NOTES AND REPORTS

NOTES ET RAPPORTS

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A NOTE ON THE INCIDENCE AND EPIDEMIOLOGICAL IMPORTANCE OF CHOLERA CARRIERS

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The appearance of cholera in Egypt in 1947 renewed interest in the possibility that convalescent and contact (" healthy ") carriers of the causative vibrios might play an important role in the spread of the infection. Moreover, since at present some consideration is being given to the advisability of meeting this supposed danger through the adoption of special quarantine procedures, it seemed well to review the literature dealing with the carrier problem in cholera since 1935, when fully reliable methods for the identification of the *Vibrio cholerae* were introduced.

Incidence and Duration of the Carrier State

Convalescent carriers

Genevray et al.[3] *(1939), Indochina:* 8 convalescents, examined 13-28 days after the commencement of an outbreak lasting 2 weeks, had no cholera vibrios in their stools.

Ying[26] *(1940), China:* 200 cases—mostly examined every 3rd day; last positive culture obtained within 1st week after onset in 76.5%, within 2nd week in 21.5%, within 3rd week in 1.5%, and within 4th week in 0.5% (1 case).

Read & Pandit[15] *(1941), India:* Out of 10 patients, 1 was free in 3 days, 6 within 5 days, and 3 on the 8th, 9th, and 13th day, respectively.

Peterson[14] *(1946), China:* 1,949 cases; average period from onset to first negative culture was 5.4 days with a standard deviation of ± 2.3. One patient remained positive for 17 days.

Reimann et al.[16] *(1946), China:* 160 cases; vibrios seldom isolated after 7th day of illness; administration of sulfonamides or streptomycin did not influence the length of the excretion period, but streptomycin reduced the number of vibrios in smears.

El-Ramli[2] *(1948), Egypt:* 689 cases; 86% were free from cholera vibrios by the 15th day from onset, 93.6% by the 20th day, and 99.6% by the 30th day. Intermittent vibrio excretion was met with, but infrequently.

Gohar & Makkawi[4] *(1948), Egypt:* " In convalescents the maximum period for the carrier state in the cases examined by us was 23 days and . . . in the great majority it was much shorter."

Kamal et al.[6] *(1948), Egypt:* Found among 1,971 convalescents, 326 (16.5%) carriers, i.e., individuals excreting vibrios for longer than 7 days. Longest period of excretion was 42 days. Out of a special group of 87 convalescents, 35.63% remained positive for 8-14 days, 33.33% for 15-21 days, 22.99% for 22-28 days, 5.75% for 29-35 days, and 2.30% (2 cases) for 36-42 days.

Intermittency of vibrio excretion was marked, the negative period being 26 days in one instance. 326 convalescents, who had been treated during the acute stage with sulfonamides, had a carrier-rate of 11.6% as against 20.5% in 244 not sulfa-treated. Sulfonamides given to carriers after clinical recovery tended to shorten the period of vibrio excretion.

Kordi[9] *(1948), Egypt:* 250 patients submitted to daily examination; in 50% the vibrios disappeared within 7 days. The longest carrier stage observed was 33 days in one instance. On the 10th day 34.4% were still positive, on the 15th day 14%, on the 20th day 6.4%, and on the 25th day 1.2%.

Shousha[19] *(1948), Egypt:* Out of 463 convalescents, 24.84% remained positive up to the 5th day from onset, 31.32% up to the 10th day, 18.79% up to the 15th day, 11.01% up to the 20th day, 6.91% up to the 25th day, 4.75% up to the 30th day, 1.29% up to the 35th day, 0.64% up to the 40th day, and 0.43% (2 cases) up to the 42nd day.

Intermittency of excretion was apparently frequent, it being stated that " the extremes of the negative period ranged from 1 to 23 days. The usual negative period was 3-6 days ".

Sulfonamides, particularly sulfaguanidine, appeared to shorten the carrier stage.

Hussein[5] *(1949), Egypt:* 250 cases; 86% were free from vibrios after 15 days, 99.6% after 20 days.

Contact (" healthy ") carriers

Smith[20] *(1938), Philippines:* Found, when examining the stools of 10,407 passengers from the mainland, 296 positive specimens (2.8%). All passengers had been inoculated at least once, 4-10 days before bacteriological examination.

Pasricha et al.[13] *(1938), India:* Detected, among 2,000 patients not suffering from cholera admitted in the course of 5 years to a Calcutta

hospital, 3 with cholera vibrios in their stools : one with ill-defined abdominal symptoms for two and a half months before admission; the second with chronic diarrhoea on admission; the third with a history of dysentery six months before admission.

Genevray et al.[3] *(1939), Indochina :* 133 contacts, examined 13-28 days after a cholera outbreak lasting 2 weeks, proved negative. All had been inoculated 1-3 weeks before stool specimens were taken.

Read & Pandit [15] *(1941), India :* Isolated, in the course of a field inquiry, cholera vibrios in about 7% of close contacts. Out of 16 of them, only 4 remained positive after 5 days from the date of onset of the last clinical cholera case occurring in the families concerned. The longest period of vibrio survival in the contacts was 9 days.

King Institute, Guindy [8] *(1941), India :* During an outbreak, cholera vibrios were isolated from 4 out of 196 specimens taken from 61 contacts. Six months after the outbreak, 237 specimens from 49 members of previously affected families gave negative results.

Omar [12] *(1947), Egypt :* Among " apartment contacts " 38 persons (21%) were found to be carriers for periods of up to 16 days. Of these 3 (8%) developed cholera, while 30% had a history of previous slight diarrhoea; 16 of the 38 carriers were children.

El-Ramli [2] *(1948), Egypt :* Detected, among 2,035 contacts, 84 carriers (4.12%) who did not show any gastro-intestinal trouble; 50% were free after the first 5 days, 91.7% after 10 days, and 100% after the maximal period of 15 days. Sulfonamides appeared to be ineffective in freeing either patients or contact carriers from cholera vibrios.

Gohar & Makkawi [4] *(1948), Egypt :* Stated that " in none of our positive contact cases did the organism persist for more than 10 days and in most cases it persisted for a much shorter period; a few did actually fall victims to the disease ". No carriers could be found in a village of over 1,500 inhabitants where a cholera outbreak had terminated about a month previously.

Kamal et al.[6] *(1948), Egypt :* Found, among 14,473 isolated intimate contacts, 497 (3.43%) carriers. Incidence varied in different regions from 0.8% to 28.8%. 123 (24.7%) of these individuals afterwards developed cholera, 85 after 3 days' isolation, 38 after 4-10 days' isolation. Contact carriers not developing cholera usually became free from vibrios on about the 10th day of isolation; in a small percentage the carrier stage lasted up to the 15th day, and some of the contacts persisted in excreting vibrios intermittently for longer periods up to a maximum of 26 days in an individual who, on daily examination, had appeared to be free from vibrios for 20 days. Administration of sulfaguanidine seemed to produce an earlier clearance of the carriers.

Among 2,411 " stampeders " and boatmen examined at quarantine stations, there were 47 carriers (1.9%), 13 of whom afterwards developed cholera during isolation.

Kordi (1948),[9] *Egypt:* Observed, among 2,037 contacts isolated in a hospital and generally examined daily, 84 carriers (4.1%). About 50% became free from vibrios after 4-5 days, the others within 15 days; 7.1% were still positive on the 10th day, 2.4% (2 individuals) on the 14th day. Only 28.5% of these carriers had been inoculated, 9.5% of them twice. There was no difference in the duration of the carrier state between inoculated and non-inoculated individuals. Two children, who had been isolated as contacts, developed cholera after having yielded negative stool samples for 10 and 11 days respectively.

Shousha[19] *(1948), Egypt:* Reported, among 13,702 contacts, a carrier incidence of 2.1%. Of the 288 carriers, 95 afterwards developed cholera. Observation of two groups totalling 141 showed a duration of the carrier state for 5 days in 65.96%, for 10 days in 27.66%, and for 15 or more days (maximum 19 days) in 6.38%.

Wahid[23] *(1948), Egypt:* Found, among 600 contacts (500 examined once, 100 twice) isolated in a hospital, 16 carriers (2.66%); 75% were carriers for not more than 2 days, the others excreted vibrios for periods of up to 7 days. In two twice-examined contacts, first positive results were obtained on the 5th and 6th day of isolation respectively. Three of the contacts (0.5%) developed cholera. Previous cholera inoculation or sulfonamide administration did not seem to influence the carrier state.

Hussein[5] *(1949), Egypt:* 84 carriers were found among 2,027 isolated contacts (4.14%). Of these 50% remained carriers for 5 days, 42.7% for 10 days, and 8.3% for 15 days (the maximal period).

Summary and discussion of literature

Though it would not be justified to base elaborate statistics on the diverse observations recorded above, it seems permissible to summarize the findings in the following four tables (tables I-IV).

TABLE I. MAXIMAL PERIODS OF VIBRIO EXCRETION IN CONVALESCENT CARRIERS

Author	Number of cases	Maximal period of vibrio excretion (days)
Read & Pandit [15]	1	13
Peterson [14]	1	17
Gohar & Makkawi [4]	1	23
Ying [26]	1	21—28
Kordi [9]	1	33
Shousha [19]	2	42

TABLE II. AVERAGE DURATION OF VIBRIO EXCRETION IN CONVALESCENT CARRIERS

Author	Number of cases	Observations
Ying [26]	200	Positive up to 7 days : 76.5 % Positive up to 10 days : 21.5 %
Read & Pandit [15]	10	Negative within 6 days : 70.0 % Negative within 8-13 days : 30.0 %
Peterson [14]	1,949	Average period of excretion 5.4 ± 2.3 days
Reimann et al. [16]	160	Excretion period usually not longer than 7 days
El-Ramli [2]	689	Negative by 15th day : 86.5 % Negative by 20th day : 93.6 %
Kamal et al. [6]	1,971	Positive not longer than 7 days : 83.5 %
Kordi [9]	250	Positive not longer than 7 days : 50.0 % Positive up to 14 days : 16.8 %
Shousha [19]	463	Positive up to 10 days : 56.16 % Positive up to 20 days : 29.80 %
Hussein [5]	250	Negative in 15 days : 86.0 % Negative in 20 days : 99.6 %

TABLE III. MAXIMAL PERIODS OF VIBRIO EXCRETION IN CONTACT CARRIERS

Author	Maximal period of vibrio excretion (days)
Wahid [23]	7
Read & Pandit [15]	9
Gohar & Makkawi [4]	10
Kordi [9]	14
El-Ramli [2]	15
Hussein [5]	15
Omar [12]	16
Shousha [19]	19
Kamal et al. [6]	26

From these data and tables it emerges that the average duration of the carrier state was appreciably shorter in contact carriers than in convalescents. While, in at least 50% of the former, stools were found positive for

TABLE IV. INCIDENCE AND AVERAGE DURATION OF VIBRIO EXCRETION IN CONTACT CARRIERS

Author	Number of cases	Percentage of carriers	Observations
Smith [20]	10,407	2.84	—
Read & Pandit [16]	—	7.0	Free after 5 days : 75.0 %
King Institute, Guindy [8]	61	6.56	—
El-Ramli [3]	2,035	4.1	Free after 5 days : 50.0 % Free after 10 days : 91.7 %
Kamal et al. [6]	14,473	3.43*	Usually free after 10 days
Kordi [9]	2,037	4.1	Free after 5 days : 50.0 % Free after 10 days : 92.9 %
Shousha [19]	13,702	2.1	Free after 5 days : 65.96 % Free after 10 days : 93.62 %
Wahid [21]	600	2.66	Free after 2 days : 75.0 % Free after 7 days : 100.0 %
Hussein [5]	2,027	4.14	Free after 5 days : 50.0 % Free after 10 days : 92.7 %

* The carrier incidence among " stampeders " and boatmen was 1.9%.

not longer than 5 days, and most of these individuals were free from vibrios after 10 days, some observers continued to obtain positive results in a considerable minority of convalescents during the second week following the onset of illness. The maximal periods of excretion in contacts were definitely shorter than those found in the case of convalescents.

As will be noted, Omar [12] found almost 50% of his positive contacts to be children or infants. The frequency of the carrier state in these age-groups was also emphasized by Khalil.[7] While this point, which seems to be supported by earlier observations, deserves attention when dealing with resident populations and groups of refugees, it is of less importance in the usual type of quarantine work where adults—e.g., groups of pilgrims or seasonal labourers—are primarily concerned.

The fear has been expressed that cholera inoculation might increase the frequency of the carrier state or prolong the period of vibrio excretion. The evidence collected above does not seem to bear this out. In fact, Kordi [9] concluded from a small series of observations that inoculation, particularly with two doses, exerted a beneficial influence. It has been

claimed by some workers that the same holds true of sulfonamide administration, but this contention has not been universally accepted.

In considering the carrier problem in cholera, it is of paramount importance to realize that vibrio excretion by convalescents and contacts is apt to be intermittent, so that repeated examinations may yield positive results in individuals who seemed to be, or to have become, free from vibrios. To cope with this situation, the Joint OIHP [a]/WHO Study-Group on Cholera at its second session, held in Paris in October 1948, recommended that the carriers should be released only after "three successive negative bacteriological examinations of their stools or rectal swabs, the second and third examinations being carried out on the fourth and seventh days after the first ".[25]

To implement this scheme during big outbreaks would not be easy, and it would be rather difficult to follow this procedure in order to detect carriers among large groups of pilgrims, seasonal labourers, or other travellers at quarantine stations. However, according to Read & Pandit [15] " it seems that examination of individuals who have not proved positive during the first 5 days after the onset of the last connected case is unlikely to detect carriers ".

Epidemiological Importance of Cholera Carriers

It will remembered that a large-scale inquiry to determine the importance of carriers in the spread of cholera was made under the auspices of the Office International d'Hygiène Publique in 1933 (see Couvy,[1] Stewart [21]). As summarized by Taylor,[22]

> " on the whole the evidence suggested that, with a very short persistence of *V. cholerae* in the intestinal tract of the convalescent or contact carrier, it was unlikely that the carrier was responsible for transmitting infection at any prolonged interval after the primary infection and consequently to places remote from cholera infected areas."

However, Taylor considered the results of the inquiry as largely inconclusive in view of the unsatisfactory knowledge available at the time in regard to cholera immunology. Referring to later investigations made in India with up-to-date methods, he stated that " the detection of a carrier before the onset of a case in the vicinity was not accomplished and positive evidence was not obtained incriminating a carrier as the source of infection ".

Seal,[18] discussing the problem of cholera endemicity in Bengal, came to identical conclusions. He noted that cholera vibrios could not be isolated from the stools of the general population or from water in the endemic areas, except in direct relation to cholera patients, and considered contact carriers and water as infective agents only " for short periods and at short range ".

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[a] Office International d'Hygiène Publique

It is in agreement with these views that actual records on infections produced by carriers are few and far between, and almost invariably not well documented; even in the instances published after 1935, H+O sera were generally used for agglutination tests. The following statements are found in the literature since 1935 :

Nicholls [11] quoted two observations made by Ciuca in Romania during the Balkan wars. One of these concerned a boy travelling home with his father, who died en route from cholera. After the boy's return, his mother and sister developed cholera within a short period. The infection had been hitherto absent in the locality and it was apparently proved that the boy was a carrier. The second and rather unconvincing instance was that of a detachment of troops returning home without undergoing quarantine procedures. A cholera outbreak, " due definitely to carrier infection ", developed following their arrival.

Russell,[17] reporting upon a large-scale cholera inquiry in Bengal, made before O-agglutinating serum had become available, mentioned without giving details that " in most of the cases of cholera, the infection appeared to have originated in previous cases; in four instances only was there strong evidence that carriers were involved ".[b]

Maitra et al.[10] referred to three cases of cholera in a gaol, the first victim being a prisoner who had been interned for several months and " could not have associated with outsiders or obtained food and drink from outside sources ". All prisoners employed in the gaol kitchen and the contacts of the actual cases were examined, and two cholera carriers were detected. Considering this as an " autochthonous " outbreak, the authors seem to have assumed that the carriers were responsible for it. However, since they were detected after manifest cases had occurred, it appears more likely that the first patient had been primarily infected by an unrecognized route.

Nicholls' study on cholera carriers in Ceylon,[11] though unfortunately also made with the aid of H+O sera, is most interesting. Examining, between 1 January 1931 and 31 July 1934, stool samples from 100,896 persons (mostly seasonal labourers) passing through quarantine en route from India, he found agglutinable vibrios on 84 occasions; 81 of the positives were obtained among labourers.

Nicholls calculated that, during the period 1924-33, at least 200 carriers must have arrived in Ceylon during a year of average immigration (the years 1931-3 were depression years). It was known on the other hand that, during the period 1924-33, there were only 10 occurrences of cholera in the areas to which the majority of the carriers went. Nine of these cholera manifestations were due to the arrival of *incubatory* carriers; the origin of the tenth outbreak could not be elucidated. Nicholls concluded, therefore,

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[b] " ... la plupart des cas de choléra ont semblé avoir comme origine des cas antérieurs; dans 4 cas seulement il y avait de fortes présomptions pour les rattacher à des porteurs ".

that the great majority of the carriers must have been excreting avirulent vibrios.

It is of great interest and importance that this conclusion, reached on epidemiological grounds, found support in laboratory observations by Bruce White which were summarized in the report [24] on the first session of the Joint OIHP/WHO Study-Group on Cholera in 1948, as follows : " At the end of the disease and during convalescence an increasing proportion of the vibrios excreted by the patient are in the process of ' roughening ' or are entirely rough. Transformation from the smooth to the rough state corresponds to a loss of pathogenicity of the organism." [24]

In attempting to summarize the evidence brought forward above, it may be stated that :

(1) Records suggesting a causative role of convalescent and contact carriers of the cholera vibrio are few and far between and almost invariably not well documented.

(2) Epidemiological observations as well as laboratory studies render it unlikely that such carriers are the source of infection.

(3) There seems, therefore, no reason to revise the opinion, held by most experts with experience in areas where cholera is endemic or frequent, that only " acute " carriers, that is, individuals late in the incubation stage, those actually ill, and possibly also those in early convalescence, are instrumental in spreading the infection.

SUMMARY

The literature from 1935 to 1948 dealing with the carrier problem of cholera is reviewed and summarized. It indicates that the average duration of the carrier state and the maximal periods of vibrio excretion are appreciably shorter in contact (" healthy ") carriers than in convalescents. Attention is drawn to the frequency of the carrier state in children; this, however, is of more significance in outbreaks among resident populations and groups of refugees than in routine quarantine work. The evidence collected does not bear out the suggestion that cholera inoculation either increases the frequency of the carrier state or prolongs the period of vibrio excretion.

The intermittent character of vibrio excretion in both convalescents and

RÉSUMÉ

L'auteur passe en revue et résume les travaux relatifs aux porteurs de germes cholériques, parus de 1935-1948. Il indique que la période moyenne durant laquelle un sujet est porteur et la durée maximum d'excrétion des vibrions sont notablement plus courtes chez les contacts ou porteurs « sains » que chez les convalescents. On peut noter que les enfants sont fréquemment porteurs de germes; ce fait cependant a un rapport moins direct avec les mesures de quarantaine courantes qu'avec l'épidémiologie locale, lors de poussées de la maladie survenant dans les populations résidentes ou les groupes de réfugiés. Les observations faites n'indiquent nullement que la vaccination anticholérique entraîne une augmentation du nombre des porteurs de germes ou prolonge la période d'excrétion de vibrions.

L'auteur souligne le caractère intermittent de l'excrétion de vibrions chez les

contacts, and the consequent desirability of repeated examination, are stressed. For practical purposes, however, it is pointed out that, according to some workers, the likelihood of detecting carriers among persons who have not proved positive during the first five days after onset of the last related case is not great.

Views on the epidemiological importance of cholera carriers are summarized in the second half of the paper. The results of a large-scale inquiry in this field, carried out under the auspices of the Office International d'Hygiène Publique in 1933, are briefly discussed; later work, although in some cases subject to the limitations imposed by the serological methods available, has indicated that the source of cholera infection is rarely traced conclusively to a carrier. Instances of the entry of a large number of carriers failing to produce a serious epidemic in the area involved have been observed. It has also been suggested that, in late stages of the disease and during convalescence, avirulent vibrios may be excreted—a theory which has found experimental support.

Thus it seems probable that only " acute " carriers, i.e., those late in the incubation stage, those actually ill, and possibly those in early convalescence, are instrumental in spreading cholera infection.

convalescents et les contacts, et, par conséquent, la nécessité d'examens répétés. Du point de vue pratique cependant, il faut remarquer avec certains auteurs la faible probabilité qui existe de dépister des porteurs parmi les personnes qui, à l'examen, n'ont pas donné de résultats positifs au cours des cinq jours suivant l'apparition des symptômes du dernier cas avec lequel elles ont été en contact.

L'importance des porteurs de germes dans l'épidémiologie du choléra fait l'objet de la seconde partie de l'article. Les résultats d'une vaste enquête sur cette question effectuée sous les auspices de l'OIHP en 1933 sont brièvement exposés. D'après des travaux récents — dont la valeur est limitée, dans certains cas, par celle des tests sérologiques eux-mêmes — il semble que l'origine d'une infection cholérique ne soit que rarement attribuable de façon certaine à un porteur de germes. On a constaté maintes fois la pénétration dans une région de nombreux porteurs, sans qu'aucune épidémie sérieuse s'ensuive. Selon certains auteurs, d'autre part, des vibrions avirulents pourraient être excrétés durant les derniers stades de l'infection et pendant la convalescence, hypothèse que l'expérience est venue confirmer.

Il semble ainsi probable que seuls les porteurs « actifs », c'est-à-dire ceux qui se trouvent au dernier stade d'incubation, les malades et peut-être les convalescents au premier stade, jouent un rôle dans la dissémination du choléra.

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