2. Golob, Meyer: Fractional Test Meal Method of Rehfuss Versus Single Test Meal of Ewald, N. Y. Med. Jour. and Med. Record, January 17, 1923.
3. Roth, J. L. A. and Bockus, H. L.: Why Do a Gastric Analysis? I. Theoretical Considerations; II. Uses of Various Procedures, Gastro-enterol., Vol. 18 No. 4, August, 1951.
4. Winkelstein, Asher and Marcus, J. M.: Excretion of Neutral Red in the Stomach in Achylia Gastrica, Jour. A. M. A., Vol. 92, April 13, 1929.
5. Golob, Meyer: Fetor Ex Ore from the Dentists' and Physicians' Standpoint, The Dental Outlook, Vol. 21, Oct. and Nov., 1934.
6. Roth, J. L. A. and Bockus, H. L.: *op. cit.*
7. Golob, Meyer: Rugae Gastrica, Their Importance in Roentgenologic Diagnosis, The Amer. Jour. of Roentg. and Rad. Therapy, Vol. 22, No. 1, 1929.
8. Held, I. W. and Goldbloom, Allen: Peptic Ulcer, Its Diagnosis and Treatment, Charles C. Thomas, Publisher, 1946.
9. Golob, Meyer: A Survey and Interpretation of the Spastic Phenomena of the Gastroenteric Tract, N. Y. Med. Jour. and Med. Rec., Nov. 21, 1923.
10. Riesman, David: Timely Topics, The Health Examiner, Vol. 1 No. 10, January, 1932.
11. Fairle, Chester W., Jr.: Chronic Gastritis as a Source of Gross Hemorrhage, The Med. Clin. of N. A., Vol. 33, No. 5, September, 1949.
12. Barowsky, Harry: When Should Gastroscopy Be Employed?, The Rev. of Gastro-Ent., Vol. 18, No. 10, October, 1951.
13. Eusterman, George B.: Chronic Non-Specific Gastritis: Significance as a Clinical Entity, Gastroenterology, Vol. 1, No. 1, January, 1943.
14. McNeer, Gordon and Barowsky, Harry: A Gastroscopic Study of the Incidence of Chronic Gastritis in Common Gastric Afflictions, The Amer. Jour. of Dig. Diseases, Vol. 6, No. 3, May, 1939.
15. Bockus, H. L.: Gastro-Enterology, Vol. I, p. 308.
16. Ricketts, R.: Gastric Analysis—Practical or Useless?, Rev. Gastro-Enter. Vol. 17, Oct., 1950, abstracted by McDonough, Francis E., Gastro-Enterol., Vol. 19, No. 2, October, 1951.

FATAL DIFFUSE HAEMORRHAGE IN CASES OF LAENNEC'S LIVER CIRRHOSIS*

KLAUS A. J. JÄRVINEN, M. D., AND ELLI LEIKOLA, M. D., Helsinki, Finland.

A HAEMORRHAGE from the gastro-intestinal tract is a rather common and severe symptom in association with liver cirrhosis. Hematemesis alone occurs in about 20 to 30 per cent of patients suffering from this disease (1,2,3). A haemorrhage from the gastro-intestinal tract was the immediate cause of death in 20 per cent of the 217 cases of liver cirrhosis examined by Evans and Gray (4). According to Cates (5) the corresponding percentage was 29 in a group of 102 patients. Douglas and Shell (6) calculated that in their material of 444 patients a gastro-intestinal haemorrhage had been the immediate cause of death in approximately 50 per cent of the cases.

Voluminous haemorrhages of the liver cirrhosis patients have in general been ascribed to a rupture of the anastomoses which have developed between the portal system and the veins in the general circulation. A haemorrhage has most often been considered as coming from the enlarged esophageal veins. However, as early as in 1900, Preble (7) described six cases of liver cirrhosis patients, who died in acute gastro-intestinal haemorrhage; nevertheless, a site for the bleeding could not be found post mortem. He explained these cases as having suffered from a diffuse capillary bleeding from the gastro-intestinal mucosa. Although some investigators have laid stress on the possibility of a diffuse gastro-intestinal bleeding in liver cirrhosis (8,9,10), very little attention has however been paid to it. Therefore, it was thought justified to present the results of a study of this problem.

MATERIAL

The material of the present work consists of 19 cases of liver cirrhosis treated in our hospital during the years 1948-1951, in whom attention was paid to the occurrence of diffuse gastro-intestinal bleeding. No cases of biliary or pigment cirrhosis were included, and such forms of liver cirrhosis which had developed on the basis of cardiac decompensation were also excluded. In addition to the routine clinical and laboratory examinations, the diagnosis was in 6 cases (cases 1,2,3,15,17 and 18) confirmed with the aid of autopsy, at which cirrhosis of the Laennec type was observed in every case. In four other cases, the diagnosis was confirmed by a histological examination of a biopsy taken at an exploratory laparotomy (cases 4,9,14 and 16). Also in these cases the biopsy revealed a cirrhosis belonging to the Laennec-type. The average age of the patients was 54.1 years. Fourteen of the patients were male and five female.

RESULTS

Eight of the patients of the present material died in the hospital. In six of these (cases 1,2,3,15,17 and 18) an autopsy was performed. In three of these (cases 1, 2 and 3) a diffuse haemorrhage from extensive areas of the gastro-intestinal tract was observed. In none of them could a localized bleeding from enlarged veins be seen. (Cases 1, 2 and 3 are described in detail.) Table I shows a comparison of some important findings in these three patients with those in the other material. The patients are grouped in the Table so that group A comprises the above three patients with diffuse gastro-intestinal bleeding as confirmed in autopsy. Group B includes all cases with haematemesis or melaena, 5 in all, but without a distinct demonstrated reason for the bleeding. (In fatal cases, permission for the autopsy was not obtained.) Group C represents patients without gastro-intestinal haemorrhage either in the history or during the stay in the hospital. The number of such cases was 11.

When group A is compared with the groups B and C in Table I, it is first observed that the age of the pa-

*From the Third Medical Clinic of the University of Helsinki; Acting chief Klaus A. J. Järvinen, M.D.
Submitted July 17, 1952.

TABLE I

The patients suffering from Liver Cirrhosis of Laennec's Type in whom the autopsy revealed that Diffuse Gastro-Intestinal Haemorrhage had been the immediate cause of death: Group A.—These are compared with patients who had bleeding of unknown origin in connection with the same disease (Group B) or no bleeding at all (Group C).

	Group A			Group B					Group C										
Case No:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Age	44	56	65	35	51	52	57	78	26	41	42	50	54	56	57	57	65	67	75
Sex	M	M	M	M	M	M	M	M	M	M	M	M	F	F	M	M	F	F	F
Alcohol abuse	++	+	−	++	++	++	++	−	−	++	++	+	−	−	−	−	−	−	−
Lues	−	−	−	+	−	−	−	−	−	−	−	−	+	+	−	−	−	−	−
Ascites	+++	+++	−	++	++	+	+++	++	−	+++	+++	−	++	−	++	+	+	−	++
Icterus index	110	17		14	90	40	24	26	26	24	110		70	55	70	45	30	30	24
	10	11		7	12	13	11	7	18	5	32	6	4	9	30	7	17	4	9
Takata	+++	++		+	++	+++	++	+++	+	+	++	+++	+++	+++	+++	++	++	++	+
Mercurie chl.	+	+		−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymol turb.	+	+		+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	−
Zinc sulph.	−	+		+	+	+	+	+	+	+						+	+	+	+
Phosphatase	5	7		5	23	18	6	19	3	16		15	9	12	14	10	69	32	46
ESR	25	49		104	62	93	125	145	5	86	23	49	118	22	40	40	128	46	69
	9	19		70	36	9	19	125	2	10	12	48	20	6	15	23	102	22	26
Serum protein	5.5	7.1		8.9	6.6	8.8	5.5	6.7	8.9	8.5	8.0			6.7		6.0	8.0	6.3	6.9
Alb./glob.	0.4	0.3		1.4	1.8	0.5	0.4	0.4	1.1	0.6				1.1		0.8	0.6	2.7	1.3
Hgb per cent	43	75		80	56	46	17	54	83	55	65	48	65	65	84	71	53	86	71
Er. mill. per cu. mm.	2.3	3.8	3.3	4.4	2.3	2.3	1.3	2.4	4.1	2.6	3.6	2.6	3.9	3.1	4.6	3.8	2.8	4.0	3.5
Index	0.93	0.98	1.07	0.90	1.20	1.00	0.65	0.95	1.01	1.05	0.87	0.88	0.83	1.04	0.91	0.93	0.94	1.07	1.01
Leukocytes per cu. mm.	630	3700	10300	6600	4200	1600	1400	3200	2500	4600	6100	2600	4900	2300	4200	4800	2000	3000	1700
Thrombocytes 1000/cu. mm.	12			106		71	53		172	154			172	67	112	122			108
Death before the 1.1.1952	D	D	D			D		D							D		D	D	

The use of alcohol is denoted with +, if the patient had clearly been abusing alcohol, and with ++, if the patient presented distinctly pathological alcoholism.

Among the results of Takata's test, the lability tests, and the alkaline phosphatase determination, the value coming most close to the time of the highest observed icterus index has been considered. The icterus index and ESR values are the observed maximum and minimum figures.

tients does not differ in these three groups. As for the sex, it is noted that the groups A and B do not include any female patients, whereas almost half of the cases in group C are female. This probably does not depend on chance due to the small number of cases, since in some more extensive investigations it has been similarly noted that gastro-intestinal haemorrhage occurs less frequently in female than in male patients suffering from liver cirrhosis (11).

As to the abuse of alcohol, which has been regarded as having an aggravating influence on the tendency to haemorrhage, due to alcoholic gastritis and vomiting caused by it (12), the groups A and B do not differ in this respect. In group C, the abuse of alcohol has been less frequent, perhaps due to the greater number of female patients in this group.

In the whole material, the number of cases with syphilis was only 4. In all of them, this disease was in the seropositive stage. Moreover, an attempt was made to exclude the possibility of a seronegative lues medicata, in addition to asking the patient, by an X-ray examination of the gluteal regions of the patient for traces of bismuth, where bismuth injections are known to leave permanent signs, according to a study made in this clinic (13). No cases of syphilis occurred among the patients of group A.

Nor does the occurrence of ascites seem to be a symptom essentially associated with diffuse gastro-intestinal haemorrhage; among the patients of group A, it was only observed in two. Moreover, it had disappeared from one of these (case 1) before the occurrence of a fatal diffuse haemorrhage.

As to Takata's test, Stolte's mercuric chloride number, the thymol test, the zinc sulphate test, alkaline phosphatase, and sedimentation rate—none of these showed any marked difference between the groups A, B, and C. The same is true of the icterus index (Meulengracht value), haemoglobin percentage, the number of erythrocytes, index, and the number of leukocytes. A tendency to anaemia was notable; in only three patients in the whole material did the Hgb percentage exceed 80, while the number of erythrocytes was above 4.5 mill. in only one. In 5 of the patients the index exceeded unity. The material shows a distinct tendency to leukopenia, as well as to thrombopenia. The blood picture shows several features characteristic of liver cirrhosis, but nothing can be found which would separate group A from the remainder. As for the thrombocytes, however, the investigation was very incomplete, particularly in group A. The determination was made only in case 1, and the observed value was the lowest in the whole material.

Although the serum protein concentration in group A is on an average somewhat lower (6.3 per cent) than in groups B (7.3 per cent) and C (7.4 per cent), the difference is in no way clear, particularly as the value in group A was obtained only from 2 patients. However, group A shows a more distinct difference from the remaining material, if attention is paid to changes in the serum protein fractions. In group A, the average serum albumin/globulin ratio (only two patients) was 0.35, in group B the corresponding value was 0.90, and in group C 1.17.

The prothrombin content of plasma was not determined in the patients of group A. In cases 4 and 8 it was 40 per cent and 76 per cent, respectively.

Enlarged veins in the lower part of the oesophagus could be observed roentgenologically in cases 1, 4, 10, 15, 17 and 18. In cases 5 and 11 the X-ray finding was negative. Haemorrhoids occurred in cases 4, 5, 16 and 17.

In the following, a detailed description is given of cases 1, 2 and 3; in these patients a fatal gastro-intestinal haemorrhage occurred which at the autopsy was found to be diffuse.

Case 1. Male, 44 years, building worker. Case history No. 3844/50. Family history for liver affections and haemorrhagic predisposition was negative. Since his youth, the patient had taken alcohol abundantly. The physical condition has been good, and he had pursued e.g. wrestling and boxing. During the last six years the patient could only be regarded definitely as an alcoholic. The general condition deteriorated progressively during this period. At the age of 41 the patient suffered from pleuropneumonia, with a slow recovery. He was admitted to the hospital at the age of 42. The pat. was at times confused, in delirium. He suffered from swelling of the abdomen, diarrhoea, occasional vomiting, and slight temperature. The physical examination of the abdomen suggested an ascites. Spider telangiectasiae were to be seen in the skin. The thenar and the hypothenar were livid, the nails biconcave. The stool contained occult blood. The urobilinogen and urobilin in urine were increased. Hgb 43 percent; Er 2.3 mill.; leukocytes 5700; nothing special in the differential count; thrombocytes 69,000; SR 12mm/1 hr.; Meulengracht 1:10, Takata ++++; Stolte's mercuric chloride number 1.02 ml (+); thymol test 0.63 ext. (+); alkaline phosphatase 6 Fo. units; total serum protein 6.1 per cent, albumin 3.1 per cent, globulin 3.0 per cent; formolgel from serum—in 12 hrs. An X-ray examination of the gall bladder with radio-opaque contrast suggested liver cirrhosis, as no contrast medium was secreted to the bladder (14). An ascites puncture gave 2.25 litres of transudate typical of liver cirrhosis. After the puncture it could be observed that the liver and the spleen were distinctly larger than normal; even the spleen could be clearly palpated. The histological examination of a liver biopsy taken through a puncture suggested an atypical liver cirrhosis which had developed on the basis of a "Speicherung." The gastro-intestinal bleeding was attributed to the roentgenologically demonstrable enlarged veins in the lower part of the oesophagus, as no cause for the bleeding could be found elsewhere. The bleeding time was 5 min. and the coagulation time 5 min. 30 sec. The condition was diagnosed as: Chronic alcoholism. Liver cirrhosis. At the beginning the patient was treated, in addition to rest and general treatment, with transfusions and penicillin (the pat. suffered also from an infection in the respiratory tract) and all the time with a diet rich in protein and with the B-vitamines. His condition improved rapidly, ascites could no longer be observed, and improvement was noticed in the liver function tests based on protein changes. After having left the hospital the pat. abstained from alcohol for six months. He then began drinking again, when epistaxis started to occur, and also vomiting, with traces of blood. He was admitted again because of severe haematemesis and melaena, being slightly in shock. The blood pressure was 130/90 mm Hg after having been 160/90 mm Hg during the previous sojourn in the hospital. There was an anaemia of Hgb at 54 per cent and leukopenia, which had occurred also during the first stay: leukocytes 1,600. There was also thrombopenia: thromb. 51,000. The bleeding time was 1 min. 45 sec. and coagulation time 5 min. 30 sec. Ascites was not to be observed. The bilirubin values of blood were normal. Takata's test—(checked twice); Stolte's mercuric chloride number 1.35 ml. (+); thymol test 0.14 ext. (−); zinc sulphate test 0.35 ext. (−).Alkaline phosphatase 3 Fo. units. Non-protein nitrogen 28 mg. per cent. Total serum protein 6.3 per cent (albumin 3.5 per cent, globulin 2.4 per cent). An electrophoretic examination gave the following values: total serum protein 7.11 per cent, alb. 3.9 per cent, αglob. 0.42 per cent, β-glob. 0.81 per cent, γ-glob. 1.94 per cent. The formolgel test from serum was negative. After having left the hospital in an improved condition the pat. went on drinking as before. Approximately a year later he was again admitted to

the hospital because of haematemesis, temperature and for petechial bleedings in the skin of the extremities. The spleen could be palpated 5 cm. below the costal arch and the liver 3 cm. below the arch. Hgb 71 per cent, Er. 3.9 mill., Leuk. 2,300 (Eos. 2.5 per cent, Bas. 1 per cent, Neutr. staff cells 4 per cent, Neutr. segm. 59 per cent, Ly. 31 per cent, Mon. 2.5 per cent), thrombocytes 11,700. Bleeding time 2 min. 55 sec., coagulation time 9 min. The patient became more icteric during his stay in the hospital. 5 days later he vomited dark, coagulated blood. A fault in the mechanism of the coagulation of blood was suspected, and the coagel retraction time was determined, but it was found to be normal (8 min.), although the fibrinogen content of the blood was subnormal (fibrin 0.12 per cent). Meulengracht was 1:110, Takata's test +++, Stolte's mercuric chloride number 0.88 ml. (+), thymol test 0.42 ext. (+), zinc sulphate test 0.90 ext. (+), alkaline phosphatase 5 Fo. units. The total protein in serum was 5.51 per cent (alb. 1.55 per cent, glob. 3.96 per cent). The formolgel test from serum was + in 45 min. The non-protein nitrogen was 51 mg per cent. Hence, the liver lesion had again considerably aggravated. A few hours after the previous haematemesis there occurred again profuse haematemesis and malaena. The patient was given a transfusion of 800 ml., and he recovered from the shock. However, the haematemesis soon recurred, and in connection with it the patient died. Because the spleen did not undergo any reduction in size during the bleeding, a lienal thrombosis is considered unlikely as a cause of the haemorrhage. *Post mortem* (performed by V. Ritama, M.D.). Abnormal findings: The mucosa of the respiratory tract was very hyperaemic. Several varicose veins were observed in the lower part of the oesophagus, but not even the smallest site of bleeding was found. There was no fluid in the abdomen. The gut was partly adherent. The peritoneum was throughout more fibrotic than usual. The liver weighed 1430 g. Its entire surface was nodular and uneven. The section surface showed pronounced fibrosis and yellow tissue islands. Microscopically the liver was in a state of advanced cirrhosis. The gallbladder and the biliary ducts showed nothing unusual. The spleen weighed 1200 g. A partial thrombosis of the vena lienalis was observed. The stomach was large and contained great amounts of fluid blood, its mucosa was haemorrhagic in the corpus, but lighter in colour in the pyloric part. The mucosa of the duodenum was also haemorrhagically infiltrated all over. Haemorrhagic areas in the mucosa were observed also lower down in the ileum and in the colon. The other parts of the intestinal mucosa looked lighter than usual and apparently fibrotic. Microscopically the mucosa of the small intestine was formed by hyaline connective tissue. In the outer layers of the muscularis and particularly in the subserosa, there was an intense, diffuse inflammatory cellular infiltration. Great inflammatory vascular changes occurred in all layers of the wall. There were also perivascular granulocyte infiltrates and fibrinoid necrosis of the wall. Similar changes were observable also in samples taken from the wall of the stomach and of the large intestine.

Autopsy diagnosis: Cirrhosis hepatis t. Laennec. Thrombosis v. lienalis Hyperplasia lienis. Fibrosis intestini. Icterus. Petechiae cutis. Gastroenterocolitis partim haemorrhagical.Varices oesophagi.

Case 2. Male, 56 years, insurance agent. Case history No. 3423/51. In addition to the findings reported in Table I: Family history negative for liver and blood diseases. First time ill at the age of 46, when a duodenal ulcer was suspected. Before this, he had been a heavy drinker for several years. Although he stopped drinking because of the dyspeptic symptoms, his general condition did not improve. During the ensuing years he had 5 or 6 attacks of pneumonia. At the age of 56 he began to suffer from recurrent diarrhoea. The patient lost weight and the abdomen began to swell. On admission to the hospital he was slightly icteric, Meulengracht 1:10, with increased urobilinogen and urobilin in the urine. The gallbladder was not visible in the X-ray examination, thus suggesting liver cirrhosis. Three litres of transudate typical of liver cirrhosis were obtained through an ascites puncture. The smooth liver could be palpated, extending 3 cm below the costal arch. Table I shows the results of the liver function tests and the protein changes. As the total protein was 7.10 per cent, alb. 1.53, glob. 5.57 per cent, the diagnosis, Cirrhosis hepatis, was evident. The patient was treated, in addition to rest and general treatment, with a diet rich in proteins, "Merck's" methionine aureomycin and B-vitamine. The condition of the patient improved rapidly; jaundice, swelling of the legs and ascites disappeared. The patient felt well and went home against the advice of the physician. After 3 weeks at home haematemesis began to appear and the abdomen swelled again. After an absence of a month from the hospital he had a severe attack of haematemesis and was brought to the clinic in a deep shock. The blood pressure was 80/35 mm Hg after having been 130/90 mm Hg previously. Before a transfusion could be given, the patient died. *Post mortem* (performed by V. Ritama, M.D.). Abnormal findings: The mucosa of the respiratory tract was hyperaemic. The mucosa of the oesophagus was reddish and several erosions could be seen in its lower part. Only a few enlarged veins were to be found, and no bleeding from them could be observed. The abdominal cavity contained 1 - 2 litres of slightly haemorrhagic fluid. The peritoneum was diffusely red, and there were no adhesions. The weight of the liver was 1300 g. Its surface was throughout nodular, the nodes being of the size of a bean or smaller. Some of them were yellowish, others greenish yellow. The section surface showed, in addition to the nodular structure, many streaks of fibrous tissue. Microscopically the hepatic tissue represented nodular cirrhosis, with fatty degeneration and round cell infiltration in the connective tissue. The gallbladder and the biliary ducts had a normal appearance. The weight of the spleen was 600 g. The thickness of the wall of the stomach was usual. Its mucosa was entirely gelatinous and diffusely infiltrated with haemorrhage. The duodenum and the jejunum excepted, the mucosa of the entire gut down to the rectum was also haemorrhagically infiltrated. Microscopically the mucosa and the submucosa of the oesophagus were sclerotic and the veins were quite engorged and their walls also sclerotized. There was diffuse, fairly marked cellular infiltration in the gastric mucosa. There also occurred diffuse cellular proliferation in the intestinal mucosa, signs of degeneration in the muscularis and slight, superficial cellular infiltration in the fat.

Autopsy diagnosis: Cirrhosis hepatis t. Laennec. Hyperplasia lienis. Oesophagitis erosiva. Venectasiae mucosae oesophagi. Gastritis et enteritis haemorrhagica diffusa. Adhaeiso pleurae l. dx. Tub. inactiva apicis pulm. dx.

Case 3. Male, 65 years, agronomist. Case history No. 3741/51. The family healthy, the patient himself had been always healthy. He had lived a regular life. The capacity for work had been good until the day of admission, except for some slight fatigue which had appeared a few weeks before the admission. During this time the appetite had fallen off and the patient had suffered from increasing thirst. At home the patient experienced an acute attack of fainting and at the same time, dark, bloody stool was excreted. When the patient recovered consciousness he began vomiting blood. He did not feel any kind of pain either in the stomach or elsewhere. He was brought to the hospital where nothing pathological could be observed except for severe symptoms of shock. There was no jaundice, and the size of the liver appeared normal as did also that of the spleen. There was no tenderness in the abdomen, and no abnormal resistances could be felt. The haematemesis recurred before blood was obtained from transfusion centre, and the patient died. Table I shows the blood picture as taken before the death. *Post mortem* (performed by V. Ritama, M.D.). Abnormal findings: The entire mucosa of the respiratory tract shows a distinct, diffuse haemorrhagic inflammation. The detaching of the oesophagus was more difficult than usual and the surrounding tissue appeared fibrotic. The mucosa of the oesophagus was diffusely haemorrhagic and quite red. Similar mucosal changes continued in the stomach and intestine, down to the rectum. The gastric mucosa was thickened and coarse, appearing granular. The less red areas had a dirty colour and were slightly greenish. In the pyloric region both on the side of the stomach and of the duodenum, there were some small rimmed ulcerations. The wall of the stomach appeared slightly thickened. The serosa of the gut was congested with blood. Microscopically the muscularis propria and particularly the muscularis mucosae appeared degenerated. The submucosa was fibrotic and its fibres hyalinized. Obvious hyaline changes could be observed in the blood vessels. Hyalinization occurred also in the mucosa. The mucosa was rich in cells and there occurred some lymphoid nodes surrounded by hyaline tissue. The mucosa of the large gut was covered by an obviously bloody mass. The connective tissue in the superficial parts of the mucosa and particularly in the submucosa

was hyalinized. The weight of the liver was 1700 g. Its entire surface was nodular. Some few of the nodes were of the size of a cherry, but the majority were as small as peas. A corresponding structure was observed in the cut surface, its colour being unusually greyish yellow. The consistency of the liver was very solid. The wall of the gall bladder was slightly thickened, but otherwise it showed a normal appearance, as did the biliary ducts. The spleen weighed 190 g.
Autopsy diagnosis: Cirrhosis hepatis t. Laennec. Inflammatio haemmorhagica mucosae oesophagi, ventriculi, intestini et tr. respiratorii. Sanguis in ventriculi et intestini. Ulcera pylori. Arteriosclerosis. Nephropathia levis. Hyperplasia lienis.

Summary of the patients of group A as described above: In addition to the findings presented in Table I and discussed in connection with it, the clinical picture and the autopsy of the above three patients showed marked similarity. Death occurred as an immediate consequence of an acute, large gastro-intestinal haemorrhage, haematemesis and melaena. In all these patients, liver cirrhosis of Laennec's type was observed. The bleeding was found to be caused in every case by an extensive haemorrhage inflammation which might cover almost whole the gastro-intestinal mucosa. No local bleeding from the varicose veins of the gastro-intestinal tract could be observed. In the microscopical examination, the pathologist paid special attention to hyaline, necrotic inflammation and vascular changes in the gastro-intestinal mucosa, which changes, however, also extended into other layers in the wall. The mucosa of the respiratory tract was also affected.

DISCUSSION

As presented above diffuse haemorrhage from the gastro-intestinal mucosa in connection with liver cirrhosis is known as a cause of haematemesis and melaena may be more common than is generally thought. Similar bleeding was observed in three of 19 liver cirrhosis patients during the period of observation (in 3 of 6 cases examined post mortem). It must be also noted that only fatal bleedings came under observation, while the cause of less profuse haemorrhages remained unexplained. As regards the treatment of the patient, this would mean that e.g. local surgical therapeutic measures for the treatment of the varices in the lower part of the oesophagus would lose their significance in the control of haematemesis.

As for the etiology of the bleeding in these cases of liver cirrhosis, the possible rôle of several factors has to be considered. An *increased pressure in the portal circulation* is a factor pointed out by e.g. Alvarez (8) and Hanssen (9) as a cause of diffuse haemorrhage. When judging the rôle of this factor attention has to be paid to the fact that in females gastro-intestinal haemorrhage—and evidently also diffuse bleeding—occurs more rarely than in men in connection with liver cirrhosis. This sex predisposition is interpreted as depending on an anatomical difference in the anastomosing parts of the portal circulation. It may be figured that in woman the well developed venous plexus of the genitals and its connections with the veins of the plexus haemorrhoidalis facilitate the connection between the portal circulation and the general circulation. Thus, the increased pressure in the portal circulation in liver cirrhosis would perhaps be more easily alleviated in women than in men, and hence the former would not so easily be afflicted with gastro-intestinal haemorrhage.

A lesion of the capillaries is considered as having a central position among the immediate causes of diffuse haemorrhage. It has been demonstrated (15) that the capillary changes, e.g. spider telangiectasiae in the skin are a typical symptom of liver cirrhosis. Quite close to this stands the assumption that in cases of diffuse bleeding these capillary changes, which also otherwise occur in liver cirrhosis, are more severe and thus would cause a haemorrhage at such a site where the pressure is high, in this case in the portal circulation. This hypothesis is supported by the observation of marked changes particularly in the small vessels and capillaries of the mucosa of the gastro-intestinal tract (necrotizing inflammation, hyalinization, sclerosis) which was found in all those patients who died in diffuse gastro-intestinal haemorrhage. A general capillary lesion is supported by the appearance of petechial bleedings on the skin of one of these patients just before the fatal haemorrhage, for the coagulation mechanism had not been much disturbed in him.

Diffuse bleeding, as haemorrhagic diathesis in general, is also caused in liver cirrhosis patients by *disturbances which are known to occur in the mechanism of the coagulation of blood*. Hypoprothrombinaemia, low fibrinogen content and thrombopenia are typical symptoms of this disease.

Attention must be paid also to the finding mentioned above that among those three patients who died in a diffuse haemorrhage, two (no determination was made on the third) showed a very low alb./glob. ratio, 0.4 and 0.3. Perhaps also this factor has something to do with the haemorrhagic diathesis. It is known that it increases transudation from capillaries (16). This finding indicates at least that the degree of the hepatic lesion has been very severe in these cases, since the protein balance had been so gravely disturbed. The same conclusion is supported by the autopsy findings. It seems that diffuse bleeding is associated with the most severe lesions of the liver.

SUMMARY

Of 19 cases of liver cirrhosis of Laennec's type, three died of haematemesis and melaena. In these three patients, the post mortem examination revealed a diffuse haemorrhage from the wall of the gastro-intestinal tract. No bleeding had occurred from the varicose veins of the lower part of the oesophagus or from corresponding formations in other parts of the gastro-intestinal tract. The results of the study are considered to suggest that such a diffuse gastro-intestinal haemorrhage is more common than generally thought in connection with liver cirrhosis. It is indicated that this possibility must be seriously considered, e.g. when planning local therapeutic measures for varicose veins of the lower part of the oesophagus, for stopping haematemesis.

It is suggested that among the factors predisposing to diffuse bleeding, the great changes of the capillaries which could be observed in all the examined cases in the wall of the gastro-intestinal tract—and for whose presence there was also indication in other situations—have an important rôle, in addition to the well known disturbances in the mechanism of the coagulation of blood as associated with liver cirrhosis. In two of the examined patients a very low albumin/globulin ratio was discovered before the fatal haemorrhage. This

finding is regarded as indicating an unusually severe lesion of the liver, an assumption confirmed by the post mortem examination. It is also pointed out that all the patients with a diffuse haemorrhage were male. It is suggested that in the female, anastomoses between the portal circulation and the systemic circulation may be performed more easily in the area of the plexus haemorrhoidalis, and thus, an elevated portal pressure might more easily be alleviated.

REFERENCES

1. Chapman, C. B., Snell, A. M., and Rowntree, L. G.: Decompensated portal cirrhosis: Report of hundred and twelve cases. J. A. Med. Assoc., 97:237, (July) 1933.
2. Ratnoff, O. D. and Patek, A. J., Jr.: Natural history of Laennec's cirrhosis of liver; analysis of 386 cases. Medicine, 21:207, (Sept.) 1942.
3. Patek, A. J., Jr., Post, J., Ratnoff, O. D., Mankin, H. and Hillman, R. V.: Dietary treatment of cirrhosis of liver; results in 124 patients observed during 10 years period. J. Am. Med. Assoc., 138:543, (Oct.) 1948.
4. Evans, N. and Gray, P. A.: Laennec cirrhosis. Report of 217 cases. J. Am. Med. Assoc., 110:1159, (April) 1938.
5. Cates, H. B.: Surgical treatment for liver cirrhosis; prognosis subsequent to omentopexy. Arch, Int. Med., 71:183, (Feb.) 1943.
6. Douglas, B. E. and Snell, A. M.: Portal cirrhosis: Analysis of 444 cases with notes on modern methods of treatment. Gastroenterology, 15:407, (July) 1950.
7. Preble, R. B.: Conclusions based on sixty cases of fatal gastro-intestinal haemorrhage due to cirrhosis of the liver. Am. J. Med. Sci., 119:263, 1900.
8. Alvarez, W. C.: Nelson new Loose-Leaf Medicine, Part V. New York, Toronto, London, p. 513 F, 1937.
9. Hanssen, O.: Nordisk Laerebog i Intern Medicine Bd III, Gyldendalske boghandel, Kobenhavn, p. 284, 1948.
10. Henschen, C.: Die Bedeutung der Leber in der Chirurgie. Arch. klin. Chir., 173:488, 1932.
11. Rolleston, H. D. and Fenton, W. J.: On the cirrhotic liver. Birmingham Med. Rev., 40:193, 1896.
12. Lichtman, S. S.: Diseases of the liver, gallbladder and bile ducts. Second Ed., Lea & Febiger, Philadelphia, p. 596, 1949.
13. Järvinen, K. A. J.: X-ray confirmation of lues medicata. Duodecim Finn., 64:569, July 1948.
14. Järvinen, K. A. J. and Paltia, V.: Differential diagnosis of hepatitis and liver cirrhosis by means of cholecystography. Am. J. Digest. Dis. 19:244 (Aug.) 1952.
15. Franke, H.: Die Capillardichte bei hepatolienalen Erkrankungen und der Einfluss der Splenektomie. Z. klin. Med., 137:86, 1940.
16. Myers, W. K. and Keefer, C. S.: Relation of plasma proteins to ascites and edema in cirrhosis of liver. Arch. Int. Med., 55:349, (March) 1935.

GRANULOMA INGUINALE ASSOCIATED WITH HEPATO-SPLENOMEGALY AND DIFFUSE PULMONARY INFILTRATION

EUNICE LASCHE* AND EDWARD S. MCCABE,** Philadelphia, Pa.

GRANULOMA inguinale was first described as a clinical entity by Conyers and Daniels (1) in 1896. Subsequently many case reports from various parts of the world described its occurrence as a chronic disease of apparently low grade contagiousness whose manifestations consisted of granulomatous lesions affecting usually but not always the genitalia or sites in the neighborhood of the genitals. Fox (2) in a review of 150 cases in the United States found occurrence of the lesions in sites distant from the genitalia area in 9%. In 1905 Donovan (3) found the characteristic intracellular bodies in smears made from the lesions.

These "Donovan bodies" which are present within the cytoplasm of the large mononuclear cells have been shown to be gram negative plump rods with polar bodies. Recently Anderson (4) has cultured them on the yolk sac of the chick embryo; she subsequently classified them as bacteria and gave them the name of Donovania granulomatis (5). Immunologically, they are similar to Friedlander bacillus (6) and a polysaccharide has been identified that gives a positive intradermal test.

The following is the report of a case of granuloma inguinale complicated by hepatomegaly, splenomegaly and diffuse pulmonary infiltration of uncertain origin.

*Resident in Medicine.

**Associate in Medicine.

Department of Medicine, Temple University, School of Medicine and Philadelphia General Hospital.

Submitted May 13, 1952.

CASE REPORT

A 25 year old, colored female was admitted to the Venereal Disease Service of the Philadelphia General Hospital with the chief complaint of burning, soreness and ulceration in the anal region. Approximately two and a half weeks previous to admission the patient noted pain in the anal area aggravated by bowel movements and ulceration in this area followed in several days, accompanied by constipation. She stated she had felt "feverish" on several occasions during the past one or two months and had noted some night sweats and anorexia. One month previous to admission she had a "cold" lasting one week. Systemic review was otherwise negative except for dysuria of two weeks duration. Past medical history consisted of typhoid fever ten years ago and one normal delivery four years ago. She was a native of South Carolina and her occupation was that of a coat trimmer. On physical examination the patient was a well developed, well nourished, young colored woman. Her temperature ranged between 98° to 100° the first two weeks of hospitalization and thereafter was normal. Blood pressure was normal. The right tonsillar area was markedly inflamed, while white mucoid patches were present on the left tonsil. Lymphadenopathy consisted of an enlarged right posterior cervical node and bilateral soft, mobile, tender inguinal nodes. The heart was normal. A few rhonchi were heard in the left base on auscultation of the lungs. The liver was enlarged with the lower border palpated at a point halfway to the um-