MANAGEMENT OF MASSIVELY BLEEDING PEPTIC ULCER*

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OPINION CONTINUES TO BE DIVIDED on the management of gross bleeding from peptic ulcer, even though clinical experience is distressingly ample in most large teaching hospitals. Reasons for confusion of thought evident in the literature of the subject are lack of precise clinical observations and careful reporting, lack of definite criteria in the selection of cases to be treated in any particular manner, variation in the quality of medical or surgical care provided, and what may be called clinical bias. Various authors have focused attention on the life-saving value of early surgical control of hemorrhage in these cases, but the ideas developed in their pioneer work have not as yet won the enthusiastic support of gastroenterologists 1-9.

It has seemed to us that advances in surgical technic and care, improvements in anesthesia, and sounder knowledge of hemorrhagic shock and its treatment[10] [11] warrant further careful evaluation of the merits of rapid blood replacement and early surgical operation in this condition. Accordingly, since January 1947 we have been testing the value of immediate large blood transfusions and gastric resection in the therapy of grossly bleeding peptic ulcer, and though the work is still in progress it is justifiable to report on methods used, clinical results to date, and tentative conclusions. At present the series comprises 54 patients, 33 of whom were operated upon, and 21 of whom were treated as control cases without operation.

A definition of terms and explanation of criteria used in the selection of cases is in order. By early operation we mean subtotal gastric resection within 24 hours of admission to the hospital. By acute hemorrhage is meant vomiting of blood or passage of blood by rectum with attendant signs of cerebral anoxia within one week of admission to the hospital. To be classified as massive the hemorrhage must have been severe enough to depress the admission red cell count to 2.5 million per cmm or less, or to reduce the circulating red cell volume to 60 per cent of normal or less. Our criteria in the selection of cases in which early operation is recommended may be tabulated, therefore, as follows:

1. The patient must have bled grossly into the upper gastro-intestinal tract within one week.
2. The admission red cell count must be 2.5 mill/cmm or less, or the circulating red cell volume must be 60 per cent of normal or less.
3. There must be reasonably good evidence for the diagnosis of peptic ulcer.

In addition, at least three liters of properly matched blood must be immedi-

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ately available. Operation is advised and carried out at once when these circumstances are present. If the bleeding has been less severe, or conditions are otherwise than as outlined, a non-surgical regimen is instituted and tests are repeated 24 hours later, or with the appearance of further signs of hemorrhage. If the patient or his referring physician show reluctance toward recommended operation, the patient is put into the control series and is treated otherwise as nearly similarly as possible. Blood is given freely and food is allowed as tolerated. Grave associated disease has not constituted a contraindication to operation in this series of cases, but rather the contrary. It seems reasonable that the rapid relief of anoxia and surgical control of hemorrhage would increase rather than impair the patient's ability to survive previously existing disease. Consequently, we have operated upon patients with advanced bilateral tuberculosis, hypertensive cardiovascular disease, extreme obesity, coronary sclerosis, pulmonary emphysema, chronic sepsis and cerebral hemorrhage. If the patient shows signs of hemorrhagic shock, the rate of administration of blood and preparation for operating are speeded up. In several instances operation was started within two hours of admission, while the patient was still hypotensive, but blood was being transfused rapidly at the same time.

Within one-half hour after admission to the hospital blood studies are made by a trained laboratory team, and blood transfusion is started immediately after samples are taken. The measurements include red cell count, hemoglobin and hematocrit, plasma volume, extracellular fluid volume, plasma protein concentration and non-protein nitrogen, plasma chloride and CO_2-combining power, and blood sugar. The analytical methods used are standard methods with which the laboratory staff has had considerable experience[12]. The blood smear is studied for type of anemia and abnormal elements, and the clotting mechanism is investigated to exclude the presence of hemorrhagic diathesis. All blood given the patient is weighed and its hemoglobin and protein content are determined beforehand. Blood loss at operation is measured and in 29 gastric resections in this series averaged 365 cc. Urine volume is measured daily and its content of cells and albumin and its specific gravity and pH are determined. In no instance was the lower nephron syndrome encountered. In patients operated upon liver biopsy is done as soon as the peritoneal cavity is opened, and the glycogen content of the specimen is measured. The blood studies are repeated within 24 hours after the operation, and again before discharge from the hospital.

The program of treatment may be briefly outlined as follows: If the criteria described are fulfilled, operation is advised within one hour after admission to the hospital, regardless of any associated disease, unless the patient is moribund from some cause other than hemorrhage from peptic ulcer. The anesthesia has been ether-oxygen mixture by endotracheal tube at the hands of a senior staff physician anesthetist. Blood is given through two cannulas before and during operation, and to a less extent afterwards.

The average interval between admission and operation has been 9.2 hours, most of which delay is occasioned in obtaining the necessary amount and type of blood.

At operation subtotal gastric resection is done with antecolic Hoffmeister anastomosis, an average of 80 per cent of the stomach being removed as shown by actual measurements. If it is a posterior wall duodenal ulcer, where feasible the ulcer is dissected out. In some instances the procedure described by Allen is employed[4]. In two cases the posterior wall duodenal ulcer had so large a crater and was surrounded by so much acute inflammatory reaction that pyloric transection was deemed advisable. An interesting problem confronts the surgeon when at operation no lesion of stomach or duodenum can be detected and no cause for hemorrhage can be made out after careful abdominal exploration. In this situation extensive gastric resection is performed without hesitation. In 5 such instances the resected specimen has shown shallow ulcers with open vessels, the stomach being involved in 4 cases and the duodenum in one.

TABLE I

	R.B.C. Mill/cmm	Vc %	Circ.Vol. R.B.C. % Norm.	Plasma Protein Gm/100cc	Plasma Volume % Norm.	Serum N.P.N. Mg/100cc
Operated on	2.5	26	48	6.0	100	53
Not operated on	2.9	29	55	5.9	97	43

Average Values for Admission Laboratory Data in Patients with Acute Massive Hemorrhage from Peptic Ulcer (Early Operation in 32, No Operation in 21)

An important technical point in some cases is evacuation of the stomach by gastrotomy before proceeding with gastric resection. The stomach is sometimes distended by a jelly-like cast of blood, and if the clot is carefully milked out through the transected lower stomach extensive gastric resection then becomes feasible.

Following operation penicillin and oxygen therapy are provided, and in the later cases streptomycin. The patient is out of bed within 24 hours for early ambulation. Sodium bicarbonate or sodium lactate is given intravenously to maintain alkalinity of the urine. As a rule little blood is given postoperatively. The average period of hospitalization following operation has been 15 days.

Of the 54 patients in the series to date 33 were operated upon early, and 21 were not operated upon, due to disinclination on the part of the patient or the referring physician. Four of the patients operated upon were found to have other causes for bleeding rather than gastroduodenal ulcer. One had esophageal varices, one hiatal hernia and peptic ulcer of the esophagus, one carcinoma of the cardia and one lymphosarcoma of the stomach. In the latter case gastric resection was performed, in the others only exploratory laparotomy. All four patients made uneventful convalescence.

With regard to diagnosis, reliance has been placed chiefly on the history and physical findings. The passage of stools containing fresh or tarry

blood had been noted by 44 of 50 patients, while 37 had vomited blood. All had either melena or hematemesis. The majority of the patients gave a history of ulcer dyspepsia, though in seven cases the symptoms were of less than six weeks' duration. In 16 patients a diagnosis of peptic ulcer had previously been made by roentgen studies. The most important physical findings were pallor, peripheral evidence of shock, and epigastric tenderness. Blood in the stool and in the gastric contents was also important. Of the entire group of 54 patients 24 showed signs of hemorrhagic shock on admission. Of these 24 patients 15 were in the operative group and the opera-

TABLE II

	Number	Age Average	Age High	Age Low	Blood given, cc Average	Blood given, cc High	Blood given, cc Low
Operated on early	33	54.6	74	22	3,600	9,400	1,000
Not operated on	21	61.0	82	35	2,040	11,000	0

Age and Amount of Blood Given in Patients Operated Upon Early and in Patients Treated Non-Surgically for Acute Massive Hemorrhage from Peptic Ulcer

tion was not postponed but resuscitation and operation were carried out concurrently. The roentgen ray has not been used as a diagnostic aid in this series of cases, as in our judgment the findings of examination under these difficult circumstances are not definitive enough to warrant delay and further manipulation.

Pathologically the bleeding ulcers of this series have fallen into two groups. More numerous have been the deep large indurated ulcers of stomach or duodenum, and often these lesions have penetrated neighboring structures. Less common have been the single or multiple shallow ulcers of stomach, or less often of duodenum, with little or no external or serosal evidence to suggest their presence. These lesions are usually associated with

TABLE III

	R.B.C. Mill/cmm	Blood Volume % Norm.	Total Cir. Hb. % Norm.	Plasma Protein Gm/100cc	Plasma Volume % Norm.	Total Cir. P.P. % Norm	Serum N.P.N. Mg/100cc
Admission	2.5	78	40.0	6.0	100	86	53
24 hours	3.8	95	68.7	6.2	110	99	41
Discharge	4.0	95	70.8	6.6	104	100	28

Average Values for Laboratory Data in 32 Patients Operated Upon Early for Acute Massive Hemorrhage from Peptic Ulcer

a short history. Hemorrhage may be fatal from these rather trivial looking lesions. The single marginal ulcer in the series to date followed gastroenterostomy done many years previously, and gastric resection had to be supplemented by resection of jejunum and transverse colon and cecostomy. Convalescence was satisfactory despite the extent of the operative procedure.

In Table I are shown admission laboratory data obtained prior to treatment in 32 patients operated upon, as compared with 21 not operated upon, average values being shown. The severity of the anemia is obvious. In appraising this factor one must always consider volume as well as concentra-

tion. The reaction to severe hemorrhage consists of shrinkage of circulating blood volume as well as anemia, hence these two laboratory findings must be taken together in setting up criteria for operation and for later assessment of the patient's condition. Plasma protein and plasma volume are far less critical factors in the survival of the patient than total circulating hemoglobin, and in both groups of patients plasma volume was normal on admission. The group treated by early operation are shown to have been more depleted than the group of patients in the control series, particularly with respect to hemoglobin values. The higher non-protein nitrogen figures probably indicate greater blood loss in the group operated upon.

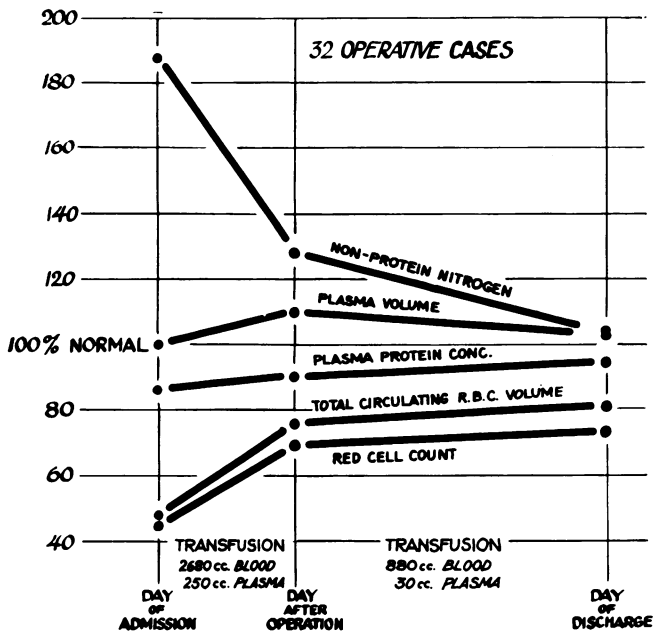

CHART I.—Study of effects of transfusion therapy on total circulating plasma protein and total circulating hemoglobin in ten cases.

In Table II appear data on age and blood transfusion therapy in the two groups of cases. Both groups of patients fell into the older age brackets, in which mortality rate is higher. It happened that the average age of the control group was somewhat greater than that of the group treated by early gastric resection. The patients operated upon received an average of 3600 cc. blood, as compared with 2040 cc. for the control group. In the control group one patient received no blood, as he died of hemorrhage within one-half hour after admission. Conditions were not strictly comparable, therefore, in the two groups of cases, though reasonably similar circumstances prevailed except for the factor of surgical operation. The patient in the non-operative group who received 11,000 cc. of blood eventually succumbed to hemorrhage.

In Table III are shown laboratory data before and after treatment in the group of patients operated upon. It is notable that total circulating hemoglobin values remained at less than 75 per cent of normal despite the administration of 3600 cc. blood, average values being considered. This raises the question of the physiologic nature of the adjustments to hemorrhage and of the subsequent reaction to replacement therapy. In Chart I are indicated further computations bearing on this subject. In 10 patients treated by early gastric resection an effort was made to determine how much of the administered hemoglobin and plasma protein remained in circulation. In all cases the hemorrhage was completely controlled by operation, and there was no reason to believe further bleeding occurred. Processing losses and losses of blood at operation were included in the computations. It is evident that the total circulating plasma protein quickly returned to normal and remained there, despite the administration of 20 to 25 per cent in excess of that theoretically required to achieve normal values. Presumably such excess plasma protein becomes a part of the "metabolic pool," as pointed out by Whipple[13] and Allen, Bogardus, Egner, and Phemister[14], and is subject to the demands of nitrogen metabolism. With respect to the fate of hemoglobin administered in theoretical surplus, the explanation is more difficult. At the end of 24 hours 22 per cent of the administered hemoglobin has apparently left the circulation, while at the end of 15 days 35 per cent is "missing," even though a serious anemia is present. There was no evidence of hemolysis in these cases as a possible explanation for the discrepancy. It is conceivable that the body reservoirs of hemoglobin, called upon in life-endangering hemorrhage, demand repayment of the loan as soon as physiologic stress is relieved. Further investigation of this question is in order. Whatever the explanation for this finding, its practical significance is that much larger amounts of blood are required in the replenishment therapy of hemorrhage than is usually realized. Unquestionably these patients have been given too little blood in the past, whether operated upon or not. Incidentally, we have seen no evidence of over-transfusion in any patient studied. Despite the frequent presence of hypertensive arteriosclerotic heart

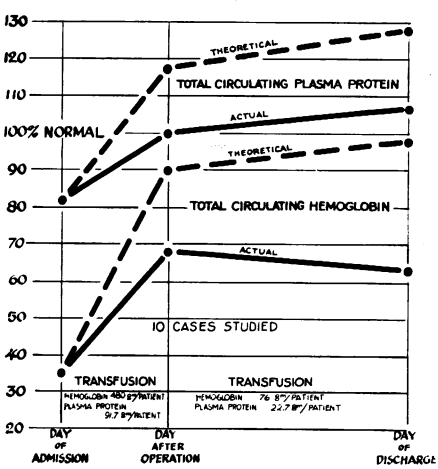

CHART II.—Average values for laboratory data in 32 operative cases of massively bleeding peptic ulcer.

disease in these patients, in none have we seen pulmonary edema, as described by Eaton in animal experiments[15], or congestive failure.

In Chart II are shown in graphic form average values for plasma protein concentration, plasma volume, red cell count and total circulating red cell volume before and after treatment in 32 patients operated upon. The average interval between points 2 and 3 was 15 days. The rapid decline of the initially elevated serum non-protein nitrogen to normal is worthy of note.

Table IV contains data bearing on carbohydrate metabolism. Elevation of blood sugar was found to be the rule in the hemorrhagic state, and the

TABLE IV

Blood Sugar Mg/100cc			Hepatic Glycogen Gm/100Gm		
Average	High	Low	Average	High	Low
164	300	112	2.9	6.2	0.3

Blood Sugar and Hepatic Glycogen Values (Liver Biopsy) in 16 Patients Operated on Early for Acute Massive Hemorrhage from Peptic Ulcer

TABLE V

	Number	Deaths
Patients treated surgicaliy.....	33	5 (15%)
Gastric ulcer	12	3
Duodenal ulcer	16	2
Marginal ulcer	1	0
Other lesions	4	0
Patients not operated on.....	21	6 (29%)

Results from Early Operative and Non-Surgical Management of Acute Hemorrhage from Peptic Ulcer

average value of 164 mg. per 100 cc. is to be compared with the normal of 80 to 120 mg. per 100 cc. for the method used. In 16 cases just after the peritoneal cavity was opened the liver was biopsied and the glycogen content of the sample was measured. Definite reduction in hepatic glycogen was the rule. Presumably both these findings are related to activity of the sympathico-adrenal system, and possibly also to preceeding deficiency in caloric intake. The evidence indicates the need for the early administration of an adequate caloric supply to these patients.

In Table V the mortality rates in the two groups of cases are indicated. The series is hardly large enough to warrant statistical analysis, but those of us concerned with the work believe that more lives are being saved by the program of early adequate blood replacement and gastric resection than by the non-surgical plan of treatment. The surgical resident staff, on whose shoulders falls the major part of the work of this rather gruelling program, are among its most enthusiastic proponents. If the resident staff is truly convinced of the value of a method—as all chiefs of teaching clinics know—the method must have real merit.

In conclusion, evidence has been presented which tends to favor early restoration of hemoglobin values and gastric resection as the method of

choice in the management of acute massive hemorrhage from peptic ulcer. The advantages of the method as seen at present are:

1. Hemorrhage is controlled directly
2. Mortality rate is lowered
3. Definitive treatment is provided for the peptic ulcer diathesis
4. Early resuscitation and relief of anoxia is achieved
5. Diagnosis is established in doubtful cases
6. Pyloric obstruction when present is relieved
7. Less blood is required in many cases

The method is not to be recommended, however, unless adequate facilities are at hand, and these may be summarized as:

1. Expert 24-hour laboratory service
2. Adequate blood bank
3. Skillful anesthesiologic service.
4. Expert surgical judgment and technique
5. Expert resident and nursing care

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DR. ALLEN O. WHIPPLE, New York: I do not know of anything more trying or more difficult than to be called in consultation on a patient who has been bleeding for days, and finally the medical group call in the surgeon to advise further therapy. Many