

Only severe cases were selected for streptomycin treatment and two cases died within 12 hours on admission.

During the convalescent period the pain subsided and the glands became small, although they remained tender for sometime. In some cases diagnosed as plague clinically or bacteriologically the adenitis relapsed with fever in the second or third week of convalescence and the glands suppurred. From these suppurred glands no *P. pestis* could be isolated. In some cases organisms of the staphylococcus group could be found.

A rather curious feature is that all the deaths that have occurred so far are amongst non-Bengalis.

AN ASSESSMENT OF THE VALUE OF PLAGUE VACCINE (HAFFKINE INSTITUTE) AS USED IN A SINGLE DOSE MASS INOCULATION

(A FIELD ENQUIRY)

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PLAGUE vaccine is extensively used now as a routine control measure in various parts of the country where the plague epidemic is prevailing. There has been an impression among people including some medical men that the plague inoculation will give more or less complete protection when constantly exposed to the risk of plague infection in the affected area which is not correct and gives a false idea regarding the protective power of the vaccine. In fact, none of the dead bacterial vaccines could be relied upon to give absolute protection against an overwhelming infection and the same is true of plague vaccine. However, recently some public health officers and medical men in the province working in the field have doubted as to whether it is of any value at all as practised now in the field in a single dose inoculation of 2 c.c. (Simeons and Chhatre, 1946). With a view to clarifying the position a field investigation was undertaken recently in this province, where plague prevailed in an epidemic form in some districts.

Field investigations in assessing the protective value of a particular vaccine have certain inherent drawbacks in that all the conditions as one obtains in control laboratory experiments cannot be fulfilled in nature. Thus, in the field investigation one has to observe the course of epidemic as it occurs in nature, which may be limited or widespread and may be extended over a long period as in plague. Again, the

risk of infection cannot be accurately ascertained as regards the intensity and duration as it affects the inoculated and uninoculated groups. This is further complicated by factors such as emigration and immigration of new groups, people are not immunized simultaneously nor all of them before the start of the epidemic, etc. The present investigation, being not a pre-planned affair and being carried out after the subsidence of the epidemic, has an added disadvantage in that the records were not properly maintained and the enquiring staff had to scrutinize the information carefully and without prejudice to obtain the relevant data.

Information was collected in detailed standard forms by the district public health staff from 3,320 infected houses in 120 plague-affected villages and seven municipal towns in 5 districts. It relates to the plague epidemic of the last season only, *i.e.* year 1946. The data thus compiled were carefully sifted and analysed by one of us (T. B. P.).

Accurate information on the state of inoculation about the persons attacked with plague was available from village records. In case of all other persons this was based on the information supplied by the persons themselves who were inoculated or the guardians in case of children. This was confirmed in many cases by the public health staff who had carried out inoculations at these villages. We also visited some places to satisfy ourselves regarding the proper recording of data by the staff.

In view of the limitations inherent in not pre-planned enquiries like this, the data compiled in this manner after careful enquiry may be considered not unsatisfactory and are undoubtedly dependable to arrive at broad conclusions. Inoculations were usually carried out by the public health staff, dispensary medical officers, and in some cases by the local medical practitioners. In all the instances a single dose inoculation was carried out and the dosage used was 2 c.c. for the adult and a proportionate one for the other groups as recommended by the Haffkine Institute. The vaccine used in all cases was a fresh one as it was issued by the Public Health Department without delay, on being received from the Haffkine Institute. It may be further stated that not all the persons were inoculated at the same time in the villages nor were they all pre-immunized, *i.e.* immunized before the start of plague infection in the village. Many times persons in a house were inoculated after the onset of a first case and these, therefore, are considered to belong to the group of 'uninoculated at risk' prior to the first case and 'inoculated at risk' group later (though strictly speaking they would come under the second group a week later when the inoculation becomes effective; see the two paras below table III). Data regarding history of inoculation were available with regard to the inmates in houses, in which there were one or two attacks of plague at different periods. In case of houses

with occurrence of more than two plague attacks at different periods, which were proportionately very few, definite information was available only regarding the time of first attack and the last attack, while that about the people inoculated after the second plague attack and before the last attack was not available.

It is observed that the people from the plague-infected houses sometimes evacuate it to avoid infection, but this evacuation is neither timely nor controlled and is very restricted during the monsoon period. The persons who evacuate from infected houses continue to be at risk whether inoculated or uninoculated as they carry plague-infected material along with their personal effects and as evacuation is not controlled they not infrequently visit their houses which they have supposed to have evacuated. These persons are, therefore, considered at risk and accordingly included in the respective two groups.

A distinction has been made regarding persons 'inoculated' and persons 'inoculated at risk' as also 'uninoculated' and 'uninoculated at risk' for judging the effect of vaccine. Only the groups at risk are taken for consideration. For

the distribution of their incidence is given in tables Ic and Id.

The value of plague vaccine is essentially determined by its effect in lowering the plague incidence, deaths and case mortality in the inoculated group when exposed to the risk of infection as compared to that obtaining in the uninoculated group under similar conditions.

Details of total incidence, deaths and case mortality and also these by districts are given below in tables I and Ia respectively.

TABLE I

Total plague incidence, deaths and case mortality rates among 'inoculated and uninoculated groups at risk' for five districts where plague enquiry was carried out

Group	Attacks	Deaths	Case mortality, per cent
Inoculated ..	1,996	509	25.4
Uninoculated ..	1,985	1,005	50.6

TABLE Ia

Statement showing plague incidence, deaths and case mortality by districts among 'inoculated and uninoculated at risk'

District	INOCULATED			UNINOCULATED		
	Attacks	Deaths	Case mortality, per cent	Attacks	Deaths	Case mortality, per cent
Poona ..	602	118	19.6	530	250	47.1
Belgaum ..	733	187	25.5	341	141	41.3
Satara ..	372	119	31.9	711	394	55.4
Ahmednagar ..	161	56	34.7	268	156	58.2
Bijapur ..	128	29	22.6	135	64	47.4

this purpose an infected house, *i.e.* a house where a rat-fall or plague case has occurred, is taken as unit. All persons residing in such a house are considered at risk and of these those uninoculated and inoculated before the occurrence of first attack are included respectively in the groups of 'uninoculated at risk' and 'inoculated at risk' and those inoculated later on, as they continue to be at risk, in the group of 'inoculated at risk'. The number in each group is sufficiently large. The accurate information regarding factors of age and sex distribution, social, economic and environmental conditions are not available regarding the two groups. However, it may be noted that both groups being mostly consisting of people residing in villages and usually of agriculturist class having more or less similar social and environmental conditions, it seems that these factors are not likely to affect materially the broad conclusions arrived at. As regards the age and sex groups

The figures in table I indicate that the case mortality rate among the inoculated is markedly lower than that among the uninoculated. The difference in the case mortality rate among the inoculated and the uninoculated in the different districts as given in table Ia follows the same pattern as in table I except for the fact that the case mortality is higher in the two districts of Satara and Ahmednagar in both the groups, *viz.* inoculated and uninoculated. Table Ia would also indicate that the relative advantage to the inoculated (as compared to the uninoculated) is less apparent as the virulence of the epidemic (high case mortality) increases, Belgaum being an exception.

In table Ib are given the details of the population of infected villages by districts, total number inoculated among them, percentage of inoculated to the total population and case mortality rates among the inoculated and the uninoculated. Thus from the table it is

TABLE Ib

Percentage inoculations in the infected village populations by districts in relation to case mortality rate among the inoculated and uninoculated groups

District	Population of infected villages	Population inoculated	Percentage of inoculated population	Case mortality rate (among inoculated), per cent	Case mortality rate (among uninoculated), per cent
1	2	3	4	5	6
Poona ..	117,203	92,195	78.6	19.6	47.1
Belgaum ..	63,812	59,621	93.4	25.5	41.3
Satara ..	70,487	42,942	60.9	31.9	55.4
Ahmednagar ..	32,245	12,490	38.7	34.7	58.2
Bijapur ..	97,089	75,568	77.8	22.6	47.2

evident that Ahmednagar with the lowest percentage of inoculated population (38.7 per cent) appears to have the highest case mortality (58.2 per cent) in the uninoculated group.

The Belgaum district with the maximum percentage of inoculation (93.4 per cent) has the lowest case mortality rate (41.3 per cent) in the uninoculated group which would indicate that the epidemic in Belgaum is of lower virulence than in other four districts. Thus from the table it would seem to suggest that the greater the amount of protective inoculation carried out in a community, less virulent is likely to be the epidemic in such a community and *vice versa* within certain limits.

Tables Ic and Id similarly give the incidence, deaths, and case mortality by different age groups and sex.

It will be seen from table Ic that in the age group 'over 45 years' the case mortality rate is slightly higher than the other two age groups both among the inoculated and uninoculated. Also the case mortality rate in the age group 'between 15 and 45 years' among the uninoculated is much lower than the other two age groups in that column.

The difference in the case mortality rate of 19.6 per cent between the inoculated and the uninoculated in the age group of 15 to 45 years as compared to that of 28.9 per cent and 30.0

TABLE Ic
Case mortality rate by different age groups

Group	INOCULATED			UNINOCULATED		
	Attacks	Deaths	Case mortality, per cent	Attacks	Deaths	Case mortality, per cent
Under 15 years ..	830	222	26.7	621	344	55.4
Between 15 and 45 years ..	949	247	26.2	1,007	461	45.8
Over 45 years ..	182	54	29.7	320	191	59.7
TOTAL ..	1,961	523	26.7	1,948	996	51.1

TABLE Id
Case mortality rates by sex

Sex	INOCULATED			UNINOCULATED		
	Attacks	Deaths	Case mortality, per cent	Attacks	Deaths	Case mortality, per cent
Male ..	773	218	28.2	699	374	53.5
Female ..	901	234	25.9	1,115	568	50.9
TOTAL ..	1,674	452	27.0	1,814	942	51.9

per cent respectively in the age groups 'under 15 years' and 'over 45 years' would suggest apparently a greater advantage from inoculation to the latter groups.

Table I*d* indicates that males have a slightly higher case mortality rate in both the inoculated and uninoculated groups.

It may be noted that sulpha-drugs (usually sulphathiazole) were extensively used in the treatment of plague cases in rural areas through the agency of epidemic and dispensary medical officers, private practitioners, through the Infectious Diseases Hospitals opened in various parts and also through the distribution of sulpha tablets by the public health staff. Many of the cases included in table I have thus been treated by sulpha-drugs. This is an added contributory factor in lowering case mortality figures. This would apply to both the groups, *viz.*, 'inoculated' and 'uninoculated'.

Table II shows the case mortality figures separately for sulpha-treated and untreated groups among the inoculated and uninoculated groups.

The group inoculated-untreated has a mortality rate of 40.2 per cent as compared with uninoculated-untreated group which has a case mortality rate of 59.4 per cent. Thus, there is a difference of 19.2 per cent between these two groups. This difference has been found to be statistically quite significant and indicates that plague vaccine has been effective in reducing the mortality by 19.2 per cent below that obtained in the uninoculated group.

Table II indicates that sulpha-drugs have been effective in reducing the case mortality still further by about 20 per cent and hence sulpha-drugs would need to be given equal importance in any plague campaign to prevent a heavy mortality from the disease. Table II also makes it clear that the contribution of sulphathiazole in lowering the case mortality in the inoculated and the uninoculated groups is not equal. Wagle (1944) found in his series of plague cases results such as 21.3 per cent in sulphathiazole-treated cases and 53.6 per cent in iodine-treated, *i.e.* non-specifically treated cases. Our results in the field compare well with this. He, however, does not

TABLE II

Case mortality rate separately for sulpha-treated and untreated groups among the inoculated and the uninoculated

Inoculated or uninoculated	TREATED WITH SULPHA-DRUGS			UNTREATED WITH SULPHA-DRUGS		
	Attacks	Deaths	Case mortality, per cent	Attacks	Deaths	Case mortality, per cent
Inoculated ..	1,586	344	21.6	410	165	40.2
Uninoculated ..	1,262	575	45.5	723	430	59.4
TOTAL ..	2,848	919	32.2	1,133	595	52.5

It will be seen that the most favoured group is the combined inoculated and sulpha-treated, having the case mortality of 21.6 per cent while the most adverse group is the combined uninoculated and untreated one with a very high case mortality rate of 59.4 per cent.

seem to have taken into account the beneficial effect of plague vaccine in assessing the results with various sulpha-drugs in his series.

Table III gives the figures of incidence, deaths, death rates and case mortality rates separately among the inoculated and uninoculated groups

TABLE III

Attack rate, death rate, case mortality rate and case mortality rate in the sulpha-treated and untreated groups among 'the inoculated and the uninoculated at risk'

Group	Number	Attacks	Attack rate, per cent	Deaths	Death rate, per cent	Case mortality rate (total), per cent	Case mortality rate in the sulpha-treated, per cent	Case mortality rate in the untreated, per cent
Inoculated at risk ..	7,660	944	12.3	185	2.4	19.5	15.3	38.4
Uninoculated at risk	4,241	1,382	32.5	652	15.3	47.1	35.5	61.7

at risk as also among the sulpha-treated and untreated ones.

In this table in calculating the figures of attacks, deaths, etc., the persons attacked with plague (or dying) within 7 days of inoculation have been included in the column of 'uninoculated at risk' as they did not have time to develop protection from plague inoculation. It will be seen from the table that the attack rate of 12.3 among the inoculated at risk as also the death rate of 2.4 among them are lower than those in the group uninoculated at risk, which are 32.5 per cent and 15.3 per cent respectively. The difference of 20.2 per cent in the attack rate among the inoculated at risk is statistically significant and indicates that the plague vaccine is definitely of value in protecting the persons against getting an attack when exposed to infection.

Difference of 12.9 per cent in the death rate in table III between the two groups is also statistically significant and indicates that the plague vaccine is of value in lowering the death rate. The value of plague vaccine appears to be much better in its effect in reducing the death rate than in reducing the attack rate and is in part enhanced by the use of sulpha-drugs as is apparent from the last two columns of table III.

TABLE IV

Plague incidence and deaths among inoculated in relation to time interval after inoculation

Time interval after inoculation	Attacks	Deaths	Case mortality, per cent
Within 3 days ..	78	38	48.7
Between 4 to 7 days.	89	22	24.7
Between 8 to 15 days.	177	42	23.7
Between 16 to 30 days.	349	63	18.5
Between 31 to 90 days.	639	153	23.9
Between 91 to 180 days.	163	37	22.6

Table IV gives the details of plague incidence among the inoculated in relation to time interval after the inoculation. It would seem to indicate that there develops an adequate immunity by about the 7th day of inoculation. The case mortality figures of the first three 'time interval' items in the table do not seem to show any adverse effect of negative phase as was suggested by Simeons and Chhatre (1946) in their series. Figures for the towns are also similar ones. In this connection it may be stated that conclusions arrived at from the laboratory experiments carried out at Lister Institute (Schütze, 1939) suggested that inoculation carried out during the incubation period in case of typhoid fever would do no harm on that account. The same would seem to be true in

case of plague inoculations and hence inoculations should not be refused to the contacts on that ground.

Summary and conclusions

1. A field investigation to assess the value of plague vaccine was carried out in 5 districts in 120 villages and 7 municipal towns affected during the plague epidemic of 1946.

2. In all 3,320 plague-infected houses comprising 3,981 plague cases were examined and data recorded from them analysed.

3. Plague vaccine as used now in a single dose has been found to be of definite value in that it reduces the case mortality rate in the inoculated by about 20 per cent when compared to that in the uninoculated group. This effect is apart from that due to sulpha-drugs which has been separately assessed.

4. The attack rate and death rate in 'inoculated persons at risk' are lower than those in 'uninoculated group at risk' and are statistically significant and indicate that the plague vaccine is of value in reducing the attack rate and death rate. However, the reduction in the attack rate observed is not marked.

5. Sulpha-drugs were used on a large scale in the treatment of plague cases in the field during the epidemic and have showed their remarkable value in reducing the death rate considerably and thus have established an equal claim with the vaccine in the control of heavy plague mortality. Ideal thing appears to be to protect persons with plague vaccine and also to provide treatment facilities with sulpha-drugs in plague-affected areas.

6. There seems to develop an adequate protective immunity response by about 7 days of inoculation. There was no adverse negative phase effect observed among those inoculated after exposure to infection and hence it would seem unwise to refuse inoculation to contacts from fear of negative phase effect.

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