

GENERAL STAFF MEETING  
UNIVERSITY HOSPITALS  
UNIVERSITY OF MINNESOTA

CONTENTS

	PAGE
I. ANNOUNCEMENTS	
1. HIGH-LIGHTS OF FIRST MEETING . . . . .	15
2. PAUL H. FESLER . . . . .	15
3. O. J. CAMPBELL . . . . .	15
4. DANCERS ATTENTION . . . . .	15
5. CLINICO-PATHOLOGICAL CONFERENCE . . . . .	15 - 16
II. ABSTRACT	
PRIMARY CARCINOMA OF PANCREAS . . . . .	16 - 19
III. CASE REPORT	
PRIMARY CARCINOMA OF THE HEAD OF THE PANCREAS. OBSTRUCTION OF THE COMMON BILE DUCT . . . . .	19 - 21
IV. ABSTRACT	
PRIMARY CARCINOMA OF THE GALL-BLADDER . . . . .	21 - 22
V. CASE REPORT	
PRIMARY CARCINOMA OF GALL-BLADDER WITH METASTASIS TO LIVER AND LUNGS . . . . .	22 - 23

## I. ANNOUNCEMENTS

### 1. High Lights of First Meeting:

Official attendance 62. Many new faces present, many old ones missing. Duck hunters will receive official excuse when spoils are presented as evidence. Dean Scammon responded graciously, briefly, appeared very interested, promised to return. Internist Beard and New Health Service Physician Watson contributed mightily to discussion of diabetes. Ophthalmologist Lane up from Northfield gave interesting comments on eye complications. Abstract was well received, new type of diet (low fat, high sugar and insulin) was discussed. Diet seems logical in view of change in cholesterol values (lower). Arteriosclerosis is very serious problem, coronary disease most frequent form in experience of discussors. Tuberculosis is infrequent today (Glen Lake experience, no cases in 3 years). Hypertension is probably frequent in disease (contrary opinion to Warren). Insulin resistant cases very rare. "Do not be afraid to use insulin especially in coma and infection" (intravenous in former?) Childhood diabetes may be different form of disease (result of infection?). Most diabetic subjects are obese, "well upholstered" individuals (life of ease). The question of removal of infected gall-bladders and stones is questionable procedure as far as tolerance is concerned (contrary). Robinowitch's work is of special interest and results will be awaited with interest. Diabetes is most often found with cataract: glaucoma with arteriosclerosis, and hypertension. Atropine should not be used after 45 years of age without considering possibility of precipitating acute glaucoma. Substitutes may be used, eserine to follow? Cases of diabetes presented many points in common. Differences: Age factor, degree of coronary disease, acute vs. chronic glaucoma, renal insufficiency vs. infection. One probable reason for diabetic mortality increase is "Once a diabetic, always a diabetic" as far as death certificates are concerned. Which at least shows tendency to write primary cause as the first cause.

"Breaking departmental technique" was well received in principle; action

depends on us. New 6th floor ward in Eustis Hospital will segregate younger from older communicable disease suspects and patients, to distinct advantage of all.

It is to be hoped all will see the advantage of cooperating with the State Department of Health Wassermann Laboratories. This is a departmental matter and should be very easy to put over. The attendance was very satisfactory and the interest good. Several of our good supporters did not get into action but will no doubt be heard from later. Which reminds us: "Please stand and face the audience when making comments." It is practically impossible to hear in the back unless this is done. Visitors are welcome at any time.

### 2. Paul H. Fesler, installed as

President of American Hospital Association, 33rd Annual Meeting, Toronto, Friday, Oct. 2, 1931. Short speech of acceptance followed. Plea: for hospitals not to sacrifice ideals of service in the interest of economy, to assume leadership in community health education, by working together to better hospital conditions for all. Congratulations from staff, best wishes for a most successful year.

### 3. O. J. Campbell will open Cancer

Conference tomorrow at 4th hour in Todd Amphitheater on "Study of End-results in Carcinoma of Breast" from University Hospitals. This was his Thesis for the Minneapolis Surgical Society and was well received. Results will be shown at end of 3, 5 and 10 year periods. Be sure to be there.

### 4. Dancers Attention:

A. T. Rasmussen, Anatomy Bldg., desires permanent faculty members who like to dance to get in touch with him at once. Reason: Faculty dancing club will swing into action for winter series of 7 or 8 dances, in about 3 weeks. Formal attire, informal hospitality. If you do not like to dance, don't tell your wife about this; if you do, this is your chance to get in good.

5. Clinico-pathological Conference starts one week from tomorrow, Friday,

Oct. 15th, under direction of Internist Henry Ulrich. Meeting to alternate with Cancer Conference in same place, same time. These meetings should prove very attractive as they were one of the highlights of last year's activity. "Get the habit, the rest is easy."

## II. ABSTRACT

### PRIMARY CARCINOMA OF THE PANCREAS

Logan Leven, M. D., Surgical Fellow University of Minnesota. Given at Cancer Conference (1930-31). Accepted for publication. Comment: Dr. Leven is to be complimented for splendid presentation of subject comparing our experience with literature, using good judgment at all times and writing very well. Interesting to note that few if any corrections were necessary when paper was handed in, truly something of which to be proud. It affords us pleasure to reprint this in abstract as we did Radiological Fellow Erickson's contribution last year on "Carcinoma of the Skin".

#### 1. Material:

(1) 32 cases of primary carcinoma of the pancreas, University Hospitals, University of Minnesota (1913-31).

(2) 99 cases from files of Department of Pathology, 1913-31, (including above). Review of history of illness, clinical course, operative treatment, and course and findings at postmortem examination.

(3) Review of pertinent literature. General statement, Carcinoma of pancreas, most frequent of all neoplastic growths, first described by Mondiere (1836).

#### 2. Types:

(1) Scirrhus. (2) Medullary (soft). (3) Gelatinous (colloid). By origin: (1) Epithelium of duct system: usually in head or body, often massive, poor definition from parenchyma. histopathology, papillary outgrowths and alveoli, cylindrical or cuboidal cells, local extensions via ducts, blood and lymph channels, or nerves, any of above gross changes.

(2) From parenchyma: diffuse, rapidly growing, alveolar arrangement, not unlike cirrhosis of gland, with associated hyperplasia of normal sometimes including islands, which may persist in malignant structure. (3) Island adenoma and

carcinoma with hyperinsulinemia (see last week). Successful operative type?

3. Cause: unknown. Theories: chronic pancreatitis, gall stones, syphilis, alcohol, trauma, developmental anomalies, etc. Possible factor cirrhosis of pancreas, e.g., like liver.

4. Incidence (Lit.) 1.3% (34 out of 2621 carcinomas); 1.76%; 2% (59 out of 2943 carcinomas). Hospital admissions: 41,949 (58), 50,494 (59), 57,143 (32) (author). Does this include all or only cases which died? Note variation.

5. Sex: Males predominate. (lit.) 566 cases; males 363, (64.1%), females 203, (35.9%) University Hospitals 32 (males 25, females 7). Department of Pathology 99 (males 67, females 32). Comment: Note close correlation (2/3 - 1/3).

6. Age: Most frequent in fifth to seventh decade, found at any age (new born?, 6 months, 2 years, etc.). University Hospitals (38 - 75 years). Department of Pathology (27 - 85 years).

Table 4. Age Distribution -- Comparison with a Collected Series

Age Grp.*	Tot. Coll. Ser.	Univ. Hosp.	Autopsy Series		
			Male	Female	Total
1-10	1	0			
11-20	11	0	0	0	0
21-30	4	0	2	0	2
31-40	24	2	5	0	5
41-50	63	6	11	6	17
51-60	82	13	18	10	28
61-70	46	10	26	11	37
71-80	23	1	4	4	8
81-90	0	0	1	0	1
Total	244	32	67	31**	98**

\* Fitcher, Friedenwald and Cullen, Boldt, Oser, Kiefer and Hale White.

\*\* The age of one case was not given reducing the totals to 31 and 98 instead of 32 and 99.

7. Location: Most frequent in head.

Table 5. Anatomical Location of Tumor

Series	Head	Body	Tail	Diffuse	Total
Coll.Ser.*	300	38	29	184	551
U. Hosp.	22	1	1	6	30
Autop.Ser.	60	4	15	18	97
Total	382	43	45	208	678
Percentage	56.3	6.3	6.6	30.7	100.

\* Series collected from Lanceraux, Mirallie, Oser, Boldt, Kiefer, Ancelet, Biach, Heiberg, Pearce, Germershausen and Segre.

8. Metastases: (lit.) First to regional nodes and liver. Small non-palpable deposits in liver. Note author found many which were bulky. Generalized growths infrequent because of short duration of disease? Extensions may produce unusual effects. 3 went to Virchow's node (in 1 it was presenting complaint).

Location	Number
Liver	59
Regional Nodes	50
Adrenals	13
Spleen	11
Carcinomatosis Peritonei	11
Lungs	11
Gall bladder and ducts	10
Extension thru diaphragm	7
Pleura	5
Peribronchial Nodes	5
Kidneys	5
Total	99

Effects: obstruction of duct of Wirsung, common bile duct, duodenum, pylorus, portal vein, inferior vena cava, ureter, etc.

9. Symptoms: Bard and Pic syndrome--progressive jaundice (no remissions?), distention of gall-bladder, absence of hepatic enlargement (probably based on small metastases theory?), subnormal temperature, rapid emaciation and cachexia. Cachexia, weight loss, anorexia, and weakness most constant (author).

(1) Weight loss: all of author's series showed some. Average 32 lbs. (Lit. 26 lbs.) Maximum (75 lbs.) Rate 1 lb. per 3.12 days; approximately, 10 lbs. a month. Very striking complaint.

(2) Jaundice: usually progressive, frequently extreme, occasionally intermittent, 3 cases. (Note this point). Of 400 cases of jaundice, Hartman found carcinoma of pancreas cause in 11.75%. (Lit.) shows sign in 70-80%. Pruritis in 50% of author's cases. Not always painless as frequently stated as it may resemble gall stone colic (important observation).

(3) Pain: (Lit.) 60 to 90% may be initial complaint. Hospital series (100%).

Types: steady, severe, dull, mid-epigastric radiating to lower back or colicky pain like gall stone attack (6 cases of authors, 2 requiring morphia) or paroxysmal umbilical pain like tabetic crises (pressure on coeliac plexus, tumor infiltration of plexus demonstrated at postmortem in one of author's cases--more if looked for?).

(4) Nausea and vomiting: (obstructive, nerve stimulation, exclusion of secretion). (Lit.) 60 to 90%. Hospital series 56%.

(5) Constipation and diarrhoea: former more frequent than latter. Bulky stools not often seen as bacteria can duplicate enzymic digestion (experimental proof).

(6) Temperature: 3 had chills and fever and 1 fever alone, 3 were subnormal. No constant subnormal finding as reported elsewhere.

10. Family history: not significant. Past history: 8 of 32 had had typhoid fever (pre-sanitary days?).

11. Physical examination: chiefly emaciation, jaundice, distended gall-bladder, and enlarged liver.

(1) Emaciation: may be extreme Series (88%).

(2) Jaundice: (Lit.) 50%. (Author) 66%. 4 had extensive hemorrhage as result (into gastro-intestinal tract) other ill-effects of jaundice may be noted. Death may occur unexpectedly and suddenly from silent or painful bleeding internally. Watch hemoglobin as well as blood pressure. Bleeding due to liver injury. (O.H.W) decompress early on this account.

(3) Palpation of liver: enlarged in 81% of series, 5 due to metastases alone, 11 to bile stasis alone.

(Contrary to Bard-Pic syndrome). Another observer found 30%.

(4) Courvosier's Law: well demonstrated in group. 14 of 20 showing jaundice (70%). At operation, 13 of 15 gall-bladders found distended, 12 of which were palpable pre-operatively. (Good!) Note law states distension of gall-bladder in carcinoma of pancreas (common duct obstruction), no enlargement in stone in duct because of gall-bladder disease. Ecklin found 175 common duct stones (23 distended gall-bladders), 139 other obstructions (121 distended bladders), in 61 cases of carcinoma of pancreas obstruction (58 distended).

(5) Tumor mass: other than gall-bladder in 7 (20%), (Lit. 20 to 40%) usually in epigastrium to right or left, usually fixed, may have transmitted pulsation or bruit from aorta.

(6) Tenderness: general abdominal common but not marked (67%) Lit. 70%.

(7) Edema and ascites: (pressure, cirrhosis, and implants over peritoneum). Edema 11, ascites 7, at autopsy 13 of 24 in hospital group, pathology series 48 of 99 (about half in both). May be chylous. Others: intestinal obstruction, dilated veins, Virchow's node, bradycardia (sometimes).

12. Laboratory: (1) X-ray to rule out gastro-intestinal and renal tumor. Typical widening of loop not always present but other displacements may be suggestive. Speed (2 of 23). Kiefer (0 of 13).

Present series: 24 examinations. In 3 picture was definite, 3 suggestive, 18 of no aid. Note: all of positive diagnoses made in last 4 years (L.G.R.)

(2) Urine: obstructive jaundice shows usual finding. Glycosuria (3), 2 diabetics in addition. Lit. (1%). Amylose (no study) of corroborative value.

Note: Laboratory is prepared to do this. Normals said to fall in rather fixed limits in 24 hour specimens.

(3) Gastric expression: 16 studies, 8 achlorhydria (over half). Lit. (about same). Duodenal contents of value. Tumor obstruction is usually complete, stone often incomplete.

(4) Blood: average hemoglobin in series (79.4%). Secondary anemia usually reported. Moderate leucocytosis in half of cases. Icterus index determined in 12 (recent test)! In 10 it was

above 90, average 136, maximum - 288. In 3 cases in which anastomoses was done (gall-bladder to stomach or intestines) it was studied. Reduction occurred as follows: 96 to 20, 118 to 32, 112 to 16. Blood amylose not done, said to be of value, low values being significant of atrophy and high of duct obstruction. Clotting time prolonged in 6 out of 19.

(5) Stool: blood in 6 out of 16 (4 were jaundiced), bile absent in 10 of 11. In 3 operated cases studied, bile returned.

13. Duration of illness: (Lit.) 6 to 8 months. Series from hospital (author) first symptom to death 6.3 months (average), i.e., operated cases 6.7, unoperated cases 6.1. Maximum in operated group 17.5, unoperated 12 months.

14. Correct clinical diagnosis: (21 out of 32) should be fairly high with tumor in head. Note: suggestive correlation with jaundice (2/3) each.

15. Treatment: High-voltage x-ray therapy in 4 cases, completed in 3. Two died before treatment was finished, the others 2 and 5 months each. Hardly a fair trial! Gold radium implants in one. Death from hemorrhage. Surgical approach difficult but operation possible. Mortality high. Anastomosis of biliary tract to gastro-intestinal system. General results in literature (63% relief, average duration of life 7.7 months, Judd and Parker). Author's result -

	<u>Simple exploration</u>			
	No. of cases	Mortality	Avg. Post-op. life of patient	Maximal survival of operations
Kiefer	8	37%	1.7 Mos.	6 Mos.
Pres. series	6	50%	1.4 "	6 "
<u>Cholecystostomy</u>				
Kiefer	4	50%	3.5 "	7 "
Pres. ser.	3	53-1/3%	5.1 "	6 "
<u>Cholecystenterostomy</u>				
Kiefer	9	22%	5.6 "	11.5 "
Pres. ser.	8	25%	4.0 "	14.5 "

Cholangitis may follow. Author also reports experimental work on radiation

of pancreas with possible application to man (in separate paper).

#### Impressions:

1. 99 cases of primary carcinoma of pancreas are reported.
2. Gross and microscopic types are described.
3. Cause unknown, incidence 1-2%, sex chiefly males, age fifth to seventh decade.
4. Location chiefly in head.
5. Metastases to liver and nodes, then elsewhere.
6. Symptoms are weight loss, (100%), jaundice (70-80%), pain (90-100%), nausea and vomiting (56-90%), usually constipation, occasionally fever.
7. Signs are emaciation (88%), jaundice, enlarged liver (80%), positive courvosiers low (70-98%), tumor other than gall-bladder (20-40%), tenderness (70%), edema and ascites (about 50%).
8. Laboratory evidence of jaundice, bleeding tendency, gastric acidity, and x-ray findings are significant.
9. Average duration of life is 6-8 months.
10. Correct clinical diagnosis parallels development of jaundice (obstruction).
11. Treatment is palliation and surgical anastomosis of gall-bladder and gastro-intestinal tract.
12. Experimental work indicates radium may be tried.

### III. CASE REPORT

#### PRIMARY CARCINOMA OF THE HEAD OF THE PANCREAS. OBSTRUCTION OF THE COMMON BILE DUCT.

The case is that of a white, male farmer, 50 years of age, admitted to the University Hospitals 9-1-31 and died 9-12-31 (11 days).

#### Pain onset

4-15-31 - Patient was suddenly seized with an attack of severe pain in the abdomen, localized to upper quadrant (right) and radiating around to the back. A few days following this, noticed jaundice which increased very rapidly. At the same time also developed slate colored stools. He became very weak and lost 25# in weight. He also had itching

of the skin beginning with the appearance of jaundice. Patient had a continuous dull pain in the upper part of the epigastrium. He consulted a physician who told him not to eat fatty foods. Patient felt better after this. Fatty and fried foods have not bothered him at any time.

#### Hospital

9-1-31 - Admitted to University Hospitals. Physical examination reveals a well-nourished and well-developed, white male, 50 years of age, who is extremely jaundiced and has excoriations over his body due to scratching. Blood pressure 90/60. Pulse 88. The liver edge is palpable about 3.0 cm. below the costal margin. Laboratory: Urine - dark brown in color, specific gravity 1.020, bilirubin present, negative for urobilin and urobilinogen. Blood-Hemoglobin 73%, wbc's 4,550, Pmn 71%, L 25%, M 1%, E 3%. Progress: Calomine lotion with 10% phenol was applied to the skin.

#### X-ray

9-2-31 - Put on a fat free high caloric diet. 1 cc. surgical pituitrin given. Non-protein nitrogen - 22.2 mg. Blood sugar - .069 mg. Icteric index - 152 units. X-ray of abdomen - no evidence of stone could be made out. Pulse is normal.

9-4-31 - Gastro-intestinal x-ray - There is some pressure on the lesser curvature of the stomach suggesting an enlarged liver. No evidence of other pathology could be definitely made out. Conclusions: Extra gastric mass, probably an enlarged liver. Blood - cholesterol 344.8, Van den Bergh's 40. Stool - clay colored, positive urobilin and benzidene (incomplete obstruction?)

#### Common duct stone?

9-5-31 - Carlsbad's salts ii drams, two times daily. Atropine sulphate gr. 1/120, three times daily. Calcium lactate dramw 1/2, three times daily. Urine - urobilin present. Surgical consultation: For common duct stone 90%. Due to the long duration of jaundice, the risk of surgery is rather high; without it, the prognosis is bad. Suggest transfer to surgery for operation. In meantime, calcium chloride 10%, 5 cc. every 48 hours, high carbohydrate diet, daily bleeding and clotting time, and force fluids.

Calcium preparation

9-8-31 - Calcium lactate drams 1/2, three times daily. Calomine lotion with 10% phenol to legs. 5 cc. of calcium chloride intravenously. Bleeding time 4' 45 seconds, clotting time 18'. Pulse and temperature are normal.

9-9-31 - Calcium lactate drams 1/2, three times daily. Atropine sulphate gr. 1/120, three times daily. Duodenal drainage, no bile. Transfused, 500 cc. blood. 10 cc. of 10% calcium chloride, intravenously. Bleeding time is now 3' 30", clotting time 7".

Operation

9-10-31 - Patient is somewhat restless and nervous. Preoperative diagnosis: Rested between common duct stone and carcinoma. The diagnosis of common duct stone was favored because of the history of attack of pain; however, the absence of chills and fever were regarded as unusual. At the time of operation, the gall-bladder was found thickened, reddened, and somewhat moderately distended. A mass was found in the region of the common bile duct which first felt like a stone or the duct itself. However, further exploration revealed that some enlarged nodes were present. One of these was removed for immediate microscopic examination. Another definitely enlarged node in the falciform ligament is observed. Microscopic diagnosis: There is an atypical proliferation of glandular epithelium in a disorderly manner. The glands are small and distinct and surrounded by a dense stroma. The cells vary in size, shape, and staining. There are a few mitotic figures. Diagnosis: Metastatic adenocarcinoma. Patient returned from the operating room conscious. Pulse is somewhat feeble, 80. Respirations 16.

Post-operative

9-11-31 - Patient perspires profusely. Hyperventilated three times daily. Patient is very jaundiced. There is no drainage from the tube. Intravenous 2000 cc. of 10% glucose and normal saline given. Morphine sulphate gr. 1/4, three times today. Pyramidon gr. x given. 7 P.M. - condition seems worse. Pulse is very weak. Respirations are slow. Temperature is elevated, 104.

Exitus

9-12-31 - Patient is very stuporous. Pulse imperceptible. Caffeine sodium benzoate gr. 7-1/2. 2:35 A.M. - patient expired.

Autopsy

The body is that of a well-developed and fairly well-nourished, elderly, white male, measuring 176 cm. in length, and weighing approximately 150#. Rigor is present. Hypostasis is purplish and posterior. There is no edema or cyanosis but there is a 4+ jaundice. Pupils measure 4 mm. and are regular. There is a recent operative incision over the right upper quadrant about 18.0 cm. in length. A drainage tube is present. There are multiple scratch marks all over the body, especially the lower extremities. There are multiple puncture wounds in both antecubital spaces.

Upon opening the PERITONEAL CAVITY, it is found to contain about 800 cc. of blood. Some of this blood is clotted and remains in the region of the liver and under the diaphragm. The APPENDIX is subcecal and free.

The PLEURAL CAVITIES contain a very slight amount of bile-tinged fluid. The PERICARDIAL SAC contains a minimal amount of fluid.

The HEART weighs 325 grams. All of the chambers are normal. The valve edges are normal and free. The coronaries show a mild amount of sclerosis. The ROOT OF THE AORTA is normal.

The RIGHT LUNG weighs 850 grams, LEFT 650 grams. The right lung shows some congestion at the base which is also present at the left but not as marked. Moderate anthracosis.

The SPLEEN weighs 325 grams and is very soft.

The LIVER weighs 2700 grams and is grayish in color on cut surface. The lower lobe, however, is somewhat reddish in appearance and much softer than the remaining portion of the liver. There is no evidence of metastases throughout substance although there is a very small whitish nodule on the anterior surface.

The GALL-BLADDER is very markedly thickened and contains a drainage tube. In tracing the gall-bladder and ducts, it is found that there is obstruction of the common bile duct by a very hard

small mass. In dissecting the mass, it is found to contain some pancreatic tissue and is really a part of the head of the pancreas. However, the rest of the pancreas is grossly normal. There are a few nodes, also, along the common bile duct which are somewhat firm. The hepatic ducts are distended and filled with white bile.

The GASTRO-INTESTINAL TRACT is normal in its entirety. No evidence of any carcinoma. However, a portion of the omentum has a gelatinous appearance and a gelatinous feel. A portion of this is taken for further microscopic study. (Shows edema). Also, the omentum of the transverse colon shows the same gelatinous colloid consistence (same). The gall-bladder is very thickened and one cut (across) shows, also, this peculiar gelatinous consistence (edema).

The ADRENALS are normal.

Each KIDNEY weighs 225 grams. The capsules strip easily revealing smooth surfaces. No evidence of infection can be seen.

The BLADDER is normal.

The organs of the HEAD and NECK are not examined.

#### DIAGNOSIS:

1. Carcinoma of pancreas, metastasis to regional nodes.
2. Obstruction of common duct.
3. Obstructive jaundice 4+.
4. Hemoperitoneum.
5. Chronic cholecystitis.
6. Recent operative incision.
7. Recent cholecystotomy.
8. Multiple puncture wounds.
9. Multiple scratch wounds.
10. Moderate anthracosis.
11. Cloudy swelling of the liver and kidneys.

#### IV. ABSTRACT

##### PRIMARY CARCINOMA OF THE GALL-BLADDER.

Diseases of the liver, gall-bladder and bile-ducts. Rolleston-McNee, Third Edition, Macmillan and Co., 691-709 (1929), Chapter: Primary Malignant Tumors of the Gall-bladder.

Comment: An excellent presentation of subject giving chief emphasis to pos-

sibility of etiologic relationship of gall stones to tumor.

#### 1. General statement:

Innocent tumors are rare in gall-bladder, not nearly so frequent as malignant growths. Primary carcinoma of gall-bladder first recorded by deStoll (1771). Flutterer (1901) reported collection of 268 cases, which included 195 since 1880. In order of frequency in organs concerned with digestion it is fifth, i.e., (1) stomach, (2) colon and cecum, (3) rectum, (4) oesophagus, (5) gall-bladder. It makes up 5% of all carcinomas examined after death. (Kaufman). Primary malignant disease of gall-bladder is almost always carcinoma. Sometimes sarcoma and melanoma are found. May be seat of secondary tumor deposits, e.g., Smithies (1919) reports 1000 cases of gall-bladder disease of which 23 were primary and 8 secondary carcinomas.

#### 2. Morbid Anatomy:

Columnar or spheroidal cells, villous or flat infiltrating, (various combinations seen). As result of metaplasia, squamous cell type may occur. Comment: squamous cell carcinoma occurs on surface and for short distance in orifices. Gall-bladder and renal pelvis are most frequent distant "surface growths". Colloid changes may so flatten cells as to make microscopic diagnosis difficult (see our case). Author does not believe in "specific cell origin" of tumors from certain cells of mucus membranes. Seldom start from papillomata. Frequency of benign papilloma (4 of 5000 removed gall-bladders, McCarty).

#### 3. Location:

Commonly starts in fundus. Other locations, midway (hourglass) or at cystic duct. Note: cystic duct tumors resemble gall-bladder growths more than bile ducts. Frequently point of origin is difficult to locate as evidence of primary tumor of gall-bladder is based on absence of viscus in tumor infiltration or presence of stone in tumor mass, in usual position of gall-bladder. (See our case). As a rule never larger than closed fist.

#### 4. Extensions: to liver, and through

ducts to duodenum or liver (as in liver tumors). Fistulae to colon (10%), duodenum (8%), stomach (6%), or abdominal wall. Pressure effects on pylorus or duodenum, bile ducts and portal vein (jaundice and ascites). Secondary growths occur in liver (50%), lymph nodes of porta hepatis and abdomen, peritoneum, ovaries, lungs, mediastinum, and Virchow's node. Distant growths may appear as primary manifestation. Abscess, peritonitis and cholangitis not infrequent.

5. Cause: Gallstones? Commonly present with tumor, e.g., 69-70-81-85-91-95-100%, according to various observers. May develop after stone removal or cholecystotomy. Statement is made tumor occurs in 4 to 14% of all cases of cholelithiasis, e.g., 20 of 141, 48 of 592 (12.3%), 13 of 300 (4.3%), 2 of 315, 23 of 500, etc. But calculi may be secondary to growth, due to stasis and inflammation. If this was true duct calculi would be common in duct tumors (which is not the case), e.g., 24 of 69 cases only. Also a comparison may be made between primary and secondary carcinoma of the gall-bladder which shows (99 primary, 94 calculi) (13 secondary, 2 calculi, also 25 secondary, 1 calculi, total 38 and 3 = 8%; other reports 5-12% of autopsy figures). But secondary growths are seldom the same as primary, i.e., more serosal than mucosal. The question has also been approached experimentally. Leitch (1924) put calculi in gall bladders of guinea-pigs. Demonstrated in this animal that mechanical factor was greater than chemical content of stone (chronic non-specific irritation) rough more than smooth stones, also pebbles, other substances. There seems to be little doubt that an etiologic relationship exists; the actual number of cases of gall stones which may become malignant is still an open question.

Comment: But does not the same difficulty of prediction also come up in chronic infection of mouth (males), carcinoma of oral cavity, stone in renal pelvis and tumor, chronic cecitis, etc. When sex is considered the factor is even more suggestive.

6. Sex: Every single report shows **females** predominate (also true of gall stones. 1913-20 in England and Wales, 2296 female deaths and 946 males from

carcinoma of gall bladder. Greater female liability to stone is (5-1, 3-2, 4-3). In 87 bile duct tumors (50 males - 37 females) like carcinoma of pancreas. Secondary carcinoma of gall-bladder (13 cases, 10 males - 3 females).

7. Age: Average 58 years (in 2 large series). Rare before 40. Extremes, 25-90. When sex is considered age factor is constant. Comment: also gall stone ages?

8. Symptoms: Pre-existing gall-stones, local and general effect of tumor. Interval between colic and tumor may be long (watch this point in taking histories). Often no history of stone is obtained? See our case? Does this mean latest stones are more apt to become seat of malignancy or does it weaken etiologic argument and favor secondary stone formation. Early complaint is often feebleness and discomfort in night, hypochondrium or attacks may seem to be regular colic. Tumor is palpable sooner or later (respiratory movement). Failure of gall bladder to fill (x-ray) contra-indicated by jaundice. With liver infiltration picture changes, (enlarged in 50%), smooth or nodular (like stasis or tumor). Jaundice (60-80%), ascites (25-40%), edema of legs, gastric symptoms, cholemia, etc.

9. Duration: Very difficult to determine since early symptoms resemble stone. When cholemia develops course is rapid. About 6 months.

10. Diagnosis: Very difficult, seldom if ever made during life. May be suspected on differential grounds (negative search for other primary). To be considered: gall stones, primary malignancy of liver, syphilis of liver, carcinoma of stomach, hepatic flexure of colon, bile ducts, head of pancreas and others.

11. Treatment: Attempts at removal seem to hasten death, e.g., Quenu (1909) collected 92 cases: operative mortality 19%; 52 were followed; of these 14 were alive at one year, only 5 or 6 were satisfactory. Tendency to hemorrhage is very great.

## 12. Impressions:

1. Innocent tumors are rare in gall-bladder; malignant growths are more frequent.

2. Primary carcinoma of gall-bladder is 5th in order of frequency in organs concerned with digestion, making up 5% of all carcinomas examined after death.

3. Metastatic carcinomas are less frequent than primary.

4. Cell types are usually combinations of columnar and spheroidal or squamous (metaplasia).

5. It commonly starts in fundus, next near cystic duct but this is difficult to determine.

6. Extends to surrounding structures, fistulae are not infrequent, pressure effects are common and distant deposits are found.

7. Distant tumors may mimic primary growths because of a silent primary.

8. Gall-stones are found in association in 69-100% of the cases.

9. Evidence points to primary rather than secondary formation.

10. Disease has been produced in guinea-pigs by the use of foreign bodies including gall stones.

11. 4-14% of gall-stones are malignant?

12. Females predominate in tumors of gall-bladder; males in bile duct and pancreatic tumors.

13. Average age is 58 years. Rare under 50. Limits 25-90 years.

14. Symptoms are those of gall-stones, local and general effects of tumor.

15. Duration is difficult to establish, probably about 6 months.

16. Diagnosis is difficult and seldom can be accurately made.

17. Treatment is palliative; surgery is apparently ineffective.

## V. CASE REPORT

### PRIMARY CARCINOMA OF GALL BLADDER WITH METASTASIS TO LIVER AND LUNGS

The case is that of a white female, 47 years of age, admitted to the University Hospitals 8-9-31 and died 9-16-31 (38 days).

### Gall-stone colic

10- -28 - Patient had a very severe attack of pain in right upper quadrant, and was in bed for two weeks at this time. The pain did not radiate to the shoulders. No jaundice nor acholic stools. Patient consulted a physician who stated she had gall stones and told her not to eat fatty foods. However, patient had no aversion to fatty foods.

### Another

7- -30 - Patient had a similar attack but only lasted one day. She lost twenty-five pounds within the next year.

### Jaundice

4-31-31 - The present attack began with jaundice. At this time, the stools were clay colored. The jaundice started very gradually and was very marked in two weeks.

### Pain

5-15-31 - Patient saw a physician who told her that she had gall stones and treated her for it. She began to have a dull pain in the right side which increased in severity.

7-15-31 - The pain was very severe at this time. Pain also developed in the right shoulder which was most severe one hour after meals.

### Diarrhea cough

7-30-31 - Patient noted very severe diarrhea and had as many as fifteen stools a day. The stools were very dark and watery. On one occasion they were definitely green. Patient began to have rather severe cough.

### Metastatic hemangio endothelioma (?)

8-9-31 - Admitted to University Hospitals. Physical examination reveals a well-developed and well-nourished, white female, lying in bed with 4+ jaundice. There is a cavernous hemangioma on the posterior border of left sternocleidomastoid muscle, 1.0 cm. in diameter. The abdomen is distended. There is a small umbilical hernia. The liver is enlarged three fingers below the costal margin which is hard and nodular; does not move on respiration. It is tender on palpation. Progress: Put on special fat free diet. Ice bag to upper right quadrant. Codeine sulphate gr. 1-1/2.

Laboratory:

8-10-31 - Patient is fairly comfortable. Blood - Hemoglobin 45%, rbc's 2,470,000, wbc's 30,000, Pmn's 85%, L 12%, M 2%, and E 1%; anisocytosis, poikilocytosis, and hypochromasia; marked shift to left. Icteric index 128 units. Bleeding time 6 minutes, clotting time 18 minutes. Urine - bilirubin 4+, urobilin and urobilinogen negative. Gastric expression - Gunsberg's reagent showed free HCL.

X-ray

8-11-31 - Carlsbad's salts drams ii, t.i.d. Atropine gr. 1/120, t.i.d. Patient feels comfortable. Stool - well formed, clay colored specimen with a few green specks; no blood, pus, nor mucus; benzidene 4+; urobilin and bilirubin negative. X-ray of right upper quadrant - plate of upper right quadrant shows no evidence of gall stones. Pulse 106, temperature to 99.6.

Complete obstruction

8-12-31 - Patient complains of some pain after eating the noon meal. Stool - clay colored, benzidene 3+, bilirubin and urobilin negative. Urine - bilirubin +, urobilin negative. Gastro-intestinal study and Chest - flat plate of the chest shows multiple densities scattered throughout the lower parts of both lungs which are no doubt metastatic in origin. Both diaphragms are very high, the right being higher than the left. The stomach is normal intrinsically, but shows definite pressure across the lesser curvature due to an enlarged mass which is undoubtedly the liver. The mass pushes the stomach to the left and posteriorly. The bulb filled out well and is normal. There is a 10% retention at 6 hours. The spleen is also enlarged and presses in on the stomach on its greater curvature.

Conclusions: Metastasis to both lungs. Negative stomach and duodenum. Enlarged liver and spleen giving pressure deformity on both the greater and lesser curvatures of the stomach and displacing it to the left. Dermatological consultation - Diagnosis - hemangioma of the neck.

8-13-31 - Patient feels fairly comfortable. Stools are clay colored. Blood chemistry - sugar .078, NPN 30.1, blood cholesterol 212.7 mg. per 100 cc. White blood count 30,500. Icteric index 96 units. Urine - bilirubin 2+. Blood Wassermann - negative. Temperature to

102.2, pulse to 100.

Calcium preparation, clotting time down

8-21-31 - Calcium chloride gr. xv, daily. Patient has no special complaints. Blood chemistry - NPN 20.3. Icteric index 128 units. Bleeding time 1'45", clotting time 7' 30". Temperature 101.8, pulse to 100.

8-25-31 - Calcium chloride gr. xv, daily. Patient feels comfortable. Passes clay colored stools. Blood chemistry - NPN 25.6. Temperature 101.6, pulse 96.

8-28-31 - Patient feels fairly comfortable. Calcium chloride gr. xv, daily. Bleeding time is now 2', clotting time 18'. Blood - Hb. 44%, Pulse to 101, temperature 100.

Clotting time up

8-29-31 - Bleeding time 2', clotting time 16'. Blood - Hb. 45%. Pulse 100, temperature 101.6.

Down

9-2-31 - Patient has no special complaints. Calcium chloride gr. xv. daily. Blood chemistry - NPN 57.6. Icteric index 128 units. Blood - 55%. Bleeding time 2' 30", clotting time 6' 30". Pulse 90, temperature 100.8.

9-8-31 - Patient has no special complaints. Calcium chloride gr. xv. daily. Mineral oil oz. i, two times daily. Fluids forced. Stools - clay colored, no pus grossly, benzidene 3+, bilirubin and urobilin negative. Pulse 108, temp. 101.2.

9-11-31 - Patient complains of pain in right upper quadrant. Pulse 112, temperature 101.6.

Hemoptysis, tumor?

9-14-31 - Patient began to expectorate bloody mucus. Codeine sulphate gr. 1-1/2. Coughs a great deal. Expectoresates a considerable amount of bright red blood. Pulse 108, temperature 101.

9-15-31 - Patient coughs at intervals. Very tired and listless. Coughs up a great deal of blood. T 102.4, P to 96.

Bleeding, exitus

9-16-31 - Patient had emesis of 200 cc. of brownish fluid. Complains of a great deal of pain. Adrenalin 1/2 cc. Codeine sulphate gr. i. Digalen i ampule. Patient seems to have some dyspnea. Caffeine sodium benzoate gr. 7-1/2. Has a great deal of pain in the right upper quadrant.

12 noon - pulse imperceptible. Slightly cyanotic. 1:00 P.M. - patient expired.

### Autopsy

The body is that of a fairly well-developed and poorly nourished, white female, measuring 160 cm. in length, and weighing approximately 130#. Rigor is present. Hypostasis is purplish and posterior. There is no edema or cyanosis. There is 4+ jaundice. Pupils measure 4 mm. in diameter and are regular. There are multiple puncture wounds in both antecubital spaces. There is a very small umbilical hernia. Striae gravidarum is present.

**PERITONEAL CAVITY.** The peritoneum is smooth and glistening. There is no fluid in the peritoneal cavity. The liver extends three fingers below the costal margin and on superficial inspection shows numerous metastatic nodules throughout. The omentum is adherent to the liver in places. The **APPENDIX** is subcecal and free.

The **PLEURAL CAVITIES** contain no fluid. The **PERICARDIAL SAC** contains a minimal amount of brownish fluid.

The **HEART** weighs 200 grams. The valve edges are free and normal. The chambers are normal. The coronaries and **ROOT OF THE AORTA** show a moderate amount of sclerosis.

The **RIGHT LUNG** weighs 600 grams, **LEFT** 675 grams. The right lung shows several, small, white metastatic nodules, measuring about 1.0 to 2.0 cm. in diameter with umbilicated centers. These are mostly situated in the lower lobe. The lower lobe is congested. The left lung shows one large metastatic nodule in the lower lobe, measuring about 6.0 cm. in diameter, and on cutting across shows breaking down and hemorrhage. There is also another nodule which had also broken down and showed hemorrhage (4.0 cm. in diameter). The lower lobe also shows congestion on this side.

The **SPLEEN** weighs 100 grams. The capsule is wrinkled and grayish in appearance. On cut section, the pulp is red and soft (not enlarged).

The **LIVER** weighs 3500 grams. There are a great many adhesions around the region of the gall bladder and liver and the omentum and coils of the intestines. These are dissected away carefully and the liver is separated away from the rest of the intestine. In

sectioning the liver across, it is found that practically all of the substance is replaced by metastatic carcinomatous nodules which are white in appearance and have umbilicated centers. Some are broken down, reddish, and show hemorrhages. The lesions vary from 2 to 15 cm. in diameter.

The **GALL-BLADDER** is situated in the carcinomatous mass. It is dissected away and the tumor probably represents the wall of the gall-bladder. This is cut across but no lumen is found. In the lower most corner of the mass the lumen and mucosa of the gall-bladder are found which contain the same white carcinomatous tumor mass which is necrotic. It contained a solitary pigment stone. It is difficult to trace out the various ducts on account of the numerous adhesions and obliteration by the carcinomatous masses in and around this region. There are hard and lymphatic nodules around the common duct which compress the duct at this point.

The **LYMPH NODES** and head of **PANCREAS** are also enlarged and involved.

The **GASTRO-INTESTINAL TRACT** shows no hemorrhage nor malignancy.

The **PANCREAS** weighs 100 grams.

The **ADRENALS** are normal.

The **RIGHT KIDNEY** weighs 225 grams, **LEFT** 200 grams. The capsules strip easily, revealing smooth surfaces. When cut across, the kidneys are greenish in appearance (bile nephrosis). The ureters and tubes are normal. When the ovaries are cut across they are found to be very hard and contain metastatic nodules.

The abdominal **LYMPH NODES** are involved down to bifurcation of the aorta.

The organs of **HEAD** and **NECK** not examined.

### DIAGNOSIS

1. Carcinoma of gall-bladder
2. Metastasis to liver
3. Metastasis to region of common duct
4. Metastasis to lungs.
5. Metastasis to abdominal nodes and ovaries.
6. Cholelithiasis.
7. Jaundice 4+
8. Multiple puncture wounds.
9. Umbilical hernia.
10. Congestion of lungs.
11. Striae gravidarum.
12. Hemoptysis (clinical).