

THE SURGICAL TREATMENT OF CHRONIC BILIARY TYPHOID CARRIERS

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It is generally agreed that the carrier problem is the most important one remaining in the eradication of residual *Bacillus typhosus* infection. Unfortunately nothing has been accomplished toward preventing a typhoid fever patient from becoming a typhoid carrier, nor, indeed, has much attention been paid to this problem in preventive medicine. Public health practice has concerned itself, instead, with the discovery, control and cure of persons in whom the carrier state has been established.

Since the establishment of typhoid fever stations in Germany at the beginning of the century, many therapeutic agents have been used in the treatment of carriers. Stertenbrink¹ reviewed the literature on the subject and called attention to the many unsuccessful attempts that had been made up until 1928. Furthermore, since then there has been no evidence of an effective curative agent except that of Gulbrandsen,² who reported four cures in 12 chronic carriers treated with deep roentgen therapy over the gallbladder. However, Forsbeck and Lampe³ were unable to effect any cures in a series of cases treated with deep roentgen therapy, although negative specimens became more frequent during treatment in some instances.

In 1888, Anton and Fütterer⁴ isolated the *B. typhosus* from the gallbladders of fatal typhoid fever cases. Later, in the German carrier campaign it was discovered that the organism could usually be found in the gallbladders of chronic carriers. Indeed, as was pointed out by Mallory and Lawson,⁵ in 1931, the persistent infection of the gallbladder in typhoid carriers usually produces a chronic inflammation of that organ which is characteristic though not pathognomonic. It has long been known that cholelithiasis is usually present in chronic typhoid carriers.

In 1908, Grimme⁶ reported a cholecystectomy performed for the purpose of curing a carrier. Since that time, this method has become an accepted, though not very common, therapeutic procedure for the cure of gallbladder carriers. In the reference of Senftner and Coughlin⁷ to the work of Bergglas⁸ and to that of Hage and Brinkmann,⁹ there is an overcount of operations performed. Of the 74 cases of Bergglas, only two were his own, 66 of the others being those already summarized by Hage and Brinkmann.

The benefits of cure by cholecystectomy accruing to the carrier, his family and the community may be summarized as follows:

- (1) The occasional case that occurs even after a person knows himself to be a typhoid carrier is prevented.
- (2) The former food-handling carrier is able to resume his occupation.
- (3) The mental depression frequently observed in carriers is relieved.
- (4) Potential or actual gallbladder disease is eradicated.
- (5) The health department is released from the expense of controlling a potential source of infection.

ELIGIBILITY CRITERIA FOR OPERATION AND FOR RELEASE OF CHRONIC BILIARY TYPHOID CARRIERS

Analysis of Previous Reports.—In the early work subsequent to Grimme's report, neither preoperative nor postoperative bile specimens were obtained, and release following cholecystectomy was based entirely upon the examination of feces. Many carriers were included in these reports who had submitted to operation because of their clinical symptoms but who were not separately classified either as to cure rates or fatality rates. Furthermore, the literature, especially foreign literature, includes many carriers of the paratyphoid group which are not separately analyzed as to fatality rates and cure rates. Finally, many of the reports include, without separate consideration, convalescent carriers who may be positive for only a few months after illness. Such a carrier has an excellent chance of clearing up spontaneously.

We have omitted the early German literature in preparing Table I because, as Bigelow and Anderson¹⁰ have pointed out, the eligibility criteria for operation and release in the earlier work were not up to the present standards. We have excluded paratyphoid carriers, typhoid carriers who have not had at least one release bile specimen in addition to release feces specimens, convalescent carriers, and persons treated otherwise than by cholecystectomy. We have included, however, cases irrespective of whether or not a preoperative bile was obtained. This analysis reduces the number of cases which can be used for a study of the effectiveness of cholecystectomy to a rather meager number.

Omitting our own series, it may be noted that about 62 per cent of all cases were returned to their communities alive and noninfectious. But if only those who were operated upon because they were carriers are considered, it may be noted that about 74 per cent were cured; and omitting the three deaths occurring in the Senftner and Coughlin series, 79.5 per cent of the cases were cured.

Determination of Gallbladder Infection.—While carriers in whom the only nidus of infection is in the intestinal wall are rare, there is little evidence as to the relative occurrence of this type of carrier. Garbat¹¹ found one intestinal carrier in 146 convalescent carriers. This, however, cannot be accepted as evidence of the occurrence of intestinal carriers among chronic

carriers.* It was not until after the development of practical duodenal drainage by Einhorn¹² that preoperative bile specimens were commonly obtained. During the past ten years, preoperative diagnostic bile specimens have been usually considered prerequisite to operation in chronic carriers essentially free from gallbladder symptoms. The procurement of a negative specimen (indicating a negative biliary tract) with positive feces would contraindicate cholecystectomy.

It has been shown, by Forsbeck and Hollon,¹³ that the reliability of a negative report on a bile specimen depends largely upon the hydrogen ion concentration of the specimen. A mixture of gastric juice and bile is usually submitted to the laboratory by the uninitiated. Such a specimen is usually highly acid. In it the typhoid organisms may be killed in less than 30 seconds after mixture has occurred. Consequently, when a negative specimen of "bile" is obtained preoperatively, it must be known definitely that the specimen is actually bile, before the case may be classified as an intestinal carrier.

In spite of the rarity of intestinal carriers it is not justifiable to subject a carrier to cholecystectomy without definitely knowing that he is a chronic bile carrier, unless the operation is indicated purely from the clinical viewpoint. Recently an illustrative case came to our attention. This person, after two positive feces, had a long series of negative feces. Without a preoperative bile drainage, she submitted to cholecystectomy on the assumption that she was a carrier. No bile was taken for culture at the time of operation. The case was probably a contact feces carrier who cleared up spontaneously before the date of operation.

On the other hand, intestinal carriers are so rare that for the purpose of analysis we may consider that feces carriers are gallbladder carriers, unless proved to be intestinal carriers by the procurement of a negative diagnostic bile specimen. This can, at most, cause but a trifling error in an analysis.

Surgical Risk.—The literature is not clear concerning the mortality rate from cholecystectomy in carriers since it is not always stated whether a carrier submitted to operation mainly to cure his carrier condition, or because of the urgency of his clinical symptoms. To deprecate surgical intervention for the cure of the carrier state because of deaths occurring among carriers operated upon because they were seriously ill with gallbladder disease is obviously illogical.

¶ In so far as surgical risk is concerned each case must be judged without regard to his carrier state, although the Michigan Department of Health as a matter of public policy does not urge cholecystectomy for any person over 50 without symptoms of gallbladder disease. On the other hand, it is considered good surgical practice to urge any good risk with gallbladder pathology to submit to cholecystectomy simply for his own welfare. Cholecystitis

* Several large states and cities have agreed on arbitrarily declaring those who have harbored the *B. typhosus* for one year or more from date of onset with typhoid fever to be chronic carriers, those for less than one year convalescent carriers.

TABLE I
RESULTS OF CHOLECYSTECTOMIES PERFORMED UPON CHRONIC BILIARY TYPHOID CARRIERS
Summarized from Data of Various Authors*

| Author | Year | Percentage of Cures | | | | | | | | | | Mortality Percentage | | | | | | | |
|--|-----------|---|-------------------------|---------------------|----------------------|----------------------|--|-------------------------|---------------------|----------------------|----------------------|---|----------|--|----------|------|------|------|------|
| | | Reason for Cholecystectomy: Gallbladder Symptoms or a Carrier | | | | | Reason for Cholecystectomy: Because a Carrier | | | | | Reason for Cholecystectomy: Gallbladder Symptoms or a Carrier | | Reason for Cholecystectomy: Because a Carrier | | | | | |
| | | Recovered or Died | Recovered Cases Only | No. Oper- ations | Per Cent Cured | Per Cent Cured | Recovered or Died | Recovered Cases Only | No. Oper- ations | Per Cent Cured | Per Cent Cured | All Ages | Under 50 | All Ages | Under 50 | | | | |
| Haaland and Haaland ¹⁵ .. | 1927 | 1 | 1 | 1 | 0.0% | 1 | 1 | 1 | 0.0% | 1 | 1 | 1 | 1 | 1 | 1 | 0.0% | 1 | 0.0% | |
| Berglass..... | 1929 | 2 | 2 | 2 | 100.0% | 2 | 2 | 100.0% | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 0.0% | 2 | 0.0% | |
| Whipple ¹⁶ | 1929 | 2 | 2 | 2 | 100.0% | 2 | 2 | 100.0% | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 0.0% | 2 | 0.0% | |
| Vogelsang and Haaland ¹⁴ .. | 1931 | 2 | 2 | 2 | 0.0% | 2 | 2 | 0.0% | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 0.0% | 2 | 0.0% | |
| Senfner and Coughlin ¹⁷ .. | 1933 | 36 | 28 | 24 | 50.0% | 24 | 24 | 64.3% | 21 | 21 | 61 | 61 | 61 | 32 | 13.1% | 42 | 7.1% | 26 | 0.0% |
| Bigelow and Anderson ¹⁸ .. | 1933 | 8 | 8 | 7 | 100.0% | 7 | 7 | 100.0% | 7 | 7 | 8 | 8 | 8 | 4 | 0.0% | 4 | 0.0% | 4 | 0.0% |
| Hanssen ¹⁷ | 1935 | 4 | 4 | 4 | 100.0% | 4 | 4 | 100.0% | 4 | 4 | 4 | 4 | 4 | ? | 0.0% | 4 | 0.0% | ? | 0.0% |
| Subtotals..... | 1927-1935 | 55 | 47 | 42 | 61.8% | 42 | 39 | 73.7% | 39 | 39 | 80 | 79.5% | 80 | 40 | 10.0% | 60 | 5.0% | 34 | 0.0% |
| Coller and Forsbeck..... | 1937 | 18 | 18 | 16 | 88.9% | 16 | 16 | 87.5% | 16 | 16 | 18 | 87.5% | 18 | 15 | 0.0% | 16 | 0.0% | 14 | 0.0% |
| Totals..... | 1927-1937 | 73 | 65 | 58 | 68.5% | 58 | 55 | 77.6% | 55 | 55 | 98 | 81.8% | 98 | 55 | 8.2% | 76 | 3.9% | 48 | 0.0% |

* In abstracting this material, paratyphoid carriers, convalescent carriers, and persons released without at least one negative bile specimen following cholecystectomy have been omitted.

is so nearly universal in chronic carriers and cholelithiasis so common, that for practical purposes it is logical to assume preoperatively the presence of gallbladder pathology. As may be noted in Table I, no deaths have been reported in any series except that of Senftner and Coughlin. In their series the fatality rate was 14.7 per cent for all cases. Of those submitting to cholecystectomy primarily for cure of the carrier state, only three or 7.1 per cent died as a result of the operation. In a personal communication Doctor Senftner has kindly supplied us with the following data concerning these three cases:

Case 1.—P. G., male, age 51. Operated upon, September 20, 1929. Died, September 23, 1929, of acute peritonitis.

Case 2.—M. G. female, age 57. Operated upon, August 12, 1922. Died, August 12, 1922, of surgical shock and acute dilatation of heart.

Case 3.—H. D., female, age 60. Operated upon, June 21, 1932. Died, July 3, 1932, of enterocolitis, toxemia, cholecystitis, cholelithiasis. Convalescing uneventfully until five days after operation.

It may be noted that all these persons were over 50 years of age. Cases 1 and 2 were inmates of state institutions for the insane, persons notoriously of low resistance.

Percentage of Cure.—In determining the percentage of cure, it is proper to include persons operated upon for clinical symptoms, provided this group is analyzed separately. While not yet proved, it would seem almost a truism, that the severity of clinical symptoms would be correlated with the extent of biliary tract involvement and therefore with the chance of cure. Vogsang and Haaland¹⁴ have suggested the probability that the rate of cure depends upon the number of years that the carrier has had gallbladder infection. Two of their carriers, of respectively 17 and 45 years' standing, were not cured by cholecystectomy. Sufficient accumulation of data may enable us to predict fairly closely the probability of cure based upon the duration of the carrier state.

PRESENT ELIGIBILITY CRITERIA FOR OPERATION AND RELEASE OF CHRONIC BILIARY TYPHOID CARRIERS IN MICHIGAN

(A) Eligibility criteria for carriers to be operated upon primarily for cure of the carrier state:

- (1) The person must be a chronic carrier.
- (2) The person must be a bile carrier.
- (3) The person must be a good surgical risk.

(B) Eligibility criteria for release after cholecystectomy: ✓

(1) Twelve consecutive feces specimens obtained at monthly intervals following operation and examined in a laboratory approved by the Michigan Department of Health shall be negative.

(2) Two consecutive bile specimens obtained during the year after operation and considered satisfactory for examination by the Michigan Depart-

ment of Health shall be examined in an approved laboratory and found to be negative.*

Results of Cholecystectomy in Michigan Series.—Our series of 18 cases has been summarized in Table II. Eleven of these cases were operated upon at the University Hospital.† All cases were chronic carriers. Twelve, or 67 per cent, had slight to marked symptoms of gallbladder disease. In two of these (Cases 5 and 16), operation was performed primarily for the relief of clinical symptoms. No deaths occurred in our series.

Of 11 preoperative bile specimens obtained ten were positive, while of 15 bile specimens obtained at operation 14 were positive. The negative preoperative bile specimen was obtained by an observer unfamiliar with the necessity of securing bile and not a gastric juice-bile mixture. The negative bile specimen obtained at operation was examined in a laboratory which had been doing but little typhoid work. In Case 1, only, it was not definitely proved by a positive bile that the person was a bile carrier. However, the patient was cured by cholecystectomy.

Of the 18 cases, three were males and 15 females. The average age at operation for the males was 35, for females 40.3. The total age incidence was 39.4. Two gave no history of having had typhoid fever. Of those giving a positive history, the duration of infection had varied from one to 38 years, with an average of 15.2 years.

The percentage of cures was 88.9 per cent. Two carriers were still feces-positive, one 14 and the other 15 months after operation. The former (Case 11) had had typhoid fever 28 years before operation, while the latter (Case 13) gave no history of having had the disease. Case 13 is still a biliary tract carrier as indicated by a positive bile obtained 15 months after operation. No postoperative bile has been obtained from Case 11. Case 6, a graduate nurse employed in a hospital, became feces-negative promptly after operation. The first postoperative bile was negative, but this was followed 18 months after operation by a positive finding. Twenty-six months after operation a third bile specimen was negative. During the two years since operation 16 negative feces specimens and no positives have been obtained. The first bile specimen obtained in the hospital where she works was not considered satisfactory by the Michigan Department of Health. We believe that this patient may have been reinfected or that she maintained a slight nidus of infection which was missed in the first bile specimen.

As can be seen in Table II, in most instances the feces became negative within a few days to three weeks after operation. However, the feces may

* If further evidence should confirm previously accumulated data,¹³ it is probable that the Michigan Department of Health will change the number of negative release biles required from two to one. Already, because of unusual circumstances, two carriers have been released with 12 negative feces and one negative bile.

† We are indebted to Drs. M. J. Darling, W. R. Clinton, and F. B. Wight, of Detroit, F. J. O'Donnell of Alpena, and C. B. Wood of Clare, each of whom has had one case under his care at other hospitals.

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RESULTS OF CHOLECYSTECTOMIES PERFORMED UPON CHRONIC BILIARY TYPHOID CARRIERS IN MICHIGAN

TABLE II

| Case No. | Sex | Age at Oper. | Years Since T. F. | Symptoms Suggesting Gallbladder Disease | Gallbladder Pathology | | | Diagnostic Bites | | Bacteriology | |
|----------|-----|--------------|-------------------|---|-----------------------|--------|---------------------|------------------|----------|-----------------------|------------------------------|
| | | | | | Chronic Cholecystitis | Stones | Other | Pre-oper. | At Oper. | Release | Specimens |
| | | | | | | | | | | Days Pos. after Oper. | No. of Negs. after Last Pos. |
| V. R. 1 | F. | 30 | 9 | Bilious attacks every 3-6 mos. from T. F. to time of oper. None in 10 mos. following | Yes | No | — | None | Neg. | 0 | 13 |
| V. R. 2 | F. | 26 | 9 | None | Yes | Yes | — | Pos. | Pos. | 308 | 16 |
| V. P. 3 | F. | 36 | 2 | None | Yes | Yes | — | None | Pos. | 64 | 13 |
| F. L. 4 | F. | 54 | 8 | Occasional sharp pain and tenderness, U. R. Q. Dull aching pain, U. R. Q. since T. F. Bilious attacks frequently. Recurrent attacks U. R. Q. Pain for past 8 yrs. | Yes | No | — | Pos. | None | 9 | 20 |
| A. K. 5 | F. | 46 | ? | None | Yes | Yes | Greatly enlarged | None | Pos. | 9 | 15 |
| L. B. 6 | F. | 36 | 13 | None | Yes | No | — | None | Pos. | 0 | 16 |
| L. H. 7 | F. | 42 | 2 | None | Yes | Yes | — | Pos. | Pos. | 0 | 16 |
| E. C. 8 | F. | 44 | 36 | Severe G. B. attacks 1929-1933. Many attacks of U. R. Q. pain. Occ. clay colored B. M. | Yes | Yes | Yes* | None | Pos. | 0 | 3 |
| D. S. 9 | M. | 51 | 16 | None | Yes | Yes | — | Pos. | Pos. | 29 | 23 |
| A. W. 10 | M. | 39 | 18 | None | No | Yes | — | Pos. | None | 0 | 2 |
| T. K. 11 | F. | 39 | 28 | Attack of jaundice 18 yrs. ago | Yes | Yes | Yes* | Pos. | Pos. | 433 | 0 |
| E. M. 12 | F. | 27 | 2 | Severe acute G. B. attacks month before oper. | Yes | No | — | Neg. | Pos. | 0 | 19 |
| D. W. 13 | F. | 44 | ? | Tenderness, U. R. Q. | Yes | Yes | 2 times normal size | None | Pos. | 460 | 0 |
| G. S. 14 | M. | 15 | 1 | G. B. symptoms during illness with typhoid fever | Yes | Yes | — | Pos. | None | 0 | 14 |
| C. A. 15 | F. | 55 | 38 | Bilious attacks 25 years. Tenderness U. R. Q. | Yes | Yes | — | Pos. | Pos. | 0 | 26 |
| M. J. 16 | F. | 48 | 22 | Pain and tenderness U. R. Q. progressively worse 13 years previous to oper. | Yes | No | — | None | Pos. | 0 | 12 |
| G. E. 17 | F. | 33 | 2 | No G. B. symptoms past 10 yrs. About 1 attack per year previously | Yes | Yes | — | Pos. | Pos. | 0 | 10 |
| I. G. 18 | F. | 45 | 37 | Treated for cholelithiasis 6 mos. before oper. Frequent U. L. Q. pain | Yes | Yes | Hepatitis | Pos. | Pos. | 16 | 14 |
| T. S. 18 | | | | | | | | | | | |

* Active chronic, purulent cholecystitis.

remain positive for a much longer time and eventually become negative, as is shown in Case 2. For two months this patient continued to submit stool specimens in spite of the fact that the specimens remained positive. Because of our inexperience, we were convinced in our own minds that this was to be a failure; however, after 308 days the feces became negative and have remained so.

Twelve patients had symptoms characteristic of cholecystitis or cholelithiasis while the remaining six patients had no symptoms even suggestive of disease of the biliary tract. Gallstones were present in 13 patients and absent in the remainder. There was a nearly uniform finding in the gallbladder on pathologic examination of chronic cholecystitis with marked lymphoid hyperplasia. In two instances, active, chronic, purulent cholecystitis was present and in two cases the gallbladder was greatly enlarged but with the common finding of chronic cholecystitis.

It is worthy of emphasis that a third of the patients had no symptoms referable to the gallbladder, nearly one-third had no stones and the changes in the gallbladder were nearly all minimal in character. In every case, however, there did exist definite changes in the gallbladder characteristic of long standing low grade infection, and aside from the cure of the carrier state, so desirable from the public health standpoint, we feel that cholecystectomy will usually improve the health of the patient to such an extent as to make it very much worth while also from the viewpoint of the individual.

SUMMARY

(1) In our series, cholecystectomy was performed on 18 chronic biliary typhoid carriers with a percentage of cure of 88.9.

(2) No deaths occurred in the series.

(3) Eligibility for cholecystectomy was based on the carrier being a gallbladder carrier and a good surgical risk.

(4) Cure was considered effected when 12 consecutive negative feces specimens and at least one (usually two) negative bile specimens were obtained.

(5) Most cases become feces-negative in from a few days to two or three weeks after operation. Hope for eventual cure may be maintained for many months, however.

(6) Mortality and cure percentages are comparable only if:

a. Typhoid and paratyphoid fever carriers are considered separately.

b. Carriers operated upon primarily for cure of the carrier state and primarily for clinical symptoms are considered separately.

c. The time elapsed since typhoid fever is taken into consideration.

d. The criteria for release are identical or at least similar.

(7) Cholecystectomy may logically be recommended as a matter of personal precaution to a chronic carrier without clinical symptoms who is a good risk.

(8) Each cure removed one more of a limited number of infection foci and thus contributes to the ultimate eradication of typhoid fever.

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