TYPHOID CARRIERS AND Vi AGGLUTININS

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Review of literature

Since Felix, Krikorian & Reitler (1935) found a carrier who had Vi agglutinins, and suggested that Vi agglutination might be a useful method for diagnosing carriers, the matter has been investigated by several workers.

Giovanardi (1936, 1936*a*), in Italy, had seven proved carriers who showed Vi agglutinins and one who did not. Cured carriers did not show Vi agglutinins, nor did a few normal persons. The lowest serum dilution used was 1 : 10.

Pijper & Crocker (1937, 1937*a*), in South Africa, described six proved carriers who had Vi agglutinins and eight apparently cured carriers of whom three still showed Vi agglutinins. They found no Vi agglutinins in seventy normal persons. The lowest serum dilution used was 1 : 20.

Felix (1938) found Vi agglutinins in twenty-three out of twenty-five proved carriers in English mental hospitals. Of 100 other inmates five showed significant titres of Vi agglutinin but no typhoid bacilli were found in them. Felix also examined sera from thirty-six known carriers from various European countries and found Vi agglutinins in thirty-three of them. He further quoted two outbreaks of typhoid fever in England in which respectively two and one carriers were found by means of the Vi agglutination test. The lowest dilution used was 1 : 5. Felix also pointed out that Vi agglutinins in non-excreting carriers may be due to the harbouring of typhoid bacilli, as illustrated by a man who had a typhoid osteitis, which case was fully described by Lane & Francis (1938).

Bhatnagar (1938), in India, gave details of three proved carriers who showed Vi agglutinins and added that he had never met a carrier who did not possess Vi agglutinins. In thousands of normal people he found no Vi agglutinins. The lowest serum dilution used was 1 : 10.

Bhatnagar, Speechly & Singh (1938), also in India, used Vi agglutination as a routine test for detecting carriers and confirmed that they had never found anybody who excreted typhoid bacilli and did not show Vi agglutinins.

Benstéd (1940), also in India, found Vi agglutinins in six out of seven proved carriers. The seventh one showed typhoid bacilli on one occasion only. One operated carrier who lost her bacilli, persisted in showing Vi agglutinins. The lowest serum dilution used was 1 : 5.

Horgan & Drysdale (1940), in Egypt, out of four proved carriers had two without Vi agglutinins. They found no typhoid bacilli in sixteen other persons who had Vi agglutinins. They called attention to the fact that random samples of the Sudan population showed Vi agglutinins in 0·3%, whilst typhoid contacts showed 8%. The lowest serum dilution used was 1 : 12·5.

Davis (1940), in Rhodesia, examined 656 random samples from natives and found forty-nine or 7·47% had Vi agglutinins. Upon further examination of twenty-six positive reactors, only one was found to be a carrier. The lowest dilution used was 1 : 5.

Eliot (1940), in America, found Vi agglutinins in forty-three out of forty-five carriers. In 219 normal persons Vi agglutinins were present in four. The lowest serum dilution used was 1 : 20.

Ferguson (1942), in South Africa, discovered two carriers by means of the Vi agglutination test.

Radowsky (1942), in Rhodesia, examined 1042 serums from natives for Vi agglutinins and found fifty-nine (5·66%) positives. From seventeen of the positive reactors typhoid bacilli were isolated in one case only. The lowest serum dilution used was 1 : 5.

W. M. Scott (1941), from his own experience and from the literature, concluded that a positive Vi agglutination test strongly suggests a chronic carrier, and that negative reactions can be dismissed with almost complete confidence in a preliminary survey.

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Nelson (1942) stated that the Vi agglutination test has now been adopted by the Hygiene Section of the Defence Force of the Union of South Africa for the elimination of typhoid carriers amongst food-handlers in the army. So far 175 persons have given a positive reaction, and for these different employment was found.

Precautionary measures against carriers in Pretoria

In Pretoria the Municipal Health Department is very much alive to the menace from chronic carriers. Several outbreaks in the past were traced to such persons. As a result the following safeguards have been instituted:

(1) The Municipal Health Department arranges for and assists dairies to have their personnel tested for Vi agglutinins. As a general rule positive reactors are not employed by dairies taking part in the scheme, but in exceptional cases permission for employment is given, one of the conditions being a series of at least three negative stool and urine examinations. The dairies concerned are allowed to advertise the fact that their personnel has been tested.

New by-laws are in preparation which will make the scheme compulsory for all dairy employees, the costs to be borne by the municipal health department.

(2) No persons are allowed to engage in work on the municipal water supplies unless they have been tested for Vi agglutinins, and found negative.

(3) All new nurses, the kitchen staff and many other employees at the General Hospital are subjected to the Vi test. Positive reactors are either not employed or taken on under conditions similar to those given in (1).

Through these precautionary measures we have had an opportunity of testing a section of the white and native population for the presence of Vi agglutinins. In this communication we are only concerned with chronic carriers, not with convalescent carriers.

Since the introduction by Bhatnagar *et al.* (1938) of the strain Vi I, we have given up the old technique of previous absorption of H and O agglutinins. In the present investigation we have used live suspensions of the strain Vi I, in dilutions from 1 : 10 to 1 : 80, with the usual precautions. We found it impracticable to use a dilution of 1 : 5, as most blood samples on arrival are slightly haemolysed, and this interferes with proper reading of results in low dilutions.

Our results with the Vi agglutination test on these samples from what may be regarded as the general population of the Transvaal, were:

Total number white persons examined	588
Total number of positives	24 (4·1 %)
Total number of natives examined	1938
Total number of positives	111 (5·7 %)

All the white positive reactors were subjected to three examinations of stool and urine. No typhoid bacilli were found.

Of the native positive reactors forty were subjected to a varying number of stool and urine examinations. The number varied from one to six. In two instances typhoid bacilli were found, in both in the urine, and on first examination. One of these proved carriers was trying to get work in a dairy, the other one applied for work on the municipal water supply. The usefulness of the method here became quite obvious.

Searching for carriers in connexion with cases

The routine investigation of cases of typhoid fever by the local Municipal Health Department includes Vi testing of possible carriers, chiefly native servants, in the surroundings of the patient. In this connexion we have examined 149 persons, of whom thirty-eight (26 %) gave a positive reaction.

In all positive reactors three examinations of stool and urine were performed. In three of these typhoid bacilli were found:

(1) A white child was notified as having typhoid fever. One of the native servants in the house showed a Vi agglutination of 1 : 80. Further examination showed typhoid bacilli in his urine. There have been no further cases in the house since his removal.

(2) An Indian child having been found with typhoid fever, suspicion fell on a recently engaged kitchen boy. His serum agglutinated Vi I up to 1 : 640. Typhoid bacilli were then found in his urine. There have been no further cases in the house since his removal.

(3) A woman in a boarding house went down with typhoid fever. The whole staff was Vi tested but there were no positive reactions. Amongst the staff was a certain native 'J'. Eight months later the proprietress of another boarding house was found to have typhoid fever. Here too the whole staff was tested, and no reactors found. Native 'J' was again amongst them, and was again found negative. Six weeks later two further persons in this second boarding house contracted typhoid fever. The Vi agglutination tests were again applied, and this time native 'J' agglutinated Vi I up to 1 : 80. Upon examination of his stool and urine typhoid bacilli were found in his urine. Native 'J' was now removed to the municipal 'carrier camp' but absconded on several occasions. On two of these occasions he was found in two different boarding houses, each time because a case of typhoid fever had been notified from these establishments, with intervals of 3 and 6 months respectively.

There is no doubt that native 'J' became a carrier, typhoid bacilli having been found in his urine after the two persons in the second boarding house fell ill. Regular examinations of his urine from that time onwards never failed to produce typhoid bacilli. His Vi agglutination too has remained positive up till now. The problem is: When did he become a carrier? Was he a carrier when he was found at the first boarding house, and did the Vi agglutination test fail on that occasion? And did it fail again when he was examined the second time? Or did he become a carrier in the second boarding house at the time when the proprietress fell ill? We believe this latter view to be correct, for two reasons. One is that when we did find Vi agglutinins in him, they were present up to the relatively high dilution of 1 : 80. The second reason is that although he is known to have been in regular employ in the town, during the 8 months separating the first two cases mentioned here, no cases of typhoid fever arose around him, whilst later on, when we had found him to be a carrier, he gave rise to cases of typhoid fever whenever he absconded and started work and was actually found again through the routine investigation of cases.

OTHER CARRIERS

During the past few years we have come across three cases of carriers which are worth mentioning:

(1) During routine testing for carriers at a military institution one native gave a positive blood test. He was then referred to us for further investigation and we found his blood agglutinated Vi bacilli up to 1 : 40, and typhoid bacilli were found in his urine on the second examination. They have since been found on nearly every occasion on which his urine was examined. Going into his past history it was found that he had previously worked at a factory where several cases of typhoid fever occurred upon his arrival, but too quickly to be caused by him. He himself did not get ill there.

(2) A woman was referred to us to see whether she was still a carrier. Her history was that she had had typhoid fever 30 years ago, whilst living overseas. She had married shortly afterwards, and two persons in her household had contracted typhoid fever. She had then been told that she was a carrier. She had now come to South Africa and wanted to know what the position was. Her Vi titre was found to be 1 : 20, and typhoid bacilli were found in her stool on the first examination. She knows of no other cases, apart from the first two, where she may have been responsible for the infection, for the whole period of nearly 30 years.

(3) An elderly lady gave the following history. She had typhoid fever 17 years ago. It left her with a cholecystitis, which was operated on, but the operation left a gall-bladder fistula. An effort to close this fistula, undertaken a year later, was of no avail, and on this occasion typhoid bacilli were found in the fistula. Since then the fistula has been open most of the time, and discharging small quantities of fluid. We examined the fluid several times and always found typhoid bacilli. Her blood had a Vi titre

of 1 : 40. At the same time we made two efforts to find typhoid bacilli in her stool, but failed. The stools were of normal colour. Here then we had a case where typhoid bacilli must be getting into the stool regularly, but could not be found on culture. As far as the patient knows, she has never infected anybody.

Discussion

With the seven proved carriers described here, there have now been recorded in the whole literature 131 proved carriers who had Vi agglutinins, and eleven proved carriers who had not. Not all the negative reactors were tested in low dilutions. It appears that Vi agglutination is not a completely reliable test for detecting carriers, it may fail in nearly 8% of true carriers, even when low serum dilutions are used. The necessity of using low serum dilutions is however quite evident from the literature. We should aim at using 1 : 5, and certainly use 1 : 10.

Using these low serum dilutions has brought out the fact that many supposedly normal persons possess quantities of Vi agglutinins of the same order as those found in proved carriers. As long as we used the lengthy absorption technique and our Vi agglutination started at 1 : 20, we found no Vi agglutinins in supposedly normal persons (1937, 1937*a*). When, however, we employed the much more satisfactory technique of direct agglutination with the Vi I strain we encountered a high percentage of positive reactors in the supposedly normal population.

Similar findings have been recorded by other workers, quoted above. The percentage of positive reactors in the supposedly normal population varies from author to author and cannot be directly compared on account of differences in technique and lack of standardization. The findings, however, are definite enough to require an explanation.

The position would be simple if these positive reactors could be proved to be carriers. The point is that this has been tried in several cases, but typhoid bacilli have only rarely been found. In other words, by taking random samples from a population, and making cultural tests on the positive reactors, very few proved carriers have come to light. These cultural tests, however, have not always been very thorough, and not always instituted under the best possible conditions. But the absence of positive results has already brought Davis (1940) and Radowsky (1942) to the conclusion that Vi agglutinins are not indicative of the carrier state.

We do not think this negative attitude is warranted. We hold that positive Vi reactors should be regarded as carriers. The word 'carrier', however, seems to need some qualification. 'Carrier' does not mean 'excreter', and there is no need to coin a new term 'harbourer'. A carrier just is a harbourer.

Vi agglutinins cannot arise without specific stimulus. They can of course persist after the stimulus has disappeared, that is their nature. We have apparently witnessed this in some of our carriers (1937). This explains that at least some persons may have Vi agglutinins in whom typhoid bacilli cannot be found.

It remains significant, however, that in populations where the incidence of typhoid fever is high, a high percentage of the population shows appreciable quantities of Vi agglutinins. In other words, under conditions where a high carrier rate would be expected, a high incidence of persons with Vi agglutinins is found. This is definitely the case in southern Africa, and there is no reason why the mental patients with their high incidence described by Felix (1938) should not be included in this category. In this connexion it is noteworthy that we found the incidence of positive Vi reactors as high

as 26% amongst persons in the immediate surroundings of patients, i.e. amongst a group of persons almost certainly containing a number of carriers, and the incidence of positive reactors amongst the general population 5·3% only. Horgan & Drysdale (1940) have published similar figures.

Looking at the matter from the point of view of the typhoid bacillus, it should be appreciated that typhoid bacilli have a very hard struggle for life. They can hardly exist outside the human body, and in the human body they are in constant danger from antibodies, bacteriophages and being overgrown by other more hardy bacteria. A high carrier rate is essential for the continued existence of typhoid bacilli.

This leads also to the explanation why the laboratory does not succeed more often in growing typhoid bacilli from what we regard as carriers. Urinary carriers of course are hardly ever missed. But faecal carriers are in a different position. Even in proved faecal carriers it is well known that the excretion is intermittent. We submit that in a very large number of cases the excretion, most of the time, is so scanty that it is missed. Stool specimens should be examined fresh, and this is not always feasible. Urines can be concentrated by centrifuging, but the quantity of stool that can be examined is always very small. We have used various media for growing typhoid bacilli from stools, including Wilson and Blair's medium, and several variations of it, but we have not got the impression that the choice of medium affects the results very much. Taking into account the considerations discussed above, there must be a number of faecal typhoid carriers who are such minimal excreters that our present-day methods must fail to grow typhoid bacilli from them. A case in point is the patient mentioned in this paper where we always and easily found typhoid bacilli in a gall-bladder fistula, but failed on two occasions to find them in her otherwise normal stools. That these 'minimal excreters' are only potentially dangerous is also evidenced from her story. We regard the urinary carrier in our country as the much more dangerous kind, especially in the form of a native servant.

SUMMARY

Seven more carriers, all possessing appreciable quantities of Vi agglutinins, are added to those already known.

Vi agglutination tests performed on 2526 inhabitants of the Transvaal, both native and white, showed that 5·3% had similar quantities of Vi agglutinins.

A fair number of these positive reactors were further examined for the presence of typhoid bacilli in their excreta, but the number of positive findings was very small.

It is argued that there are a large number of typhoid faecal carriers who are such minimal excreters that the typhoid bacilli in their stools escape detection.

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