

The campaign against typhoid and paratyphoid B in western Norway. Results of cholecystectomy

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INTRODUCTION

At the beginning of this century a considerable number of typhoid and paratyphoid B cases were notified every year in western Norway. The figures also remained high during the First World War and the following years. However, since 1922 there has been a uniform decline, and in recent years only a few cases have been notified.

The distribution of the two diseases has been exceedingly uneven in the various districts in western Norway. Such distribution is a cogent argument for the opinion that the infection is conveyed by chronic carriers. The first chronic carrier in western Norway was detected in 1918 (Madsen, 1918). In 1920 the guiding principles were formulated for the institution of a systematic campaign against enteric diseases in western Norway. In particular, great pains have been taken to discover the original sources of infection in the form of chronic carriers. Since 1918, 147 individuals have been found to be chronic carriers, 84 being carriers of *Salmonella typhi*, and 63 of *Salmonella paratyphi B*. The chronic carriers of older date discovered by systematic searching for the source of infection among the contacts of new cases of typhoid, numbered 91. Among these chronic carriers were 37 who had previously suffered from enteric fever. Twelve of these were first found to be carriers more than 20 years after infection, and several of them were not found to be carriers till after the age of 70. Cases kept under constant control from the time of their illness and found to discharge the specific organisms after recovery from it, numbered 39. Three were found to be carriers following bacteriological examination of gall-bladders after their removal on account of attacks of biliary colic. On systematic bacteriological examination of the gall-bladder carried out at all the post-mortem examinations conducted at The Gade Institute, 14 individuals were found to have been carriers. In only 2 of these cases had there been a history of enteric fever.

Of the 147 chronic carriers, 23 were males and 124 females. Thus, in this material women were much in the majority, accounting for 84% of the chronic carriers. Most of the carriers were elderly folk, 96 (65%) being over the age of 50 when their carrier state was discovered. There were 37 carriers over the age of 70 at this stage. Prigge (1912) associated the high chronic carrier rate in elderly persons with the incidence of gall-stones, which also rises with age. The post-mortem material from the Bergen City Hospital for the period 1912-28 (Vogelsang, 1929), consisting of

2690 individuals over the age of 20, showed a gall-stone rate of 6·5 %, 3·9 % for men and 9·8 % for women. There was a considerable rise in this rate among women around the age of 50. A similar rise came at a higher age in men. It is therefore possible that the greater liability of elderly women to suffer from gall-stones contributes to the frequency with which they become chronic carriers.

From time to time attempts have been made to cure the chronic state by various means. Occasional cures have been reported as a result of various procedures, but further investigations have shown them to be ineffective in most cases. As the carrier state in the majority of cases depends on processes in the gall-bladder, we have tried to cure the carriers by operation.

OPERATION ON CHRONIC CARRIERS

Among the 147 chronic carriers who discharged the specific organism in the faeces, there were 14 in whom this condition was not discovered till a post-mortem examination was made. Among the remaining 133 there were 66 on whom operations were performed with a view to curing the carrier state.

Cholecystotomy

In 2 cases, only cholecystotomy could be performed. In a 50-year-old workman's wife the operation was limited to cholecystotomy because of the state of her gall-bladder, which contained pus and 12–14 stones of the size of a walnut. There was also an angular stone as large as a pea in the much thickened cystic duct. *S. paratyphi B* was found in the biliary fistula up to 4 days after the operation. All the later bacteriological examinations gave negative results. She was considered cured.

The other, a 58-year-old farmer, stated that he had suffered from typhoid 40 years earlier. As the position of the gall-bladder was abnormal and because it was firmly adherent to the common bile duct and portal vein, only cholecystotomy was performed. The biliary fistula took 2 months to close, and discharge of *S. typhi* in the faeces continued.

Thus, in 1 of the 2 cases in which cholecystotomy was performed, a cure of the carrier state was effected, while it persisted in the other case.

Cholecystectomy

The gall-bladders of 64 chronic typhoid and paratyphoid B carriers were removed by operation with the results given in Table 1. Two died as a result of the operation, 9 remained carriers, 53 are considered cured. A distinction can be made between the two infections, but this does not demonstrate any striking difference in the results achieved following operation in chronic typhoid or chronic paratyphoid B carriers.

Two deaths and 9 failures to achieve sterilization may seem to bulk large in relation to so small a total as 64 cases. On the other hand, the 64 cases included 53 cures. The operation was therefore successful in four-fifths of the cases.

Two deaths must be related to the operation. A 56-year-old farmer's wife was

detected as a chronic carrier $7\frac{1}{2}$ years after she had suffered from typhoid. She was examined in the Bergen City Hospital and, as she had myocarditis, she was advised against operation. However, she herself wished to have the operation, and a cholecystectomy was carried out at her urgent request in another hospital. She died of heart failure 10 days after the operation.

Table 1. Results of cholecystectomy

Specific organism	Died	Remained carrier	Considered cured	Total
<i>S. typhi</i>	1	6	31	38
<i>S. paratyphi B</i>	1	3	22	26
Total	2	9	53	64

A technical mistake was made during the operation on an insane woman who was operated on at the age of 39, $1\frac{3}{4}$ years after she had suffered from paratyphoid B. Her death from cholaemia 6 days after the operation was caused by the common bile duct having been divided and ligated about 8 cm. above the papilla of Vater.

CHRONIC CARRIERS WITH NORMAL STERILE GALL-BLADDERS

The gall-bladders of two individuals who remained carriers were found at the operation to be perfectly normal, without stone formation. Microscopical examinations showed no pathological changes in the walls of the gall-bladders, and bacteriological examinations showed the contents of the gall-bladders to be sterile. Both these carriers continued to discharge *S. typhi* with the faeces after the operation. As in both cases the gall-bladder was found to be macroscopically and microscopically normal, to contain sterile bile and no stones, it seems unlikely that the focus of infection was situated higher up in the bile passages or in the liver. As, however, the duodenal contents continued to contain *S. typhi* after the operation, it seems natural to suspect a focus of infection in the neighbourhood of the duodenum. As the canal of Wirsung opens into the common bile duct below the cystic duct, it is conceivable that these 2 carriers continued to discharge *S. typhi* because of a focus of infection in this canal or in the pancreas. On X-ray examination, no pancreatic stones were found. As both carriers are still alive, though very old women, the seat of infection in both these cases must remain in doubt for the present.

CONTINUED DISCHARGE OF THE SPECIFIC GERM AFTER OPERATION

A female shop assistant was 24 years old when operated on, $1\frac{1}{2}$ years after she had suffered from paratyphoid B. A biliary fistula communicating with the exterior remained open. She died from tuberculosis $1\frac{1}{2}$ years after the operation without being rid of *S. paratyphi B*, which was found in the liver together with tuberculous necrosis.

Of the other 6 carriers who continued to discharge the specific germ after operation, the time of infection is unknown in one (Table 2). In the other 5 the operation

was carried out 4 and 5 months, 1 year, 17 and 46 years respectively, after infection. The age at the time of the operation was in 1 case 30 years, in 4 cases between 50 and 60, and in 1 case 63 years. The carrier who was operated on 5 months after infection died of a cerebral tumour 7 years after the operation. At the post-mortem examination *S. paratyphi B* was cultivated from the common bile duct and the hepatic duct. It therefore seems that the specific process may in a few cases be situated at a higher level in the bile passages of the liver, as well as in the gall-bladder.

Table 2. *Interval between infection and operation*

Interval	Died	Remained carrier	Considered cured	Total
3 months	—	—	1	1
4 months	—	1	1	2
5 months	—	1	2	3
$\frac{1}{2}$ year	—	—	4	4
$\frac{3}{4}$ year	—	—	2	2
1 year	—	1	6	7
1 $\frac{1}{2}$ –2 years	1	1	2	4
2–3 years	—	—	3	3
3 years	—	—	1	1
4–5 years	—	1	1	2
5–10 years	1	—	2	3
10–15 years	—	1	1	2
15–20 years	—	1	3	4
30–39 years	—	—	1	1
40–49 years	—	1	3	4
50 years	—	—	2	2
Unknown	—	1	18	19
	2	9	53	64

In typhoid fever a histological examination reveals necrotic foci in the liver. Bile congestion may easily arise as a result of inanition, meteorism and the like, and it may well be that a focus formed in the liver may provide favourable conditions for the further growth of the organisms.

CRITERIA OF CURE

The number of bacteriological examinations of chronic carriers after operation has varied with the duration of excretion of the organisms. Though some carriers were found to be negative at every examination after operation, others were found to harbour the specific organism for varying intervals of time after operation before the carrier state ceased.

Bacteriological examination usually started from 4 to 6 days after operation and continued at intervals of a few days. In 14 patients only faeces were examined, and in most of these the operation was performed before the introduction of duodenal intubation as a routine procedure. No carrier was regarded as cured until he had had at least five consecutive negative faecal tests; in fact there were only 2 carriers who did not have more than this minimum number.

Otherwise, we have attached much greater importance to a negative duodenal

test than to a negative faecal test. Since the introduction of duodenal intubation as a routine procedure after the operation, we have required a minimum of three consecutive negative faecal tests and one negative duodenal test; there were, however, only six carriers who did not have more than this minimum number of negative results.

Table 3. *Numbers of consecutive negative examinations after operation*

No. of negative tests		No. of carriers
Faeces	Duodenal contents	
5	—	2 } 14
6	—	
7	—	
8	—	
9	—	
10	—	
22	—	
3	1	6 } 39
4	1	
5	1	
6	1	
7	1	
11	1	
13	1	
26	1	
3	2	
4	2	
5	2	
6	2	
7	2	
9	2	
10	2	
13	2	
14	2	
7	4	1
6	5	1

Sixteen carriers showed only negative results after operation. In the other carriers the consecutive negative results recorded in Table 3 followed some positive results. It was particularly in the carriers whose first tests after operation were positive that more than one negative duodenal test was required before the carrier was considered cured. In most of these carriers the faeces had become negative within the 1st month after operation, but the last two in Table 3 showed positive faecal results over a considerable period. For this reason these two carriers were not considered cured until they had had four and five negative duodenal tests respectively in addition to the negative faecal tests.

Although in certain patients it might have been desirable to undertake further tests, most of them had so many consecutive negative results that the chances of our being mistaken in regarding them as cured are very small indeed. It is now many years since several of these carriers were operated on, and in the interval no case of enteric fever has occurred which could be connected with any of them.

INDICATIONS FOR OPERATION

The experiences provided by the present material point to the following indications for operation and the time at which it should be undertaken:

The specific organism must be demonstrable in the bile by duodenal intubation.

If, at the same time, cholecystography indicates stones in the gall-bladder, the operation should be carried out when the carrier state has lasted at least 3 months after the end of the illness.

If X-ray examinations indicate only functional disturbances of the gall-bladder, the operation ought not to be carried out less than 6 months after the end of the illness.

If the functional activity of the gall-bladder is shown on X-ray examination to be normal, it is as well to be reserved in recommending operation.

Most individuals must experience quite a severe physical shock when told they are chronic carriers. Because of this state, many of them cannot continue in their former occupation, and the most conscientious of them are in constant terror of infecting those about them. A few of our carriers have committed suicide. With the growing realization by the public that removal of the gall-bladder offers chances of a cure of the carrier state, there will be a growing demand by chronic carriers for this remedy, which, as matters are at the present time, would seem to be difficult to prevent.

In recent years several investigators have tried to cure the carrier state with antibiotics. Further investigations are needed here. However, it is to be hoped that we shall soon have in our hands an antibiotic or other drug which is excreted by the liver in such concentrations that it will be able to kill the specific organisms and thereby cure the carrier state of these really unhappy individuals.

SUMMARY

1. The first chronic carrier in western Norway was discovered in 1918. Since then 147 individuals have been found to be chronic carriers, 84 being carriers of *S. typhi* and 63 of *S. paratyphi B*.

2. Of the 147 chronic carriers 23 were males and 124 females. Most of the carriers were elderly folk, 96 over the age of 50 and 37 over the age of 70 when their carrier state was discovered. There is a considerable rise in the incidence of gall-stones among women around the age of 50, while a similar rise comes at a higher age in men. This sex difference may be a contributory cause of the larger number of female carriers.

3. Operations were performed on 66 chronic carriers with a view to curing the carrier state. In 2 cases, only cystotomy could be performed because of the state of the gall-bladder. In one of these the carrier state was cured, while it persisted in the other.

4. The gall-bladders of 64 chronic carriers were removed by operation with the following results: 2 died as a result of the operation, 9 remained carriers, and 53 are considered cured. The operation was therefore successful in four-fifths of the cases.

The gall-bladders of 2 individuals who remained carriers were found at operation

to be sterile and perfectly normal, without stone formation. Two other individuals who remained carriers have later died, $1\frac{1}{2}$ and 7 years after their operations. In both cases *S. paratyphi B* was cultivated from the common bile duct and the hepatic duct. The specific process may therefore in a few cases be situated at a higher level in the bile passages of the liver.

5. The interval between infection and operation varied from 3 months to 50 years. The 2 carriers who had the longest interval are both cured.

6. Indications for operation are given on the basis of the experiences provided by the present material.

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