THE LIFE HISTORY OF PATIENTS WITH CIRRHOSIS OF THE LIVER AND BLEEDING ESOPHAGEAL VARICES*

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CREDIT FOR THE renewed interest in the surgical treatment of patients with bleeding esophageal varices unquestionably belongs to Drs. Whipple and Blakemore. Since their reports in 1945,[3, 27] the American literature has contained numerous papers,† both experimental and clinical, describing various surgical attacks on the cirrhotic patient with an upper gastro-intestinal hemorrhage. Most of the reports are enthusiastic and give one the impression that, although more time is necessary for a final evaluation of the end results, the present data indicate that there are several operations which influence favorably the natural course of this disease.[1, 4, 16, 19, 21, 25] Of all these procedures, the venous shunts between branches of the portal and caval systems are described as the most rational and satisfactory treatment available at the present time.[5, 6, 14, 15]

Before one is able to conclude that a given surgical procedure is beneficial, it is essential to know what will happen to a comparable group of patients who are not operated upon. The majority of the authors describing the results of their operations refer at some time to one of the following considerations:

1. A study of the life history of patients with Laennec's cirrhosis indicated that at the end of one year after their first hemorrhage from varices, 70 per cent were dead (Ratnoff and Patek[20]).

2. The unpublished report of Shull revealed that only 37 per cent of the cirrhotic patients who bled were alive one year after the diagnosis of esophageal varices was made. In his group of 108 patients, 83 per cent died from all causes, but 45 per cent of those who died succumbed to massive gastro-intestinal hemorrhage (Linton[15]).

3. At the Mayo Clinic, nearly one-half of the traced cirrhotic patients with hematemesis secondary to ruptured varices died within the first year, and nearly four-fifths died in less than seven years (Douglas and Snell[10]).

4. Because many die from their bleeding varices, the implication is frequently made that all patients with esophageal varices are doomed some day to bleed to death.[14]

Many surgeons use one or more of these statements as the justification for their operative attacks, and as a comparison for their end results.

There are several reasons why these observations may not accurately reflect the prognosis of the cirrhotic patient with bleeding esophageal varices who is admitted to our wards today. The original 386 cases of Ratnoff and Patek[20] (106 with hematemesis) comprised patients studied before 1938, their more recent paper of 124 cases (42 with hematemesis) covered the years 1938 to 1948; the study of Shull at the Massachusetts General Hospital of 108 cirrhotics who bled was derived from the years 1934 to

* Submitted for publication June, 1954.

† The *Index Medicus* lists 87 references during the five-year period from January, 1949, through December, 1953.

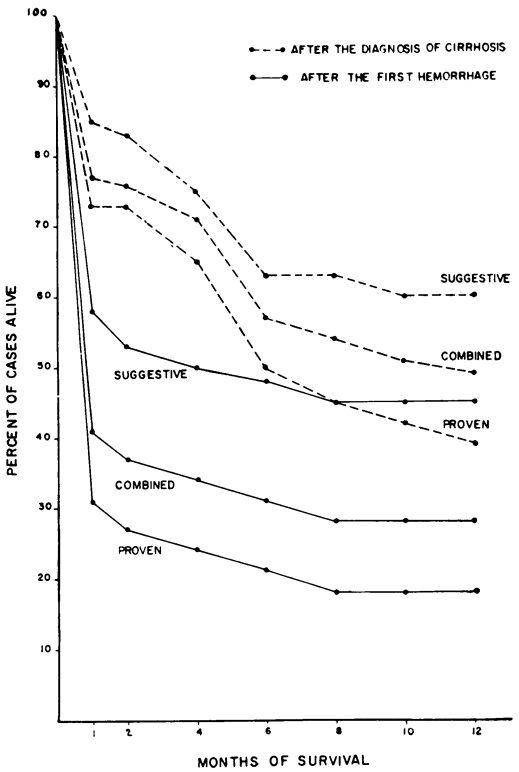

FIG. 1. The survival of patients after the diagnosis of cirrhosis has been made and after the first hemorrhage has been sustained.

1945; and, finally, the report of Douglas and Snell[10] of 444 cases (71 with hematemesis) was obtained from patients seen at the Mayo Clinic between 1940 and 1945. It is readily apparent that many of the cases in these control series were seen at times when blood transfusions were not administered liberally, when the advantages of the modern dietary regimens for liver disease were not routinely utilized, when many of the present antibiotics were not available, and when esophageal balloon tamponade was not employed. If attention is paid to the statement of Snell,[24] that hepatic coma, gastrointestinal hemorrhage and intercurrent infection are the principal predisposing causes of death in cirrhosis, then it seems likely that the life history of our cirrhotic population today should be different from that reported in the earlier studies.

The validity of the assumption that all patients with esophageal varices will some day bleed to death is open to question. Linton has made the statement that, "in a few instances patients have been followed in our clinic for a number of years, after varices have been demonstrated, without evidence of bleeding from them." Many cirrhotics who have been autopsied in our department of pathology (Mallory Institute of Pathology) and found to have esophageal varices, not only did not die of hemorrhage, but also never bled during the course of their disease. To our knowledge, there is no evidence at present that a patient with varices who has never bled has a prognosis as poor as the one who has at some time ruptured his varix and sustained a significant hemorrhage. While this may later be shown to be true, it seems rather radical at present to expose these patients to the risks of a portacaval shunt, as some surgeons are doing today.[14]

Because we felt the need for a more detailed and relatively recent control series, we were stimulated to begin this study of the cirrhotic patient with bleeding esophageal varices who did not receive surgical therapy, but who was exposed to most of the advantages of modern medical management. Only after this and other similar studies will we be in a position to assess accurately the value of any surgical procedure for this disease.

CLINICAL MATERIAL

While patients with cirrhosis of the liver may sustain a fatal upper gastro-intestinal hemorrhage from many lesions of the esophagus, stomach, or duodenum, three-fourths of these patients autopsied at the Mallory Institute of Pathology were found to have esophageal varices as the only lesion responsible for their hemorrhage.[9] During the years 1944 through March, 1954, we were able to collect the records of 112 patients admitted to the Boston City Hospital with cirrhosis of the liver, who had bled on 176

occasions, the source of which seemed to suggest esophageal varices. Thirty-four additional cases were excluded because of one or more of the following reasons:

1. A cause other than or in addition to the varices was found to explain the hemorrhage either by roentgenogram, esophagoscopy or postmortem examination. This group included cases of peptic ulcer, hiatus hernia, gastritis and duodenitis.

2. The bleeding episode was questionable, and not significant enough to send the patient to his doctor or to the hospital.

3. The diagnosis of cirrhosis was not definite.

4. An operation was performed at the time of the initial bleeding episode, which usually resulted in the patient's death.

Of the 112 patients studied, ten were cases whose course might have been altered by the operation to which they were subjected after their initial hemorrhage had ceased. Therefore, they were included only as patients who had survived hemorrhage. The remaining 102 cases received no surgical treatment and constitute our control series.* A control group which does not include all patients subjected to surgery might be considered one which omits many of the more favorable cases. This is not entirely true here. During the past ten years at the Boston City Hospital, there were only a small number of patients with good liver reserve subjected to either a portacaval shunt or an esophageal resection, and almost as many patients with advanced decompensation of the liver who had some other operative procedure. Thus, it is a fortunate circumstance that the cases excluded are divided nearly equally as regards the status of their livers.

TABLE I. *Comparison of Prothrombin Times and Blood Findings Suggesting Hypersplenism in Cirrhotics Who Have and Who Have Not Bled.*

	Bleeders		Non-bleeders	
	Cases	Percent	Cases	Percent
Prothrombin Time				
Near normal	50	77	45	90
Markedly prolonged	15	23	5	10
White Blood Cell Count				
Over 5,000	88	89	46	92
Below 5,000	11	11	4	8
Abnormal differential	0	0	0	0
Platelets				
Normal	85	91	45	90
Decreased	8	9	5	10

The diagnosis of cirrhosis was made on the basis of history, physical findings, and laboratory data indicating damage to the liver in 59 cases, and by needle biopsy of the liver or postmortem examination in 43 cases. There was no doubt in our minds that these patients had cirrhosis and a gastrointestinal hemorrhage, but we found it necessary to divide them into two groups, relative to the source of the hemorrhage. The first group, comprising 62 patients, we have called *proven* (group P), indicating that the source of their bleeding was determined to be their esophageal varices by either roentgenogram, esophagoscopy, control by esophageal balloon tamponade, or postmortem confirmation. The second group, designated as *suggestive but not proven* (hereafter referred to as "group S"), comprised 40 cases in which the clinical diagnosis was ruptured esophageal varices; there was no ulcer history, and the gastro-intestinal series was negative or reported as questionable for varices.

* This statement needs some modification. There were three patients in this group who were operated upon more than a year after their initial hemorrhage. Since other writers as well as ourselves have used this period of one year as the critical time for survival,[10, 11, 18] beyond which the prognosis is more favorable, we felt justified in including them. Whether their operation altered the natural course of their disease beyond this time is immaterial to our discussion. There was also one patient who was bleeding to death from her varices, with a Sengstaken-Blakemore tube in place, when the desperate surgery was undertaken. Unquestionably, this patient died from her disease and not from the surgery.

TABLE II. *Comparison of Clinical and Laboratory Findings in the "Proven" and "Strongly Suggestive" Groups of Cirrhotic Patients with an Upper Gastro-intestinal Hemorrhage.**

Clinical Data	P %	S %	C %	Laboratory Data	P %	S %	C %
Cause of Death:				Bromsulphathalein Retention:			
Coma	59	43	54	0–35%	40	57	45
Exsanguination	41	57	46	Over 35%	60	43	55
Severity of the Hemorrhage:				Cephalin Flocculation:			
Mild	13	27	19	0, 1+, 2+	35	45	39
Significant	29	23	26	3+, 4+	65	55	61
Severe	58	50	55	Total Protein or Serum Albumin:			
Ascites:				Normal	62	79	69
Absent	30	52	38	Decreased	38	21	31
Present	70	48	62	Prothrombin Time:			
Jaundice:				Near normal	63	96	77
Absent	63	55	60	Prolonged	37	4	23
Present	37	45	40				
Hepatomegaly:				P—"Proven" Group—62 Cases			
Absent	32	23	28	S—"Strongly Suggestive" Group—40 Cases			
Present	68	77	72	C—Combined (Control) Group—102 Cases			

*See text for more detailed explanation of these groupings.

This group of *suggestive but not proven* was included for several reasons. First, because the evidence seemed strongly in favor of varices as the cause of the hemorrhage; secondly, because it is not an uncommon experience to have a cirrhotic with a significant bleeding episode in whom varices can not be definitely demonstrated; and thirdly, so that we could compare the course of these patients with the proven group.

There is another possible reservation which the critical reader might introduce at this point. Admittedly, these patients have cirrhosis and the cause of any significant gastro-intestinal hemorrhage is usually attributed to esophageal varices when other lesions in the esophagus, stomach, and duodenum have been ruled out.[20] However, what about the abnormalities in the hemostatic processes which are known to be present in these patients? These include decreased platelets, prolonged prothrombin time, increased capillary fragility, and other still not completely understood defects in the clotting mechanism.[28] We have attempted to clarify part of this matter in regard to the thrombocytopenia and hypothrombinemia by comparing the data in our bleeders with 50 other proven cirrhotics, who died without having bled. Table I indicates that there are minimal differences between the two groups in the depression of the white cells, abnormal differential smears, or platelets. The prothrombin time differences are not very marked and when subjected to the chi square analysis, reveals that the likelihood of the differences being due to chance occurrence is 11.4 per cent.

We have, therefore, a group of 102 known cirrhotics who have had at least one gastro-intestinal hemorrhage, 62 of which have been proven to be due to esophageal varices and 40 of which are very suggestively due to the same cause. Before we go on to compare these two groups and study the characteristics of all our bleeders, it seems advisable to define the terminology which we plan to use.

DEFINITION OF TERMS

Throughout the remainder of this paper certain clinical categorization and laboratory findings will be discussed. These may be described as follows:

1. *Survival after diagnosis* refers to the time that the patient lives after the diagnosis of cirrhosis of the liver has been made by his family physician, or during his hospitalization period.

2. *Survival after the first hemorrhage* is probably self-explanatory, with the addi-

tional notation that all hemorrhages refer to either episodes of hematemesis or melena or both, which were of sufficient concern to result in the patient being hospitalized.

3. *Cause of death* is described as due either to coma or to exsanguination in all but one of the 88 patients who died. The latter term describes the patient who dies in shock a very short time after entry despite vigorous efforts at blood replacement and, when possible, esophageal balloon tamponade. The patient whose blood volume and circulation can be restored, but who shortly thereafter loses consciousness and shows evidence of further hepatic decompensation, is recorded as dying of hepatic coma.

4. *Severity of the hemorrhage* is considered as *mild*, when the hematemesis or melena are simply recognized, as *significant* when shock is either impending or present and transfusions up to 2,000 ml. of blood are required, and as *severe* when the shock state is marked and more than 2,000 ml. of blood is given. Recognizedly, these subdivisions are somewhat arbitrary. Nevertheless, it is our belief that they serve as a better clinical yardstick to measure the serious nature of a hemorrhage than do the determinations of hematocrit, hemoglobin or red blood cells. Thus, some of our patients who had exsanguinating hemorrhages were found to have an hematocrit over 35 and a red cell count over four million. Perhaps the one laboratory test which would offer more accuracy would be the blood volume determination, but this has not been done. From the clinical viewpoint these subdivisions seem to characterize three different groups of bleeding cirrhotic patients, whom we meet in our hospital.

5. *Ascites, jaundice,* and *hepatomegaly* are recorded as absent and present, the former including those cases where any doubt exists.

6. *Bromsulphathalein* (phenoltetrabromphthalein sodium sulfonate) *retention* is divided into the values from 0 to 35 per cent and over 35 per cent throughout most of the discussion. This represents the 45-minute readings, when 5 mg. of dye per kilogram of body weight is given.[28]

7. *Cephalin flocculation* data are combined into the more favorable group of 0, 1+, or 2+, and the more ominous of 3+ and 4+.

8. *Total protein or serum albumin* are considered as *normal* or *decreased.* When the A/G ratio has been obtained, then any albumin value under 3 Gm. per cent places the patient in the *decreased* category. If only the total protein has been determined, a value under 5 Gm. per cent (our low normal reading) places the patient in the same group. Admittedly there is a drawback in not having all albumin determinations, for some patients with serum protein levels over five may have values such as 2.5/3.5. Thus we are probably including some patients with poor albumin values in our *normal* group.

9. *Prothrombin time* is separated into *near normal* and *prolonged* divisions. Previous writers[5, 16] have considered a value of four seconds longer than the control as indicating a serious prolongation of the prothrombin time. We have accepted this. Where our data has been recorded in per cent values, several curves of prothrombin concentration suggested that any value below 40 per cent was closely comparable to this degree of hypoprothrombinemia. Thus any patient with a prothrombin time more than four seconds above the control, or a concentration below 40 per cent of normal, is considered in the *prolonged* group, while all others are recorded as *near normal.*

CLINICAL DATA

Our first comparison is concerned with the group of patients we have labeled *proven* (Group P), in that only varices were found as the source of their hemorrhage, and the *strongly suggestive* cases (Group S) in whom the clinical picture was very similar but the varices were not demonstrable. The

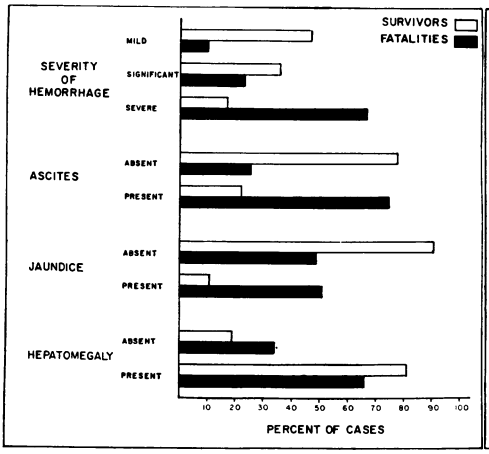

FIG. 2

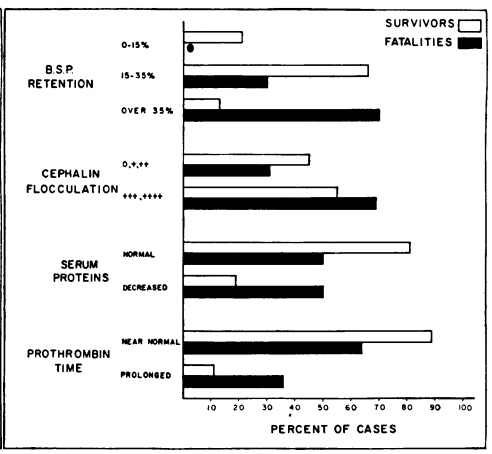

FIG. 3

FIG. 2. A demonstration of the differences in the physical findings among those patients who survive and those who succumb to their initial hemorrhage from varices.

FIG. 3. A demonstration of the differences in several hepatic function tests among those patients who survive and those who succumb to their initial hemorrhage from varices.

62 patients in Group P sustained 88 hemorrhages (averaging 1.4 per patient), and 66 per cent of these bleeding episodes led to death; while the 40 patients in Group S experienced 60 hemorrhages (1.5 per patient), of which 43 per cent resulted in death. This somewhat more favorable finding in Group S is also observed elsewhere. Figure 1 illustrates the survival times in months both after the diagnosis of cirrhosis has been made and after the first hemorrhage has occurred. The slopes are closely parallel between the proven and suggestive groups except that the prognosis is continually more favorable in the latter. The steepness of the slopes during the first month reflects two facts; namely, (a) that the diagnosis is first made in some patients just before death, and (b) that the first hemorrhage takes the lives of many patients (42 per cent of Group S, 69 per cent of Group P, and 59 per cent of the combined cases). One year after the diagnosis of cirrhosis had been made, 49 per cent of our patients were alive, while at a comparable time after their first hemorrhage only 28 per cent were still living.

To continue our comparison between the proven and suggestive cases, Table II has been constructed. The slightly higher incidence of exsanguination as a cause of death in Group S (57 per cent compared to 41 per cent) probably reflects the fact that the suggestive cases, by definition, contained those who exsanguinated before the source of hemorrhage could be determined, and upon whom postmortem examination was not permitted. The severity of the hemorrhages in the two groups were fairly similar except for a smaller number of mild hemorrhages in Group P (13 per cent as against 27 per cent). Turning to the physical findings, it may be noted that more patients in Group S were free of ascites, but that jaundice and hepatomegaly were not significantly different. The bromsulphathalein retention, cephalin flocculation, serum proteins, and prothrombin times all point toward slightly more favorable values for Group S. Thus, it becomes apparent that the suggestive cases differ from the proven ones in that the former live a little longer after the diagnosis of cirrhosis is made, have a somewhat higher percentage of mild hemorrhages, a greater number survive their first hemorrhage, ascites is not quite as prevalent, and the liver functions indicate slightly less damage.

Do these findings mean that bleeding cirrhotic patients in whom the varices can not be definitely identified, but in whom other causes have been ruled out, are not bleeding from varices? We feel strongly that the answer to this question is *no*. An analysis of the 40 cases placed in the *suggestive* rather than the *proven* group may help to clarify our answer. These patients were either too sick to accomplish a satisfactory work-up, or were discharged from the hospital before all their studies were completed. In the former category, there were 16 patients who exsanguinated within a day or two and 12 patients who died in coma usually in a five- to six-day period. Nine roentgenologic examinations were carried out in these 28 desperately ill patients, four of which showed some suspicion of varices in the esophagus. Similar cases in which postmortem examination was permitted could obviously be placed in the *proven* group, but by definition these 28 could only be considered as *strongly suggestive*. Twelve patients were discharged without having had the source of their hemorrhage located. Only eight of these patients had roentgenologic examinations performed, and none were esophagoscoped. Most of the 12 patients therefore represent either incompleteness in the work-up, or failure of the diagnostic method employed to identify their varices. Perhaps if esophagoscopy and repeat gastro-intestinal series had been done in all, we might have been able to put many of these 12 in the *proven* group.[7]

TABLE III. *Comparison Between Patients Dying of Exsanguination and Those Dying of Hepatic Coma.*

	Cause of Death		
	Exsanguination %	Coma %	All Deaths %
Duration of life more than one year after the diagnosis of cirrhosis...	47	39	43
Ascites present.....	60	83	72
Jaundice present.....	43	49	45
Hepatomegaly present.....	73	66	69
Bromsulphathalein retention greater than 35%.....	56	68	65
Cephalin flocculation 3 + to 4 +..	77	56	64
Serum proteins below 5 grams percent or albumin below 3 grams percent.....	38	34	35
Prothrombin time more than 4 seconds longer than normal.....	14	39	30

To summarize, the cases in which we were not able to prove that the varices were the source of the hemorrhage consisted of 28 seriously ill patients who died within a few days of entry to the hospital, and 12 patients upon whom our work-up was incomplete. It is important to understand that in these 28 patients the prognosis and hepatic functions were as poor as those in Group P, while in the 12 the outlook was better. Thus, the somewhat more favorable findings in the over-all picture of Group S. Objections may be raised by some readers to the inclusion of these 12 cases as cirrhotics who have bled from varices. In eight, peptic ulcer and malignancy were definitely ruled out by roentgenologic examination, and in the four, nothing in their history suggested ulcer. The occasional difficulty in identifying varices by all of our clinical diagnostic methods is recognized by many physicians who meet these patients.[17, 20] Under these circumstances, it seems unreasonable to postulate some obscure cause for the hemorrhage in a proven cirrhotic simply because the varices were not identified. It is our feeling that a greater error would be introduced by omitting the 12 patients than might exist by including them. For these reasons, we have combined the 40 suggestive cases with the 62 proven ones in order to study the life history of 102 cirrhotic patients with bleeding esophageal varices.

The seriousness of the bleeding is reemphasized by our data, even though we have readily available blood for transfusion, and the recent use of esophageal balloon tamponade. Of these 102 patients admitted to the Boston City Hospital during the stated ten-year period, 88 died, and in these a hemorrhage was the precipitating or causative

TABLE IV. *Comparison of the Clinical and Laboratory Findings in Cirrhotic Patients Bleeding from Esophageal Varices According to the Severity of the Hemorrhage.*

	All Deaths %	Severity of Hemorrhage			Severe Hemorrhages	
		Mild %	Significant %	Severe %	Died of: Coma %	Died of: Exsanguination %
Duration of life more than one year after the diagnosis of cirrhosis	43	71	33	39	24	46
Ascites present	72	92	89	59	59	59
Jaundice present	45	46	44	46	53	44
Hepatomegaly present	69	62	61	75	76	74
Bromsulphathalein retention greater than 35%	65	75	70	58	55	62
Cephalin flocculation 3+ to 4+	64	46	50	76	75	76
Serum proteins below 5 grams percent or albumin below 3 grams percent	35	31	27	43	50	40
Prothrombin time more than 4 seconds longer than normal	30	25	43	27	50	15

factor in 84. Forty-seven per cent of the patients lived more than one year after the diagnosis of cirrhosis was made, but only 28 per cent lived this period of time after their first hemorrhage. While it is frightening to realize that 60 per cent of our bleeding cirrhotics will die of their first hemorrhage, it is also important to note that of the 40 per cent surviving the initial hemorrhage, only one-third will die during the subsequent year, and two-thirds will be alive longer than one year. Coma and exsanguination were almost equally divided as the cause of death. The hemorrhage was severe (indicating the presence of shock and the need for transfusion of more than 2,000 ml. of blood) in over half the cases. Ascites was present in 62 per cent, jaundice in 40 per cent, and hepatomegaly in 72 per cent. Marked impairment of bromsulphathalein excretion and cephalin flocculation was indicated in well over one-half the cases, while serum protein abnormalities were present in at least one-third, and prothrombin content severely deficient in almost one-fourth of the cases.

At this time, a number of questions arise, the answers to which might prove helpful in understanding the course of this disease:

(a) Is there any difference between the patient who dies of hepatic coma and the one who exsanguinates?

(b) How important is the severity of the hemorrhage at the time of the patient's death?

(c) What differentiates, if anything, the patient who survives his *initial hemorrhage* from the one who succumbs?

(d) Are patients with non-fatal hemorrhages different from those with fatal hemorrhages?

Attempts to clarify these matters are made in Tables III and IV and in Figure 2.

In comparing those who died in coma with those who exsanguinated, it might have been expected that the latter would have less evidence of serious hepatic disease. However, as seen in Table III, 47 per cent of the exsanguinated group have had cirrhosis over one year as contrasted to 39 per cent of the coma group. Thus, the hemorrhage can not be considered an accident occurring early in the course of the disease. On the other hand, it is true that significantly more patients in the coma group have ascites, 83 per cent as against 60 per cent, but jaundice and hepatomegaly are present in close proportions. The hepatic functions indicate that severe BSP retention (over 35 per cent) and markedly prolonged prothrombin time (more than four seconds above normal) are less among those who exsanguinate, but the cephalin flocculation and serum protein values are somewhat

worse in this same group. It is not readily apparent from these data that the patients who have an exsanguinating hemorrhage from their varices have less advanced cirrhosis than those who die in hepatic coma.

Table IV separates the 88 patients who died into the three groups characterizing the severity of their hemorrhage. The reason for and manner of this separation have been described previously (definition of terms section). It might have been anticipated that the patents with mild and significant hemorrhages, most of whom die in coma, would show clinical and laboratory evidence of more marked decompensation of the liver. But again, the findings are not very striking. Incidentally, it is interesting to note that there is no correlation between the prolongation of the prothrombin time and the severity of the hemorrhage. The suggestion has been made by others[18] that in the patients who have a severe hemorrhage there are some who die of their hepatic disease and others in whom the bleeding episode is an accident leading to their death. In the 56 patients with a severe hemorrhage, 17 died in coma after bleeding had ceased and 39 died of exsanguination. This separation has been included in Table IV, and again many similarities are noted. All the evidence seems to point to the fact that there are not very striking differences with respect to disease of the liver between the patient who dies in hepatic coma and the one who exsanguinates, nor is the severity of the hemorrhage related to a more or less advanced state of liver decompensation at the end of their lives. This is in marked contrast to the findings among patients who survive their hemorrhages!

As mentioned earlier, 42 patients survived their initial hemorrhage, 32 of whom are part of the study of the surgically untreated cases and ten of whom could not be included in our control series because they had some operative procedure within a year after their initial hemorrhage which might have altered the course of their disease. However, these are all patients with cirrhosis of the liver who withstood an episode of bleeding from their varices. Those who survive have their hemorrhages recorded (Fig. 2) as mild in about one-half, significant in one-third, and severe in one-sixth, in contrast to the patients who die where it may be seen that only one-tenth have a mild hemorrhage and two-thirds a severe one. Ascites and jaundice were absent in over three-fourths of those who live, while in the others ascites was present in three-fourths and jaundice present in one-half. The significance of hepatomegaly is obscure. An enlarged liver does not indicate either a poorer or a more favorable prognosis. When the laboratory data are examined (Fig. 3) only 13 per cent of the patients who lived had a bromsulphathalein retention over 35 per cent in 45 minutes in contrast to those who died, 70 per cent of whom had this severe degree of retention. The differences in cephalin flocculation are also significant, but not so marked. Of the survivors, only 19 per cent had serum proteins under 5 Gm. per cent, and 11 per cent a prothrombin time greater than four seconds above normal, while in the fatal group 50 per cent had unsatisfactory serum proteins, and 36 per cent a serious prolongation of their prothrombin time. These differences strongly suggest that the patient who tolerates his initial hemorrhage does so because the bleeding is frequently milder and his hepatic compensation better than the patient who succumbs.

Are these facts applicable only to the first hemorrhage, or is a similar pattern found in respect to any hemorrhage? The data in Table V indicates that these same findings of a milder hemorrhage and a better state of liver compensation differentiate the patients who live from the ones who die subsequent to any episode of bleeding from their varices.

DISCUSSION

Numerous problems are encountered in studying the natural life history of a patient

with cirrhosis of the liver who has had an upper gastro-intestinal hemorrhage. Three questions that immediately present themselves may be listed as follows:

(1) How accurate is the diagnosis of cirrhosis?
(2) Are the varices the source of the hemorrhage?
(3) Is the prognosis changing by present-day management?

Accuracy of the diagnosis. The first study of Ratnoff and Patek[20] in 1942, comprised a review of 865 charts of several of the larger New York hospitals from which 386 cases were selected because they contained enough data to substantiate the diagnosis. One hundred seventy-eight of these were proven to be cirrhosis on microscopic examination, and 208 were presumptive, but based on fairly good clinical evidence. Their second paper,[18] in 1948, comprised 124 patients treated over a ten-year period who were hospitalized in some stage of hepatic failure. Of these the diagnosis was made microscopically in 59 per cent. While the first paper is entitled, *The Natural Life History of Laennec's Cirrhosis,* it is not quite clear how they excluded the postnecrotic and biliary types with microscopic proof in only 46 per cent of their cases. The second paper does state that in it they have made no differentiation between the postnecrotic and Laennec varieties. The report of Shull (quoted by Linton[15]) is composed of 108 cirrhotics with a gastro-intestinal hemorrhage who were admitted to the Massachusetts General Hospital during the years 1934 to 1945. In the majority of these cases the diagnosis of cirrhosis was made on clinical grounds. They also did not separate their cirrhotics into groups. Douglas and Snell[10] studied 1,165 cases seen at the Mayo Clinic during the years 1940 through 1944, of which 444 were considered to be uncomplicated Laennec's cirrhosis on strict diagnostic criteria. Since only 32.9 per cent were confirmed by biopsy, it seems unlikely that they differentiated too carefully between the portal, postnecrotic, and biliary types. Henrikson published data on 162 cases from the Minneapolis General and the University of Minnesota Hospitals, of which 84 were proved and 78 probable. Thus it may be seen that in several good control studies[10, 12, 13, 15, 18, 20] the diagnosis of cirrhosis is made on microscopic grounds in almost one-half of the cases (Table VI). There is little doubt as to the presence of cirrhosis in the others which were diagnosed from the clinical and laboratory findings. To be sure, a microscopic examination of every liver would be ideal. This would insure complete accuracy and also allow for the differentiation between the Laennec's, the postnecrotic and the biliary varieties. But often this is not possible nor, in our opinion, is it necessary for this type of study. The patient with a suggestive history of cirrhosis, who has physical findings pointing to decompensation of the liver (ascites, jaundice, hepatomegaly or splenomegaly), whose hepatic functions indicate damage, and who, in addition, experiences an intestinal hemorrhage, has cirrhosis of the liver until proven otherwise. The accuracy of our clinical impression under these circumstances should be quite high. The need for differentiating between

TABLE V. *Comparison of Clinical and Laboratory Data of Cirrhotic Patients Who Withstand or Succumb to a Hemorrhage from Their Esophageal Varices.*

Clinical Data	Survivors %	Fatalities %
Severity of the hemorrhage:		
Mild	42	12
Significant	42	21
Severe	16	67
Ascites present	22	73
Jaundice present	16	48
Hepatomegaly present	85	70
Liver Function Tests		
B. S. P. retention over 35%	19	64
Cephalin flocculation 3 + to 4 +	57	6
Serum proteins under 5 grams percent	20	38
Prothrombin time more than 4 seconds above normal	9	31

TABLE VI. *Evidence for the Diagnosis of Cirrhosis and of Varices as the Source of the Hemorrhage in Several Control Studies.*

Authors	Hospitals	Years of Study	All Cases of Cirrhosis			Cases with Hemorrhage Due to Varices		
			Nos.	Clinical %	Microscopic %	Nos.	Clinical %	Laboratory* %
Ratnoff and Patek	Several New York Hospitals	1916–1938	386	54	46	106	not stated	
Patek, et al.	Presbyterian Hospital	1938–1948	124	41	59	42	52	48
Shull	Mass. Gen. Hospital	1934–1945	108	majority	—	108	—	majority
Linton	Mass. Gen. Hospital	1946–1950	99	—	majority	99	33	67
Henrikson	U. of Minn. and Minn. Gen. Hospital	1916–1932	162	48	52	38	not stated	
Douglas and Snell	Mayo Clinic	1940–1944	444	67	33	71	30	70
Higgins	San Francisco City & County Hospitals	1919–1947	—	not stated		115	27	73
Nachlas, et al.	Boston City Hospital	1944–1954	102	58	42	102	39	61

*The laboratory findings which definitely identified the varices were either roentgenologic demonstration, esophagoscopic visualization, control by balloon tamponade or postmortem examination.

the varieties of chronic disease of the liver seems unnecessary, because of the fact that each group develops hepatic insufficiency and some degree of portal hypertension, one of which usually leads to death.

Varices as the source of the hemorrhage. Given a patient with proven cirrhosis who has a significant gastro-intestinal hemorrhage, the second problem that arises is the source of the bleeding. When malignancy, peptic ulcer, gastritis, and hiatus hernia have been ruled out and varices are demonstrated, it seems fairly safe to incriminate the varices. However, when these other causes have been eliminated, but the varices cannot be identified, are we accurate in blaming them? In the control studies referred to,[10, 13, 15, 18] the varices were proven to be the source of the hemorrhage in two-thirds of the cases (Table VI). This degree of accuracy is probably the highest that can be obtained inasmuch as over 50 per cent of the cases come to the hospital desperately ill and die within a short time.[20] Nevertheless, there is little doubt that the vast majority of these patients represent variceal bleeders. In the cases where surgical therapy is undertaken and the results reported, the varices should be identified as the source of the hemorrhage in every case.

Effect of recent management on the prognosis. The patient with cirrhosis of the liver has a better prognosis today than he had ten to 15 years ago. Until 1942, numerous papers emphasized the major role which infection played.[11, 12, 20] Pneumonia and peritonitis were found to be responsible for death in 16 to 37 per cent.[20] The importance of antibiotics is emphasized by the report of Douglas and Snell[10] in 1950, at which time they found only 4.7 per cent of their deaths due to pneumonia, while the previous figure from the same clinic in 1942 was 26 per cent. Hepatic insufficiency is also apparently being delayed by better dietary and vitamin regimens. The first study of Ratnoff and Patek[20] (1942) indicated that only 32 per cent of their cirrhotic patients were alive one year after the onset of ascites. However, in their treated group,[18] reported in 1948, 65 per cent of this same group were alive at the end of the first year. As antibiotics reduced the deaths from infection and good dietary management improved their hepatic reserve, one might anticipate that the bleeders would also be aided by the liberal use of blood transfusions and by esophageal balloon tamponade (described by Rowntree, *et al.*, 1947[22]). Unfortunately, this does not seem to be the case. Even though we have

not employed tamponade in many cases of this series, we have had a number of recent experiences which are very discouraging. In 14 patients upon whom esophageal balloon tamponade was attempted, results were reported as fair to satisfactory in ten. Nevertheless, all of these individuals subsequently died of coma.

There are at least three reasons why transfusions and tamponade have not significantly altered the prognosis of the bleeder. In the first place, some of the patients exsanguinate very rapidly. Secondly, many patients with good hepatic reserve survive their hemorrhage without medical assistance. And finally, a significant number of patients only have hemorrhages of moderate severity which either stop or can be controlled, but who, nevertheless, go on to hepatic coma and death. It is difficult to estimate with any degree of accuracy how many patients—if any—with a severe hemorrhage would have survived if their bleeding had been controlled. Although the life of the non-bleeding cirrhotic patient is unquestionably being prolonged, when a hemorrhage does occur there is no evidence that any non-operative measures can prolong life. In 1942, Ratnoff and Patek[20] noted that at the end of one year after a bleeding episode only 30 per cent of their patients were alive. Of these 102 cases admitted to the Boston City Hospital during the past ten years, only 28 per cent were living after the same period of time following their hemorrhage.

If non-operative measures cannot alter the life history of the cirrhotic patient after he ruptures his varix, can surgery accomplish this? Although there are many operations described in the literature which purport to do this,[1, 2, 5, 14, 17, 19, 21, 25] the evidence is not very conclusive. Perhaps this is due to the difficulties encountered in reporting the results of surgery in a very selected group of cases. Obviously, when one establishes criteria for the selection of patients to be submitted to operation, one cannot compare the end results in this group with the entire population of bleeding cirrhotics. Over nine years have passed since the portacaval shunt operations were popularized,[3, 27] and a somewhat shorter period of time since mediastinal packing,[25] resection of the lower esophagus,[19] radical subtotal gastrectomy,[1] and ligation of the hepatic and splenic arteries[2, 21] have been employed in these patients. We should be able to ascertain just how well these procedures have prevented hemorrhage, and if they have prolonged life. We would like to suggest that the answers to these questions might become apparent if the following specifications are adhered to in future reports:

1. Extrahepatic portal obstruction should not be reported with cases of portal hypertension due to cirrhosis. The natural courses of these two disease groups are entirely different.

2. The diagnosis of cirrhosis should be based on strict criteria, and the varices should be demonstrated in all cases where surgery is undertaken.

3. At the present time, the evidence strongly suggests that only patients who have bled from their varices should be operated upon. There would be no means of evaluating the results of surgery in patients who have not bled.

4. The entire bleeding cirrhotic population admitted to the hospital should comprise the series. The percentage of those selected for surgery and the clinical and laboratory findings of the degree of hepatic insufficiency should be recorded.

5. The total number of patients in this series who are alive at the end of one year after their hemorrhage will give some indication as to the value of the operative procedures employed.

Patients who are bleeding from their varices should probably be considered from two viewpoints. There are those who will die during their first hemorrhage, necessitating emergency surgery if this is to be prevented; and there are those who will survive, allow-

ing more definitive procedures at a more propitious time. But, is it possible to differentiate the two groups? In this control series of 102 cases, 60 of the patients died within a month of their first hemorrhage. Of these, 19 died in hepatic coma following a mild or significant hemorrhage, while 41 had a severe hemorrhage. Surgical attempts to control the bleeding in the former 19 would be futile, whereas some salvage might be expected in the latter 41. Even a procedure which carried a 50 per cent or 75 per cent mortality would obviously be beneficial in this group of patients who all die with non-operative treatment. The serious nature of any severe hemorrhage is readily apparent when it is realized that in the entire 176 hemorrhages studied, 68 were classified as severe and were experienced by 65 patients, 56 of whom were dead within one month, three within six months, four were alive more than six months, and two have only been followed for a three-month period at this time. Unquestionably, the mortality will be high, but the thought of doing emergency surgery on all patients with a severe hemorrhage should be seriously considered. The problem is no longer a matter of how many will die during the operation, but rather can any be saved by operation!

On the other hand, different considerations affect the patient who has survived his initial hemorrhage. Of the 102 cases, 42 patients fell in this category and only one-third of these died during the subsequent year. Any operative attack upon these patients must carry a respectably low mortality, and must demonstrate its value by keeping more than two-thirds of these patients alive longer than one year after their initial hemorrhage.

SUMMARY

The purpose of this paper has been to study the life history of the cirrhotic patient who bleeds from his varices. Although many difficulties are encountered which might limit its scientific accuracy, such a study produces a great deal of useful information when strict criteria are adhered to. Recognizing the possibility of some slight error, the following statements appear to be well founded:

1. The patient with proven cirrhosis of the liver who has a significant upper gastrointestinal hemorrhage can be said to be bleeding from esophageal varices when the other more common lesions of the stomach and duodenum are ruled out. With careful and repeated examinations, the varices should be demonstrated in many cases.

2. Hypoprothrombinemia and hypersplenism probably play a very minor role in the large majority of the bleeders.

3. While the first hemorrhage takes the lives of 60 per cent of the cases, a patient who survives this episode has two out of three chances of being alive at the end of one year.

4. At the time of death, the differences in the clinical and laboratory signs of hepatic decompensation between those dying of exsanguination and those dying in hepatic coma are not very striking.

5. In contrast to this finding, marked differences were noted in the signs of liver reserve in the patients surviving a hemorrhage as compared to those dying.

6. The severity of the hemorrhage and the evidence of hepatic compensation are the important features in estimating the prognosis of the cirrhotic patient with a ruptured esophageal varix.

7. A thorough analysis of the cases treated surgically, a one-year follow-up study, and a careful comparison with the control series should demonstrate the value of the surgical procedure employed.

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