Transfusion in Upper Gastrointestinal Hemorrhage

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IN THIS PAPER we propose to discuss the indications for blood transfusion in upper gastrointestinal hemorrhage, the methods by which it is possible to determine the quantity of blood lost and to be replaced, the technic and the limitations of blood transfusions, and the results of treatment. We shall restrict our remarks to hemorrhage from intrinsic lesions of the upper gastrointestinal tract and exclude from their scope bleeding which occurs as a result of portal hypertension, since cirrhosis of the liver is a comparatively rare disease among patients admitted to our hospital, and our small experience of this condition does not qualify us to write about it. By contrast, hemorrhage from peptic ulcers and other lesions of the stomach and duodenum is frequent, and the conclusions which will be reported are based on a study of 286 patients, 206 men and 80 women, with a total of 297 admissions. These were treated by means of a uniform regimen first introduced in our hospital in May 1952, and described by us in 1954.[1] The diagnoses in our series are set out in Table 1.

Some years ago transfusions were rarely given in gastrointestinal hemorrhage, not only because the procedure itself was somewhat unfamiliar and the supply of blood generally inadequate, but also because it was thought that the hypotension which accompanies extensive hemorrhage is an important factor in arresting it, and that transfusion, by raising the blood pressure, might cause bleeding to recur. Although this attitude has changed, so that blood is now given freely (sometimes too freely) in many cases of hematemesis, there is still much disagreement about the choice of patients to be transfused, the quantity of blood to be given, and indeed the aims of transfusion.

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THE AIMS OF TRANSFUSION

The first and most obvious aim of blood transfusion is the relief of symptoms. If a patient is in shock, if he is obviously pale, restless, or sweating, if hemorrhage is continuing at a brisk rate, if the blood pressure is low and the pulse rate high, the need for blood is evident and urgent. No less important, however, is a second aim: to make the patient able to withstand further bleeding, should it occur, and surgical intervention, if it is found to be eventually necessary. A patient with a normal hemoglobin level is capable of tolerating considerable losses of blood without immediate danger

TABLE 1. Diagnosis in 286 Patients with Upper Gastrointestinal Hemorrhage[a]

Diagnosis	Male	Female
Gastric ulcer	46	16
Duodenal ulcer	77	24
Stomal ulcer	6	0
Esophageal ulcer	2	0
Ulcer not visualized	59	32
Hiatus hernia	3	2
Gastritis	4	4
Tumor of stomach (carcinoma, leiomyoma)	9	2
Total	206	80

[a]Six patients were admitted twice, 1 patient three times, and 1 patient four times. Total number of admissions 297.

to his life. Hemorrhage recurring when anemia is already established has a much more serious import, and the hazards of operating on anemic patients have been amply demonstrated.

INDICATIONS

Every patient who has lost blood is less able to stand up to further hemorrhage than if he had not bled. There is no way of foretelling which patient will suffer a recurrence of his hemorrhage; nor is it often easy to be certain whether the original bleeding has actually ceased or is still continuing. As will be shown presently, the size of the blood loss is difficult to gauge, and conventional methods of doing so frequently underestimate it. For these reasons, it is our opinion that in every case in which there is good evidence that blood has been lost from the upper gastrointestinal tract, transfusions should be given and continued until the loss has been quantitatively replaced.

BLOOD LOSS

Evidence

The commonest evidence is obtained from the history given by the patient. This is, however, often inaccurate and may be fallacious. Bright blood, when vomited, is easily recognized, but the distinction between hematemesis and hemoptysis may not be readily made. A frequent report concerns "brown" liquid which has been vomited and which may represent altered blood but is often of an altogether different nature. Melena may continue for considerable periods before it is noticed, particularly, as is often the case, if the patient has been taking an iron preparation. In every instance, the significance of an observation is increased if the patient has felt faint or actually fainted during or after vomiting. Melenous bowel content may be retained for several days before it is passed, and in these rather common cases of obscure bleeding general symptoms alone may raise the suspicion of upper gastrointestinal hemorrhage. It is well recognized that where overt hemorrhage has occurred, its size can only rarely be gauged from the patient's account.

Hematologic estimations are used to confirm the fact that bleeding has taken place, and to estimate the size of the blood loss. The usual methods are estimations of the hemoglobin level, the red cell count, or the hematocrit. Many physicians use the results so obtained as a yardstick for prescribing treatment, transfusions being given or withheld and their size being determined according to the degree of anemia revealed by these means. This criterion is useful only when bleeding has proceeded slowly, or when much time has elapsed since its occurrence. The reason is that hemorrhage means the loss of whole blood, and that the hemoglobin level of the blood remaining in the body will be unchanged until hemodilution occurs as a result of the entry of tissue fluid into the circulation, which will restore the volume of the blood but by so doing lower its concentration. If blood is lost slowly, hemodilution takes place pari passu with the bleeding, but in rapid hemorrhage it lags, so that estimations of the hemoglobin or red cell level can give no true picture of the loss. Thus in such cases there is a poor correlation between the hemoglobin level and the quantity of blood which has been lost.[1, 2] Moreover, until the blood volume has become stabilized, repeated hemoglobin estimations are of doubtful value, for a falling level

could indicate either continuing hemorrhage or merely progressive hemodilution. These difficulties can be avoided if estimations are made not of the hemoglobin level but of the blood volume, for by means of comparing the actual volume with that calculated to be normal for the patient in question, the quantity of blood lost can be ascertained with an accuracy great enough for practical needs.

Technic of Blood-Volume Estimation

The blood volume can be calculated either from measurements of the volume of the plasma or of the red cells, in either case combined with an estimation of the venous hematocrit. The calculated figure will vary slightly according to the method used, but the differences are unimportant in practice. We have so far used the Evans blue dye-dilution method of Gregersen[3] for the determination of the plasma volume (V_P), and the venous hematocrit corrected according to Mollison[4] for calculating from it the total blood volume (V_B) and the total red cell mass (V_R). The only reason for employing this method is that we have found it convenient, but any other method, such as the direct estimation of the V_R by means of radioactive chromium,[5] will serve the same purpose, provided it is capable of giving rapid and accurate results under emergency conditions. We would accept any method by which one can estimate the V_R in 1 hour or less.

Repeated estimations of the V_P in nonbleeding subjects have been found to agree to within 5 per cent. If successive estimations of a patient's V_P should therefore show a difference significantly greater than 5 per cent, it may be concluded that an actual change has occurred in the interval. The initial blood loss is determined by comparing the patient's actual V_B with his "ideal" one, which may be calculated from published tables. This calculation is, however, beset by some uncertainties, for the normal V_B varies not only with age and weight but also with the individual's build; fat people have a V_B relatively smaller, and lean and muscular ones a V_B larger than the ideal. Thus the patient's normal V_B before the hemorrhage began may not have been identical with the ideal, and a comparison of the actual volume with the ideal may underestimate or overestimate the blood loss. Experience helps in overcoming this difficulty by teaching to alter slightly the ideal V_B in patients of an obviously nonideal body build.

Size of Blood Loss

The amount of blood lost in upper gastrointestinal hemorrhage is extremely variable, and we have been impressed with the difficulties of estimating it from the patient's clinical condition. In general, the tendency is to underestimate it, for in contrast with traumatic injury, much larger blood volume deficits may be necessary before signs of shock are apparent. Whereas a reduction in the blood volume of 30 per cent or more is often regarded as predisposing to shock, we have frequently seen much greater deficits in patients who, clinically, appeared in good condition and also showed remarkably little pallor. The rapidity of bleeding is of obvious importance in the production of symptoms, but this does not appear to be the only cause of the differences which we have observed.

TABLE 2. Reduction in Red Cell Mass (Per Cent of Normal)*

Reduction in red cell mass (%)	No. patients	% patients
0–19	6	2.6
20–49	96	41.2
50 and over	131	56.2

*Two hundred thirty-three patients not yet transfused or suffering from hemorrhage recurring after transfusion.

In gaging the size of the blood loss, we take most notice of the reduction in the red cell mass (V_R), since this is the guide to the size of the transfusion which is to be given. Table 2 shows this reduction in all our patients who, at the time of the blood-volume estimation, had either not been transfused or had had bleeding recurring after transfusion. (It should be noted that it is unnecessary to withhold transfusion because a blood-volume estimation is to be carried out; as long as the quantity of blood transfused is known, it can be taken into account in calculating the blood loss.) It will be seen that among these 233 patients only 6 had a blood loss producing less than a 20 per cent reduction in the V_R. By contrast, 56.2 per cent had lost one half or more of their total V_R, several of them in the vicinity of 80 per cent. Correlation with the hemoglobin level was good in those patients who had bled slowly and had had time to dilute their blood, but absent in the cases with rapid hemorrhage. Thus we have seen a loss of 70 per cent of the V_R associated with a hemoglobin level of 10 Gm. per 100 ml. and 55 per cent with 12 Gm. per 100 ml.

ADMINISTRATION OF TRANSFUSION

Quantity of Blood

It is our practice to replace quantitatively all the blood which has been lost, except where hemorrhage has been obviously slow and long-continued, when it is likely that the circulation has become partially adjusted to a reduced blood volume and a complete replacement of the deficit might overload it. In such cases, especially in aged patients, we aim at a restoration of the V_R to about 80 per cent of normal. Blood is dispensed in units of 540 ml. of citrated blood, each containing an average of 200 ml. of red cells. If the V_R deficit has therefore been calculated as being 1000 ml., the transfusion will consist of five units of whole blood, or in many cases the packed red cells derived from five units.

TABLE 3. Quantity of Blood Given (296 Admissions)

No. Units*	Liters*	No. cases
0–2	0– 1.1	23
3–4	1.7– 2.3	59
5–6	2.8– 3.4	69
7–8	4.0– 4.5	61
9–10	5.1– 5.7	20
11–15	6.3– 8.5	34
16–20	9.0–11.4	16
Over 20	Over 11.4	14

*Average 8.0 units, 4.5 liters.

Table 3 shows the quantity of blood given in 296 admissions. The average of eight units per patient is unusually large, but is somewhat inflated by a comparatively small number of very large transfusions which were administered to patients with long-continued or recurrent bleeding and those undergoing emergency surgical treatment. The median figure is six units. Only 27 per cent of all patients received fewer than five units of blood.

Mode of Administration

Blood is administered by means of the continuous-drip method, at a standard rate of one unit (540 ml.) every 4 hours. This rate is, however, exceeded for the first one or two units in the more severe cases of hemorrhage, and always when the patient's condition does not respond to the slower rate. When bleeding is very rapid—as

may be shown by the passage of bright blood per os or per rectum —it is essential to keep pace with it by increasing the speed of transfusion, and patients who are to be prepared for emergency operations must have a safe blood volume; in many such cases blood must be given at very rapid rates, under positive pressure, and sometimes simultaneously into several veins. The need for constant personal supervision of all transfusions by a responsible medical officer cannot be overemphasized. Where packed red cells are used, the standard rate of transfusion is one half that for normal blood, and where the initial V_R is very low in a patient who has already largely restored his V_B by hemodilution, packed red cells must be given very slowly in order to avoid circulatory overloading.

Dangers

Blood transfusions given for any reason whatever carry certain dangers such as reactions of incompatibility, the administration of infected blood, and the transmission of the virus of serum hepatitis. Because of these, it is incumbent on any physician to restrict the number of transfusions to those considered essential for the patient's well-being. We regard all transfusions given to patients with blood loss from upper gastrointestinal hemorrhage as essential and are therefore willing to accept these inevitable risks. To date, there has been no case in our series in which death or serious illness could be attributed to the causes enumerated.

In the specific instance of transfusion for hematemesis or melena, the danger most commonly anticipated in the older literature was a renewal of bleeding because of the transfusion. This has not occurred in any of our patients as far as we have been able to determine. It appears more dangerous to prolong an existing hypotension by withholding transfusion than to run the risk of recurrent bleeding by raising the blood pressure to a safe level. All the same, it is probably important to give blood as slowly as is possible in the existing circumstances, so as to increase the blood volume slowly and raise the blood pressure gradually.

Overtransfusion is another danger which has been rightly stressed, and this is of particular importance when transfusions are as large as they are apt to be where a complete replacement of the blood loss is attempted. It is for this reason that administration must be supervised by experienced personnel who are familiar

with the signs of circulatory overloading and able to adjust the rate of flow and the quantity of blood in accordance with the patient's condition. A rule-of-thumb policy is apt to be disastrous. In this series of 297 admissions there were 2 deaths in old men of 79 and 84 years, respectively, in which an overrapid transfusion was thought to have possibly contributed to the fatal outcome. These point to the special care which must be taken in old patients and those suffering from complicating diseases. That even frail patients can, however, be treated successfully is shown by the case of a woman of 81 who, having lost 63 per cent of her V_R, made a good recovery from an emergency gastrectomy for gastric ulcer, following the transfusion of ten units of blood. In this connection, it is emphasized that severe hemorrhage in elderly patients not infrequently produces symptoms of coronary insufficiency, with or without congestive heart failure, and that myocardial infarction has been seen by us on a number of occasions. These patients should be treated by means of cautious transfusions, for symptoms, including failure, are likely to be dramatically relieved rather than aggravated by them.

The development of a bleeding tendency following massive transfusion has been recently reported from several quarters. This is primarily the result of a thrombocytopenia (which may develop when more than fourteen units of blood are given in 48 hours);[6] other, so far unexplained changes in the blood-clotting mechanism have also been noted.[7, 8] Although we have not noticed any difficulties in our series which we could attribute with certainty to an increased hemorrhagic tendency, the possibility of such a tendency arising provides an argument against an indefinite continuation of transfusion and in favor of early surgical intervention where hemorrhage shows no sign of ceasing. Citric acid intoxication is another danger of massive transfusion which has lately been studied[9] and can be minimized by the continuous intravenous administration of calcium chloride.

Duration

In the majority of cases seen in our hospital, hemorrhage had either ceased before admission or it stopped shortly after it. It is frequently difficult to be certain whether or not hemorrhage is continuing, as both the clinical and hematologic signs may be misleading. We have used repeated estimations of the V_B to obtain infor-

mation, for by comparing successive estimates, taking into account any blood which has been given in the intervening period, it is possible to show whether or not significant further bleeding has occurred. This matter has been discussed previously.[1]

There is a minority of cases in which hemorrhage continues or recurs after admission to hospital. In these cases the blood volume falls again after having been restored by transfusion, and continued transfusions are required in order to maintain it near normal. There is then a question how long to persist with a conservative regimen of treatment in the hope that bleeding may cease spontaneously, or alternatively when to recommend surgical intervention. Such difficulties do not arise in places where there is a rule either against emergency surgery in any eventuality, or to operate in every case. At this moment most observers, including ourselves, recommend an intermediate course, with operation reserved for those patients who fail to respond to conservative treatment or relapse under it. It is important to identify as soon as possible these refractory patients, since the risks of emergency operations increase the longer these are delayed, one reason being the development of an increasing tendency to bleed after long-continued massive transfusions.

In our hospital, it is recommended that an operation be carried out in every case in which significant hemorrhage continues 48 hours after admission or recurs at any time. In some instances the decision to operate is made at an early stage, especially when bleeding is obviously so severe and rapid that it is difficult to maintain the blood volume even when transfusions are very rapid. Our patients are initially admitted to surgical wards, but they are always given the benefit of conservative treatment in the early stages; only when this is seen to have failed after a full trial of adequate blood replacement and ancillary measures (diet, sedation, etc.) is surgery recommended. Two days is the maximum time ordinarily permitted for an evaluation of the effect of conservative treatment. The operation of choice is partial gastrectomy.

Table 4 shows the initial treatment given in the 297 admissions of our complete series. It will be seen that only 36 or 12.2 per cent had emergency operations, but we believe that several others would have profited from surgical treatment. The mortality (Table 5) was considerably higher with surgical than with conservative treatment, but as the former was given to the most severely ill patients,

this must be expected; it is probable that a very much higher proportion of these patients would have died if operation had been withheld.

DISCUSSION

We regard blood transfusion as the most important single measure in the initial treatment of upper gastrointestinal hemorrhage. By its use, together with other conservative means, the great majority of patients can be tided over the acute stages of their illness without recourse to surgery. Where bleeding fails to be arrested

TABLE 4. Initial Treatment

Treatment	No.	%
Conservative	261	87.8
Operative[a]		
Gastric ulcer	16	12.2
Duodenal ulcer	14	
Gastritis	4	
No lesion found	2	

[a]The age of patients treated by emergency operation ranged from 30 to 81 years and averaged 57.8 years.

TABLE 5. Mortality According to Initial Treatment

Treatment	Survivals	Deaths	Mortality (%)
Conservative	245	16	6.1
Surgical[a]	29	7	19.4
TOTAL	274	23	7.7

[a]Partial gastrectomy: 5 deaths in 34 operations (14.7%)

under conservative treatment, transfusion is able to maintain the patient's condition in a state in which an operation can be performed without prohibitive risks.

Transfusion is of particular importance in the case of patients in the older age groups and with complicating diseases because their tissues, particularly the vital organs like the heart, brain, liver, and kidneys, are less resistant to long-continued anemic anoxia than those of younger and healthier people. The rapid rise with increasing age of the death rate from upper gastrointestinal hemorrhage is a well-known fact which is borne out by our own experience (Table 6). Whereas no patient under 40 died, the mortality rate was 12.0 per cent among those between 60 and 90. Old

people "tolerate" transfusions as well as younger ones and are more likely to die if they are inadequate. Because of their intolerance to anemia, it is vital to consider early operation if bleeding should continue in such patients. For similar reasons, the presence of complicating conditions like cardiac or renal disease speaks often in favor rather than against early surgery.

During the 4 years which our own study has so far continued, we have noted that the severer degrees of hemorrhage occur especially in middle-aged and elderly patients. Among our 297 admissions 74.8 per cent were more than 50, 52.8 per cent more than 60, and 27.3 per cent more than 70 years old. Members of a population such as this, in addition to their age, are also subject to many

TABLE 6. Mortality According to Age

Age	Survivals	Deaths	Mortality (%)[a]
0–29	13	0	0
30–39	21	0	0
40–49	38	2	5.0
50–59	63	2	3.1
60–69	66	10	13.1
70–79	64	6	8.6
80–89	9	3	25.0
TOTALS	274	23	7.7

[a]Mortality under 40 0; mortality under 50 2.7%; mortality 40–60 3.8%; mortality 60–90 12.0%.

chronic complicating diseases, and for both reasons it appears of paramount importance that they receive the optimum amount of blood and are treated by means of early operation where this is indicated. It is probable that the large size of the average transfusion given in our hospital (see Table 3) is partly accounted for by the large proportion of old people in our series.

SUMMARY

1. The aim of blood transfusion in upper gastrointestinal hemorrhage is the restoration and maintenance of a normal blood volume.

2. Evidence of the size of the blood loss is often difficult to obtain from the clinical history or from the hemoglobin level, red cell count, or hematocrit. It should be estimated by means of determination of the blood volume.

3. The lost blood should be replaced quantitatively.

4. It is dangerous to continue transfusions and other conservative means of treatment indefinitely in the face of long-persisting or recurrent hemorrhage. A definite time limit is recommended for the trial of such measures, after which emergency surgery should be carried out.

5. Adequate transfusion and early operation are of particular importance in the treatment of frail or elderly patients.

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