

Cholera Incidence in a Population Offered Cholera Vaccination: Comparison of Cooperative and Uncooperative Groups*

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From May 1964 to December 1965, a controlled field trial of the effectiveness of cholera and cholera El Tor vaccines was conducted in Negros Occidental, Philippines. Some people did not volunteer for vaccination, and of those who did some received cholera vaccine and others a control (typhoid) vaccine. After analysing the incidence of cholera among these three groups it was found that the morbidity and mortality rates were significantly higher in the unvaccinated group than in either the control vaccine group or the cholera vaccine group. This would indicate that the unvaccinated group is basically different from the vaccinated control group. The clinical course of the disease was the same whether the patient had been vaccinated or not. The reasons for non-vaccination were investigated and should be taken into account by public health agencies when immunization programmes are being planned.

Earlier field studies of enteric vaccines (Cvjetanović, 1961; Yugoslav Typhoid Commission, 1964) have demonstrated that volunteers who accept vaccination have lower attack rates than people who are uncooperative and do not volunteer. In view of the public health importance of this finding we wanted to find out whether the volunteers in anti-cholera vaccination campaigns also differed from those who did not volunteer.

From May 1964 to December 1965 a controlled field trial of the effectiveness of cholera and cholera El Tor vaccines was conducted by the Joint Philippines-Japan-WHO Cholera Committee in the Province of Negros Occidental, Philippines (Azurin et al., 1967).

The study area included 24 towns and cities, and during the controlled trial three kinds of cholera vaccine and one control vaccine were administered. The number of people given the control vaccine is shown in Table 1, together with the number in the unvaccinated group. The trial was designed and

Table 1. Age distribution of population in unvaccinated and control vaccine groups

Age group (years)	Unvaccinated group		Control vaccine group	
	No.	% of total	No.	% of total
<1	32 100	4.24	1 600	1.09
1-4	110 800	14.66	23 000	15.67
5-9	113 000	14.95	33 600	22.89
10-14	96 700	12.79	21 300	14.51
15-24	144 100	19.06	26 200	17.85
25-34	96 800	12.81	18 900	12.87
35-44	67 000	8.87	10 300	7.02
45-54	47 500	6.29	7 200	4.90
55-64	28 000	3.71	2 600	1.77
≥65	19 800	2.62	2 100	1.43
Total	755 800	100.00	146 800	100.00

* This study is part of the joint Philippines-Japan-WHO studies on cholera.

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carried out in accordance with the principles of strictly controlled field trials.

During the surveillance phase, which lasted 18 months (6 June 1964 to 5 December 1965), intensive case finding was conducted in the whole

trial area. All laboratory-confirmed cases, and when possible their contacts, were followed up whether the patients had been vaccinated or not. The results of the controlled field trials and incidence of cholera among the vaccinated and control groups have already been reported (Azurin et al., 1967).

In this paper the occurrence of cholera cases among the unvaccinated group in the trial area, and their clinical features, are analysed and compared with those of people who volunteered for vaccination: the causes of non-vaccination among the unvaccinated group were also investigated. This information may help in understanding the disease, in the planning of future vaccine trials, and in the implementation of mass vaccination campaigns by public health agencies.

The materials used and the methods followed have already been described (Azurin et al. 1967).

RESULTS

In the whole trial area, 1 388 symptomatic cases of cholera, confirmed as being caused by the El Tor vibrio, were detected in the unvaccinated group. Of these cases, 1 314 were followed up: 74 cases were not followed up because the patients lived in inaccessible places. For purposes of comparison, the results from 3 experimental groups are presented here: (1) the unvaccinated group, representing people who, for one reason or another, did not take part in the trial; (2) the control vaccine group who were given typhoid vaccine; (3) the cholera vaccine group. The latter group includes those people who received one of the three cholera vaccines used in the field trial. The patients in the unvaccinated group were asked to give reasons for their non-vaccination.

Morbidity

The surveillance teams found a total of 1 887 symptomatic cases during the 18-month period of case finding. The attack rates of the different groups are shown in Table 2. The lowest attack rate was for the vaccinated group and the highest rate occurred in the unvaccinated group: the group vaccinated with the control vaccine occupied a middle position.

These results show that volunteers (control group) tended to have a lower attack rate than those who did not volunteer (unvaccinated group) and that the reasons for this are not concerned with the immunity produced as a result of the administration of cholera vaccine.

Table 2. Cholera cases among the unvaccinated and vaccinated groups, 6 June 1964 to 5 December 1965

Group	Population	No. of cases	Case rate per 100 000
Unvaccinated group	755 800	1 388	184
Control vaccine group	146 800	171	116
Cholera vaccine group	437 200	328	75
Total	1 339 800	1 887	141

Mortality. The total number of deaths was 171 (Table 3). The highest death rate, in the unvaccinated group, was double the rate in the volunteering group that received the control vaccine.

Table 3. Cholera deaths among the unvaccinated and vaccinated groups, 6 June 1964 to 5 December 1965

Group	Population	No. of deaths	Death rate per 100 000
Unvaccinated group	755 800	132	17.5
Control vaccine group	146 800	13	8.9
Cholera vaccine group	437 200	26	5.9
Total	1 339 800	171	12.8

Case-fatality ratios

Table 4 shows the ratios between the numbers of deaths and the numbers of cases for each of the three

Table 4. Case-fatality rates in the unvaccinated and vaccinated groups, 6 June 1964 to 5 December 1965

Group	No. of cases	No. of deaths	Case-fatality ratio (%)
Unvaccinated group	1 388	132	9.5
Placebo group	171	13	7.6
Cholera vaccine group	328	26	7.9
Total	1 887	171	9.1

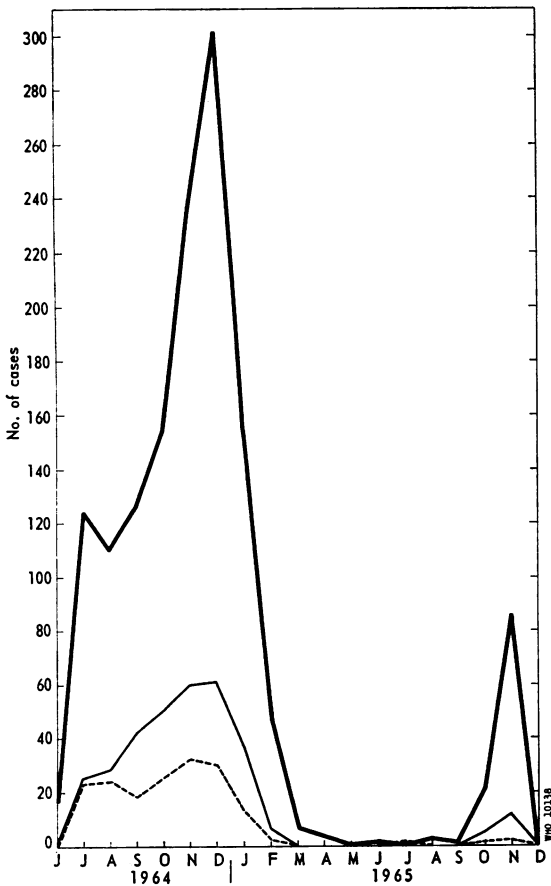


Fig. 1. Number of cholera cases in the vaccinated and unvaccinated groups from June 1964 to December 1965 (heavy solid line : unvaccinated ; light solid line : cholera vaccine ; dashed line : control vaccine).

groups. The rate for the unvaccinated group was slightly higher than that for either of the two groups of volunteers.

Epidemic curve

Fig. 1 shows the distribution of the 1 887 cholera cases by groups and by months of onset. While the number of cases in the unvaccinated group was much higher than that in the vaccinated group, the trends were distinctly the same, with peaks during November and December 1965.

Distribution of cases by age, sex, and socio-economic class

The percentage distribution of cases among the different age groups is shown in Table 5, and this

may be compared with the percentage distribution by age group of the persons in each experimental group. The table shows that the disease was particularly prevalent in the 1-4-year age group in all experimental groups and that there was a much lower prevalence between the ages of 5 and 25 years. Above the age of 25 years the disease was again more prevalent.

The sex distribution of cases was about even in all groups, whether vaccinated or not. The socio-economic characteristics of the unvaccinated and the vaccinated groups were also about equal.

Clinical characteristics of the disease

The duration of diarrhoea and the quantities of fluids administered parenterally were determined for 1 185 and 1 143, respectively, of the 1 256 surviving cases in the unvaccinated group and for all the surviving vaccinated cases. Clinical symptoms were also recorded for all cases whether they survived or not. No differences were found between the groups in any of these characteristics.

Carrier rates

Wherever possible the contacts of confirmed cases among the unvaccinated group were followed up and carrier rates were determined. Out of 1 884 unvaccinated contacts of the unvaccinated cases, 192 carriers were confirmed. This represents a carrier rate of 10.2%. The corresponding rates for the control vaccine group (38 carriers among 458 contacts investigated) and for the groups given cholera vaccines (73 carriers among 1 391 contacts investigated) are 8.3% and 5.2%, respectively.

Reasons for non-vaccination

During the interview with each patient with confirmed cholera an attempt was made to find out why persons in the unvaccinated group had not accepted vaccination during the campaign.

Apart from those who gave no reason, the largest group were those who claimed to have been vaccinated before (18.6%). About 18.4% simply refused vaccination without giving an excuse, while 16.3% were out at the time the vaccinating teams visited their homes, 10.5% were sick (most of these complained of fever and a few had diarrhoea at the time), and 5% were pregnant (pregnancy and any form of illness, particularly fever and diarrhoea, were considered to be contraindications to immunization in this vaccine trial). Only a small fraction

Table 5. Cholera cases by age in the unvaccinated and vaccinated groups, 6 June 1964 to 5 December 1965

Age-group (years)	Unvaccinated group			Control vaccine group			Cholera vaccine group		
	Percentage of total population	No. of cases	Percentage of total cases	Percentage of total population	No. of cases	Percentage of total cases	Percentage of total population	No. of cases	Percentage of total cases
<1	3.2	27	1.9	1.1	1	0.6	1.2	14	4.3
1-4	10.2	289	20.8	15.7	45	26.3	15.6	96	29.3
5-9	10.9	122	8.8	22.9	29	17.0	20.9	68	20.7
10-14	10.7	50	3.6	14.5	11	6.4	16.4	22	6.7
15-24	23.1	173	12.5	17.8	17	10.0	18.0	19	5.8
25-34	16.1	222	16.0	12.9	22	12.8	11.2	34	10.3
35-44	10.7	152	11.0	7.0	14	8.2	7.4	33	10.1
45-54	7.5	150	10.8	4.9	9	5.3	5.7	20	6.1
55-64	4.2	104	7.5	1.8	13	7.6	2.3	14	4.3
≥65	3.4	99	7.1	1.4	10	5.8	1.3	8	2.4
Total	100.0	1 388	100.0	100.0	171	100.0	100.0	328	100.0

(5.8%) said their areas of residence were not covered by the vaccinating teams. It is apparent from this analysis that most of these unvaccinated people could have been vaccinated if they had wished.

DISCUSSION

During the 18-month period following the immunization phase of the cholera vaccine field trial, surveillance showed that the attack rate in the group that had not volunteered for vaccination was almost 60% higher than in the volunteer group who received control vaccine. The mortality rates followed a similar pattern, the rate in the unvaccinated group being twice that in the control vaccine group.

This difference between the incidence of cholera in the uncooperative and cooperative groups is similar to that demonstrated earlier in studies with typhoid vaccine (Cvjetanović, 1961; Yugoslav Typhoid Commission, 1964). It was demonstrated that the people who did not volunteer for anti-typhoid immunization were also more exposed to other infections caused by poor sanitation (e.g., infectious hepatitis) and it is probable that those who did not take part in the anti-cholera vaccination were also more exposed to all other enteric infections owing to lack of personal hygiene. Apparently the uncooperative sections of the population have a

lower standard of hygiene and are less health conscious than those who readily accept vaccination. Volunteers for vaccination probably also take other measures to protect their health and thus are less likely to contract the disease than those who do not.

The reasons given by the patients who contracted cholera in the unvaccinated group for their non-vaccination should be of interest to both administrators and health educators. Those who simply refused vaccination and those who claimed to have been vaccinated before constituted more than one-third of the total cases. A sizeable percentage of those in the unvaccinated group who contracted cholera were out at the time the immunization teams called or had transient illnesses at the time. Absenteeism could be markedly reduced if the vaccination teams were to make repeat visits at suitable times. Furthermore, expanding the area covered by the teams would also help to reduce the percentage of persons not vaccinated.

Public health agencies should take into consideration the above reasons for non-vaccination when planning mass immunization campaigns, and as the uncooperative sections of the population are likely to have a higher rate of infection than those who volunteer for vaccination action should be taken to include them in public health measures as much as possible.

RÉSUMÉ

INCIDENCE COMPARÉE DU CHOLÉRA DANS DES GROUPES DE POPULATION
AYANT ACCEPTÉ OU REFUSÉ LA VACCINATION

Le présent article est une analyse des cas de choléra apparus dans un groupe vacciné et un groupe non vacciné lors d'un essai pratique contrôlé sur l'efficacité de la vaccination contre *Vibrio cholerae* et son biotype El Tor, organisé conjointement par le Gouvernement des Philippines, le Gouvernement du Japon et l'OMS dans la province du Negros Occidental (Philippines) entre mai 1964 et décembre 1965. La région intéressée comprenait 24 agglomérations urbaines. Trois types différents de vaccin anticholérique et un vaccin témoin (vaccin antityphoïdique) ont été administrés à 584 000 des 1 339 800 habitants de cette zone. Tous les cas de choléra, qu'ils se soient déclarés chez des personnes vaccinées ou non, ont été confirmés au laboratoire et chacun d'entre eux a fait l'objet d'une étude approfondie.

Aux fins de comparaison, les sujets soumis à l'essai ont été répartis en trois groupes: a) les sujets non vaccinés, b) les sujets ayant reçu le vaccin de contrôle et c) les sujets vaccinés par l'un des trois vaccins anticholériques. On a enregistré 1388 cas de choléra clinique confirmé dans le groupe non vacciné et 499 cas dans le groupe vacciné, soit un total de 1887 cas. Les diffé-

rences des taux de morbidité entre les trois groupes étaient statistiquement significatives. Les taux de morbidité et de mortalité par choléra étaient significativement plus élevés dans le groupe non vacciné que dans le groupe vacciné et dans celui qui avait reçu le vaccin témoin, ce qui semblerait indiquer que le groupe non vacciné est fondamentalement différent du groupe vacciné. Les caractéristiques cliniques de la maladie étaient comparables dans les trois groupes, et l'évolution était apparemment la même, que le sujet ait été vacciné ou non. En ce qui concerne le nombre des porteurs de germes, la vaccination paraît le réduire, mais dans une proportion qui n'est pas statistiquement significative.

Les auteurs énumèrent les différentes raisons pour lesquelles la vaccination n'a pu être pratiquée; les principales sont le refus pur et simple, la maladie, l'absence au moment du passage de l'équipe sanitaire, la grossesse et la déclaration d'une vaccination antérieure.

Il faudrait donc que les services de santé publique adoptent des mesures administratives et apportent certaines modifications aux campagnes de vaccination pour tenir compte de ces diverses raisons et en atténuer les répercussions, en particulier dans les groupes vulnérables.

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