VOL. II THURSDAY, FEBRUARY 26, 1931 NO. 20

GENERAL STAFF MEETING
UNIVERSITY HOSPITALS

CONTENTS

PUBLICATION FINANCED BY CITIZENS AID SOCIETY

ANNOUNCEMENTS:

1. Clinico-Pathological Conference:
Friday, 11:00 A.M. Todd Amphitheater, February 27, 1931. Chronic osteomyelitis; amyloidosis anduremia.

2. Trip:
To Chicago to view progress of Central Scientific Exhibit at Headquarters of American Medical Association, 535 N. Dearborn St., Chicago. All visitors to Chicago invited to visit demonstration. Purpose: to save for more extended observation outstanding adaptable exhibits from Annual Meeting. Exhibits in place in permanent form (models, pictures, specimens, charts, stereographis, etc).

Tularemia. Walter M. Simpson, Minneapolis Session, 1928.

Lymphoblastoma. Paul A. O'Leary and Hamilton Montgomery. Minneapolis Session, 1928.

Stereographs of the living Eye. Arthur J. Bedell. Minneapolis Session, 1928.

Leprosy. A Study in Natural Photography. O. E. Denney. Minneapolis Session, 1928.

Cutaneous Granulomas. F. J. Eichenlaub, C. W. Finnerud, Howard Fox, Henry H. Mazen, Oliver S. Ormsby, James Herbert Mitchell, William Allen Pusey, Bedford Shelmire, selected from the exhibit under the auspices of the Section on Dermatology and Syphilology. Minneapolis Session, 1928.

Undulant Fever. A. V. Hardy, Portland Session, 1929.

Cutaneous Manifestations of Syphilis. C. W. Finnerud, Howard Fox, George M. MacKee, James Herbert Mitchell, Edward A. Oliver, William Allen Pusey, Bedford Shelmire, Erwin P. Zeisler, selected from the exhibit under the auspices of the Section on Dermatology and Syphilology. Detroit Session, 1930.

Histopathology of Cutaneous Syphilis. Hamilton Montgomery and J. A. Hookey. Detroit Session, 1930.

Bone Repair Following Fracture and Experimental Extra-Skeletal Bone Production. Clay Ray Murray. Detroit Session, 1930.

Prostatic Disease. H. C. Bumpus, Jr., Detroit Session, 1930.

Impressions: University of Minnesota gaining ground, because of forward looking group, progressive, becoming better known. Dr. Fishbein paid fine tribute to staff meeting and visit here. Spoke at meeting of staff of St. Anne's Hospital on West Side. Progressive group, good organization, large, well-equipped institution, 250 beds, 60 bassinets, large obstetrical service, good pathologist (Weiss), fine spirit; meeting also attended by undertakers in interest of "post" cooperation, finest courtesy ever received at any place.

3. Honored:

Drs. Henry Michelson and Sam Schweitzer elected to membership in Vienna Dermatological Society. Personal tribute by Dr. W. A. Pusey, Dean of Dermatologists, Chicago: "Minneapolis has finest group of Dermatologists for size of city of any place in this country. Michelson is a credit to any place". Thank you!

II. ABSTRACTS:

Jaundice - Abstr. O'Brien and Rufe.

Visible jaundice is due to bilirubin deposits in tissues (follows hyperbilirubinemia). Mann on hepatectomized dogs demonstrated conversion of hemoglobin into bilirubin in reticulo-endothelial cells of spleen, liver and bone marrow. Normal pathway of execretion is by way of polygonal cells of liver. Bilirubin isthreshold substance (normal amount being constantly present). McNee believes polygonal cells are tubules with blind ends, free end passing into bile capillary. Surrounding tubules are vascular capillaries lined with Kupfers cells composed of reticuloendothelium which carry blood from portal to central to hepatic vein.

Types of jaundice:

1. Bilirubin reabsorbed after passage through the vascular channel and polygonal cells back into blood stream and lymphatics (extra biliary obstruction).
2. Abnormally large production of bilirubin or precursars or impediment of passage through endothelial cells of capillaries which allows substance to enter general circulation without passage through hepatic cells proper (hemolytic).
3. Hepatic injury, functional or otherwise, which causes normally formed bilirubin to fail of excretion; also that which has passed through polygonal cells may be reabsorbed (toxic or infectious).

Comment: Theoretical conception based on combination of physical and pathological observations and liver tests, chiefly Van den Bergh.

Abstract: A study of the causes of jaundice in 400 cases. Hartman, H.R. Med. Clin. of N. Amer. Vol. XI, 1383-1388 (May) 1928.

Jaundice is an important sign of biliary tract disease (but not pathognomonic). Classification based on McNee's anatomonical classification. Group I - Circulatory or splenic group. Group 2 - Hepatic origin. Group 3 - Extrahepatic biliary origin. Series showed (1) 7%, (2) 31%, (3) 62%.

Table I 400 cases of jaundice		Per cent
Group 1. Hemolytic jaundice	Total	7.00
" 2. Catarrhal jaundice		11.50
Intrahepatic jaundice (biliary cirrhosis, late portal cirrhosis, yellow atrophy)		11.25
Carcinoma of liver (primary and secondary)		6.75
Toxic jaundice		1.00
Dissociated jaundice		0.50
	Total	38.00
Group 3. Choledocholithiasis		19.75
Carcinoma of gallbladder, ducts or pancreas		17.25
Stricture of ducts (common or hepatic)		9.25
Pancreatitis		5.75
Extrinsic pressure on common duct (edema, enlarged lymphatics, gall stones in bladder, empyema of gallbladder, etc.)		4.50

Cholangitis	4.00
Inflammatory reaction	1.25
Contraction of common duct	0.25
Total	62.00

Comments: Groups 1 and 2 may be surgical; 3 usually (at least) is exploratory. Distinction between "catarrhal" and "Toxic" is probably etiological rather than real. Diagnosis of pancreatitis (unqualified) is debatable.

Table 2. 400 cases of jaundice as to pathological origin. (Same group)

	Per Cent
Carcinoma	
Pancreas	11.75
Gallbladder or ducts	5.50
Metastatic, primary in stomach, rectum, ovary and generalized	3.75
Liver	3.00
Total	24.00
Intrahepatic:	
Catarrhal	11.50
Cirrhosis	11.25
Total	22.75
Choledocholithiasis	19.75
Structure (common, hepatic ducts)	9.25
Hemolytic jaundice	7.00
Extrinsic pressure on common duct	4.50
Cholangitis	4.00
Inflammatory reaction	1.25
Toxic jaundice	1.00
Dissociated jaundice	0.50
Contraction of common duct	0.25
Total	100.00

Comments: Note frequency of carcinoma (24%) intrahepatic jaundice (cirrhosis and catarrhal) (22.75%) and common duct stone (19.75%). Also half of malignant jaundice (11.75%) from pancreas.

Summary: Carcinoma is the most common single cause of jaundice. Extrahepatic biliary jaundice is almost as frequent. Stricture of ducts is usually postoperative but may be primary. With hemolytic jaundice it is 4th in frequency. The classification was undoubtedly based on "clinical" and not "laboratory" jaundice which accounts for absence of some well known causes of mild jaundice.

Abstract: Intrahepatic jaundice. Snell, A. and Jordan, F. M. Northwest Medicine, XXIX 295-303 (July) 1930.

Toxic or infectious jaundice

Process varies from cloudy swelling to necrosis (hepatitis). Also includes degeneration. Sometimes seen in chronic, passive congestion, chronic degenerative proliferative changes and cirrhosis (both primary and as the result of extrabiliary obstruction). Attempts at regeneration (nodular hyperplasia) is frequently seen at postmortem in fatal cases. Why is jaundice produced by these varied processes? The suggestion is made that it is due to changes in the hepatic cells, cholangitis of the finer capillaries (bile), and a combination of processes.

Classification - Etiologic

A. Infectious jaundice:

1. Epidemic or catarrhal jaundice, including campaign jaundice (recovery as a rule except for cases which go on to acute atrophy. Portal obstruction may be terminal).
2. Diffuse hepatitis (Parasitic)
3. Spirochetal (Weil's disease, syphilis).

B. Toxic jaundice - Drugs, industrial poisons and disease.

1. Drugs:
   1. Arsenic (organic and inorganic), 2. Cinchophen (atrophan) oxyl iodide, etc., 3. Chloroform, carbon tetrachloride, 4. Yatren.

II. Industrial poisoning.
   1. Phosphorus, picric acid. 2. Arsenic. 3. Trinitrotoluene (TNT), Tetachlorethane ("airplane dope"), Toleuylendinandin, 4. Arsenuretted hydrogen.

III. Systemic diseases.
   1. Exophthalmic goiter.
   2. Pneumonia, sepsis, typhoid fever (focal necrosis) yellow fever, dysentery, relapsing fever.
   3. Toxemia of pregnancy.

C. Circulatory jaundice:
   1. Chronic passive congestion.

D. Inflammatory and suppurative jaundice:
   1. Cholangitis (usually with obstruction).
   2. Pylephlibitis.

E. Jaundice with cirrhosis:
   1. Portal (yearly and late, often constant andlow).
   2. Bilary and mixed types (usually obstructuve).

F. Subacute or acute yellow atrophy:
   1. Primary.
   2. Secondary to any of the above.

In Mayo Clinic group composed about 25% of total, which is low estimate? compared with private practice because of larger numbers of epidemic or catarrhal forms seen by practitioner. Common intrahepatic types seen at the Clinic were (1) Catarrhal or infectious. (2) Drugs - usually cinchophen and arsophenamin, (3) cirrhosis. Acute single injury shows possible recovery. Multiple or chronic insults tend to go on to permanent liver damage.

Clinical picture:

Extremely variable. Usually jaundice which is insidious and painless with a prodromal pruritis (especially from drugs) epidemic forms usually show initial gastro-intestinal disturbance, general malaise and slight fever. Severe symptoms or crampy, colicky pains are infrequent. There may be temporary stoppage of bile escape into gastro-intestinal tract although most cases studied at Clinic showed bile on 2nd or 3rd aspiration. This may be due to fact that patients were not seen until 2nd or 3rd week of disease. Bilirubin curves in epidemic or infectious forms show high level and gradual subsidance. Acute or subacute forms of hepatitis show slight fluctuating level. Only early do they vary in amount. Other forms of hepatitis and cirrhosis value lower, vary slightly from day to day, also true of passive congestion.

Treatment:

No specific treatment. Very little influence on course of disease, by treatment used. Possibilities are: early recognition of etiology (chemical poison), high carbohydrate diet, as it has been definitely shown that protein is harmful to an injured liver. Intravenous glucose, sometimes associated with insulin (without any good reason). Calcium salts, mechanism unknown. Transfusion of blood, especially before operative attempt. Duodenal drainage is chiefly diagnostic. It is said to shorten the course of the arsphenamin group.

No cholagogues are indicated although decholin has been tried. Absence of surgical interference except for definite indications. Prolonged surgical drainage in obstructive cases may be of value. Splenectomy for cirrhosis and attempt to establish collateral circulation when portal system is involved.

Abstract: Clinical Interpretation of Blood Examinations, Kilduffe, R. A. 1st edition, Lea and Febiger, 367-391, 1931.

1. Functions of liver.
   1. Secretion of bile.
   2. Formation and storage of glycogen.
   3. Manufacture of urea.
   4. Detoxicification (portal and general).
   5. Manufacture of erythrocytes (embryonic).
   6. Destruction erythrocytes (bilirubin).
   7. Formation of fibrinogen and antithrombin.
   8. Possible desaturation and direct oxidation of fats (storage in animals).
   9. Storage of iron (at least under pathological conditions, i.e. pernicious anemia).

Some of these functions are partial, others are complete. It is this complexity which makes tests so variable and difficult to evaluate.

II. Carbohydrate tests:

Administer 100 grams of levulose to fasting patient and examine urine at hourly intervals for 4 hours. Based on extirpation of liver of frog, when only sugar not used up was levulose (Strauss 1901). Evaluated by Friedman and Strouse (1914), and Finkelstein and Dannenberg (1925). May indicate in general way functional disability, but other organs may compensate. Not clear cut or conclusive. Absent in known cases of liver disease; present in normal liver. Other sugars have been used (lactose and dextrose). Opinion the same.

III. Fibrinogen reaction (Whipple 1911)

Quantitative determination of fibrinogen in oxalated plasma. Normal 350 to 618 mg. per 100 cc. Reduced in extirpation of liver and cases of injury with chloroform and phosphorus. Evaluation: other tissues concerned in same process, so test is of little practical value. Occasionally positive in cirrhosis. Negative or normal findings not of significance.

IV. Nitrogen function (Blood nitrogen partition test).

Simultaneous determination of total non-protein nitrogen, urea nitrogen, aminoacid nitrogen. Based on relation of liver to urea formation and metabolism of amino acids. Of some value in establishing hepatic functional deficiency but not quantitative. Clinical information not of value.

V. Ferments in blood

1. Lipase (Whipple, et al. 1913).

Lipolytic function varied from normal in certain liver disorders; not of proven value.

2. Ghedini's ferment test

Based on unproved assumption liver is source of ferment capable of converting glycogen into maltose, isomaltose and glucose. Really involves 2 ferments (diastase and maltase) no value.

3. Goodposture's test (1914)

In some cases of cirrhosis the blood shows fibrinolytic ferment. Rountree, Marshall, Chesney (1914) state that the ferment is not found in the absence of cirrhosis; others state test is not of value. Not extensively used.

VI. Protein metabolism

1. Widal's Hemoclastic Crisis (1920). Proteopexic function: to arrest and transform peptones, proteoses, and other disintegrating proteins from portal vein during digestion. Test - Fast 5 hours, count leucocytes; give one glass (200 grams) milk. Leucocyte count every 20 minutes for 2 hours. Normal: leucocytosis. Liver disturbance: leukopenia (usually in first hour). When gross damage is present the test gives corroboratory evidence. May be only sign of liver injury (functional). Others consider variations normal (coincidence). However, it has been shown that milk may depress the leucocyte count in pneumonia. (Reported case of drop of 17,200 cells after injection of one glass of milk). Test of doubtful value, but may be used in conjunction with others.

2. Protein test for urea formation (Cohen and Levin, 1927). Based on normal conversion by liver of animo acids to urea. (1) Fasting patient. Examine blood for quantitative sugar, urea and quantitative Van den Bergh. Use part of blood for dye standard. (2) Inject dye. Authors first used phenoltetrachlorein, later bromsulphthalein. (3) Withdraw blood (15, 30 & 60 minutes) for dye determinations. (4) Give 1-1/2 grams of levulose by mouth per kilo of body weight and determine blood sugar every 30 minutes for 2-3 hours. (5) Given one gram of protein (white meat of chicken) per kilo of body weight and determine blood urea in 4 hours. Results: Normal blood urea increased after protein meal as does sugar after glucose. Blood urea increase 50-75% above fasting level in 4 hours. In liver injury increase is much diminished, usually below 50% and sometimes none. When liver returns to normal protein test shows correlation. Tests were checked by authors, that is procedures 1 to 4 with 5 and correlations said to be present. Not extensively developed?

VII. Dye execretion

1. Tetrachlorphthalein (Rowntree, et al. 1913). Original by Orndorff and Black (1908). First determined amount excreted in feces 48 hours after intravenous injection. Soon discarded. McNeil (1916) estimated amount in bile by duodenal siphonage. 3 minute appearance time normal within 2 hours after injection. Rosenthal (1922) determined amount in serum (15 and 60 minutes). Dose 5 mg. or 0.1 cc. of solution per kilo of body weight. Inject slowly, avoid extravasation. Collect blood in 60 minutes and divide into two tubes. In 1 tube of serum, add 10% NaOH and in the other 5% Hcl. Read in colorimeter. Results: (-3%) normal. (4-8%) partial insufficiency. (Over 8) marked impairment. Regarded as of value by Rowntree (1925) but shows possible toxicity and difficult to develop non-irritating solution. Definite limitations of test because it is not quantitative. Some question as to whether or not it is removed by the liver selectively as no one has been able to account for more than 75% of the dye in the bile and complete absorption takes place in from 24-48 hours in cases of total obstruction by way of the kidney.

2. Rose Bengal (tetra-iodotetrabrom fluorescein). Delprat, Epstein, Kerr (1926). Ideal because it is a non-toxic crystalloid solution eliminated almost entirely by the liver and remains in circulation a sufficient time to allow determination. But it is markedly photodynamic and the patient and the specimen must be protected during the test. Patient should be kept from light for at least one hour after the test is completed. Technic is in general similar to other dyes but specific instructions must be followed. The purpose is to determine the amount of dye which the liver can excrete in 8 minutes. There is a control, a 2 minute specimen and an 8 minute specimen. The normal amount excreted in 8 minutes is 11.5% which is 60% of total possible 19.1%. Anything above 60% retention is abnormal. 19.1% being 100% retention is based on experimental work. Greatly used in estimating the effect on the liver of syphilis and drugs used in the treatment of same. It shows that in certain cases of secondary syphilis there is a hepatitis and injury followed by recovery. It is also valuable in estimating the amount of damage from drugs.

3. Bromsulphalein (phenoltetrabrom phthalein sodium sulphate). Rosenthal and White (1925). Normal rabbits excrete 85% of dye in bile in one hour. Extirpation of liver causes almost 100% retention. Inject 2 mg. per kilo body weight or divide weight by 55 to determine the number of cc. of solution to use. Withdraw 4-5 cc. in 30 minutes. Also a sample in 5 minutes for early hepatic disease. Treat the dye as in the first test, with sodium hydroxide and Hcl acid. Standards available which read from 10-100%. Figure percentage on this basis. Being extensively used at the present time and has been found to be of value in estimating liver damage from anesthetic. Example: a series of dogs were given anesthesia and the following results found. All dogs showed injury from chloroform which took 8 days to recover from 1/2 hour anesthesia and from 1 hour - 6? weeks. Ether recovered in 24 hours but showed definite transitory damage. Nitrous oxide and ethylene did not show any damage at all. Large doses of morphine, like ether, definite transitory effect recovery in 24 hours. Cyanosis increased toxicity of all anesthesia which injures liver. Other dyes suggested: Azorubin-S (Tada and Nakashima 1924) use 4 cc. of 1% solution of dye intravenously. The dye appears in bile after magnesium sulphate stimulation; normal time 17 minutes. The test has not been studied very much. Tetraiodophenolphthalein (Behrend and Heesch, 1926) used in combination with x-ray of gallbladder. Is being studied at present time.

VIII. Bilirubinemia

1. Fouchets (1917)

Trichloracetic acid plus ferric chloride plus increased amount of bilirubin in serum equals green color. Gives positive test in concentration of 1-60,000 or more. Normal concentration 1-600,000. Replaced by others because it lacks a definite quantitative feature only indicating range between normal and abnormal.

2. Van den Bergh (1915)

Bilirubin in acid alcohol solution combines with Erhlich's diazo reagent to form purple dye (azobilirubin). Quantitative standard 1-32,000 equals 1-200,000 azobilirubin (one unit). Standard is troublesome because of technical features.

Qualitative reactions: 1. Direct. A. Immediate (30 seconds). B. Delayed (after long standing). C. Biphasic - appears promptly but is intensified after definite but variable period. 2. Indirect. No reaction with serum but appears promptly with filtrate secured by precipitation of pure proteins with alcohol. 3. Icterus index. Compare color of blood serum with 1-10,000 (value 1) solution of potassium bichromate. Serum should be free from hemolysis or cloudiness (i.e. fasting specimen in dry tubes). Other colors should be ruled out (i.e, carotinenia, eggs, vegetables, etc.). Normal range 4-6, average 5, Latent jaundice 6-15. Clinical jaundice 15+. Clinical jaundice about 16 units usually. Test the greatest value of all.

Significance of bilirubin test.

1. Normal bile obstructed at ducts (cholemia).
2. Bilirubin unable to reach ducts because of injury to liver cells (hyperbilirubinemia).
3. Bilirubin formed rapidly or in increased amount to pass through liver (hyperbilirubinemia).

Original theory was that bilirubin undergoes some change as it passes through liver, resulting in direct reaction given by bile which has passed through and indirect reaction by bile which results from hemolytic jaundice. Other ideas are that one form of bilirubin is an alkaline salt (ammonium) which gives a direct reaction and the indirect reaction is given by the normal free acid. There are other theories in regard to its association with the plasma. At the present time literature is full of confusion and is very difficult to evaluate. The present status (probable) is that (1) the direct reaction is given by free bilirubin, and (2) the indirect reaction by bilirubin in combination with plasma.

Obstructive jaundice	Direct immediate positive	Indirect positive
Non-Obstructive jaundice	" positive	" negative
Hemolytic jaundice	negative	" positive

Direct delayed is secured in normal or occasionally in delayed excretion of bile, biphasic in combinations of obstructive jaundice and liver injury. All the reactions are not this clear cut. Other interpretations are that the differences are due to the duration of the jaundice, whether or not the kidney is able to separate the pigments which are excreted by it and also whether or not it is a simple quantitative feature?.

The icterus index should be used in cases of gallbladder disease, heart failure, alcoholism, catarrhal jaundice, all anemias, pneumonia, chronic sepsis, malaria, typhoid, trichiniasis, drug treatment, especially arsenic. Its chief value is (1) Diagnosis of jaundice, indicating the amount of bilirubin retention. (2) Following the course (i.e., taking specimens at frequent intervals and charting a curve). (3) Demonstrating latent jaundice.

Abstracts:

Laboratory Medicine, Nicholson, D. 1st Edition, Lea and Febiger, 1930. Also Clinical Diagnosis by Laboratory Method, Todd & Sanford, 6th Edition, W. B. Saunders, 1927.

Urine:

Urine tests of value in jaundice. Although bilirubin can be absorbed back into blood from intestine and excreted again in bile, most of pigment reaching intestine is reduced to urobilin by action of bacteria. Some of urobilin is excreted in feces; some is absorbed into blood. Under normal conditions most of urobilin absorbed into blood stream is removed by liver to be excreted in bile or to be conserved for unknown purposes. Under certain conditions the liver becomes unable to remove it efficiently from blood stream, and quite large amounts may pass from the blood into urine. This is basis for the urobilin and urobilinogen tests on the urine in jaundice.

Bilirubinuria

Bilirubin in excessive amounts in urine causes yellow foam. (reliable test), but will not show minute amounts. Add to 5 cc. of urine equal amount of concentrated HCl acid. After mixing add a few drops of hydrogen peroxide and green color which develops after a minute denotes presence of bile. A few drops of Obermeyer's reagent gives a green color to urine if bile is present. Gmelins - Rosenbach test - yellow nitric acid on filter paper saturated with suspected urine. Play of colors (green blue). Blue and red may be produced by indican and urobilin, violet by iodine. Best technique precipitate with lime water, filter and touch precipitate with a drop of acid. Bilirubin is carried down as insoluable calcium compound which concentrates pigment and avoids interfering substances. Overlay urine with tincture of iodine diluted 9 times its volume with alcohol and emerald green color at zone of contact denotes bile pigment. It is convenient to use a conical glass one side of which is painted white.

Evaluation:

Bilirubin is found in greatest amounts in obstructive jaundice and jaundice due to liver injury. It is said not to occur in the urine in hemolytic jaundice.

Urobilin

Same significance as urobilinogen. To 10 cc. of urine in test tube add a few drops of Lugol's solution to transform the chromogen into pigment. Add 10 cc. of saturated alcohol solution of zinc acetate or zinc chloride (filter). A greenish fluorescence, best seen when tube is held in sunshine against a black background (concentrated light with a lens) shows urobilin. The fluorescence

becomes more marked after an hour or two. Bile pigment, if present, should be previously removed by adding 1/5 volume of 10% calcium chloride solution and filtering.

Urobilinogen

To a few cubic cm. of urine in a test tube, add a few crystals of para-dimethylamino benzaldehyd (mate definitely acid with HCl). In the presence of pathologic amounts of urobilinogen, a cherry red color appears. This is best seen by viewing the tube over top of a sheet of white paper. Normal amounts will cause the red color only when the urine is heated. Quantitative determination on single specimens of urine may be made by this test after the manner of Wallace and Diamond. The urine is diluted with tap water, and the concentration is expressed in terms of dilution. Evaluation. Both urobilin and urobilinogen occur normally in the urine. They are increased in hemolytic jaundice, liver injury and partial obstruction. Absent in complete obstruction because of the theoretic assumption that bile does not reach the intestinal tract and therefore cannot be converted into these substances.

Urobilin in Feces

This is done by testing for urobilin by rubbing a small quantity of fecal matter with saturated mecuric chloride solution and allowing it to stand for 24 hours. Urobilin will give a red color which will likewise impart it to such microscopic structures as are stained with urobilin. Green color shows presence of unchanged bilirubin and is not seen normally. Other means of testing the patency of the bile ducts is to pass a duodenal tube, aspirate contents and test for bile.

Comment: Laboratory tests of greatest value: 1. Icterus index (curves); 2. Bilirubin (urine). 3. Urobilin, urobil inogen (urine). 4. Urobilin (feces). 5. Duodenal siphonage. To be tried (again): 1 Van den Bergh? for attempted correlation of dye tests - bromsulphalein. Others: 1. carbohydrate; 2. Widal; 3. Protein test; 4. Rose Bengal. None are absolutely diagnostic but aid in grouping cases.

II. CASE REPORT

ACUTE SUPPURATIVE APPENDICITIS AND PERITONITIS, APPENDECTOMY, TOXIC JAUNDICE. Path. Pearson

The case is that of an elderly white male laborer (road man) 67 years old, admitted to the University Hospital 1-23-31 and died 1-28-31 (5 days).
January 1930 - Began to have attacks of palpitation, dyspnea, orthopnea and marked edema of the ankles and hands. Physician said the condition was caused by heart disease due to high blood pressure. On bed rest and digitalis for one month he improved greatly. Has been on digitalis therapy until December 1930 with no return of symptoms. At this time he began to complain of occasional vague pain in the right side.
1-16-31 - Attacks of moderately severe upper abdominal pain accompanied by anorexia.
1-17-31 - Complains of stiffness, tenderness and constant moderate dull aching pain over the entire abdomen. Stayed in bed part of the day. Anorexia still present. Noted that urine was dark brown color.
1-18-31 - Pain became more severe and was localized more on the right than the left side. Relieved somewhat by hot applications. Anorexia present.
1-21-31 - Had greenish emesis in A. M. Constipation began.
1-22-31 - Past history - Negative. No history of inflammatory rheumatism. Family history not obtained.
1-23-31 - Admitted to the University Hospital at 6:10 P.M.

Physical Examination - Fairly well developed and nourished white male in a semi-stuporous condition, covered with profuse, cold perspiration and complaining of severe abdominal pain. Breathing is labored. Chest is negative. B.P. 130/90. Beat irregular in rhythm and force (auricular fibrillation). Definite rigidity of both recti (upper and lower abdomen). No definite point of tenderness. No rebound tenderness. No distention. No pain on deep palpation. Slight pitting edema of the extremities. Rectal examination negative. Laboratory - Urine - brownish in color. 2 plus albumen. Spec. gravity 1026. 2-3 WBcs. WBCs 12,100. P 80 T 99.4. 6:45 P.M. catheterized and 50 cc. obtained. 10 P.M. Hypodermoclysis 2,000 cc. Ice bag to the abdomen. 11:40 P.M. Sent up to Surgery. Operation began 12:05 P.M. and ended 12:42 P.M. (time 37"). Operation revealed considerable, foul smelling, yellow, purulent material through the entire peritoneal cavity. Cecum, ileum and omentum were all plastered together in the right lower quadrant. Appendix was extremely necrotic, with markedly edematous and friable meso-appendix. The appendix was amputated. 5 Penrose drains were inserted. After the operation condition was very poor. Systolic B.P. 46. 11:50 P.M. M.S. gr. 1/4 P 80, x T 99.4-102.

1-24-31 - 1 A.M. - Returned from Surgery. Condition is very poor. Pulse weak and irregular. Adrenalin mm. x, digalen 2 cc. Intravenous glucose 10% given. B.P. 126/70. Auricular fibrillation is present. 1:20 A.M. Pulse 120, irregular. R 20 and stertorous. 10:30 A.M. Digalen 2 cc. Put up in a semi-Fowler position. 2,000 cc. subcutaneous saline given. 1 P.M. Patient is very drowsy. 2 P.M. P 78, fairly strong. Permanent catheter inserted and 325 cc. urine obtained. 4:30 P.M. Digalen 1 cc. 9:45 P.M. Proctoclysis of tap water started. 10:45 P.M. Pulse 76 and irregular. Very drowsy. 70% alcohol and dry dressings applied. Voided 100 cc. blood tinged urine. Smear taken from appendix showed no bacteria. Hb. 122%, WBc 10,950, Pmns 85%, L 11%, M 4%. Group IV. P 70-80, T 102.2-103.2

1-25-31 - Jaundice of trunk and extremities and sclera are noted. Cardiac rate 120-130. Complains of no pain. Alcohol 70% with dry dressing applied. 4 A.M. Pulse strong - 68. Urine deep red color. 8:30 A.M. Digalen 1 cc. P irregular - 72. 2,000 cc. of intravenous 10% saline. 1:45 P.M. Proctoclysis 1000 cc. 2:30 P.M. Digalen 1 cc. given. 9 P.M. Digalen 1 cc. Involuntary urination. 10:50 P.M. P 68 and irregular. Complains of pain when he coughs. P 66-82, T from 97.6-100.6.

1-26-31 - Jaundice is deepening. 12:30 A.M. States that he aches all over the body. Is very restless. M.S. gr. 1/6 given. 2:30 A.M. Digalen 1 cc. P is irregular - 72 and fairly strong. 7 A.M. Foul odor from the wound with moderate amount of drainage. S. S. enema with good results. 4:40 P.M. Subcutaneous 2,000 cc. saline. 8:30 P.M. Digalen 1 cc. Patient is perspiring and seems a great deal weaker. 9:45 P.M. M.S. gr. i/6 given. Urinalysis showed bile 2 plus. Urobilin - 0. Urobilinogen - 2 plus. Icterus index of 80 units. P 80-120. T 98.6-103.

1-27-31 - Jaundice is about the same. Condition seems worse. Very stuporous. Dressings changed b.i.d. Foul odor with a moderate amount of drainage is noted. Digalen 1 cc. q.i.d. 12:45 P.M. Intravenous 10% glucose given. R 40, P 108. 3:45 P.M. M.S. gr. i/6. P 118, R 36. 7 P.M. Involuntary urination and defecation. Breathing is more irregular 38. P 128. 7:30 P.M. Cheyne-Stokes respirations noted at intervals. Proctoclysis started. 9 P.M. Caf. sod. benz. gr. viiss given. P irregular but strong, digalen 1 cc. 9:30 P.M. There is a lot of mucus in the throat. Atropin gr. 1/150 given. P 136, R Cheyne-Stoke. Chest is clear on auscultation. WBC 17,800, P 84-130. T 100-104.4.

1-28-31 - Jaundice is about the same. Digalen 1 cc. q.i.d. Cheyne-Stoke's breathing. Does not respond. There is twitching of all the muscles. R 44, P is getting weaker. P to 136, T 106.4. Caf. sod. benz. gr. vviiss given. 4:20 A.M. died.

Autopsy: The subcutaneous fat over the anterior abdominal wall measures 5 cm. in thickness. The wound edges are rather firmly held together but when separated show a greenish black discoloration and softening. The odor is that of colon bacilli. When the peritoneal cavity is opened, the omentum is rolled up in the

upper portion and the operative wound. The coils of the small intestine contain a small amount of gas. There is discoloration of the right half of the colon and when this is liberated, a large amount of thin, grayish yellow foul smelling fluid esapes from the right middle portion. The surface of the peritoneum is congested, covered with exudate and shows numerous hemorrhages. The omentum, which is in the region of the appendix, is covered with exudate and can be liberated without difficulty. The intestinal coils are matted together by adhesions in the right side of the abdomen. When the omentum was liberated, purulent exudate was found in the region of the gallbladder. There is no purulent exudate beneath the right dome of the diaphragm nor down in the pelvis. The diaphragm is at the 3rd rib on the right, 3rd interspace on the left. The appendix is absent. There is thickening of the fat in the region of the appendix and a purulent exudate involving several coils of small intestine. There are firm, fibrous adhesions, mainly at the apices, on both sides. There are a few in the posterior and lateral regions. The pericardial sac is normal.

The spleen weighs 240 grams. The capsule is slate-colored, wrinkled, and shows a diffuse collection of hyaline. There is slight softening present. There is one raised yellowish nodule. The liver weighs 1600 grams. The surface is smooth and a peculiar grayish-brown. Section does not reveal very much swelling, but marked cloudiness is seen. No abscesses are found. The hepatic bile ducts are carefully dissected out and no obstruction seen. The entrance of the portal vein into the liver is very carefully examined and no thrombosis found. The gallbladder is moderately distended and contains a moderate amount of dark brown bile. The stomach shows a slight collection of gas. The small intestine is normal, except in the region of the operation wound where a collection of exudate is found which has been previously described. The large intestine, except in the region of the right lower quadrant, is essentially normal.

DIAGNOSIS:

1. Acute suppurative appendicitis.
2. Local peritonitis.
3. Toxic jaundice (acute)
4. Congestion and edema of lungs.
5. Pulmonary emphysema.
6. Pleural adhesions.
7. Hypertension heart.
8. Acute splenitis.
9. Cloudy swelling of heart & kidneys.
10. Operation wound.
11. Puncture wounds.
12. Hypertrophy of prostate; and,
13. trabeculation of bladder, and hypertrophy.
14. Hemorrhages of mucous membrane.
15. Ileus.

Comment:

Elderly man with hypertensive cardiac failure develops acute appendicitis. Operation on 6th day. Poor postoperative reaction. Deep jaundice starting on 2nd postoperative day. Death on 5th. Pylephlebitis suggested but chills absent. Liver showed bile stasis, cloudy swelling. No necrosis, exudate or rupture of bile capillaries. Type of liver injury which may accompany any infection.

Abstract:

Pylephlebitis of Appendicular Origin. Schlitz, C. F. Northwest Medicine, XXIX, 36-38, (January) 1930.

Report of 19 year old girl with history of repeated attacks of appendicitis. At time of operation appendix showed suppurative lesion and gangrenous tip. Removed and drained. Small amount of serous fluid in peritoneal cavity. Mesentery was thickened but not friable; few enlarged glands. Three days post-operative condition considered good except pulse to 120, temperature to 100, or less. 4th day began to vomit. Small amount of wound drainage. Extreme pain in epigastrium and toxic appearance. Wound opened but nothing was found to account for change in condition. Condition remained about same, until 13th day (severe chill.) Temperature to 103. Vomiting worse, pain in epigastrium more severe, restless. Chills continued in severity. 28th day diagnosis; pylephlebitis. Emaciation from vomiting extreme. Aspiration for pus in region of liver negative.

On 30th day chills stopped, vomiting continued. Six weeks later temperature normal taking nourishment in small quantities. Marked ascites had developed, lost 54#. Ascites repeatedly aspirated. Legs had become contracted. Straightened out and put in casts. Six months after operation was able to walk, weighed 115# and was in good condition. Said to be uncommon outcome of this serious condition. Author quotes: Colp, R.-S.G.& O. 43,627-645 (November) 1926. Frequency 2,841 cases of acute appendicitis (1916 to 1925.) 9 cases, or .3% pylephlebitis found. Appendix varied greatly in severity of original disease, from acute inflammation to gangrene and abscess. Veins in mesentery were already thrombosed. At operation in some.

Possible complications: (1) Bacterial emboli without thrombi to liver, (multiple abscesses), the portal vein and radicals normal. (2). Extension of thromboses through ileo-colic vein to radicals to portal to liver (abscesses). Right lobe commonly involved. (Note: Recent work indicating a specific current in portal circulation). Process may remain in ileo-colic vein as hard, retro-peritoneal strand. Perivenous abscesses or retro-peritoneal phlegmon. Petro-peritoneal lymph nodes and lymphatics participate in process and infectious material may be carried. Jaundice may be present. Local lesions: in and about appendix may even heal. If the process is as advanced at the time of operation, attempts have been made to ligate or remove infected vein. (good policy?) Collateral circulation usually adequate veins on left sife of abdomen usually not involved. Chills during course of acute appendicitis indicate portal or general blood stream discharge of bacteria or emboli and are a sign of grave importance. Note in case under discussion today, this feature was absent although it was suggested clinically. Absence of chills spoke against pylephlebitis as cause of jaundice. No thrombosis were demonstrated but the source of the liver injury may have been bacterial emboli and the process seen before abscess formation had chance to take place.

IV. CASE REPORT:

CARCINOMA OF STOMACH (MALIGNANT ULCER). ACUTE HEMORRHAGIC PNEUMONIA.
Path. - Pearson.

The case is that of a white male adult, 62 years of age, admitted to the University Hospital 12-16-30 and died 1-11-31 (26 days).
1928 - Began to have some food distress, aggravated by eating meat or some sour food. Relieved by drinking milk and cream and eating Bland diet. Also complained of belching of gas. No relief with soda.
1929 - Trouble became progressively worse. Treated by a physician for ulcer of the stomach with no relief. Marked constipation.
June 1929 - Progressive weakness began and patient lost about 50# during the next 6 months. There was a constant dull, aching pain in the epigastrium, not relieved by food.
November 11, 1930 - Noticed fullness in abdomen. Emesis of a quart of dark brown fluid, foul-smelling.
11-15-30 - Stools were black and tarry. Patient felt a mass in the epigastric region.
Past history - Negative.
Family history - Father and mother died of old age at 75 years. 2 brothers living and well, 2 sisters living and well. No history of cancer in the family.
Marital history - Negative.
12-1-30 - Admitted to the University Hospital dispensary where a diagnosis of probable carcinoma with secondary anemia was made. Laboratory - Hb. 55%, RBcs 3,600,000, WBcs 9,500. Urine - negative.
12-2-30 - Wassermann - State Board and Larson negative. Stools - Gregorson positive. Gastric expression at this time was not successful.

12-3-30 - X-ray - There is a marked infiltration of the lesser curvature in about the middle third with a considerable irregularity suggesting malignant infiltration. A very large, penetrating ulcer can be made out in this region which is very irregular on its upper portion. There is also some lack of filling in the prepyloric region. Appearance suggests carcinoma with ulceration. At 6 hours the stomach is empty and the head of the meal is in the cecum. Conclusions: Carcinoma of the stomach with ulceration.
12-16-30 - Admitted to the University Hospitals. Physical examination - Shows well developed and fairly well nourished elderly white male laborer with marked pallor of the skin and mucus membranes. The chest is negative. B.P. 96/60. Pulse 114, regular and strong. There is a fullness and indefinite mass in the epigastrium slightly to the left of the midline. There is slight tenderness on deep palpation in this region. The liver edge can be palpated 2 fingers below the costal margin. There was no evidence of metastases to the superficial lymph nodes. Rectal examination showed enlarged prostate. Virchow's node not palpable. Rectal shelf masses (?) 2 out of 3 observers.
Laboratory - Urine negative. Hb. 31%. RBcs 1,540,000, WBcs 9,500, Pmns 87, L 13. Marked hypochromasia and anisocytosis. Moderate polychromatophilia and poikylocytosis. T 99.4, P 120.
12-17-30 - Complains of nausea. Emesis of 150 cc. of brownish fluid. T 99.6, P 104.
12-18-30 - Emesis of 400 cc. of brownish fluid. Tube inserted for histamine test. 200 cc. of brownish fluid withdrawn.

	Free NCl	Total Acid	
1st specimen	55	70	
2nd "	54	70	
3rd "	80	92	
4th "	89	108	P. 100, T. Normal.

12-19-30 - Complains of slight pain in the abdomen. Codeine gr. 1/2 given. Urine negative. Stools hard, black and tarry. Gregerson positive. P 108, T normal.
12-22-30 - No complaint. Given 500 cc. of blood through vein. S.S. enema. T. 99.2, P 92.
12-23-30 - Complains of some pain in the left chest, upon breathing.
12-26-30 - No complaints. S.S. enema given. Mineral oil 1 oz. 2 times daily begun. Hb. 23%. Urine negative.
12-31-30 - Feels comfortable. 500 cc. unmodified blood given by vein.
1-3-31 - Feels comfortable. Gastric lavage 350 cc. retention. Hb. 32%. P and T Normal.
1-4-31 - Feels good. 2 donors used and 1000 cc. unmodified blood given by vein. T and P normal.
1-6-31 - Gastric lavage. 350 cc. residual. No complaints except itching of hands. Hb. 57%. B.U.N. 23.33 mg.
1-7-31 - No complaints. Gastric lavage. 65 cc. retention in forenoon and 50 cc. in P.M. X-ray - Shows the same infiltration on the lesser curvature. The ulcer has decreased considerably in size. May be due to lack of filling although this is not entirely definite. Believed to be carcinomatous ulcer although benign ulcer could not be entirely excluded. Conclusions: 1. Probably carcinamatous ulcer on lesser curvature of posterior wall. 2. Probably carcinomatous infiltration of lesser curvature and posterior wall of stomach.
1-8-31 - Patient's left ankle swollen and discolored. 2000 cc. 5% glucose in saline intravenously. Gastric lavage 250 cc. retention. T and P normal.
1-9-31 - Ankle still swollen and discolored. Gastric lavage 50 cc. retention. Operation begun at 2:50 P.M. using 4 cc. of spinocain and 1 ampule ephedrine. 3 cc. discarded and the remainder expanded to 8 cc. 3:55 P.M. Ethylene begun. 4:30 P.M. Ether begun. Operation revealed a large, crater-like lesion in the midportion of the stomach. There were no peritoneal implants. There was some doubt as to whether or not the lesion was an ulcer or a carcinoma. A Polya type

of anastomosis was made, and lower 2/3 of stomach removed. Time for operation 2-1/2 hours. Pathological diagnosis - ulcerated scirrhous carcinoma. Intravenous 2500 cc. of 10% glucose given postoperatively. Catheterized 300 cc. urine obtained. 1500 cc. saline proctoclysis. Hyperventilated 2 times daily. M.S. gr. 1/2 twice daily. Postoperative condition fairly good. P 124 and regular. T 97. B.P. 130/70.

1-10-31- 2 A.M. Patient voided 400 cc. 3:30 A.M. patient voided 400 cc. 4 A.M. B.P. 98/64. Breathing is more rapid and shallow and there was considerable belching of gas. 5:30 A.M. patient is restless. 9 A.M. 1000 cc. 10% glucose given intravenously. Hyperventilated 5 minutes. P 132. Voided 150 cc. 1 P.M. B.P. 72/40. M.S. gr. 1/4. Intravenous saline 200 cc. 500 cc. whole blood given, per vein. B.P. after transfusion was the same as before. Calcium chlorides 15 gr. intravenously, T 104 (2), P 24, R 24. Voided 50 cc. 5:30 P.M. 1200 cc. dark fluid aspirated from stomach and patient lavaged with hot sod. bicarb. 6 P.M. M.S. gr. 1/4. Voided 100 cc. 2500 cc. 10% glucose by vein. Patient seems weaker. 11:30 P.M. 250 cc. brownish fluid aspirated from the stomach. Lavage with hot water. Complains of occasional pain in the chest. Breathing more labored and pulse more rapid. B.P. 88/56. Examinations showed no breath sounds over the left lower chest. Pleural friction rub was also heard. Hb. 52%, RBcs 3,380,000. P 120-140, T 97-104.6, R 16-34.

1-11-31 - General condition worse. Hyperventilated 5 minutes t.i.d. 12:30 P.M. M.S. gr. 1/4. 1000 cc. normal saline by hyperdermoclysis. 3 A.M. Breathing more labored and shallow. P 148. 4 A.M. Patient is more stuporous. 5A.M. B.P. is 100/60. 6 A.M. P 148. Condition about the same. Responds poorly. B.P. 92/56. 7:45 A.M. Rales were heard on both sides of the chest, particularly posteriorly at the bases. Abdomen is soft and there is no distention. 8 A.M. T 105, P 142, R 36. 9 A.M. Hyperventilated 3 minutes. Breathing better following this treatment. Voided 50 cc. 9:30 A.M. There is definite dullness over the rt. base. Tympany over the left lower chest. X-ray - showed considerable mottling in the uppoer portion of the right long field which probably represents a beginning pneumonia which is not entirely consolidated. At this time there appears to be a slight amount of density at the left base, but this is not particularly definite. Oxygen started. Hyperventilation 3 minutes. T 106 (R), P 142, R 36. Breathes with a respiratory grunt. B.P. 76/52. 2:50 P.M. 10% glucose by vein started. 1 ampule of calcium chloride injected per vein. 4:45 P.M. Pulse rapid and irregular. Digalen 1 cc. Rapidly growing worse. 8 P.M. condition very poor, P imperceptible. T from 104 to 106.2 (R), P 140-158 (R) R 36. 8:56 P.M. died.

Autopsy -

The subcutaneous fat over the anterior abdominal wall is 3 cm. in thickness. The diaphragm is at the 4th rib on the right, the 4th interspace on the left. The appendix is subcecal and free. There is approximately 1 liter of brick red, cloudy fluid without any fibrin, in the peritoneal cavity. The investinal coils are not distended except for the jejunal loop making up the enterostomy. For approximately 1 meter away from the operative site, there is a dark bluish green discoloration of the lumen of the small intestine. When opened this is found to be due to brownish black old blood. The entire small intestine shows slight congestion. There is also congestion of the vessels of the perietal peritoneum. The large intestine contains a moderate amount of gas and fecal material. There is a mass of feces in the hepatic flexure. No evidence of peritonitis. The source of this free fluid is probably the duodenal stump. No reaction is seen about this so this is probably a postmortem affair. More than 2/3 of the stomach has been resected. More of the greater curvature is left than the lesser. The anastomosis which is anterior to the colon is 8 cm. in length. No evidence of metastases seen. There is one small hard, calcified nodule the right side of the prostatic flexus of veins (phlebalith).

The right lung weighs 1,150 grams, the left 1050. Marked anthracosis is present. There is dark bluish discoloration of the dorsal surfaces of both lower lobes and the lower portion of the upper lobes. Bilateral interlobar adhesions

are present. The surface of the right lung is slightly roughened due to liberated adhesions. Crepitation is definitely reduced. The lungs have a heavy, boggy feeling. On section marked congestion and edema are seen. There is slight emphysema of the upper lobes. On section both lungs show diffuse hemorrhagic congestion and edema. No definite areas of consolidation. The cut surface has a meaty appearance. A large amount of hemorrhagic fluid is expressed on pressure. There is a small healed subpleural tubercle in the right upper lobe and a calcified node at the hilus. The bronchi show marked congestion and a few hemorrhages.

DIAGNOSIS:

1. Gastric ulcer (Malignant)
2. Partial resection of stomach.
3. Anastomosis of stomach to jejuna (anterior).
4. Acute hemorrhagic bronchopneumonia.
5. Ascites (postmortem).
6. Acute splenitis.
7. Cloudy swelling of heart, liver and kidneys.
8. Fatty metamorphosis of liver.
9. Old blood in small intestine.
10. Pleural adhesions.
11. Old healed tuberculosis.
12. Slight hydrothorax.
13. Cardiac hypertrophy and dilation.(400)
14. Cholesterosis of gallbladder.
15. Hypertrophy of middle lobe of prostate.
16. Hyperplasia of upper abdominal nodes.
17. Abdominal operation wounds.
18. Antecubital wounds.
19. Varicosities of left leg.

Comment: Non-pyloric ulcer with infiltration in base and side walls. (ulcerated carcinoma). Note acidity and mixed clinical history of ulcer and carcinoma. (Food relief, frank hemorrhage (ulcer) "meat" distress, constant pain, weight loss cancer age (malignancy). Terminal complication - diffuse hemorrhagic pneumonia.

V. ABSTRACTS:

Gastric Secretion in Carcinoma of the Stomach. Polland, W.S. and Bloomfield, A.L. John Hopkins Hospital Bulletin, XLVII, 307-322 (January to June) 1930.

1. Literature

Golding Bird (1842) is credited with describing diminution of Hcl in cancer of stomach. Original description is vague andthe case was probably pyloric stenosis due to ulcer. Von d. Velden (1879) made first purposeful studies and found absence of Hcl in carcinmoa of the stomach. Miehe (1890) found free Hcl in carcinoma but agreed it was usually absent. Other reports. Boas (1911) anacidity 77.5%. Smithies and Oschner (1916) free acid from 0 to 73. Hartman, Mayo Clinic (1922) 551 cases, none of which were believed to follow ulcer, found anacidity 53.7%, hypo-acidity 15.7%, normal acidity 17.4%, hyperacidity 4.5%. Brown (1927) states that acid is absent in more than 75% of the cases. Few observers observe hyperacidity.

II. Conditions where acid is present.

According to the literature (1) early carcinoma, (2) small pyloric growth, (3) carcinoma on ulcer basis. Author disagrees with this contention.

III. Material. 19 verified cases of carcinoma of stomach (operation or autopsy). Patients in terminal stages, huge growths, or extensive metastases were not used. Purpose to study various types and not statistical group. Fasting material

was aspirated histamine 0.1 mg. per 10 kilo body weight were given subcutaneously and 3-6 10 minute collections were made. Studies were made of gross appearance, amount, acidity, PH and ferment. In a few cases chlorides, nitrogen and total base were determined. Correlations were made with clinical features of size and position of growth. A few were followed as to variation and end result.

IV. Results

1. Gross characteristics - Small volume tenacious, mucoid grey or brownish material in some bloody and foul. Others were thin and clear, but still no acid was present. Where nearly normal acid values were obtained, the juice was usually colorless, clear and without special note.

2. Volume - Small in all. Anacidity - figures usually showed less than 10 cc. of secretion. Usually 1 to 5 cc. No true rise after histamine indicating no true reaction, only mucus. Even when acid was present, the amount was subnormal.

3. Acid - Majority have anacidity (di-methyl indicator). Several were subnormal only 3 near normal. Low values may be obtained in other conditions (gastritis?) PH in anacidity is usually 6-8. In some the PH was 3-5 with no acid.present by indicator method, indicating some was being secreted.

4. Pepsin - Determined in 5 cases. No specific information obtained as amount varied with rate of acid secretion. Some pepsin was demonstrated when acid was absent. This is an old observation.

5. Mucus - Large amounts were not secured, contrary to recorded opinion. No true mucorrhea, only very small amount.

6. Chlorides - Fixed base and nitrogen (2 determinations). No specific findings.

7. Relation to size, position and duration of growth - No definite conclusion. All cases with free Hcl in this series had pyloric lesions (see our case) but anacidity occurred with lesions at any part of the stomach. One case was followed after resection without change in secretion. No evidence of metastases at the time. One was followed through progressive increase in size of the growth without change, acid in this case being present at all times. Another showed functional improvement, if anything, with the continuation of the growth. These observations are not in accord with the undocumented statement made so often in the literature that acid decreases as the growth extends.

Theories: That gastric secretion might be altered in advanced ulcerating carcinoma has seemed natural enough to most writers who have studied the subject, but it is more difficult to understand how a small growth, localized in the submucosa of the pyloric region could cause an anacidity. The following theories have been suggested:

1. Neutralization of gastric juice by duodenal contents.
2. Suppression of gastric secretion by mucus.
3. Injury ofthe acid bearing glands of the pylorus by the growth.
4. Interference of gastric nerves by growth.
5. Neutralization or inhibition of gastric juice by alkaline products of the growth.
6. Chloride starvation.
7. Gastritis, associated with the growth.

Comment: Of these the one which has been most widely held is that gastritis, associated with growth is responsible for change in the secretion. Lebert (1878) found in 41 out of 56 cases, extensive gastritis, even at distance from growth. Rosenheim (1888) investigated question very carefully. (Extensive gastritis found in 14 stomachs with cancer in which anacidity had been present during life). Another case of verified cancer with normal acid showed no gastritis at autopsy. A large number of observers from 1888 to 1928 have studied the question and all agree as to frequency of diffuse gastritis or areas of gastritis in stomach, seat of cancer, and feel that changes in secretion are due to this rather than to the growth itself Konjetzny and Saltzman (1913) produced positive evidence on

pathological side by demonstrated histological transitions from gastritis to actual cancer. Hurst supported this view on clinical grounds: (1) But does this neutralization of gastric juice occur from duodenal contents. Had there been regurgitation in author's series, there would probably been increased volumes. Bile is also absent. (2) Gastric secretion is not suppressed by mucus because mucus is present in such small amounts. (3) Injury of acid bearing glands of pylorus by growth cannot be supported because very high values in both acid and volume have been found in cases of huge pyloric ulcers. Normal values may also be obtained in quite large pyloric carcinomas, where as anacidity may exist with small ones. The most important reason is, of course, that acid producing cells do not exist at pylorus. (4) Does interference by the growth with gastric nerves cause change. Recent stimulation and depression of nerves to acid secretion in health and disease answers question in negative. (5) No support for idea that neutralization or inhibition of secretion by alkaline products of the cancer is cause. (6) General chloride depletion of body was once suggested but benign lesions with marked vomiting still show acid.

Summary - 1. Gastritis is associated with carcinoma. 2. Most observers have concluded or assumed that growth produces a gastritis. 3. Authors believe all evidence points the other way. Agree with Mathieu's long neglected view that gastritis precedes growth and carcinoma is prone to occur in stomachs already seat of chronic changes.

Abstract: Multiple Adenopapillomata of the Stomach with Report of Case Showing Varying Degrees of Malignancy. Ackman, F.D., Canada Med. Association Hournal, 23, 391-199, (September) 1930.

Introduction:

Prior to 1909 multiple polypoid adenomata of stomach had been recognized only at postmortem and condition was therefore thought to be uncommon. Modern advances in diagnostic laboratory methods, particularly routine roentgenological examinations of stomach, have however, shown that condition is not rare and can be recognized clinically. First observed Brissard (1885) and classified by Menetrier (1888), (1) polyadenoma "polypeux", (2) polyadenoma "en nappe". Classification still generally accepted. Also advanced theory that disease is due to chronic gastritis. Wegele (1909) first antemortem diagnosis (operation). Prior 49 cases reported were postmortems. 39 cases have been reported since 1909 (more than 2/3 were diagnosed clinically). See Brunn and Pearl, S.G. & O. 43: 559- 1926. (84 proved cases, 5 of their own.)

I. Incidence (Mayo)

Wide diversity of opinion, but considered rare?. Carmen recognized two in 50,000 gastric-roentgen-ray examinations. Probably not a true statement of frequency. Age - youngest 20 - oldest 82. Average 53. 20-30 (3), 30-40 (11), 40-50 (8), 50-60 (21), 60-70 (17), 70-80 (8), over 80 (2). Ages in 8 cases not given. Females 31, males 32, sex not given 23.

II. Etiology

1. Anlangen becomes separated during early development.
2. Familial tendency (debatable).
3. Chronic irritation.
4. Chronic gastritis.

Konjetzny noted gradual transformation from chronic gastritis to adenoma and even to carcinoma. Many admit the inflammatory origin, but also suggest familiar tendency and even possibility of a congenital cause. Fibiger produced adenomata in stomachs of rats by feeding a certain nematode whose intermediate host is cockroach. Mature parasite grows in gastric wall of rat and results in papillomatous formation. Two Japanese investigators produced polyps by injecting

coal tar into gastric mucosa of rats. All experimental evidence inclines toward the "acquired" theory and emphasizes role of irritants.

III. Pathology

"Polypeux" group characterized grossly by pedunculations and marked lobulations, cystic dilatations of glands (almost constant finding.) Type more common and thought to be result of hypertrophic involvement of glands at neck of duct with resultant blocking. More uncommon "en nappe" (7 previously reported cases). Present case making 8. Mostly sessile, flattened plaques composed of closely packed folds of hypertrophied mucosa, rarely containing cysts, and more rarely peduncular. (Except when mechanical factors exert traction). Type represents true hyperplasia of cells at fundal end of gastric glands. Both types of tumor may be present. Others show Brunner's glands. Occur most frequently in distal third of stomach and on greater curvature and vary in number from 3-800. Sometimes large polyps are surrounded by smaller ones. Vary in size from few mm. to tumors filling stomach; all are fairly soft. Vary in color from pale grey to reddish brown, depending on vascularity, amount of degeneration and whether or not hemorrhages are present. Hemorrhage and ulceration fairly common. The tumors are covered with a thick mucus of egg-albumin consistence, which also is spread over surrounding gastric mucosa. (Finding is characteristic). Gastric wall itself is usually thickened and congested. Polypeux type, histologically, shows well developed elongated stalk of connective tissue supporting fairly orderly adenomatous pattern of glands lined by single layer of columnar, cuboidal or flattened epithelium. Dilated glands are filled with mucus. In other variety glandular arrangement is more irregularly adenomatous. Mitotic figures are very uncommon. Inflammatory reaction is extensive, for the most part small cells and plasma cells predominating, but in some areas polymorphonuclear leucocytes may be so numerous as to give the appearance of abscess formation.

IV. Malignancy.

Malignant transformation was found in 12% to 20%.

V. Symptomatology.

May run long course without symptoms. When present vary in character and degree, depending upon kind of tumor, location and size. Epigastric discomfort, sensation of pressure or weight is said to be first symptom, subsequently pain. Epigastric pain is most common symptom, (27%). Pain may be burning or colicky. relieved by food, in others without effect. Nausea frequent and vomiting in small number. Vomitus is said to be characteristic (mucus). Development of anorexia, anemia, asthenia or constipation is about as frequent as vomiting. Hematemesis occurred in 8 of the cases reported and was the primary symptom in 4. Fatal bleeding is unknown. Occult blood is more frequent. Achlorhydria is almost always present; diarrhea is frequent finding. Pedunculated tumors may cause acute or chronic obstruction. How much of the symptoms are due to the tumors and how much to the associated gastritis cannot be determined?

VI. Diagnosis.

Frequently overlooked clinically. X-ray is most valuable means of diagnosis. Gastric analysis also affords help. Absence of free HCl and low total acidity were found in over 90% of the cases. Occasionally tumor tissue has been found in the stomach washing. Large quantities of thick, viscid mucus are said to be characteristic and occult or manifest blood has been found in over half. Gastroscopy offers aid. Anemia may be marked. Chief differential points are from chronic gastritis, gastric ulcer, carcinoma and syphilis.

VII. Prognosis and Complications.

Little is known of prognosis. Malignant changes not uncommon. Micro-

scopic recognition of early malignant changes is often difficult. Must rest on actual invasion of submucosa although cases with metastases have shown no such invasion.

VIII. Treatment.

On account of the danger of malignancy the lesion should be completely excised, partial resection of the stomach being the operation of choice. Extent will usually be determined by degree of involvement. Sometimes a large tumor can be removed and the outlying growths excised and their bases cauterized. Radium used in one case successfully. Author reports a case in which there was absence of gastric symptoms prior to bleeding. Large pedunculated polyp which prolapsed through the pylorus without leading to obstructive symptoms. Malignant transformation had occurred, partial gastrectomy was performed, and the patient made uneventful recovery. Microscopic sections showed malignant transformation of polyp.

IX. Summary.

1. 88 cases of multiple gastric adenopapillomata are to be found in literature.

2. The condition is generally thought to be inflammatory in origin although congenital or familial tendency has been noted.

3. No characteristic symptomatology (epigastric pain is frequent symptom). Hematemesis occasionally first sign.

4. Of laboratory diagnostic aids roentgenogram is most important. Achlorhydria is practically a constant finding, and when combined with an excessive amount of mucus is considered suggestive.

5. Malignant transformation is common but rarely multiple. (15-20%).