Fazenda Churega, as previously noted, none had been vaccinated in March. In fact, the vaccination teams did not visit this fazenda. The 95 persons on this fazenda were vaccinated during the epidemic investigation. Half of the vaccines were primary vaccines; among those under five years, 84% received primary vaccination.

Age-group (years)	Number of vaccinations			Per cent. primary vaccination
	Primary	Revaccination	Total	
0-4	21	4	25	84.0
5-14	26	12	38	68.4
15-29	7	6	13	53.8
30 and over	4	15	19	21.0
TOTAL	58	37	95	50.5

From the survey results in Branquinhas City, the total population by age group was estimated and attack rates computed as shown below.

SMALLPOX ATTACK RATES FOR BRANQUINHAS CITY

Age-group	Population		Cases	Attack rates (%)
	Survey	Total*		
<1	15	50	6	12.0
1-4	55	184	8	4.3
5-14	125	418	14	3.3
15-29	120	402	10	2.5
30 and over	116	388	1	0.3
Unknown	17	57	-	-
TOTAL	448	1 499	39	2.6

* Estimated from: survey results x_1 (3.346) = Total X_1

The high attack rate in children under one year of age is notable. Of the six cases under one year of age, three were under eight months of age, including the only death, a seven-month old, who was not yet three months of age in March at the time of the campaign and was not considered eligible for vaccination. The other two, one-month old and a two-month old, were born since the campaign in March.

Discussion

This investigation demonstrates the problems that can occur in a smallpox eradication programme without independent concurrent assessment. Although the vaccination teams reported 100% of the population vaccinated, in reality only half were vaccinated.

From discussions with those concerned with the programme and with local authorities, it was apparent that the team responsible for vaccination in Branquinhas was poorly surpervised and almost certainly falsified the records. The team was discharged.

Since this outbreak evaluation teams have been trained and added to the staff in all state-wide systematic vaccination programmes in Brazil.[1] This system of independent assessment not only determines vaccination coverage but also vaccination take rates as a continuing measure of vaccine potency and vaccination technique in the field.

The only death in this outbreak occurred in a seven month old child. Although the case fatality rate for variola minor ranges between 1 and 3% in Brazil, case fatality rates among those under one year of age are usually much higher. During 1967, the case fatality rate in Sao Paulo City was 11.4% for the 44 cases under one year of age as compared to 0.5% for the 607 cases one year of age or older.[2] Similar results have been observed during the past 10 years both in Sao Paulo City and Sao Paulo State.

Reporting Unit	10 year period	Case fatality rate (%)	
		Under 1 year	1 year and over
Sao Paulo - Capital[2]	1958-1967	8.5	0.6
Sao Paulo - Interior[3]	1957-1966	6.5	0.9

In Branquinhas City, the unusually high attack rate of 12% in children under one year of age is to be particularly noted since it was the policy of the smallpox eradication programme in Brazil, as well as in some other countries, not to vaccinate infants less than three months of age. However, due to the high risk of contracting smallpox and the higher case of fatality rate under one year of age, children from the time of birth should be eligible for vaccination in endemic areas. The use of smallpox vaccine from the time of birth has been shown to be both safe and effective.[4,5]

It should also be noted that the attack rate in persons 30 years of age and older was only 0.3%. During 1968 in Brazil, among 2181 cases for which data are available, only 11% were over the age of 30.[6] This undoubtedly can be attributed to a higher level of immunity in older persons. For example, in Fazenda Churega, 79% of those 30 years of age or older had been vaccinated at least once in their lifetime compared to only 29% of those less than 30 years of age. It appears therefore that particular emphasis in the programme should be directed toward vaccinating those younger than 30 years of age.

The importance of the population centres as foci for transmission of smallpox has been repeatedly noted. Such was the case in this outbreak. Smallpox occurred in the rural areas and in Fazenda Churega long after the outbreak had been well established in Branquinhas City. If Branquinhas had been well vaccinated, neither of these areas would have been afflicted. An identical situation occurred in the Municipio of Luziania, Goias, earlier in 1967.[7] Smallpox occurred first in the city of Luziania and subsequently spread to a nearby fazenda. If Luziania had been well vaccinated, once again, there would have been no focus of infection where these persons could have become infected.

ANNEX

For the survey of vaccination coverage, it was decided to select a sample of households in each of the areas for study. In assessing the vaccination coverage by age-group in given geographic areas, it was desired that the estimate of vaccination coverage should be correct within $\pm$10% with a 95% probability of accuracy in any given age-group. Four age-groups were defined for study purposes: 0-4, 5-14, 15-29, and 30 years and older. The 0-4 age-group was employed as an index group for calculation of the sample size as this group necessarily included the smallest number of individuals. An adequate sample in this age-group ensured an adequate sample in the older age-groups. The vaccination coverage of the population was expected to be anywhere from some percentage (p) less than 50% to 100%. Since the product of p and q (i.e. 1 - p) increases as p moves towards 0.5, a conservative estimate of the number required in the sample is obtained by choosing for p the value nearest to 0.5 in the range in which p is thought likely to lie. Therefore, p = 0.50 was utilized in the calculation of sample size. For Branquinhas, this was calculated as follows:

$$n = \frac{t^2 pq}{d^2}$$

where p = 0.50
q = 0.50
d = 0.10, the margin of error
t = 1.96, the value for d < 0.10 at the 95% confidence level

$$n = \frac{3.84\ (0.50)\ (0.50)}{0.0100} = \frac{0.96}{0.01} = 96$$

To compensate for the increase in variation resulting from within family correlation, the sample size calculated was multiplied by a cluster coefficient.[8,9] Serfling has estimated this cluster coefficient for smallpox immunization in children under five years of age to be 1.85 which would give a sample size of 178.[10] In addition, a vacancy and/or not at home rate of about 12% had to be taken into account. Thus another 22 children were added to the sample to make the sample size an even 200.

In developing areas, approximately 20% of the population is under five years of age. In an average household size is five persons per household, one can expect one child under five in every household. With these assumptions, the number of children under five and the number of household is synonymous. Therefore, to obtain 200 children under five, a sample of 200 is required

However, the sample size can be reduced by means of a finite population correction (fpc) if the sample size (n) is large relative to the total group to be sampled (N). In Branquinhas, N = 350 (estimated number of households in the city) and the necessary sample size may be reduced as follows:

$$fpc = \frac{N}{1 + n/N} = \frac{200}{1 + 200/350} = \frac{200}{1.571} = 127$$

To sample 127 households, one-third of the 350 houses in Branquinhas were visited, utili- a random number between one and three to begin the survey (in other words, a systematic sample with a random start).

The same type of calculations were employed for Usino Campo Verde where there were an estimated 60 households:

$$fpc = \frac{200}{1 + 200/60} = \frac{200}{4.333} = 46$$

In this area, more than two-thirds of the total households needed to be sampled, but due to logistical considerations, one-half of the households, or every other household, were sampled with a random start. In effect the acceptable margin of error (d) was increased from $\pm$ 10% to $\pm$ 12% if, in fact, p was equal to 0.5.

Annex

On Fazenda Churega there were 20 households and here all households were visited.

Confidence limits for the survey results were calculated in accordance with the method described by Cochran.[11]

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FIG. 1. SMALLPOX CASES BY WEEK OF ONSET - BRANQUINHAS OUTBREAK, BRAZIL 1967