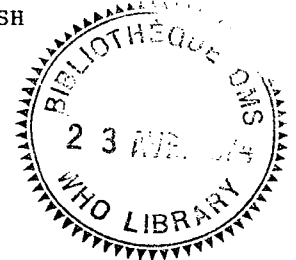




THE 1972 SMALLPOX OUTBREAK IN KHULNA MUNICIPALITY, BANGLADESH
II. EFFECTIVENESS OF SURVEILLANCE AND CONTAINMENT
IN URBAN EPIDEMIC CONTROL¹

by

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SUMMARY

Between 28 April and 22 June 1972, 1 384 smallpox cases and 372 deaths were detected in Khulna Municipality, Bangladesh. Within three weeks of instituting surveillance and containment activities the entire city-wide epidemic was under control. Active surveillance detected over 84% of all new cases, as estimated by dividing the number of cemetery registered "pox" burials by the observed case fatality rate. Ninety per cent of family contacts of detected cases were vaccinated in the course of three home visits. Only 75% were vaccinated at the time of the first visit but intrafamilial transmission essentially ceased at that time. The secondary attack rate among families first visited within one week of onset of their index case was 1.2%, compared with 22.2% for those first visited after five or more weeks had elapsed. Few if any individuals vaccinated as late as five days into their incubation period developed clinical disease. Vaccination performed after that time still reduced the clinical attack rate, on the average, by 50%. These results suggest that selective epidemiologic control can be highly effective in aborting intense smallpox epidemics, and that the search of cemetery burial registers is a useful means of reconstructing the actual course of an epidemic and determining the thoroughness of case detection.

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INTRODUCTION

Much of the success of the World Health Organization's smallpox eradication programme⁽¹⁾ has been attributed to three technical innovations: widespread availability of lyophilized vaccine, introduction of the bifurcated needle, and substitution of surveillance and containment for simple mass vaccination. Of these, the last has been credited with being the most important⁽²⁾.

Since before the time of Jenner, perhaps as long as 1000 years ago⁽³⁾, inoculation with live virus, at first variola but later vaccinia, has been an effective prophylactic measure against smallpox. The technique of mass vaccination extended this protection to large segments of the population, but its effectiveness in eradicating the disease, especially in underdeveloped countries, proved disappointing. Most programmes, no matter how well executed, rarely attained vaccination rates of more than 80 per cent, leaving behind relatively large concentrations of transient slum dwellers capable of propagating the disease (2, 4-6).

Because of similar experiences and the logistical problem of achieving even modest levels of protection, Dixon⁽³⁾ despaired of eradication through mass vaccination and instead proposed concentrating on foci of infection. This evolved, in the course of the highly successful West African Programme, into active "surveillance and containment", with intensification of activities during seasonal lulls when transmission was naturally decreased and the number of foci smaller⁽⁷⁾. By concentrating on case detection, outbreak investigation, and vaccination of contacts, smallpox was eradicated without achieving a high level of immunity in the population^(7,8).

With the tenacious hold that smallpox appears to have on the Indian subcontinent, the locus of over 90% of the world's cases⁽⁹⁾, a detailed assessment of the surveillance and containment procedure and its value in controlling explosive urban epidemics might prove useful in adapting it to differing local conditions. The opportunity for such an assessment was provided by the recent outbreak of smallpox in Khulna, Bangladesh. The background, history, and epidemiologic features of this outbreak are described in part I of this report⁽¹⁰⁾ and elsewhere⁽¹¹⁾.

MATERIALS AND METHODS

Although the municipal health staff included almost 100 multi-purpose workers who were involved at least part of the time in smallpox control, preliminary investigations revealed large numbers of unreported cases as well as poor vaccination coverage of family contacts in "contained" outbreaks. Therefore, beginning in late April, all smallpox activities within the municipality were centralized under a single Sanitary Inspector who was designated overall "coordinator". Eight four-man teams, also drawn from existing municipal health personnel, were trained in surveillance and containment techniques. Assisted by a sanitary inspector from the central Smallpox Eradication Programme in Dacca, the coordinator made daily visits to the Infectious Disease Hospital and the city's bazaars in search of cases. He delivered teams to the homes of these cases where they compiled a census of each affected family and attempted to vaccinate all members of the family and compound (the cluster of patrilineally related houses opening on a common courtyard) or bustee (urban slum). They then conducted a house by house search of the adjacent compounds or bustees, and any family with a history of either a smallpox case or death since independence was treated in the same manner as the index family. An attempt was made to revisit all infected families at least two more times: one to two days after the initial visit and again three weeks later, in order to vaccinate individuals missed during the previous visits and to record any subsequent cases.

The teams assembled at the end of each day to review their progress and plan the next day's activities. Spot checks on their work were carried out by the two sanitary inspectors.

Three vaccinators were also placed on duty at the Infectious Disease Hospital to vaccinate all individuals (patients, visitors, staff) who entered the premises. Their rotations were staggered to ensure coverage from dawn to midnight, seven days a week. The adequacy of their work was checked by the coordinator on his daily visits.

Vaccinations were all done with sterile bifurcated needles according to accepted procedure, and only lyophilized vaccine meeting WHO standards of potency was used.

RESULTS

Figure 1 depicts the epidemic curve for the municipality at large, divided into its three component sectors. Because of limited manpower, each sector was attended to in turn, beginning with the area with the most cases. Although data to be presented later suggest that these are only rough approximations of the actual epidemic, especially during the pre-surveillance period, they serve as useful indices of the course of events.

In each of the three sectors of the city, as well as the non-Bengali refugee camp (figure 2), there was a striking temporal relationship between the onset of control activities and the decline in the number of new cases. The one-week lag approximates the period required for completion of initial visits, as well as the minimal interval, as will be shown, for development of significant protection following vaccination. In addition, the point of the interruption in the epidemic was different for each. The middle sector of the city was not reached until its curve had plateaued for some weeks, suggesting this might be the "natural" course of a neighbourhood outbreak. The first and last areas were reached much earlier - the former after the epidemic had peaked and been at plateau for one week and the latter before any plateau had occurred; yet the results were the same for each.

The success of surveillance and containment depends upon the thoroughness of case detection and vaccination of contacts as well as the speed of onset of protection following vaccination. Each of these aspects of the programme will be examined separately.

CASE DETECTION

In the period from 16 December 1971 (Independence) to 27 April 1972, a total of 77 cases were officially reported by the municipal health authorities, none of them in April. Surveillance and containment activities began on 28 April. Within nine days a total of 702 cases were uncovered, 80 per cent of them active. The detected numbers of active, fatal, and healed cases declined with each successive week. By 22 June a total of 1 384 cases had been enumerated: 1 117 in the municipality at large and 267 in the Kalishpur Bihari camp.

In order to document the true scope of the epidemic and to verify the completeness of case detection, a search was made of local cemetery burial registers, and all burials reportedly due to "pox" were noted. The "expected" number of cases was then estimated by dividing the number of such burials by the age-specific case fatality ratios for the town at large(10).

Burial data were most complete for the refugee camp: all burials took place in a single nearby cemetery, and a separate register was maintained by camp attendants. One hundred fifty-five such deaths were uncovered, representing an estimated 399 cases (table 1).

By comparison, surveillance detected only 267 cases, two-thirds of the estimated total. Since this large public cemetery served the whole northern sector of the city, it is conceivable that some of the persons listed in the camp burial register had not actually been inhabitants of the camp. Table 2 indicates this is unlikely to have been the case. The age distributions of the estimated and detected cases in the camp are almost identical, and quite different from cases detected in the municipality.

Kalishpur cemetery burials and detected cases by week of occurrence (figure 2) indicate that after onset of surveillance activities, early in week 18, burials lagged an expected two to three weeks⁽¹⁰⁾ behind the peak of detected cases. However, before that period, deaths actually outnumbered recorded cases. At the age-adjusted case fatality rate of 38.8 per 100, these 49 burials represent an estimated 126 cases. Since only four cases that might have contributed to these deaths were detected during the period, these "missed" cases would account for almost 75 per cent (122/166) of the discrepancy between the detected and expected numbers (table 2). This suggests that almost the entire discrepancy was due to undetected cases that occurred at least two weeks before the onset of surveillance activities. Roughly 84 per cent (229/273) of all cases with onset after that time were detected.

The situation in the municipality at large was more complex. In addition to two large public cemeteries which maintain burial registers, there are numerous small "unauthorized" ones that do not. Figure 3 presents detected cases and burial-registered deaths by week of occurrence. The onset of the epidemic and control activities occurred in different parts of the city at different times⁽¹⁰⁾. Unfortunately, the burial registered deaths were not identified by neighbourhood or origin, obscuring in part the relationship between onset of surveillance and completeness of case detection. Even so, for the period following initiation of surveillance activities in the city, late in week 17, the two curves are strikingly similar, with the burial curve lagging an expected two weeks behind detected cases. In contrast, during the pre-surveillance period there were large numbers of deaths in the absence of expected numbers of retrospectively detected cases. If we assume this same pattern was true of the unauthorized cemeteries, then once again case detection was far more effective for new than old cases, and the actual size of the epidemic was far larger than here reported.

The existence of unauthorized cemeteries makes accurate assessment of actual case detection rates less certain. In addition to the 438 registered burials, an additional 239 smallpox burials were located by questioning attendants at nine unauthorized cemeteries. One hundred thirteen of these smallpox victims could be traced and their ages were ascertained. Assuming all 239 had an age distribution similar to that of the 113, there were at least 677 smallpox burials in Khulna between weeks 1 and 21 (when the registers were reviewed) which represent an estimated 1923 cases. Eight hundred twenty cases were actually detected during the period, or approximately 43 per cent of the estimated total. Retrospective case detection uncovered only 31 per cent (264/866) of the estimated number of cases which occurred during the pre-surveillance period; however, once surveillance had begun in at least one sector of the city, 53 per cent (556/1057) of the expected number of cases were detected. If retrospective and prospective detection rates could be calculated for each sector of the city separately, the proportion of new cases detected prospectively would undoubtedly be much higher.

VACCINATION COVERAGE

Excluding active cases, the containment teams failed to vaccinate 10 per cent of the members of infected Khulna families, even with three visits to their homes. Age specific "missed" rates ranged from a low of 1 per cent for those under the age of three years to a high of 13 per cent for those 15 years and over. The rates did not vary with prior vaccination status.

Ninety-eight per cent of all persons missed were five years or older, and almost half were adult males. Questioning of their relatives revealed that 51 per cent had been vaccinated in the past, 21 per cent had not, and 28 per cent were of unknown status.

Of all persons vaccinated, 83 per cent were vaccinated at the first visit and an additional 13 per cent at the second visit. Only 4 per cent of all vaccinations (and only 2 per cent of all primaries) were given at the third visit. Refusals accounted for less than 5 per cent of missed individuals. Most simply were not at home.

A different approach was taken in the "non-Bengali" refugee camp. Because of the intense crowding and the persistent rumor of impending closure of the camp and dispersion of its inhabitants, mass vaccination was added to ongoing surveillance and containment. Three approaches were tried: tent by tent visitation, vaccination at a central station without coercion, and mandatory vaccination before receipt of relief supplies. The last method was at least four times more effective than the others. The number of vaccinations performed in a single eight-hour day by eight-man teams were 1174, 526 and 4075, respectively. After two days a Pedojet was procured. In two weeks, 31 000 vaccinations (representing at least 75 per cent of the estimated maximum population of the camp at any time) were given.

EFFECT OF INTERVENTION ON THE FAMILY OUTBREAK

Two basic assumptions underlie our containment technique: family contacts are at the greatest risk of infection, and their vaccination, after onset of the family's index case, can still protect them from developing clinical disease. If correct, families first visited (and vaccinated) soon after onset of their primary case should have had a lower attack rate than those visited later. Table 3 indicates that this indeed was the case.

To ensure that each family had completed its outbreak, calculations were based only on families to which our last visit was at least five weeks after onset of a majority of the cases and not less than four weeks after the onset of the most recent case. The secondary attack rate is defined as all cases occurring seven or more days after onset of the index case. Although "true" secondary cases, resulting from household exposure, should not appear until the end of the second week, we wanted to determine whether protection occurred even before that time, among those persons with coprimary (extra-household-acquired) infections.

There was a steady rise in attack rates with elapsed time. Families visited within two weeks after onset of their initial case had a subsequent attack rate of only 1.9 per 100, compared with 37.5 per 100 for those first visited after nine or more weeks had elapsed. The extraordinary rate in the latter group was the result of late reintroductions (cases occurring at least six weeks after any preceding family case) in five of 15 of these families. If these late reintroductions are removed, this group's rate falls to 19 per 100, about the same as in families with intervention between weeks 5 and 8. Since over 90 per cent of all cases in infected families occur within five weeks of onset of rash in the index case (10), this is not surprising.

Of particular interest is the very low attack rate among families visited within one week after onset of their index case. Even if vaccination prevented all subsequent intrafamily transmission, some individuals, already incubating the disease, might still be expected to become ill. Since others have shown that the mean incubation period (from exposure to onset of rash) is 14 days (12), this would include, at a minimum, all cases expected in the second week. With an "uninfluenced" overall attack rate in

infected families of 35.8 per 100, and 9 per cent of all cases having their onset in the second week (10), this amounts to at least 3.2 additional cases per 100 individuals. The attack rate among those visited within the first week, however, was only 1.2 per 100, or one-third the minimum expected ($p < .025$). This suggests that vaccination well into the incubation period was effective. If we assume that vaccination took place on the average in the middle of the first week (it was probably somewhat later) and that all the cases "expected" in the second week occurred in the middle of that week, then there was a mean interval between vaccination and expected onset of rash of seven days. With a mean incubation period of 14 days, vaccination administered on the average seven days into the incubation period appears to have reduced the clinical attack rate by at least two-thirds. For those vaccinated during the second week the attack rate was only 2.2 per 100, and while this is not a statistically significant difference from 3.2 per 100, it suggests that vaccination administered even later in the incubation period might still have a limited effect.

SUBSEQUENT ATTACK RATES AMONG VACCINATED AND "MISSED" INDIVIDUALS

A comparison of attack rates of individuals vaccinated and not vaccinated during the team's first two visits to their homes further confirms the effectiveness of vaccination among family contacts. These data are presented in table 4 for the three-week period between the second and third visits. Although 63 per cent of all cases within this period occurred among individuals vaccinated by the teams, their attack rate was only one-fourth that of those who were not vaccinated ($p < .0001$). This difference persists in comparisons of all age-specific and "previous vaccine status" specific attack rates although it is greatest among preschool children.

The time of onset of rash among the cases in both groups (table 5) provides another estimate of the effectiveness of vaccination administered during the incubation period. Day 1 is the day of vaccination in those vaccinated (over 90 per cent on visit 1, the rest approximately one to two days later at the second visit) and the day of the initial home visit in those not vaccinated. The difference is striking. Except for a single individual, all disease among the vaccinated group occurred within nine days of vaccination. Among the unvaccinated group, less than half the cases occurred within this period.

Since the longest interval between vaccination and onset of rash was nine days, and the average incubation period is 14 days (12), vaccination as late as five days into the incubation period appears to have been highly, if not completely effective in preventing clinical disease. It also appears that vaccination after that time was still moderately effective. Unfortunately, the appropriate denominator for making such a comparison, the number of individuals five or more days into their incubation period at the time of the first home visit, is lacking. If, however, we assume that the distribution of incubation periods was similar among those who were and were not vaccinated, the populations of vaccinated and unvaccinated individuals can serve as reasonable denominators for calculating relative attack rates. Although the numbers are small, cumulative attack rates (table 5) suggest a definite trend, with onset of protection between seven and nine days following vaccination (five to seven days into the incubation period). The 14 vaccinated cases with onset of rash between zero and nine days after vaccination represent an attack rate of 7.9 per 1000 (14/1772). By contrast, the four missed cases with onset of rash during this same period represent an attack rate of 14.4 per 1000 (4/277). Thus, vaccination performed five or more days into the incubation period may have reduced the clinical case rate by about one-half ($p < .01$).

DISCUSSION

"Surveillance and containment" proved effective in the West African smallpox eradication programmes. Our experience in Khulna now suggests it can be equally effective in controlling intense urban epidemics in Asia.

The Khulna epidemic was brought rapidly under control through selective immunization of high risk groups: family and compound contacts of infected cases, residents and visitors to the Infectious Disease Hospital^(13,14), and inhabitants of refugee camps. Mass vaccination was not undertaken in the municipality during this period, and we can assume the general level of immunity in the population remained essentially the same.

The diagnosis of fatal cases is relatively easy, especially during an epidemic, even for minimally educated cemetery workers. Since age and vaccination-specific case fatality ratios vary little from one area to another^(14,15), burial registers are a useful means of reconstructing the course of an outbreak and determining the thoroughness of case detection. Centralization of smallpox activities under a single individual and establishment of well-trained teams whose sole function was smallpox control resulted in a tremendous increase in case finding⁽⁴⁾, although it was never complete.

Slum inhabitants, who contributed the overwhelming number of cases, are notoriously difficult to trace and vaccinate^(4,14). In this study, 10 per cent of family contacts escaped vaccination, even with three home visits. Fortunately, their omission seems to have made little difference: intra family transmission essentially ceased after the first home visit. The speed with which the epidemic was brought under control was therefore limited only by the number of available workers (rate of coverage of infected families and their immediate compounds) and the delay between inoculation and onset of protection.

Vaccination administered as late as five to seven days into the incubation period was found to be highly effective in preventing onset of clinical disease. Vaccination after that time still seems to reduce the clinical attack rate by roughly one-half, although this reduction undoubtedly decreases the later vaccination is performed. Ricketts and his contemporaries observed exactly the same results over half a century ago⁽³⁾.

Mack et al.⁽¹⁶⁾ found that surveillance, as practiced in rural West Pakistan, identified outbreaks relatively late in their course, and therefore suggested ignoring family contacts and concentrating instead on adjacent households and compounds. Our data suggest that in a large urban epidemic active surveillance can locate infected families early in the course of their outbreak, and intervention as late as the third week can have a dramatic effect on their attack rate. When the epidemic is as intense as in Khulna and late reintroductions are common, intervention might still be effective as late as the fifth to seventh week of a family's outbreak. However, since over 60 per cent of all cases were the result of extra-household exposure⁽¹⁰⁾, vaccination of compound and bustee contacts remains of equal or greater importance.

Despite the close temporal relationship between the onset of control activities and the decline in the number of new cases in the three different areas of the city and in the refugee camp, the response was more rapid and dramatic than we would have anticipated, even with our own relatively favorable post-exposure vaccination efficacy data. While intriguing, it suggests other factors might have been operating, most probably a natural waning of the epidemic.

As we discovered in Khulna⁽¹⁰⁾ and has been reported by others^(14,17), municipalities are important foci in propagating smallpox and are frequently responsible for its periodic reintroduction into the countryside. Urban surveillance and containment must therefore

be retained as control activities move into the countryside. Failure to appreciate this principle resulted in the resurgence of the epidemic in Khulna⁽¹¹⁾.

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TABLE 1

Cemetery burials and estimation of actual number of cases, Kalishpur Bihari Camp, January-June, 1972

Age (years)	Burials	Case/ Fatality*	Estimated No.** of cases
0-2	54	55.1	98
3-4	47	46.3	102
5-14	47	28.6	164
≥ 15	7	19.8	35
All ages	155	(38.8) [‡]	399

* From reference 10

** Number of burials/case fatality

[‡] 155/399 or 38.8%. This differs from the overall municipality rate (33.1%) because of a difference in age distribution of cases.

TABLE 2

Age distribution of estimated and detected cases, in Kalishpur, and detected cases in Khulna Municipality, January-June, 1972

Age (years)	Kalishpur Cases				Khulna Cases	
	Estimated		Detected*		Detected**	
	No.	%	No.	%	No.	%
0-2	98	24.6	68	29.2	197	18.4
3-4	102	25.5	52	22.3	178	16.6
5-14	164	41.1	99	42.3	407	37.9
≥ 15	35	8.8	14	6.0	291	27.1
All ages	399	100.0	233	99.8	1073	100.0

* 34 cases lacking age data are omitted.

** 44 cases lacking age data are omitted.

TABLE 3
Secondary* attack rate by week of intervention in
family epidemic, Khulna Municipality

Week of intervention ⁺ after onset on index case	Cases	Rate/100	Combined ⁺ rate †
1	2	1.2	1.9
2	11	2.2	
3	42	10.0	12.0
4	31	16.4	
5	57	21.3	19.8
6	11	14.4	
7	15	27.3	26.0
8	11	24.4	
9	17	41.5	37.5
≥ 10	13	33.3	

* All cases occurring within one week of onset of rash in the first family case are omitted from both cases and contacts.

+ Onset of rash in first family member is taken as day 1, week 1.

† Differences which are statistically significant: 1-2:3-4 $p < .0001$; 3-4:5-6 $p < .002$; 5-6:7 ≥ 10, $p < .005$. (When "corrected" this difference disappears).

TABLE 4
Subsequent attack rate* among individuals vaccinated
and not vaccinated by containment teams on first
two visits

Previous Vaccination Status	Vaccinated by team			Not vaccinated by team		
	Contacts	Cases	Rate/ 1000	Contacts	Cases	Rate/ 1000
Vaccinated	1276	3	2.4	152	2	13.2
Unvaccinated	414	10	24.2	54	5	92.6
Unknown	82	2	24.4	71	2	28.2
Total	1772	15	8.5	277	9	32.5

* During the 3-week interval between the second and third home visits.

TABLE 5
Family members with onset of rash following
containment

Day* of onset	Vaccinated		Unvaccinated	
	No.	Cumulative rate/100	No.	Cumulative rate/100
2	3	1.7	1	3.6
4	2	2.8		3.6
6	6	6.2	1	7.2
8	3	7.9	2	10.8
10		7.9	2	21.7
12		7.9	1	25.3
≥ 16	1	8.5	2	32.5
Total	15	8.5	9	32.5

* Among individuals who were vaccinated, day 1 is the time of vaccination either at the first household visit (>90% of the subsequent cases) or 1-2 days later at the second. Among individuals who were not vaccinated, Day 1 is the time of the first household visit.

Figure 1: Week of onset of smallpox cases in the three sectors comprising Khulna municipality (excludes refugee camp). Week 1 began on 2 January 1972. The arrows indicate initiation of surveillance and control in each of the sectors.

Figure 2: Cemetery burials and onset of smallpox cases, by week, Kalishpur refugee camp. Week 1 began on 2 January 1972. The arrow indicates initiation of surveillance and containment and mass vaccination in the camp. Burial registers reviewed during calendar week 21.

Figure 3: Cemetery burials and onset of smallpox cases, by week, Khulna Municipality (excludes refugee camp). Week 1 began on 2 January 1972. The arrow indicates initiation of surveillance and containment in the municipality. Burial registers reviewed during calendar week 21.

Fig. 1 CASES OF SMALLPOX, BY WEEK OF ONSET, KHULNA MUNICIPALITY

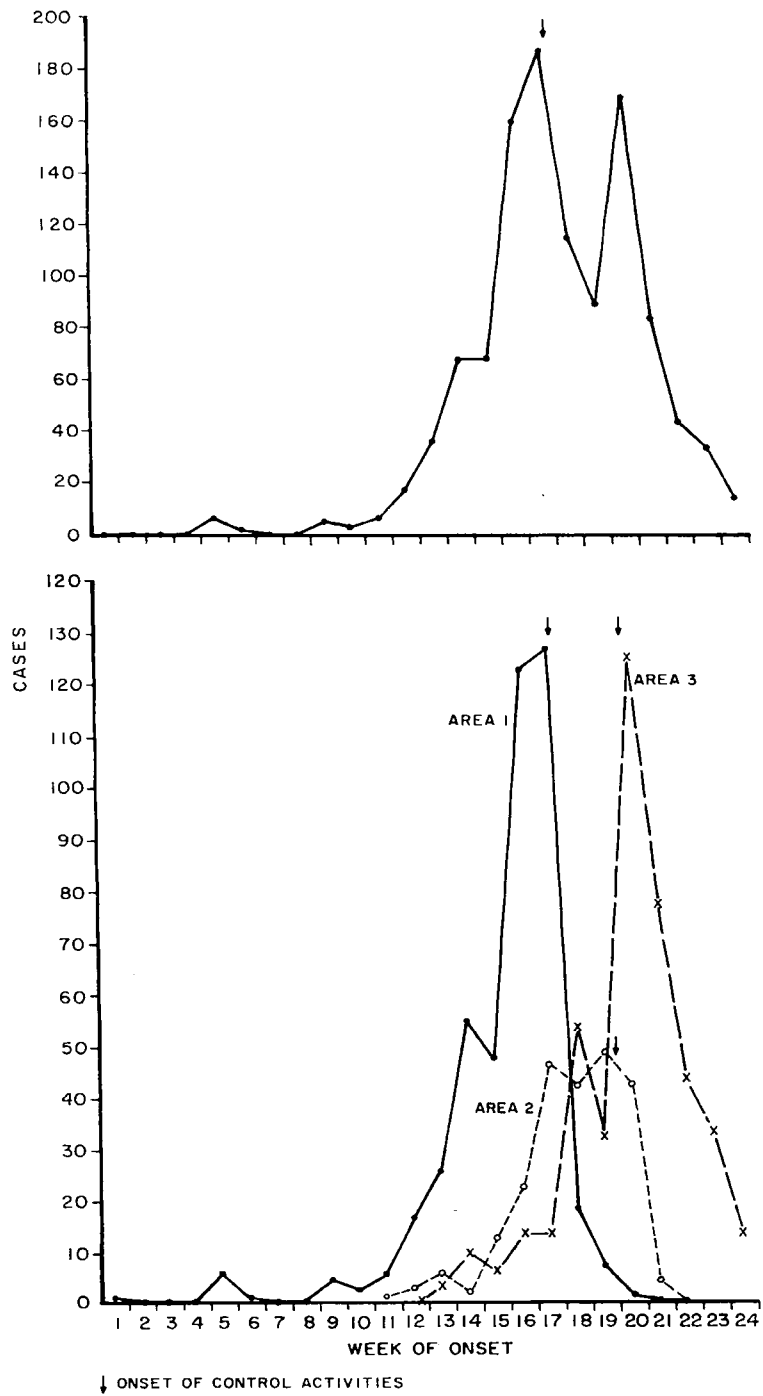


Fig. 2 CASES OF SMALLPOX AND CEMETARY BURIALS, KALISHPUR BIHARI CAMP

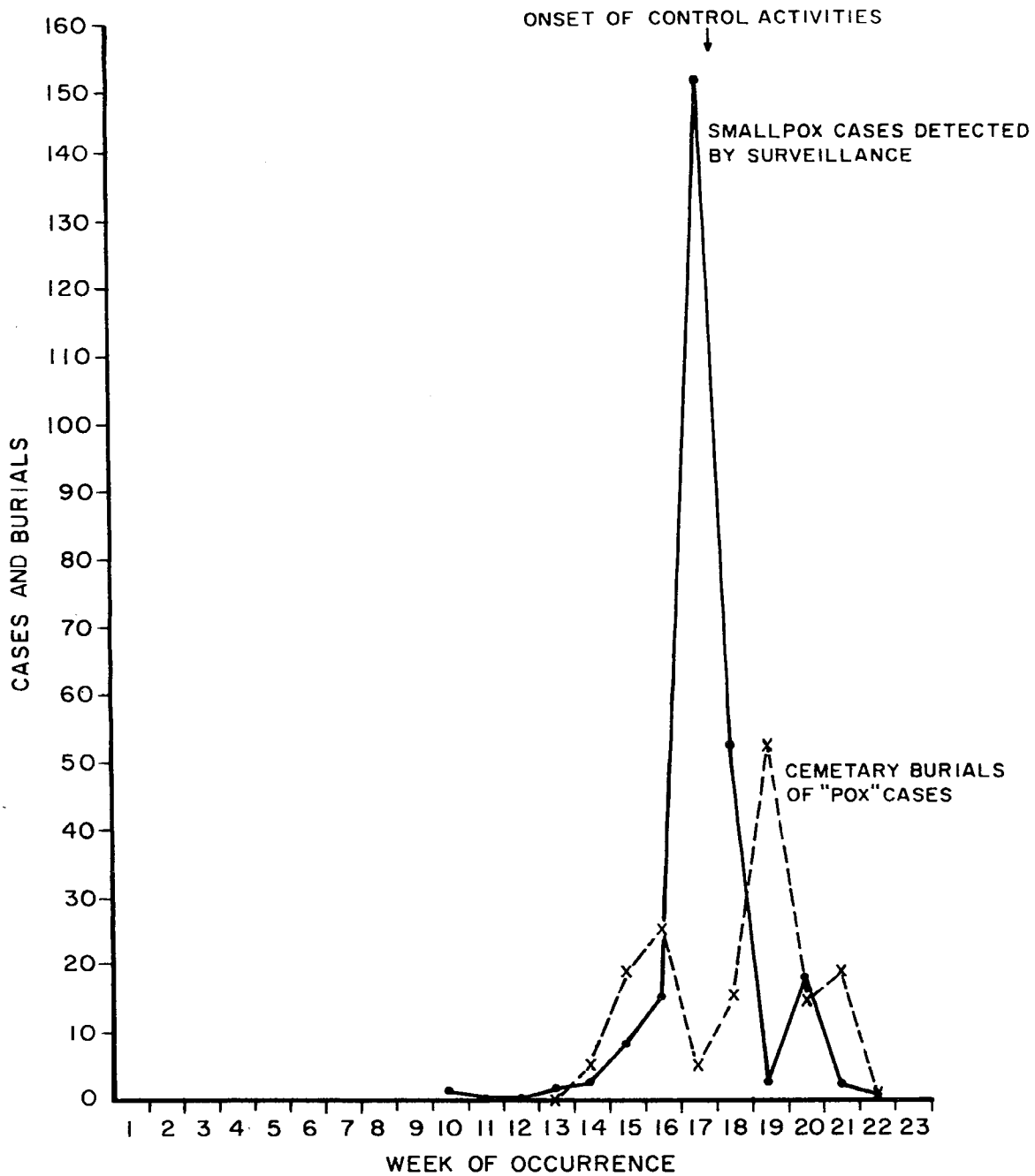


Fig. 3 CASES OF SMALLPOX AND CEMETARY BURIALS, KHULNA MUNICIPALITY

