TREATMENT OF ACUTE GASTRO-DUODENAL HAEMORRHAGE

WITH PARTICULAR REFERENCE TO QUANTITATIVE BLOOD REPLACEMENT

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During the year beginning in May, 1952, we treated patients with acute gastro-duodenal haemorrhage by a method incorporating the following principal features: (1) initial treatment by conservative measures; (2) early estimation, by means of a blood-volume determination, of the amount of blood lost; (3) quantitative replacement of the blood lost; (4) repetition of the blood-volume estimation to determine if haemorrhage has ceased or has recommenced; (5) early surgical intervention in cases of haemorrhage continuing or recurring in spite of conservative treatment.

We have been impressed with the increased saving in life since the inception of this therapeutic regime, and, while our own trial continues, publication of clinical detailed results obtained to date seems to be warranted.

The treatment of acute gastro-duodenal haemorrhage is still controversial. Agreement is lacking on such points as the diet to be given, the quantity of blood to be administered and the rate of transfusion, and the indications for emergency surgical operations.

It is difficult to compare the results furnished by various means of treatment, because of fundamental differences in the material reported on by the authors. Such differences are particularly noteworthy in the age and social grouping of patients studied and in the average severity of the haemorrhage: whereas some authors include all cases of bleeding in their series, others select only those of "severe" or "massive" haemorrhage; and the criteria by which the assessment of the severity is made vary widely.

One further source of differences among the various published accounts is worthy of emphasis. While some report "personal" series treated by outstanding specialists in this field, others summarize work carried out at general hospitals by heterogeneous medical groups without special facilities for selection or segregation of patients. The treatment described in this paper was carried out by a staff of general physicians and surgeons of varying experience, and the results represent the work of some 15 individuals. We believe that a similar scheme could readily be organized at any well-equipped general hospital.

Definition.—The term "gastro-duodenal haemorrhage" as used here denotes bleeding arising from intrinsic lesions of the stomach or duodenum. It excludes bleeding from oesophageal varices. "Acute" means bleeding at or shortly before the first examination.

Principles of Treatment

At Christchurch Hospital, at the present time, all patients stated to be suffering from acute gastro-duodenal bleeding are initially admitted to a surgical ward and seen by the surgeon dealing with acute cases. A physician is always on call, particularly when a patient's suitability for operation is being considered. Emphasis is laid on conservative treatment in the early stages, and adequate blood transfusion is regarded as its most important part. Only when this is seen to have failed to arrest the bleeding, or in cases of recurrent haemorrhage, is surgical intervention considered. We believe that non-arrest of bleeding should be diagnosed within 48 hours of admission and that the decision to operate should be made during that period.

Blood Transfusion

The purpose of blood transfusion is twofold: to relieve shock and other symptoms resulting directly from loss of blood and to raise the patient's haemoglobin concentration to a level permitting adequate oxygenation of vital organs, such as the heart, liver, kidneys, and brain, and giving the best possible chance to the surgeon if he should be forced to intervene. It is widely recognized that emergency surgery carried out on anaemic patients is beset with a high and possibly prohibitive mortality, especially if the anaemia is of any length of standing. Prevention and rectification of anaemia seem to us to be the most important single aim in the initial treatment of acute gastro-duodenal haemorrhage, and we believe that, whenever there is evidence that blood has been lost, the extent of the loss should be ascertained and the deficit made good as rapidly as possible.

It was pointed out by Bennett *et al.* (1938) that in the early stages of most cases of acute haemorrhage an examination of the peripheral blood alone can give no valid information about the amount of blood lost, because cells and plasma are lost in equal proportion, and anaemia cannot be diagnosed until the plasma volume is restored by means of haemodilution. This classical paper has not received the attention it merits, and the severity of haemorrhage is still estimated by most investigators in terms of the haemoglobin level or red-cell count. Thus Crohn (1953) defines "massive" haemorrhage as that which is accompanied by shock and a lowering of the red-cell count to 3,000,000 or less per c.mm. or the haemoglobin level to 7.5 g. or less per 100 ml. In our series, following the advice of Bennett *et al.*, we have estimated the blood loss by means of a determination of the blood volume, and have used the figures so obtained for prescribing the quantity of blood to be transfused, the aim being restoration of the total red-cell mass to the figure calculated to be normal for each patient.

Other Therapeutic Measures

The diet is regulated according to individual requirements. Although we do not regard initial starvation as desirable we have found that many patients suffering from considerable degrees of gastro-duodenal haemorrhage tolerate early feeding badly and prefer to take only sips of fluid, at least during the first 12 hours. We give a semi-liquid gastric diet as soon as patients can take it comfortably. Nothing seems to be gained by forcing patients to eat or drink in the intervals between haematemeses.

Colloidal antacids have generally been given from an early stage, especially where pain persisted.

Sedation seems an important aspect of treatment, and includes not only drugs (we prefer not to use morphine in patients who are vomiting) but also liberal reassurance by the attending practitioner. When apprehensive patients are suddenly translated to an unfamiliar environment and then subjected to a series of investigations, which though necessary are puzzling to them, brief explanations and friendly reassurance can do much to ensure the success of treatment.

Surgery

During recent years it has become evident that in certain cases haemorrhage from the stomach or duodenum will not

subside under conservative treatment, however long continued, and that surgical removal or obliteration of the bleeding lesion is necessary. Two courses are open to the surgeon: either to operate on all except mild cases of haemorrhage (Finsterer, 1939; Stewart *et al.*, 1950) or to attempt to select those patients in whom conservative treatment is likely to be unsuccessful. We have adopted the second course, subjecting to emergency surgical treatment two classes of patients: (1) Those who in spite of conservative treatment, including adequate blood transfusion, showed evidence of bleeding at the end of 48 hours' observation in hospital—the operation, preceded by appropriate measures of resuscitation, being performed as soon as such a diagnosis had been made. (2) Those who, following cessation of the original haemorrhage, showed evidence of recurrent bleeding while still in hospital.

The operation of choice was partial gastrectomy, but in one case this was not thought to be feasible because of the patient's poor condition, and a local repair was done.

Technique of Blood-volume Estimation

We have used exclusively Gregersen's (1944) Evans blue method for determining the plasma volume (V_P), and have found it convenient and accurate enough for emergency use. Only slight modifications in Gregersen's technique have been necessary in our series. Thus the chromogenicity of the dye used by us was so high that the recommended injection of 25 mg. could sometimes not be repeated within 48 hours without producing a rather alarming slaty-grey staining of the patient's skin and mucosae. For this reason we injected the full dose only in exceptionally large patients, while in those of small and medium stature we gave 15 to 20 mg. on each occasion. Calibration standards were prepared from dye diluted solely with plasma. We have now performed well over 300 blood-volume estimations with this dye and have noted no sign of toxicity in any patient.

In the calculation of the total blood volume (V_B) and the total red-cell mass (V_C) we have made use of the venous haematocrit reading, multiplying it by a factor of 0.96 to correct for trapped plasma. We realize that an error was thereby introduced, as the total body haematocrit reading is lower than that of the venous haematocrit, and that the correction factor 0.86 would have given a more accurate result (Mollison, 1951). For the purpose of computing the amount of blood to be transfused the calculated V_C was compared with the "ideal" V_C . The latter was obtained by multiplying the patient's "ideal" weight (from Life Tables, using the patient's height and age) by the figure 36 ml. per kg. body weight. The work of Reeve and Veall (1949) has indicated that 30 ml. of red cells per kg. is a better estimate of the "ideal" V_C . The second error thus introduced into our calculations acted in the opposite direction to the first and partly cancelled it. We have calculated that by using the older figures mentioned we overestimated blood losses by from $\frac{1}{2}$ to $1\frac{1}{2}$ pints (284 to 850 ml.) per patient, according to the severity of the haemorrhage. This error does not appear to invalidate the results of our investigations, which were carried out under emergency conditions and not intended to supply fundamental data. When successive blood-volume estimations were compared for the purpose of establishing the presence or absence of continued bleeding the errors mentioned above did not influence our calculations, as we were comparing two sets of figures both obtained with the use of the same factors.

Using the Evans blue technique in non-bleeding patients, we have found successive estimations of the V_P to agree to within 5%, as claimed by Gregersen. Great care in injecting the dye, in removing samples of blood, and in estimating dye concentrations (using a Coleman spectrophotometer at a wavelength of 625 m μ) was, however, necessary to obtain such results, and all these operations were carried out by experienced senior laboratory staff. As few of our patients were able to take much food at the time of our examinations we have had little trouble with turbid plasma samples. Difficulties occasionally arose in estimating the

height and weight of gravely ill patients, and in some cases we found it inadvisable to use the "ideal" weight for calculating the "ideal" V_C owing either to the presence of gross obesity or to malnutrition. In these cases we used a figure lying between the actual and the "ideal" weight.

Technique of Transfusion

All patients were transfused by means of the continuous-drip method with either stored whole blood or packed red cells. The normal rate of transfusion was one pint (570 ml.) in four hours. This rate was generally exceeded for the first one or two bottles of blood in the more severe cases of haemorrhage; when active bleeding was obviously proceeding, and particularly when patients were being prepared for emergency operations, blood was often given at very rapid rates and sometimes simultaneously into two veins.

As already stated, our aim was to restore the total V_C to the "ideal" by means of transfusion. For this purpose we assumed a pint bottle of stored blood to contain 200 to 220 ml. of red cells. If, therefore, we found a deficit of 1,000 ml. in the V_C we would give four to five bottles of whole blood. Packed red cells were often given when a patient's V_P was found to be large compared with his V_C , and especially when heart failure was present. In a few cases incipient congestive heart failure with a large V_P appeared to make it advisable to leave the patients with a blood volume of only about 80% of the calculated normal.

Material

During the year since the adoption of this therapeutic regime we treated 88 cases of acute gastro-duodenal haemorrhage: males, 69 (78%); female, 19 (22%). Five of these were admitted twice during the year, so that the series comprises 93 separate admissions. In addition several other patients were on admission thought to be suffering from haematemesis or melaena, but were on investigation found to have lost only insignificant amounts of blood. We decided to exclude these from our series. Table I shows the age

TABLE I

Age Incidence among 93 admissions (88 patients):					
0-29 years	..	..	2	60-69 years	..
30-39 "	..	..	4	70-79 "	..
40-49 "	..	..	13	80-89 "	..
50-59 "	..	..	15		24
Average Age, 62.6 years:					
Over 50 years	..	..	74 (78.5%)		31
" 60 "	..	..	59 (63.5%)		31
" 70 "	..	..	35 (37.7%)		4

incidence among our patients. It will be seen that the great majority were middle-aged or elderly. This is in contrast to many other published accounts in which acute gastro-duodenal haemorrhage appeared to be most common among the younger age groups. As has been found by others, men were more commonly affected than women, although their preponderance was unusually heavy in our material.

Diagnosis

The diagnoses made in our 88 patients were as follows: gastric ulcer, 29 (male 25, female 4); duodenal ulcer, 26 (male 19, female 7); stomal ulcer, 2; probably peptic ulcer, 4; ulcer not visualized, 20; hiatus hernia, 2; gastritis, 3; carcinoma of stomach, 2. A definite diagnosis is indicated only when it was proved radiographically, at gastroscopy, operation, or necropsy. The group of four patients classed as cases of "probable peptic ulcer" had ulcers proved on previous occasions, but no ulcer was found during the current admission. Patients listed under the heading "ulcer not visualized" had strong histories pointing to peptic ulceration, but no actual lesion could be demonstrated. The policy at our hospital has so far been to wait at least one week after presumptive cessation of the haemorrhage before undertaking radiological or gastroscopic studies. Inevitably some of the more acute ulcers must have healed in the intervening period and their visualization thus became

impossible. A few emergency radiological examinations were carried out immediately before operation. In two cases no lesions were found at operation, but after gastrectomy bleeding ceased. It is probable that in at least one of these a high gastric ulcer was left behind.

Results

Table II shows the reduction in the red-cell mass found in those patients who had not been transfused at the time when their blood volume was first estimated, and in another six

TABLE II.—*Reduction in Red-cell Mass (% of Normal) .*

	0-19%	20-49%	50+%
Patients not yet transfused	4	24	35
transfused but suffering from recurrent haemorrhages	—	1	5
Total	4 (6%)	25 (36%)	40 (58%)

who had recurrent haemorrhages after their first transfusion. Following the suggestion of Bennett *et al.*, we have arranged these individuals into three groups according to the magnitude of the blood loss. The "mild" group, with a reduction of up to 19% in their V_C , comprised 6% of the total; the "moderate" group, with a reduction of 20 to 49% in the V_C , 36%; and the "severe" group 58%. The last-named group lost more than 50% of their V_C . If a reduction in the V_C of 40% or more had been taken as implying "severe" or "massive" haemorrhage, as was done by Stewart *et al.* (1950), 78% of our patients would have fallen into this class.

The quantity of blood given is indicated in Table III. It will be seen that only about 25% had small transfusions of up to 4 pints (2.3 litres), while over 20% had more than

TABLE III.—*Quantity of Blood Given (93 Admissions)*

0-2 pints (0-1.1 l.)	7	9-10 pints (5.1-5.7 l.) .. .	5
3-4 " (1.7-2.3 l.)	16	11-15 " (6.3-8.5 l.)	13
5-6 " (2.8-3.4 l.)	22	16-20 " (9.0-11.4 l.)	4
7-8 " (4.0-4.5 l.)	23	Over 20 " (over 11.4 l.)	3
Average, 7.9 pints (4.49 l.)			

10 pints (5.7 litres) each. The average, 7.9 pints (4.49 litres) per patient, is among the highest reported. It equals that used by Stewart *et al.* in their patients undergoing emergency surgical treatment.

In the great majority of our patients the initial treatment was solely by medical means (Table IV). Only 14% had

TABLE IV.—*Initial Treatment*

Medical	80 (86%)
Surgical (Gastrectomy, 12; Closure of ulcer, 1)	13 (14%)
Diagnosis in surgical cases:	
Gastric ulcer	6
Duodenal ulcer	3
Gastritis	2
No lesion discovered	2

emergency surgical operations. "Interval" gastrectomies were carried out in another 17 patients (18%) after cessation of the bleeding. One-third of all individuals therefore underwent operations either during or after the haemorrhage.

Among 93 admissions there were seven deaths, making a mortality rate of 7.5% (Table V). One further patient died from a cerebral haemorrhage ten days after cessation of

TABLE V.—*Mortality*

	Survivals	Deaths	Mortality
Medical treatment	75	5	6.6%
Surgical treatment	11	2	15.4%
Total	86	7	7.5%

a bout of melaena. As he had advanced arterial disease with hypertension and a history of a previous cerebral accident, we believe that his death was coincidental with the condition for which he was admitted and that he should not be

included in our list of deaths from the effect of acute gastro-duodenal haemorrhage. With medical treatment alone the mortality was 6.6%, while among the 13 patients treated surgically two died (15.4%). If the patient treated by cauterization of the bleeding vessel who succumbed to a recurrent haemorrhage is omitted from the "surgical" group, the mortality among the 12 patients treated by emergency partial gastrectomy was 8.3%.

Particulars of the fatal cases are given in Table VI. Their average age was 65.4 years and did not differ significantly from that for the whole series. Several of them had serious

TABLE VI.—*Particulars of Fatal Cases*

Age	Sex	Diagnosis	Operation	Complications	Cause of Death	Death avoidable
71	M	Gastric ulcer (acute)	Closure of ulcer	Severe chronic asthma with heart failure	Recurrent haemorrhage	?
59	M	Gastric ulcer	—	Hypertension and obesity	Uncontrolled haemorrhage	+
45	F	"	—	Abdominal and generalized tuberculosis	"	—
84	M	Duodenal ulcer	—	Senility. ? Excessive blood transfusion	Heart failure	?
70	F	Gastric ulcer	—		Uncontrolled haemorrhage	+
67	M	Duodenal ulcer	Partial gastrectomy		Inhalation of vomit at operation for repair of ruptured gastrectomy wound	+
62	M	Gastric ulcer	—	Perforation of gastric ulcer	Shock and haemorrhage	?

complicating diseases and were obviously poor surgical risks. Nevertheless we feel that at least three might have been saved by more rapid transfusion followed by operation. Only one patient, a 45-year-old Maori woman with gross abdominal and general tuberculosis in addition to an enormous gastric ulcer, appears in retrospect to have been doomed, whatever the treatment.

The following three cases are quoted to illustrate some of the details of our methods of diagnosing and treating acute gastro-duodenal haemorrhage.

Case 77

A man aged 37 was admitted eight hours after having vomited a small quantity of brownish fluid; he felt faint. He had had a similar episode nine years previously, when a diagnosis of duodenal ulcer was made. On examination he was a rather pale young man but not in distress. His pulse rate was 100; blood pressure 170/110; haemoglobin, 14 g. per 100 ml. Within two hours of admission the blood volume was found to be: V_B 62% of normal, V_P 68%, V_C 55%, indicating a deficit of 6 to 7 pints (3.4 to 4 litres) of blood (see Fig. 1). As this was an early case in the series

FIG. 1.—Case 77; blood-volume estimations.

and the patient's condition seemed to be good, no action was taken at this stage, but the blood volume estimation was repeated three days later. During this time there had been no further vomiting, the bowels had not moved, and the patient felt moderately well. The haemoglobin had fallen to 8.5 g. per 100 ml. The second estimation showed V_B 60%, V_P 84%, and V_C 33%, suggesting a further loss of about 3 pints (1.7 litres) of blood, with partial restoration of the plasma volume. Transfusion was now started, a total of 7 pints (4 litres) of whole blood being given. Further estimations demonstrated that the gain in V_C equalled the quantity of red cells administered, and this was evidence that bleeding had ceased. Large stools containing altered blood were passed from the fifth day onward. Radiography later demonstrated considerable deformity of the duodenal cap. The patient also suffered from advanced essential hypertension.

Comment.—This case history demonstrates an instance of an almost silent haemorrhage from a duodenal ulcer. On admission the patient's condition was good and his haemoglobin level normal. Yet a blood-volume estimation revealed a very considerable red-cell deficit. It was later possible to show by the same means first a further haemorrhage and then its arrest, all before there had been any overt signs of bleeding. When melaena occurred it was proved not to indicate renewed bleeding.

Case 53

A man aged 67 was admitted four days after a fainting spell. There was no vomiting or melaena. He had had abdominal pain for two and a half years. During a recent cholecystectomy for the relief of this pain a mass was discovered on the posterior surface of the stomach and interpreted as a probable penetrating gastric ulcer. Soon after admission the patient passed a large melaena and collapsed. His blood pressure was 90/55; haemoglobin, 8 g. per 100 ml. Blood-volume estimation showed V_B 73% of normal, V_P 98%, V_C 42% (Fig. 2), indicating a total deficit of about 6 pints (3.4 litres) of blood. A transfusion was started, with improvement of his condition. A second blood-volume estimation 36 hours later showed V_B 97%, V_P 105%, V_C 80%, and no significant difference between the quantity of blood administered and retained. It was concluded that bleeding had then been arrested.

FIG. 2.—Case 53; blood-volume estimations.

Twenty-four hours later the patient collapsed again and passed another stool containing much blood. Blood-volume estimation showed V_B 53%, V_P 64%, V_C 40%. Emergency operation was decided upon, and was carried out after the transfusion of 6 pints (3.4 litres) of blood in three hours. At operation the splenic artery was found eroded by a large gastric ulcer adherent to the pancreas. The artery was tied and subtotal gastrectomy with splenectomy was performed, the ulcer being oversewn. The patient recovered. A total of 23 pints (13 litres) of blood had been given.

Comment.—The interest of this case lies in the use of blood-volume estimations to show a temporary arrest of bleeding and also the extent of both the primary and the recurrent haemorrhage. The blood volume was initially almost completely replaced by means of transfusion, and we believe that this enabled the patient to withstand the effects of the grave recurrent haemorrhage and to be prepared for a major emergency operation, which was successful.

Case 39

A man aged 47 was admitted with a history of severe upper abdominal pain for the past four days, black stools for two days, and vomiting of bright blood shortly before

FIG. 3.—Case 39; blood-volume estimations.

arrival in the ward. He had had indigestion for seven to eight years, and asthma for the same period. He was shocked, sweating, and orthopnoeic. His blood pressure was 78/50. His chest was emphysematous, and there were marked movements of the accessory respiratory muscles. Blood-volume estimation showed V_B 65% of normal, V_P 70%, V_C 58% (Fig. 3), with an estimated deficit of $3\frac{1}{2}$ pints (2 litres) of blood. Overnight he was given 3 pints (1.7 litres) of blood with clinical improvement, but a second blood-volume estimation, which showed V_B 71%, V_P 89%, V_C 49%, suggested a further loss of about 4 pints (2.3 litres) of blood when the transfused blood was taken into account. Further transfusions were given, his condition remaining poor mainly because of severe asthma. The next day there was great improvement and the blood volume was substantially normal. It was concluded that bleeding had now ceased, and the patient continued to make progress. Daily haemoglobin estimations showed a steady level, but six days later it was noted that it had dropped by 6 g. per 100 ml. in 24 hours. The patient looked a little pale, but his clinical condition was excellent and there had been no overt bleeding. An emergency operation was now carried out following the rapid transfusion of 4 pints (2.3 litres) of blood. Two large gastric ulcers were discovered—one with a large actively bleeding artery in its floor. After a partial gastrectomy the patient recovered. A total of 15 pints (8.5 litres) of blood had been given.

Comment.—This patient, in addition to bleeding from gastric ulcers, was suffering from severe chronic asthma and emphysema, and his condition during the first two days was extremely poor and probably precluded surgery. By means of repeated blood-volume estimations it was possible to show arrest of the bleeding within 48 hours of admission. Adequate blood transfusion restored his blood volume to normal and so improved his clinical condition that gastrectomy could be safely undertaken a week later, when haemorrhage recurred.

Discussion

The scheme of treatment here described was introduced in an effort to improve our results, which we had judged to be unsatisfactory. There were two fundamental considerations which led us to its adoption :

(1) It appeared improbable that we should be able to gauge the extent and duration of bleeding by the means usually employed—namely, an analysis of the clinical features plus estimations of the haemoglobin content of the peripheral blood. We therefore tested the possibility of using blood-volume estimations.

(2) We regarded prompt replacement of the lost blood as the single most important measure in conservative treatment, and also as an indispensable preliminary to surgery. The usually quoted indications for transfusion did not appear precise enough; it seemed logical, once the extent of the blood loss had been determined, to replace it as completely as possible and thereby to give the patient an optimum chance of healing his ulcer and of withstanding further bleeding, should that occur.

Below we examine the validity of these two considerations in the light of our findings.

The results of the initial blood-volume estimations are shown in Fig. 4, where the V_C on the abscissa is charted against the initial haemoglobin concentration. Only those

FIG. 4.—Results of initial blood-volume estimations.

patients who had not been previously transfused are included. It will be seen that, as might be expected, there is a general positive correlation between the two levels; however, more significantly, there are numerous striking exceptions in which a high initial haemoglobin concentration is paired with a low V_C . The findings reproduced in Fig. 4 are summarized in Table VII. In column 4 of this we also give the amount of blood calculated to be necessary to raise the initial V_C to normal in all patients in the various groups of severity. For instance, among the seven patients with initial haemoglobin concentrations of 4 to 5.9 g. per 100 ml. the initial V_C was 23 to 44% of normal, and 7 to 11 bottles of blood would have been required in individual cases to bring the V_C to the calculated normal. Again there is a general correlation between the initial haemoglobin level and the average amount of blood required. But the departures from the average become more and more marked as the initial haemo-

TABLE VII.—Correlation Between Initial Haemoglobin Level and Red-cell Mass (63 Admissions Previously Untreated)

Initial Hb (g. per 100 ml.)	No. of Patients in each Group	Initial red-cell Mass (% of Normal)	No. of Bottles of Blood required to raise Red-cell Mass to 100%
2-4	1	17	
4-5.9	7	23-44	7-11
6-7.9	15	25-61	6-10
8-9.9	16	31-88	2-8
10-11.9	14	30-87	1.5-9
12+	10	43-81	2.5-9.5

globin level rises. Thus among the 10 patients with levels exceeding 12 g. per 100 ml. the initial V_C varied from 43 to 81% of normal and the quantity of blood required to raise it to normal from 2.5 to 9.5 bottles.

We believe that these figures show vividly the difficulty of gauging the severity of bleeding from haemoglobin estimations. Whereas the lower levels generally give a good indication, the higher ones often do not; the reason is that the high haemoglobin levels tend to be found soon after an acute haemorrhage and before there has been time for haemodilution to occur. At that time there is no possibility of knowing the eventual haemoglobin level or how soon it will be reached. Consequently it is impossible to estimate the quantity of blood which it will be necessary to give.

The problem of establishing continuance or cessation of bleeding in some cases is too well known to need elaboration; yet on its solution depends the treatment to be given. By means of repeated blood-volume estimations we have often been able to come to a definite decision, and to distinguish between the two causes of a falling haemoglobin level—haemodilution and continued bleeding. In this connexion the limits of accuracy of our method must be taken into account: before it was possible to diagnose further loss of blood the difference in successive estimations must exceed the experimental error. We have taken deficits in excess of 200 ml. of red cells as positive evidence of bleeding. There have been only a few cases in which interpretation of the findings was doubtful.

The indications and purpose of blood transfusion in acute gastro-duodenal haemorrhage vary with the views of different authors writing on the subject: "the presence of sweating or restlessness; anaemic pallor, as shown in the palms of the hands and in the conjunctivae; or a haemoglobin level of 60% or under are our indications for immediate transfusion" (Ogilvie *et al.*, 1952); "the object [of transfusion] was to make the patient fit enough to stand a possible recurrence of haemorrhage or an emergency operation" (Ferguson and Wyman, 1951); "give [blood] at an estimated hydrated 3,000,000 [R.B.C. per c.mm.] and stop at 4,000,000" (Rossett and Stephenson, 1952); "transfusion in every case" (Alsbrough *et al.*, 1952); "early transfusion with the aim of raising the red-cell count to 3,500,000 per c.mm." (Gott *et al.*, 1952). These few excerpts from recent papers show the wide divergence of opinion which still exists. In most of the older publications transfusion was the exception rather than the rule.

We regard transfusions as being of prophylactic as well as of immediate therapeutic value. When symptoms and signs of shock are present transfusion is obviously a matter of urgency; but people may lose large amounts of blood without accompanying shock, and the fallacy of judging the size of the loss from haemoglobin estimations has already been pointed out. Such patients may readily develop severe shock if further bleeding takes place, and their resuscitation at that stage may be a problem of the greatest difficulty, while emergency surgery may then be impossible. Moreover, a mild or moderate haemorrhage may progress to a severe one. Further, it is well recognized that the presence of anaemia impairs the action of organs like the heart, liver, and kidneys, and probably also the chances of healing at the ulcer site. It is likely that patients over 50 are progressively less tolerant of anaemia, and that this accounts for the rising mortality in the older age groups. Nearly 80% of

our patients were over 50. These arguments have persuaded us to transfuse every case of acute gastro-duodenal haemorrhage and to attempt to replace completely all the red cells which have been lost.

Many observers have in the past stated their fear lest transfusion may cause renewed bleeding once it has been arrested. Like other recent authors, we have found no evidence of this happening in our patients. It is probably of some importance to give the blood slowly so as to increase the blood volume and raise the blood pressure gradually, but this should not preclude rapid administration where there are signs of shock or the patient has to be prepared for emergency surgery. It is likely that prolonged hypotension contributes significantly to the fatal outcome in some cases, and slow transfusion may not be adequate to raise a dangerously low blood pressure to a safe level.

The transfusions given by us were generally large and often massive. The danger of overtransfusion has been widely discussed, and in our patients we have watched carefully for any signs which might have indicated it. It is gratifying that with one exception these have been completely absent. The exception was a man of 84 who died several days after arrest of bleeding from a chronic duodenal ulcer and after transfusion of 7 pints (4 litres) of whole blood. At necropsy moderate pulmonary oedema was present; possibly this was partly caused by the transfusion and might have been avoided if packed red cells had been given instead of whole blood. This patient was, however, extremely senile, and death did not occur during or soon after transfusion; nor were any signs of respiratory distress noted at any stage. For these reasons the significance of the transfusion causing death was doubtful. This fatality occurred early in our series, and since then we have often given packed red cells instead of whole blood, especially when the history of bleeding extended over several days and when the plasma volume was in the vicinity of normal. It should also be mentioned that severe haemorrhage in elderly patients sometimes causes signs of acute coronary insufficiency with or without congestive heart failure, and that in this series there were several instances—at least three with actual myocardial infarction. All of these were greatly benefited by adequate transfusions, and the signs of failure disappeared as a result.

Downie's (1952) suggestion that administration of large quantities of stored blood might interfere with wound-healing if surgery became necessary has not been borne out by our experience. It is improbable that the requirements of these patients could be met entirely from fresh as opposed to stored blood, however adequate the resources of the transfusion service.

It is not our purpose to discuss the still controversial question of the place of emergency operations in the treatment of acute gastro-duodenal haemorrhage. With the indications previously quoted such operations were performed in 14% of our patients. Mainly through lack of sufficiently vigorous resuscitation, it was impossible to make fit for surgery several other patients who might have profited from it and who died in its absence. We believe that 15 to 20% of the members of a series composed like ours will probably need to be operated on in the acute stage. Our mortality rate of 8.3% in 12 partial gastrectomies—several of which were performed on patients with serious complicating diseases—seems encouraging, and to bear out the statement made by Amendola (1952) that emergency subtotal gastrectomy if performed early may be done without significantly greater risk than the elective procedure. We are prepared to believe that our total mortality rate could have been lowered if we had followed the policy of Stewart *et al.* (1950), who perform emergency gastrectomy on all patients who have had a blood loss in excess of 40% of their V.C. This would have involved operations on nearly 80% of our patients, or about 75 emergency gastrectomies in one year. Emergency surgery on this scale would appear to demand very special facilities, which unfortunately do not at present exist at our hospital.

Comparison with a Control Series

We mentioned above the difficulty of comparing the results yielded by different methods of treatment of acute gastro-duodenal haemorrhage. Nevertheless some standard of comparison is necessary in order to assess the success of any therapeutic regime. For this reason we have analysed a second unselected series of 93 patients with acute gastro-duodenal haemorrhage who were treated at Christchurch Hospital during the eighteen months immediately preceding the introduction of the new regime.

This control series consisted of 68 men and 25 women, with an average age of 59 years; 71% were over 50 and 47% over 60 years. This series was therefore slightly younger than the experimental series. In 86 patients (92.5%) treatment was medical and in 7 (7.5%) by means of emergency surgery. The amount of blood given to these patients varied from 0 to 21 pints (11.9 litres), with an average of 2½ pints (1.4 litres). Half the patients received no transfusions. The distribution of diagnoses was very nearly the same in both series. The mortality rate among the controls was 17.2% (16 cases), with an average age of 64 years. One of the deaths followed emergency surgery.

The experimental and the control series appear comparable as regards age and sex distribution and diagnosis. It is difficult to compare the severity of bleeding as no blood-volume estimations were done on the controls. From a scrutiny of the clinical records it appears, however, that no gross difference existed, and such differences were not in any case likely to be important in what amounts to the two halves of one continuous list of 186 admissions. The two series differ, however, greatly in the quantity of blood which was given to individual patients. Whereas an average of 7.9 pints (4.5 litres) was transfused in the experimental series, the controls received only 2½ pints (1.4 litres), and 50%, among them three fatal cases, were not transfused at all. Five other fatal cases received fewer than 4 pints (2.3 litres) each. The percentage of emergency operations performed on the controls was about half that in the experimental series. We believe that these differences in treatment were probably largely responsible for the reduced mortality rate in the experimental series (7.5% as against 17.2%). This reduction of over 50% in the total mortality is statistically significant ($\chi^2=4.02$; $P<0.05>0.02$).

When comparing our results with those reported in the literature we can take into account only those series which resemble ours in age distribution and severity of bleeding. After a careful search we have found only one report which fulfils these conditions. Tanner (1951) includes in his "Period No. 5" a total of 74 patients 55% of whom were aged over 60 and 34% over 70; 18% of these had emergency operations. The total mortality was 13.5%. In Avery Jones's (1947) series of 411 cases the total mortality was 7.8%. The average age was, however, distinctly lower (33% over 60), although at the time of publication this appeared to be the oldest known series. It was interesting that among Avery Jones's patients 12% of those between 60 and 69 and 21% of those aged 70 and over died. The comparable figures for the present experimental series are 8.3% and 8.6% respectively. We may therefore conclude that our results compare favourably with those of other authors who were working with material similar to that encountered by us. It may also be tentatively concluded that increasing age among patients suffering from acute gastro-duodenal haemorrhage does not necessarily lead to a rapidly increasing mortality rate, provided that the criteria of severity and the methods of treatment are equally applied in all age groups. Of these methods the most important would appear to be early adequate blood transfusion together with emergency surgical operation in suitably chosen cases.

Summary

A method of treating patients with acute gastro-duodenal haemorrhage is described. Its most impor-

tant features are early complete replacement of the lost blood in all patients, and emergency surgical operation in selected cases.

Employment of this method led to a halving of the mortality rate at Christchurch Hospital.

The results in a series of 93 admissions compare favourably with those reported in the literature.

We acknowledge with gratitude the help of Mr. J. T. Murray, hospital biochemist, who standardized and supervised the blood-volume estimations and made many important contributions to our work; and of Drs. A. F. Burry and A. V. Kurta, who assisted throughout the course of these investigations. The following surgeons and physicians were in charge of the patients included in the experimental series: M. H. Aiken, L. A. Bennett, W. H. Bremner, P. W. Cotter, W. M. Cotter, J. K. Davidson, H. E. H. Denham, D. McK. Dickson, M. K. Gray, J. F. Landreth, D. G. Radcliffe, and W. L. F. Utley. Without their help and co-operation this work could not have been undertaken.

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ARSENAMIDE TREATMENT OF FILARIASIS DUE TO *W. BANCROFTI* AND *A. PERSTANS*

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Arsenamide is a trivalent arsenical, and has the formula: $(\text{COOH} \cdot \text{CH}_2 \cdot \text{S})_2 = \text{As} \begin{array}{c} \diagup \quad \diagdown \\ \text{---} \end{array} \text{CO} \cdot \text{NH}_2$. It was first employed in the treatment of *Wuchereria bancrofti* infections by Thetford *et al.* (1948), when they reported the treatment of six cases. Since then the compound has been used by various other workers as summarized in the discussion below. This paper describes the results obtained in the arsenamide treatment of 37 cases of filariasis in Gambia, British West Africa, and the action of suramin in two trypanosomiasis patients whose blood contained *bancrofti* microfilariae.

Methods.—Four groups of cases were investigated: (1) Two cases of yaws were treated under close observation in the ward as a preliminary test for tolerance. (2) Eleven cases of filariasis were treated in the ward under similar close observation. (3) Twenty-one cases were treated in a village; among these there was one fatality due to acute hepatic necrosis. (4) Five cases were treated in the ward with low doses and special

precautions against toxic effects. For the present work the drug was supplied in 5-ml. ampoules of 2.5% buffered solution.

Group 1. Two Cases of Yaws

Case 1.—A man aged 46 complained of pain all over the body. He weighed 60 kg. He was given one intravenous injection of 5 ml. arsenamide, followed the next day by one injection of 7.5 ml. and then 10 ml. daily for 10 days (2 mg./kg. arsenamide, 3 mg./kg., and then 4 mg./kg.). He vomited after the fifth and sixth injections; occasionally a trace of albumin was found in the urine. During treatment he lost 3 kg. in weight, which he subsequently regained. His previous symptoms cleared up.

Case 2.—A man aged 25 had ulcers on the legs and on an arm. He weighed 66 kg. He was given the same injections as in Case 1 (1.9 mg./kg. arsenamide, 2.8 mg./kg., and then 3.8 mg./kg.). He did not vomit at all, but lost 2 kg. in weight, which was regained; occasionally a faint trace of albumin was found in the urine. The ulcers cleared up rapidly.

These cases suggested that 10 ml. of the solution (approximately 4 mg./kg.) daily would be tolerated. The dose level which was adopted for the trial against *W. bancrofti* was half this—namely, 5 ml. (about 2 mg./kg.) daily for 12 days.

Group 2. Cases of Filariasis Treated in Hospital

Eleven cases were treated in the research ward at Fajara. On admission the patients were examined clinically for any contraindication to treatment; and then two or three days were allowed to elapse so that the microfilaria cycle could settle after the change in habits. At 10 p.m. on the evening before the injections of the drug were to begin, two lots of 20 c.mm. blood were taken from the finger-tip and spread on a slide for enumeration of microfilariae in the usual way. Throughout the trial all the slides were examined and the microfilariae enumerated by one of us (J. A. McF.). All subsequent measured quantities of blood in the cases treated in the ward were taken within a few minutes of 10 p.m. Conditions were further standardized by all the injections being given in most cases within a few minutes of 10 a.m. The urines from these cases were examined daily for albumin, each patient was weighed daily, and a watch was kept for any signs of toxicity of the drug, particularly vomiting.

Results

Table I records the microfilariae counts of the 11 patients treated in the ward. Four to five days after the first injection the total number of *bancrofti* microfilariae had decreased by 22%; at nine days it had decreased by 86%; and at 12 days the total reduction was 98%. Subsequently, only occasional microfilariae were found in the blood of these patients. Finally, when the last blood samples were taken (at six months) all the patients were free from microfilariae except for one who still had two microfilariae per 40 c.mm., and one who still had one microfilariae per 40 c.mm. (at three months).

In eight of the patients *perstans* microfilariae were also present initially; 70–200 days after treatment their total numbers were reduced by 70%, and in four the blood became negative.

Toxic Features

Vomiting.—Three patients vomited occasionally. One other patient (Case 10) vomited a quarter to three hours after each injection; she was receiving the largest dose per kg. of body weight, and treatment was stopped.

Headache (4 cases).—This is difficult to assess, as it is a common complaint among Africans.

Signs of Death of Adult Worms or Allergic Reactions.—Two patients had pyrexia. One other patient developed enlarged tender glands in the axilla and one developed a tender epididymis.

Loss of Weight (1 case).—This was the patient (Case 10) who vomited considerably.