

# THE INCIDENCE OF GALLSTONES AND THEIR CORRELATION WITH OTHER DISEASES\*

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MANY REPORTS on the incidence of gallstones have been published. Comparisons of the statistical data presented in these reports are difficult or impossible, for the data have been analyzed in different ways by the various authors. Frequently, there was no separation of the patients as to sex, age groups or color. One purpose of this report is to show that such a separation is necessary and the second purpose of this report is to demonstrate that certain diseases have an actual correlation with gallstones.

## MATERIAL

This report is based upon an analysis of 26,895 consecutive autopsies performed at the Philadelphia General Hospital during a period of 20 years, from the beginning of 1920 to the close of 1939 and of 7771 consecutive autopsies performed at the Jefferson Medical College Hospital from the beginning of 1920 to the end of 1949. The great majority of patients admitted to the Philadelphia General Hospital are indigent, chronic or aged sick with provisions made for a small percentage of sick who are employees of the city government. About 40 per cent of the patients admitted to Jefferson Hospital are indigent or free ward patients, the remainder coming from all classes and income groups. The data from each hospital were analyzed separately but no significant differences were

noted. They are, therefore, combined and presented as one group.

## METHOD

All cases in which autopsy was performed and all cases with gallstones were recorded as to sex, color and age by decades. All diseases having a probable correlation with gallstones were similarly recorded.

## INCIDENCE OF GALLSTONES

Stated in the orthodox manner, of the 34,666 autopsies reviewed, gallstones were found in 3448 cases or in 9.94 per cent of all cases. This figure has little or no significance, for no gallstones were found in 4887 autopsies on individuals less than 20 years of age in this series. Since gallstones rarely occur before the age of 20 years, all autopsies below this age should be eliminated from consideration. Therefore, of the 29,779 autopsies performed on patients over 20 years of age, gallstones were present in 11.6 per cent.

## DISTRIBUTION OF MATERIAL ACCORDING TO AGE, SEX AND COLOR

The incidence of gallstones differed with age, sex and color as indicated in Table I. The incidence of gallstones increased progressively in successive decades. This incidence according to age was found to differ as regards sex. The total incidence of gallstones was greater in the white female (21.7

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per cent) than in the white male (9.7 per cent) with a ratio of 2.2 to 1. The incidence of gallstones also differed as regards color. The total incidence of gallstones was greater in the colored female (8.7 per cent) than in the colored male (3.25 per cent) with a ratio of 2.7 to 1. However, the total incidence was greater in both white males and females than in the colored race. Further analysis showed that, in white females, stones doubled in frequency of incidence in successive decades from the third through the sixth, with a slower progressive increase to the tenth decade, when a considerable increase again occurred. Marked increases in incidence occurred between the ages of 50 to 60 years and above 90 years of age. Gallstones occurred sporadically in white males up to the age of 50 years, becoming significant after the age of 60 and continuing to form beyond the age of 90 years. In colored females, the first significant increase in the incidence of gallstones occurred between the ages of 60 to 70 years, with a more marked increase between the ages of 80 to 90, followed by a considerable decrease beyond the age of 90 years. In the colored male, a significant increase in gallstones occurred at a much later period, that is, between the ages of 80 to 90 years, followed by a decrease in incidence as in the colored female. Gallstones, therefore, seemed to make their real appearance in the white female between 50 and 60 years of age, in the white male between 60 and 70 years, in the colored female between 60 and 70 years and in the colored male between 80 to 90 years. Especially significant, therefore, was the incidence of gallstones in individuals 50 years of age or more occurring in 27.8 per cent of white females, 12.4 per cent of white males, 14 per cent of colored females and 6 per cent of colored males. These data also show that new stones continued to form through all the later decades of life in white males and females whereas, in the colored race, new

stones apparently formed only to the age of 90 years.

Many authors have attempted to explain the difference in the incidence of gallstones in men and women on the basis that pregnancy accounted for the larger incidence in women. Robertson and Dochat<sup>29</sup> have furnished an extensive review of this subject. They concluded that their data did not support the view that pregnancy alone could account for the relatively increased frequency of gallstones in women. Robertson<sup>28</sup> stated that gallstones in both men and women are formed almost exclusively during the active sex life of the individual. My data do not support this statement. On the contrary, gallstones appeared to form with greater frequency in both sexes and both colors with the diminution and cessation of sexual activity. Construction of a curve of incidence of gallstones showed that the first high point reached its peak in the climacterium in white women, that is, between the age of 50-60 years, but the second and higher peak occurred after the age of 90 years. In colored females, the first high point reached its peak between 60 and 70 years, presumably a period of relative sexual inactivity, with a second higher peak between the ages of 80 to 90 years. The peak of incidence occurred one decade later in males than in females, that is, between the ages of 60 to 70 years in white males and 70 to 80 years in colored males. It may be admitted that sexual activity continues to a later age in men than in women, but a rising curve of incidence continued with almost equal degree beyond the accepted period of sexual activity.

A review of the literature with a view to comparing the statistical data herein presented with that previously published was attempted. This was difficult, for there was no separation as to sex, color or age group as in the reports of Naunyn,<sup>25</sup> Scheel,<sup>31</sup> Lotzin<sup>18</sup> and Martenson.<sup>20</sup> The data for the incidence of gallstones in males and

females by age groups but without separation into white or colored of each sex were furnished by Mosher,<sup>24</sup> Mentzer,<sup>21</sup> Ophüls,<sup>26</sup> Dessau<sup>5</sup> and Robertson<sup>28</sup> in this country and by Hamilton<sup>8</sup> in Australia. In Table II are included the data furnished by Hansen<sup>9</sup> (Norway), Gross<sup>7</sup> (Great Britain) and Crump<sup>3</sup> (Germany) occurring in white males and females only. Also included are the data for both sexes, both white and colored, furnished by Jaffe<sup>10</sup> (Chicago), Ludlow<sup>19</sup> (Cleveland) and Lopis<sup>17</sup> (South Africa). Wide differences in incidence of gallstones were reported from Europe, but

per cent in white females, 0.28 per cent in white males (a ratio of 1.7 to 1), 0.21 per cent in colored females and 0.13 per cent in colored males (a ratio of 1.5 to 1). On the other hand, the incidence of carcinoma of the gallbladder in those patients harboring gallstones was 2.5 per cent in white females, 1.6 per cent in white males (a ratio of about 1.5 to 1), 3 per cent in colored females and 5 per cent in colored males (a ratio of 1 to 1.6). The higher incidence of carcinoma of the gallbladder with gallstones in the colored race seemed remarkable but may not be significant, since relatively few cases

TABLE I.—*The Incidence of Gallstones.*

Age	Total Cases	Female White		Total Cases	Male White		Total Cases	Female Colored		Total Cases	Male Colored	
		Number with Gall-stones	Per Cent with Gall-stones		Number with Gall-stones	Per Cent with Gall-stones		Number with Gall-stones	Per Cent with Gall-stones		Number with Gall-stones	Per Cent with Gall-stones
20-30	592	25	4.2	576	5	0.9	999	20	2.0	735	2	0.3
30-40	816	70	8.6	1126	24	2.1	967	50	5.2	975	9	0.9
40-50	1156	140	12.1	1941	81	4.2	1005	99	9.8	1141	24	2.1
50-60	1495	348	23.3	2906	220	7.6	859	89	10.4	1033	43	4.2
60-70	1852	510	27.5	3153	395	12.5	502	84	16.7	689	53	7.7
70-80	1402	429	30.6	2081	342	16.4	265	50	18.9	320	21	6.6
80-90	412	144	34.9	583	125	21.4	44	11	25.0	66	9	13.6
90+	36	16	44.4	31	8	25.8	10	1	10.0	11	1	9.1
All cases	7761	1682	21.7	12397	1200	9.7	4651	404	8.7	4970	162	3.25

some of these may have been due to the relatively small series of cases included in the reports.

#### DISEASES AND PATHOLOGIC CHANGES HAVING CORRELATION WITH GALLSTONES

A significant positive correlation with gallstones was found in primary carcinoma of the gallbladder, diabetes mellitus, acute pancreatitis with and without fat necrosis and portal cirrhosis, and a questionable correlation was noted with peptic ulcer and pernicious anemia. A determination of the incidence of gallstones in tuberculosis also seemed worthwhile because of the general impression among pathologists of a decreased incidence of gallstones in this disease.

*Primary Carcinoma of the Gallbladder.* The incidence of carcinoma of the gallbladder in the general autopsy series was 0.47

were included in this group. That carcinoma of the gallbladder was associated with a markedly increased incidence in the frequency of gallstones is shown in Table III. The highest incidence of gallstones (64.3 per cent) occurred in white females with carcinoma of the gallbladder. There was approximately a three-fold increase in the number of gallstones in both white and colored females, a five-fold increase in white males and a ten-fold increase in colored males.

Mohardt,<sup>22</sup> in a collective review of primary carcinoma of the gallbladder, stated that the percentage of cases in which stones occurred varied between 65 and 100 per cent, with the lowest incidence of 64.6 per cent reported by Judd and Gray.<sup>14</sup> He also stated that the incidence of cancer of the gallbladder in patients having stones was

THE INCIDENCE OF GALLSTONES

4 to 5 per cent. These figures are higher than those presented above. It has been frequently stated in the literature that cholelithiasis was about four times more frequent in women than in men, as was also carcinoma of the gallbladder. My data show that cholelithiasis was 2.2 to 2.7 times more frequent in women, and that carcinoma of

cent in white males, 348.0 per cent in colored females and 183.1 per cent in colored males. In diabetics beyond 50 years of age, gallstones were present in approximately one of every two white females, one of every three colored females, one of every five white males and one of every seven colored males.

TABLE II.—*The Incidence of Gallstones.*

	Female Num- ber of Autopsies	White Per cent with Gall- stones	Per Cent With Gallstones									
			0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90+
Hansen	542	31.2	...	....	12.5	19.6	28.2	36.2	32.8	39.3	....	....
Gross	3400	12.4	...	0.3	2.5	5.5	14.2	24.2	35.4	40.7	21.0	....
Crump	550	37.8	...	....	14.5	12.0	25.0	37.0	48.0	51.0	....	....
Jaffe	?	17.6	...	....	5.0	11.5	21.9	17.07	29.03	24.44	....	....
Ludlow	1387	10.45	...	1.54	4.92	7.39	16.66	22.62	24.76	26.83	50.0	....
Lopis	684	19.7	0.0	0.0	8.43	16.66	14.87	26.27	26.01	33.3	40.0	0.0
Lieber	7761	21.7	...	....	4.2	8.6	12.1	23.3	27.5	30.6	34.9	44.4
	Male	White										
Hansen	649	19.0	...	....	1.8	6.7	12.8	14.0	25.1	34.8	....	....
Gross	6131	6.2	...	....	1.0	1.7	5.0	10.3	15.0	19.6	34.0	....
Crump	450	26.2	...	....	0.0	6.1	24.0	14.0	35.0	54.0	53.0	....
Jaffe	?	6.76	...	....	0.0	1.45	4.2	6.7	11.2	13.9	....	....
Ludlow	2392	5.77	0.0	0.88	2.52	2.4	6.3	10.66	15.09	13.73	0.0	0.0
Lopis	1182	9.3	0.0	3.3	0.0	0.0	5.4	9.3	14.06	16.12	33.0	0.8
Lieber	12397	9.67	...	....	0.86	2.1	4.2	7.6	12.5	16.4	21.4	25.0
	Female	Colored										
Jaffe	?	10.23	...	....	3.28	7.5	12.24	16.27	25.0	20.0	....	....
Ludlow	461	7.6	0.0	0.0	1.92	7.02	14.1	21.95	33.3	12.5	100.	0.0
Lopis	578	5.7	0.0	0.0	3.95	8.07	7.31	17.5	0.0	0.0	0.0	0.0
Lieber	4651	8.7	...	....	2.0	5.2	9.8	10.4	16.7	18.9	25.0	10.0
	Male	Colored										
Jaffe	?	1.04	...	....	0.0	0.73	0.0	1.86	4.34	6.66	....	....
Ludlow	560	3.04	0.0	0.0	0.0	1.4	3.48	12.35	5.56	0.0	0.0	0.0
Lopis	1099	2.0	0.0	0.0	0.05	1.38	0.82	3.73	0.0	30.76	0.0	0.0
Lieber	4970	3.25	...	....	0.27	0.92	2.1	4.2	7.7	6.6	13.6	9.1

the gallbladder was about 1.5 times more frequent in women than in men.

*Diabetes Mellitus.* There was a total of 1259 cases of diabetes, in 381 of which gallstones were present (30.2 per cent). Table IV shows that an appreciable increase in the incidence of gallstones in diabetics occurred in each age group beyond the third decade and in each color of both sexes. Comparison of Tables I and IV demonstrated that there was a total increase in the incidence of gallstones in this disease of 77.4 per cent in white females, 84.5 per

No comparable figures or data could be found in the literature. Seckel<sup>32</sup> found only 26 patients with gallstones among 430 cases of diabetes (6 per cent). Jones and his associates,<sup>11</sup> from examination of the duodenal contents of 68 diabetic patients, concluded that 15 (22 per cent) had gallstones. Wilder<sup>34</sup> found gallstones in 16 (28 per cent) of 58 cases of diabetes examined post-mortem. Woehrmann<sup>35</sup> found gallbladder disease in 160 of 677 diabetic patients (23.6 per cent) but did not indicate the number with gallstones. Similarly, Katsch<sup>15</sup> reported

gallbladder changes in 14 of 36 cases of diabetes (39 per cent). Warren<sup>33</sup> found gallstones at autopsy in 140, or 31 per cent of 453 cases of diabetes over 30 years of age, whereas in 500 consecutive autopsies on non-diabetic patients of the same age group, gallstones were found in only 21 per cent. Dry and Tessner<sup>6</sup> reported that gallstones were present or had been removed

in diabetics than in non-diabetics, concluded that gallbladder disease could not be regarded as a primary factor in the causation of diabetes. Robertson<sup>28</sup> has provided an excellent review of the various theories that have been proposed to explain the presence of gallstones. Commenting on the more frequent occurrence of gallstones in diabetics, he stated that he was unable to

TABLE III.—Incidence of Gallstones in Primary Carcinoma of the Gallbladder.

	Female White			Male White			Female Colored			Male Colored		
	Num- ber of Cases	with Gall- stones	Per Cent with Gall- stones	Num- ber of Cases	with Gall- stones	Per Cent with Gall- stones	Num- ber or Cases	with Gall- stones	Per Cent with Gall- stones	Num- ber of Cases	with Gall- stones	Per Cent with Gall- stones
20-30	0	0	....	0	0	....	0	0	....	0	0	....
30-40	1	0	....	0	0	....	0	0	....	0	0	....
40-50	4	2	50.0	6	3	50.0	1	0	....	0	0	....
50-60	6	3	50.0	5	2	40.0	3	0	....	2	1	50.0
60-70	16	11	68.7	16	6	37.5	5	2	40.0	6	2	33.3
70-80	13	9	69.2	7	4	57.1	2	1	50.0	0	0	....
80-90	2	2	100.0	5	4	80.0	1	0	....	0	0	....
Total	42	27	64.3	39	19	48.7	12	3	25.0	8	3	37.5

TABLE IV.—Incidence of Gallstones in Diabetes Mellitus.

Age	Female White			Male White			Female Colored			Male Colored		
	Num- ber of Cases	with Gall- stones	Per Cent with Gall- stones	Num- ber of Cases	with Gall- stones	Per Cent with Gall- stones	Num- ber of Cases	with Gall- stones	Per Cent with Gall- stones	Num- ber of Cases	with Gall- stones	Per Cent with Gall- stones
20-30	12	0	0.0	8	0	0.0	8	1	12.5	3	0	0.0
30-40	12	2	16.6	6	1	16.6	12	1	9.3	11	0	0.0
40-50	37	7	19.0	16	2	12.5	32	6	18.7	20	1	5.0
50-60	131	41	31.3	42	4	9.5	115	34	29.4	25	2	8.0
60-70	163	77	47.2	81	11	13.5	130	49	37.7	13	2	15.4
70-80	111	50	45.0	91	22	24.2	102	41	40.2	3	1	33.3
80-90	8	5	62.5	52	13	25.0	7	4	57.0	1	1	100.0
90+	1	1	100.0	5	1	20.0	1	1	100.0	0	0	0.0
Total	475	183	38.5	301	54	17.9	407	137	33.7	76	7	9.2

surgically in 50 or 27 per cent of 182 cases of diabetes. Robertson,<sup>28</sup> reviewing the statistics of 4671 postmortem examinations performed at the Mayo Clinic on patients over 20 years of age, stated that gallstones occurred in 17 per cent of men and 30 per cent of women, whereas in 76 cases of diabetes, gallstones were present in 33 per cent of men and 43 per cent of women. Wilder<sup>34</sup> stated that disease of the gallbladder was an etiologic factor of importance in diabetes. However, Joslin and his associates,<sup>13</sup> commenting on the more frequent occurrence of cholelithiasis and cholecys-

titis in diabetics than in non-diabetics, find a single author who could support the possibility that diabetes favored the formation of stones and that almost all authors were agreed that diabetes, when it occurs, follows the presence of gallstones. My data do not furnish any demonstrable clues as to why an increased number of stones are found in diabetics. Nor can any explanation be offered for the considerably greater increase in the incidence of gallstones in colored than in white diabetics.

*Acute Pancreatitis With or Without Fat Necroses.* There was a total of 105 cases in this series. Other cases occurring postoper-

THE INCIDENCE OF GALLSTONES

actively or as a result of rupture of a viscus or mesenteric thrombosis were not included. Although there were an insufficient number of cases for adequate analysis, Table V does show several features of interest. There was a great increase in the incidence of gallstones in all decades in white men and women, particularly the latter. Gallstones were found in 77 per cent

indication of reflux of bile into the pancreatic duct as a probable cause in the production of acute pancreatitis. In the remaining 103 cases, the relationship between gallstones and pancreatitis remained unexplained.

Molander and Bell<sup>23</sup> presented statistical data on 158 cases of acute hemorrhagic pancreatitis occurring in 41,663 persons exam-

TABLE V.—Incidence of Gallstones in Acute Pancreatitis and Fat Necroses or Both.

Age	Female White			Male White			Female Colored			Male Colored		
	Number of Cases	with Gall-stones	Per Cent	Number of Cases	with Gall-stones	Per Cent	Number of Cases	with Gall-stones	Per Cent	Number of Cases	with Gall-stones	Per Cent
20-30	1	0	0.0	0	0	0.0	1	0	0.0	4	0	....
30-40	2	0	0.0	0	0	0.0	5	0	0.0	8	1	12.5
40-50	4	2	50.0	4	2	50.0	6	2	33.3	3	0	....
50-60	13	13	100.0	6	2	33.3	1	0	0.0	4	0	....
60-70	15	11	73.3	9	4	44.4	5	2	40.0	2	0	....
70-80	6	4	66.6	4	0	0.0	0	0	0.0	0	0	....
80-90	1	0	0.0	1	0	0.0	0	0	0.0	0	0	....
Total	42	30	71.4	24	8	33.3	18	4	22.2	21	1	4.7

TABLE VI.—Incidence of Gallstones in Portal Cirrhosis.

Age	Female White			Male White			Female Colored			Male Colored		
	Number of Cases	with Gall-stones	Per Cent	Number of Cases	with Gall-stones	Per Cent	Number of Cases	with Gall-stones	Per Cent	Number of Cases	with Gall-stones	Per Cent
20-30	4	0	0.0	6	0	0.0	0	0	0.0	5	1	20.0
30-40	12	2	16.6	35	2	5.7	5	0	0.0	12	1	8.3
40-50	47	9	19.1	81	9	11.1	12	1	8.3	17	0	0.0
50-60	65	29	30.7	104	12	11.5	13	3	23.0	22	1	4.6
60-70	58	22	38.0	116	24	20.6	5	0	0.0	10	0	0.0
70-80	31	13	41.9	42	8	19.0	3	1	33.3	3	0	0.0
80-90	7	4	57.1	11	0	0.0	0	0	0.0	0	0	0.0
Total	224	70	31.2	395	55	13.9	38	5	13.2	69	3	4.3

of white women and in 33 per cent of white men over the age of 40 years, approximately a three-fold increase in the incidence of gallstones in both sexes. No case with gallstones occurred before the age of 40 years. Of the 18 cases of acute pancreatitis in colored women, four cases (22.2 per cent) showed gallstones. Of 21 cases of acute pancreatitis in colored men, only one case (4.7 per cent) was associated with gallstones. Calculous obstruction of the common bile duct was found in six cases, and in two others gallstones were present in the duct but did not produce obstruction. In only two of the six cases was there an

ined postmortem, including 26,262 males and 15,401 females. These cases were divided by age and sex groups but not by color. There were 93 males and 67 females showing acute hemorrhagic pancreatitis. None of these cases were associated with cholelithiasis prior to the age of 30 years. In each decade following the fourth, the percentage of cases associated with gallstones in males was 28.6, 25, 32, 50, and 33.3 respectively and in females 37.5, 85, 85.7, 90, 57.1 and 50 per cent respectively. They stated that in about two-thirds of the males and one-third of females with acute pancreatitis, this disease developed in the absence

of gallstones, but since gallstones were found about six times as frequently in both males and females with acute pancreatitis as in the general autopsy population, there must have been some causal relation between the two findings. Roberts, Baggenstoss and Comfort<sup>27</sup> stated that 25 patients

*Portal Cirrhosis.* Portal cirrhosis was associated with gallstones in 31.2 per cent of white women, 13.9 per cent of white men, 13.2 per cent of colored women and 4.3 per cent of colored men. The essential data on this relationship are presented in Table VI. Comparison of this table with Table I

TABLE VII.—*The Incidence of Gallstones in Gastric Ulcer, Duodenal Ulcer and Peptic Ulcers Collectively.*

Age	Female White			Male White			Female Colored			Male Colored		
	Total Cases	Number with Gall-stones	Per Cent with Gall-stones	Total Cases	Number with Gall-stones	Per Cent with Gall-stones	Total Cases	Number with Gall-stones	Per Cent with Gall-stones	Total Cases	Number with Gall-stones	Per Cent with Gall-stones
<b>Gastric Ulcers</b>												
20-30	4	0	0.0	2	0	0.0	6	1	16.6	2	0	0.0
30-40	5	0	0.0	12	0	0.0	4	0	0.0	17	1	5.9
40-50	13	0	0.0	44	0	0.0	10	0	0.0	29	0	0.0
50-60	18	7	38.9	68	2	2.9	9	3	33.3	25	0	0.0
60-70	21	6	28.6	59	6	10.2	9	2	22.2	14	0	0.0
70-80	24	9	37.5	36	7	19.4	5	0	0.0	6	0	0.0
80-90	5	0	0.0	14	1	7.1	3	1	33.3	1	0	0.0
90+	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
All cases	91	22	24.2	235	16	6.8	46	7	15.2	94	1	1.1
<b>Duodenal Ulcers</b>												
20-30	3	0	0.0	3	0	0.0	7	0	0.0	7	0	0.0
30-40	3	0	0.0	24	4	16.6	7	1	14.2	15	1	6.6
40-50	10	1	10.0	52	3	5.8	7	0	0.0	13	0	0.0
50-60	9	3	33.3	40	5	12.5	11	3	27.2	6	0	0.0
60-70	19	8	42.1	51	8	15.7	6	1	16.6	5	0	0.0
70-80	12	1	8.2	45	4	8.9	6	4	66.6	1	0	0.0
80-90	8	3	37.5	11	1	9.1	1	0	0.0	0	0	0.0
90+	2	1	50.0	0	0	0.0	0	0	0.0	0	0	0.0
All cases	66	17	25.7	226	25	11.1	45	9	20.0	47	1	2.1
<b>All Peptic Ulcers</b>												
20-30	7	0	0.0	5	0	0.0	13	1	7.7	9	0	0.0
30-40	8	0	0.0	41	5	12.2	11	1	9.1	32	1	3.1
40-50	24	1	4.1	101	4	4.0	20	0	0.0	42	0	0.0
50-60	27	10	37.0	112	9	8.0	23	6	26.1	32	1	3.1
60-70	43	14	32.5	114	14	12.3	16	2	12.5	22	0	0.0
70-80	38	10	26.3	85	12	14.1	13	6	46.1	7	0	0.0
80-90	15	3	20.0	27	1	3.7	4	1	25.0	1	0	0.0
90+	3	1	33.3	0	0	0.0	0	0	0.0	0	0	0.0
All cases	165	39	23.6	485	45	9.3	100	17	17.0	145	2	1.4

died with acute pancreatic necroses among 13,788 patients. The records were incomplete in two cases. In only two of the remaining 23 cases (9 per cent), was an entirely normal biliary tract encountered. In 19 of the remaining 23 cases (83 per cent), the gallbladder showed signs of chronic inflammatory disease. Fifteen of the 22 gallbladders (68 per cent) examined contained gallstones. No data as to sex, age groups or color were supplied.

shows that there was a moderate increase in the incidence of gallstones in portal cirrhosis. There was a 43 per cent increase in incidence of gallstones in white men and women, 52 per cent in colored women and 32 per cent in colored men.

Klopstock<sup>16</sup> reported finding gallstones in 8 per cent of 209 males and in 17 per cent of 41 females with portal cirrhosis. According to Rolleston and McNee,<sup>30</sup> gallstones occurred slightly more often in cirrhosis

than in ordinary cases, for in 200 cases of cirrhosis examined after death, gallstones were found in 26, or 13 per cent. Martenson<sup>20</sup> found gallstones in 34 of his 105 cases of cirrhosis (32.3 per cent) occurring in women and in 48 of his 252 cases of cirrhosis (19 per cent) in men.

*Peptic Ulcer.* There was a total of 895 patients with peptic ulcer, in 103 of which

gallstones in white females and of 74.7 per cent in colored females, whereas a decreased incidence of 30 per cent occurred in white males and of 66 per cent in colored males. In patients with duodenal ulcer, there was an increased incidence of gallstones of 18.4 per cent in white females, 130 per cent in colored females and 14.4 per cent in white males, but colored males

TABLE VIII.—Incidence of Gallstones in Pernicious Anemia.

Age	Female White			Male White			Female Colored			Male Colored		
	Num-ber of Cases	with Gall-stones	Per Cent with Gall-stones	Num-ber of Cases	with Gall-stones	Per Cent with Gall-stones	Num-ber of Cases	with Gall-stones	Per Cent with Gall-stones	Num-ber of Cases	with Gall-stones	Per Cent with Gall-stones
20-30	1	0	0.0	0	0	0.0	1	0	0.0	0	0	0.0
30-40	2	0	0.0	3	0	0.0	1	0	0.0	0	0	0.0
40-50	15	0	0.0	7	0	0.0	5	0	0.0	0	0	0.0
50-60	14	1	7.1	12	0	0.0	3	0	0.0	5	0	0.0
60-70	22	8	36.3	16	0	0.0	0	0	0.0	1	0	0.0
70-80	5	2	40.0	7	2	28.5	0	0	0.0	0	0	0.0
80-90	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Total	59	11	18.6	45	2	4.4	10	0	0.0	6	0	0.0

TABLE IX.—Incidence of Gallstones in Tuberculosis.

Age	Female White			Male White			Female Colored			Male Colored		
	Num-ber of Cases	with Gall-stones	Per Cent with Gall-stones	Num-ber of Cases	with Gall-stones	Per Cent with Gall-stones	Num-ber of Cases	with Gall-stones	Per Cent with Gall-stones	Num-ber of Cases	with Gall-stones	Per Cent with Gall-stones
20-30	206	7	3.4	177	3	1.7	559	6	1.1	431	2	0.4
30-40	187	7	3.7	270	4	1.5	318	9	2.8	387	5	1.3
40-50	137	8	5.8	368	10	2.7	154	7	4.6	257	4	1.5
50-60	88	15	17.0	369	18	4.9	92	14	15.2	140	2	1.4
60-70	75	14	18.6	264	23	8.7	34	12	35.3	71	5	7.0
70-80	42	10	23.8	105	11	10.4	20	11	55.0	27	1	3.7
80-90	11	3	27.2	9	0	0.0	4	3	75.0	5	0	0.0
Total	746	64	8.6	1562	69	4.4	1181	62	5.3	1318	19	1.4

gallstones were also present (11.5 per cent). The essential data are presented in Table VII under the three headings of gastric ulcers, duodenal ulcers and peptic ulcers, collectively. Included in the last group were also those cases with ulcers in both the stomach and duodenum, not included in the first two groups. Gallstones were present in 46, or 9.87 per cent of 466 cases of gastric ulcer, and in 52, or 13.5 per cent of 384 cases of duodenal ulcer. A comparison of the data presented in Table VII with those in Table I showed that, in patients with gastric ulcer, there was a slight increase of 11.5 per cent in the incidence of

gallstones in white females and of 74.7 per cent in colored females, whereas a decreased incidence of 30 per cent occurred in white males and of 66 per cent in colored males. In patients with duodenal ulcer, there was an increased incidence of gallstones of 18.4 per cent in white females, 130 per cent in colored females and 14.4 per cent in white males, but colored males

showed a decreased incidence of 35 per cent. Considering peptic ulcers, collectively, there was an increased incidence of gallstones of 8.8 per cent in white females and of 95.4 per cent in colored females, but a decreased incidence of 4.1 per cent occurred in white males and 56.9 per cent in colored males.

These data indicated that there was practically no difference in the incidence of gallstones between peptic ulcers, collectively (11.5 per cent) and the general autopsy population (11.6 per cent) without consideration of sex, age and color. However, a significant increase in the incidence



of gallstones was noted in the colored female in each of the three groups, namely, gastric, duodenal and peptic ulcers, collectively. Only a slight increase in the incidence of gallstones was noted in white females in each of the three groups. Colored males showed a consistently decreased incidence of gallstones in all three groups. A decreased incidence of gallstones also occurred in white males with gastric ulcer and peptic ulcers, collectively but an increased incidence of approximately 20 per cent occurred with duodenal ulcers.

The greater number of gastric ulcers than duodenal ulcers in this series was noteworthy. The ratio of gastric to duodenal ulcers in the 769 cases from the Philadelphia General Hospital was 1.45 in white females, 1.17 in white males, 1.12 in colored females and 2.1 in colored males. The ratio of gastric to duodenal ulcers in the 126 cases from the Jefferson Hospital was 1.0 in white females, 0.62 in white males, and 1.25 in colored males; no gastric ulcers and only four duodenal ulcers were found in colored females. No explanation could be determined for the larger number of gastric ulcers which occurred at the Philadelphia General Hospital.

Little statistical data as to the incidence of gallstones in peptic ulcer could be found in the literature. Gross<sup>7</sup> found among his 4000 control cases, 173 cases (4.33 per cent) of gastric ulcer and 230 cases (5.75 per cent) of duodenal ulcer. Among the 405 cases with gallstones, there were 19 cases (4.69 per cent) of gastric ulcer and 21 cases (5.19 per cent) of duodenal ulcer. He concluded that there was no association between gastric or duodenal ulcers and cholelithiasis.

*Pernicious Anemia.* There was a total of 120 cases of pernicious anemia distributed in the manner indicated in Table VIII. Gallstones were present in 13 cases (10.8 per cent). No gallstones were found in the 16 cases of pernicious anemia occurring in

colored males and females. Stones were absent in white women up to the age of 50 years and in white men up to the age of 70 years. There was a total decreased incidence of gallstones of 14.4 per cent in white females and of 54.6 per cent in white males.

The prevailing view is that cholecystic disease is frequently concomitant with pernicious anemia. Jones and Joyce<sup>12</sup> stated that they were able to demonstrate chronic infection of the gallbladder in all 13 of their cases; gallstones were present in one case. In a subsequent paper, they added nine cases, one of which was associated with gallstones, and concluded that in every case of pernicious anemia with which they worked personally, a chronic infection of the gallbladder had been positively demonstrated. Davidson and Gulland<sup>4</sup> stated that they were impressed by the frequency of gallstones in pernicious anemia. Brown,<sup>2</sup> in 18,200 autopsies, found 151 cases with pernicious anemia, of which 15.9 per cent had either cholecystitis or cholelithiasis. Boyden and Layne<sup>1</sup> reviewed 31,311 necropsies and found 105 cases with pernicious anemia. They described an increasing incidence of gallbladder disease with age. They found gallstones in 19 of these cases (18.1 per cent) with an incidence of 5 per cent in the decade 41-50, 7 per cent in the decade 51-60, 22 per cent in the decade 61-70, 35 per cent in the decade 71-80 and 50 per cent in the decade 81-90.

*Tuberculosis.* There was a total of 4807 cases of tuberculosis, and gallstones were present in 214 of these cases (4.4 per cent). An analysis of the data presented in Table IX when compared with those in Table I showed that there was a decreased incidence of gallstones in white females, both white and colored males, and in colored females up to 50 years of age. An increased incidence of gallstones occurred in colored females after the age of 50. The incidence of gallstones in the general colored female population after the age of 50 was 14.0 per

THE INCIDENCE OF GALLSTONES

TABLE X.—Per Cent of Gallstones in Various Diseases.

Age	All Cases	Carcinoma of Gallbladder	Acute Pancreatitis			Portal Cirrhosis	Peptic Ulcers	Pernicious Anemia	Tuberculosis
			Diabetes	and/or Fat Necroses					
<b>Female White</b>									
20-30	4.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.4
30-40	8.6	0.0	16.6	0.0	16.6	0.0	0.0	0.0	3.7
40-50	12.1	50.0	19.0	50.0	19.1	4.1	0.0	0.0	5.8
50-60	23.3	50.0	31.3	100.0	30.7	37.0	7.1	7.1	17.0
60-70	27.5	68.7	47.2	73.3	38.0	32.5	36.3	36.3	18.6
70-80	30.6	69.2	45.0	66.6	41.9	26.3	40.0	40.0	23.8
80-90	34.9	100.0	62.5	0.0	57.1	20.0	0.0	0.0	27.2
90+	44.4	....	100.0	0.0	....	33.3	....	....	...
Total	21.7	64.3	38.5	71.4	31.2	23.6	18.6	18.6	8.6
<b>Male White</b>									
20-30	0.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.7
30-40	2.1	0.0	16.6	0.0	5.7	12.2	0.0	0.0	1.5
40-50	4.2	50.0	12.5	50.0	11.1	4.0	0.0	0.0	2.7
50-60	7.6	40.0	9.5	33.3	11.5	8.0	0.0	0.0	4.9
60-70	12.5	37.5	13.5	44.4	20.6	12.3	0.0	0.0	8.7
70-80	16.4	57.1	24.2	0.0	19.0	14.1	28.5	28.5	10.4
80-90	21.4	80.0	25.0	0.0	0.0	3.7	0.0	0.0	0.0
90+	25.8	....	20.0	....	....	0.0	....	....	...
Total	9.7	48.7	17.9	33.3	13.9	9.3	4.4	4.4	4.4
<b>Female Colored</b>									
20-30	2.0	0.0	12.5	0.0	0.0	7.7	0.0	0.0	1.1
30-40	5.2	0.0	9.3	0.0	0.0	9.1	0.0	0.0	2.8
40-50	9.8	0.0	18.7	33.3	8.3	0.0	0.0	0.0	4.6
50-60	10.4	0.0	29.4	0.0	23.0	26.1	0.0	0.0	15.2
60-70	16.7	40.0	37.7	40.0	0.0	12.5	0.0	0.0	35.3
70-80	18.9	50.0	40.2	0.0	33.3	46.1	0.0	0.0	55.0
80-90	25.0	0.0	57.0	0.0	0.0	25.0	0.0	0.0	75.0
90+	10.0	....	100.0	....	....	0.0	....	....	...
Total	8.7	25.0	33.7	22.2	13.2	17.0	0.0	0.0	5.3
<b>Male Colored</b>									
20-30	0.3	0.0	0.0	0.0	20.0	0.0	0.0	0.0	0.4
30-40	0.9	0.0	0.0	12.5	8.3	3.1	0.0	0.0	1.3
40-50	2.1	0.0	5.0	0.0	0.0	0.0	0.0	0.0	1.5
50-60	4.2	50.0	8.0	0.0	4.6	3.1	0.0	0.0	1.4
60-70	7.7	33.3	15.4	0.0	0.0	0.0	0.0	0.0	7.0
70-80	6.6	0.0	33.3	0.0	0.0	0.0	0.0	0.0	3.7
80-90	13.6	0.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0
90+	9.1	....	....	....	....	....	....	....	...
Total	3.2	37.5	9.2	4.7	4.3	1.4	0.0	0.0	1.4

cent as contrasted with the incidence of 26.6 per cent which occurred in those with tuberculosis.

Table X provides a concise, readily accessible comparison of the percentage incidence of gallstones by sex, age groups and color in the general autopsy population as contrasted with their incidence in primary carcinoma of the gallbladder, diabetes mellitus, acute pancreatitis, portal cirrhosis, peptic ulcer, pernicious anemia and tuberculosis.

SUMMARY AND CONCLUSIONS

1. Gallstones were present in 11.6 per cent of 29,779 autopsied patients 20 years or more old. The incidence of gallstones differed with age, sex and color. There was a progressive increase in the incidence of gallstones from one decade to the next. The incidence of gallstones was greater in the white than in the colored race and greater in females than in males. There was a ratio of 2.2 to 1 of white females to white males and a ratio of 2.7 to 1 of colored females

to colored males. The first high point in the incidence of gallstones in white females occurred between the ages of 50 to 60 years and between 60-70 years in colored females. In males, this occurred one decade later, that is, between the ages of 60-70 years in white males and between 70-80 years in colored males. Gallstones continued to form through all the decades of life in white males and females and up to the age of 90 years in colored males and females. Greater increase in the incidence of gallstones was concomitant with a diminution of and cessation of sexual activity.

2. Carcinoma of the gallbladder was associated with a three-fold increase in the number of gallstones in females, a five-fold increase in white males and a ten-fold increase in colored males.

3. Gallstones were present in 30.2 per cent of all diabetic patients beyond 20 years of age. An appreciable increase in the incidence of gallstones occurred in each age group and in both sexes of each color. This increased incidence in gallstones was considerably greater in the colored than in the white race. In diabetics 50 years of age or more, gallstones were present in approximately one of every two white females, one of every three colored females, one of every five white males and one of every seven colored males.

4. Gallstones were found in three-fourths of all white females and one-third of all white males with acute pancreatitis. No case with gallstones occurred before the age of 40 years. Of 18 cases of acute pancreatitis with or without fat necroses in colored females, four cases (22.2 per cent) were associated with gallstones and of 21 cases of this disease in colored males, only one case (4.7 per cent) showed gallstones.

5. A moderate increase in the incidence of gallstones occurred in portal cirrhosis in both sexes of each color.

6. An increased incidence of gallstones occurred in both white and colored females

with gastric, duodenal and peptic ulcers, collectively. Conversely, a decreased incidence of gallstones occurred in males except for a slightly increased incidence of stones in white males with duodenal ulcer.

7. Pernicious anemia was associated with a decreased incidence of gallstones in both sexes of both colors.

8. A decreased incidence of gallstones occurred in tuberculosis in both sexes, both white and colored, except in colored females 50 years old or more, who showed a two-fold increase in the number of stones.

## BIBLIOGRAPHY

- 1 Boyden, E. A., and J. A. Layne: The Gallbladder in Patients with Pernicious Anemia. *Gastroenterology*, 4: 121, 1945.
- 2 Brown, M. R.: The Pathology of the Gastrointestinal Tract in Pernicious Anemia and Subacute Combined Degeneration of the Spinal Cord. *New England J. Med.*, 210: 473, 1934.
- 3 Crump, C.: The Incidence of Gallstones and Gallbladder Disease. *Surg., Gynec. & Obst.*, 53: 447, 1931.
- 4 Davidson, L. S. P., and G. L. Gulland: *Pernicious Anemia*, London, 1930, Henry Kimpton.
- 5 Dessau, F. I.: The Incidence of Gallstones in the Higher Age Groups. *New England J. Med.*, 229: 464, 1943.
- 6 Dry, T. J., and C. F. Tessner: Postmortem Findings in Cases of Diabetes. *Minnesota Med.*, 24: 96, 1941.
- 7 Gross, D. B. M.: A Statistical Study of Cholelithiasis. *J. Path. & Bact.*, 32: 503, 1929.
- 8 Hamilton, I.: Gallstones Found Post-Mortem. *M. J. Australia*, 2: 78, 1932.
- 9 Hansen, S.: Undersøgelse over Cholelithiasis. *Ugesk. f. Laeger*, 84: 405, 1922.
- 10 Jaffe, R. H.: Cholelithiasis. A Statistical Study with Special Reference to Its Frequency in the Colored Race. *J. Lab. & Clin. Med.*, 18: 1220, 1936.
- 11 Jones, C. M., W. B. Castle and H. B. Mulholland: Pancreatic and Hepatic Activity in Diabetes Mellitus. *Arch. Int. Med.*, 35: 315, 1925.
- 12 Jones, N. W., and T. M. Joyce: Infection of the Gallbladder in Relation to Pernicious Anemia. *Am. J. M. Sc.*, 168: 469, 1924. Further Remarks on Infection of the Gallbladder in Relation to Chronic (Pernicious) Anemia, *ibid.*, 173: 566, 1927.

- 13 Joslin, E. P., H. F. Root, P. White, A. Marble and C. C. Bailey: *The Treatment of Diabetes Mellitus*, Ed. 8, Phila., 1946, Lea & Febiger, p. 554.
- 14 Judd, E. S., and H. K. Gray: *Carcinoma of the Gallbladder and Bile Ducts*. Surg., Gynec. and Obst., **55**: 308, 1932.
- 15 Katsch, G.: Ueber den sekundären Diabetes nach Cholecystopathie. *Deutsch. med. Wchnschr.*, **2**: 1508, 1928.
- 16 Klopstock, F.: Ueber Milztumor, Ikterus and Ascites bei Lebercirrhose. *Virchow's Arch. f. path. Anat.*, **187**: 111, 1907.
- 17 Lopis, S.: The Incidence of Cholelithiasis in the Bantu. *Clin. Proc.*, **6**: 338, 1947.
- 18 Lotzin, R.: Ueber die Beziehungen der Gallensteine zum Krebs der extrahepatischen Gallenwege; zugleich ein Beitrag zur Lehre von den Gallen steinwanderungen und dem Hydrops der Gallenwege. *Beitr. f. klin. Chir.*, **139**: 525, 1926.
- 19 Ludlow, A. J.: Autopsy Incidence of Cholelithiasis. *Am. J. M. Sc.*, **193**: 481, 1937.
- 20 Martenson, K. M.: The Incidence of Gallstones in Sweden. *Arch. Surg.*, **34**: 650, 1937.
- 21 Mentzer, S. H.: A Clinical and Pathologic Study of Cholecystitis and Cholelithiasis. *Surg., Gynec. & Obst.*, **42**: 782, 1926.
- 22 Mohardt, J. H.: *Carcinoma of the Gallbladder. Collective Review*. Surg., Gynec. & Obst. (*Internat. Abstr. Surg.*), **69**: 440, 1939.
- 23 Molander, D. W., and E. T. Bell: Relation of Cholelithiasis to Acute Hemorrhagic Pancreatitis. *Arch. Path.*, **41**: 17, 1946.
- 24 Mosher, C. D.: Abstract: The Frequency of Gall-Stones in the United States. *Bull. Johns Hopkins Hosp.*, **12**: 253, 1901.
- 25 Naunyn, B.: *A Treatise on Cholelithiasis* (Translated by Archibald E. Garrod), London, 1896, The New Sydenham Society.
- 26 Ophüls, W.: *Stanford Univ. Pub. Med. Sc.*, **1**: 131, 1921, cited by Warren.
- 27 Roberts, W. J., A. H. Baggenstoss and M. W. Comfort: Acute Pancreatic Necrosis. A Clinicopathologic Study. *Am. J. Clin. Path.*, **20**: 742, 1950.
- 28 Robertson, H. E.: The Preponderance of Gallstones in Women. *Surg., Gynec. & Obst. (Internat. Abstr. Surg.)*, **80**: 1, 1945.
- 29 Robertson, H. E., and G. R. Dochat: Pregnancy and Gallstones. *Surg., Gynec. & Obst. (Internat. Abstr. Surg.)*, **78**: 193, 1944.
- 30 Rolleston, H., and J. W. McNee: *Diseases of the Liver, Gallbladder and Bile Ducts*. London, 1929, Macmillan Co., p. 238.
- 31 Schetl, V.: Undersøgelser over Cholelithiasis. *Ugesk. f. Laeger.*, **73**: 1757, 1911.
- 32 Seckel, H.: Observations on Heredofamilial and Constitutional Diseases of Metabolism in Diabetes Mellitus. *Ztschr. f. klin. Med.*, **102**: 195, 1925.
- 33 Warren, S.: *The Pathology of Diabetes Mellitus*. Ed. 2, Phila., 1938, Lea & Febiger, p. 106.
- 34 Wilder, R. M.: Necropsy Findings in Diabetes. *South M. J.*, **19**: 241, 1926.
- 35 Woehрман, W.: Diabetes bei und nach Gallenblasenerkrankungen. *Ztschr. f. klin. Med.*, **108**: 646, 1928.

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#### ERRATUM NOTICE

In the January, 1952, issue of ANNALS OF SURGERY, on page 101 of the article "Surgical Decompression in Biliary Obstruction: A New Operative Procedure" by Mark A. Hayes, M.D., Ph.D., and Frederick A. Collier, M.S., M.D., a plate of illustration was printed upside down, thus labeling Figures 7, 6, 5 and 4 incorrectly as Figures 4, 5, 6 and 7, respectively. ANNALS OF SURGERY regrets any misinterpretations which may have resulted from this error.