BLOOD VOLUME IN SURGICAL DISORDERS

By W. C. WILSON, M.B., F.R.C.S.E.

Regius Professor of Surgery, University of Aberdeen

Methods of measuring the circulating blood volume in man have been available for the past fifty years but the surgical disorders in which measurements have been recorded are rather few. This is the more surprising when one considers the striking blood volume changes which have been found in one surgical disorder, severe trauma. Doubtless many clinicians have been deterred by the technical difficulties of most methods and even more by the conflict of opinion on their accuracy. Yet it may be argued that there are now methods to hand which are simple and precise enough for clinical investigation, and that a wider application of blood volume measurement might lead to new knowledge. My colleagues—Mr P. H. Theron, Mr C. D. L. Cromar, Mrs S. Konstam and Mrs I. E. James—and I have made numerous measurements in surgical disorders over the past four years and have found that, new knowledge apart, they have paid an unsought dividend in improved therapy. But that, after all, is a common enough experience. In this lecture I shall deal in the main with the blood volume in abdominal emergencies and surgical operations; recent work, relevant to the main theme, on haemorrhage and trauma will be reviewed and an account, necessarily brief, will be given of methods of blood volume estimation.

Blood Volume Estimation in Man

Four methods which seem to have the best claims to convenience and precision will be mentioned but there are many others which are modifications or are based on similar principles.

(a) The carbon monoxide method, introduced by Haldane and Smith (1900), measures directly the red cell volume. The subject inhales a known volume of CO from a closed, re-breathing circuit and the blood concentration of CO is measured when equilibrium in the system has been reached. The precision of the method has been much enhanced by improved methods of measuring small quantities of CO in blood (Scholander and Roughton, 1943) and a great advantage is that the estimation is unaffected by hæmolyisis or cloudiness of samples. It is still uncertain, however, how much CO leaves the blood to combine with other substances like myoglobin. Slow losses can be allowed for (Root, Roughton and Gregersen, 1946) but not rapid losses. The total blood volume is calculated from the red cell volume and the hæmatocrit of venous blood. The question of the hæmatocrit will be discussed later.

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(b) The dye-haematocrit method of Keith, Rowntree and Geraghty (1915) measures directly the plasma volume and from the plasma volume and the haematocrit of venous blood the total blood volume is calculated. A known quantity of a non-toxic, non-diffusible dye is injected intravenously, the dye concentration of the plasma is measured after time is allowed for mixing in the circulation and from the dilution of dye in the plasma the plasma volume is calculated. The blue dye T-1824 (Evans Blue) has now supplanted the red dyes (vital red and Congo red). Plasma dye concentrations are measured by a photoelectric absorptiometer with a high degree of precision provided there is no haemolysis or cloudiness of the samples; extraction of dye (Harington, Pochin and Squire, 1940) is time-consuming and complicated. When dye concentrations are plotted against time the curve shows an initial steep fall, up to about nine minutes after injection, followed by a slowly falling straight-line “disappearance slope.” It is assumed that the initial fall coincides with the time of mixing in the blood, and that dye leaves the circulation during mixing at the same rate as during the later phase; on this assumption the disappearance slope can be extrapolated back to the time of injection to give what would, theoretically, have been the value of dye concentration if no loss had occurred. Unfortunately the technique used varies considerably. There is no accepted rule on the number or timing of samples. Plotting of dye concentrations is usually done linearly, but sometimes semi-logarithmically (Noble and Gregersen, 1946). Extrapolation is not always employed; Davis (1942) uses a single sample taken at ten minutes after injection, while Harington, Pochin and Squire (1940) average the concentrations at 10, 20 and 60 minutes.

(c) The differential agglutination method (Ashby, 1919) is an ingenious procedure. A group A subject is transfused with a known number of group O red cells and, after time is allowed for mixing, blood samples are taken. The group A cells of the sample are agglutinated with a potent antiserum and the group O cells are counted. Details of the method with recent improvements can be found in papers by Barnes, Loutit and Reeve (1948a, b).

(d) The radioactive isotope method measures the red cell volume. The principle is that red cells labelled by radioactive iron (Gibson, Peacock, Seligman and Sack, 1946) or radioactive phosphorus (P32) (Hevesy and Zerahn, 1942; Hevesy, Köster, Sorensen, Warburg and Zerahn, 1944; Mayerson, Lyons, Parson, Nieset and Trautman, 1948; Reeve and Veall, 1949) are injected intravenously, blood samples are drawn at intervals afterwards and their radioactivity measured. The most recent method of Reeve and Veall (1949) seems to be one of considerable precision.

Discussion of Methods

It is not known which method, if any, measures the true blood volume. Barnes, Loutit and Reeve (1948a, b) have compared the
dye-haematocrit with the differential agglutination method and Reeve and Veall (1949) have compared the dye-haematocrit with the radioactive $\text{P}_{32}$ method. In both instances the red cell volume by dye-haematocrit is higher than by the other methods, and by a very constant amount (ratio $1:0.85$). It is now recognised that in the conventional haematocrit 4 or 5 per cent. of the plasma is trapped in the red cell column (Gregersen and Schiro, 1938). But the discrepancy between the dye-haematocrit and $\text{P}_{32}$ red cell volume is still present after correcting for this error (Reeve and Veall, 1949). The explanation given for the discrepancy is that the venous haematocrit is higher than the body haematocrit (the red cell-plasma ratio of all the blood in the body) which, in turn, is higher than the haematocrit of blood in the smallest blood vessels. That some difference between the haematocrits exists is supported by evidence from various sources. On the other hand, the blood volumes measured by CO and dye-haematocrit have been found to correspond quite closely (Root, Roughton and Gregersen, 1946; Courtice and Gunton, 1949a, b) and the accuracy of the CO measurement has stood the test of bleeding and transfusing blood. These results suggest that the difference between venous and body haematocrit is insignificant or, at least, is too small to affect the calculation of blood volume from the corrected venous haematocrit. This opinion is shared by Mayerson et al. (1948), who compared the dye-haematocrit with the $\text{P}_{32}$ method, but in their work the venous haematocrit is corrected for the trapping of 8.5 per cent. plasma in the cell column—a figure confirming Chapin and Ross (1942), but higher than that found by Root et al. or Reeve and Veall. The CO cell volume, apparently, has not been compared directly with the $\text{P}_{32}$ or differential agglutination cell volumes. The question of the relative accuracy of the methods thus remains undecided.

From the standpoint of convenience the dye-haematocrit has a long lead over the others, especially for the investigation of acute and dangerous reduction of blood volume. The CO method is not without risk in these circumstances, and the others are too restricted in their application or too complicated.

Our Own Methods

We selected the dye-haematocrit method (T-1824) for our investigations. Our methods in investigating peritonitis have already been detailed (Theron and Wilson, 1949) but they have been modified for research problems requiring greater accuracy. Important points are emphasised below.

All patients are investigated under basal conditions and in the post-absorptive state. Injections of dye are made from a specially calibrated syringe. Blood samples are taken without stasis and therefore from the femoral vein or artery when the circulation is greatly depressed. Samples are taken at 10, 20 and 30 minutes after injection and the dye disappearance slope extrapolated to injection
time. Plasma dye concentrations are determined in the usual way using a photoelectric absorptiometer and a dye calibration curve previously constructed for the sample of dye in use; the determinations are completed within one or two hours of taking samples. As a check on the spun haematocrit, Hb. is estimated by an accurate photoelectric method. The specific gravity of blood and plasma is measured (copper sulphate), giving figures for Hb., haematocrit and plasma proteins. Corrections are made: (a) for dilution by heparin, (b) for fluid shifts into or out of the circulation (Noble and Gregersen, 1946), (c) on the spun haematocrit figure (0.95). When swelling of the red cells occurs (see Dyson, Plaut, and Vaughan, 1944) the haematocrit figure is derived from the Hb. estimation and similarly corrected.

A simpler method can be adopted for routine clinical work. A single sample is taken at ten minutes after injection and the haematocrit is derived from the Hb. or specific gravity estimations. According to Noble and Gregersen this method of estimating plasma volume involves an average error of 1.3 per cent. (corrected for fluid shifts) or 3.3 per cent. (uncorrected).

HÆMORRHAGE AND SEVERE TRAUMA

It must be admitted that the numerous investigations made during the recent war on haemorrhage and severe trauma have produced little that is new or startling; here and there, however, they have cleared up doubtful points or determined a change of emphasis.

Blood volume changes after haemorrhage have been studied in man by removal of 540 ml. blood (Dyson, Plaut and Vaughan, 1944) and of larger amounts up to 1200 ml. (Ebert, Stead and Gibson, 1941). After the smaller bleedings dilution begins as early as thirty minutes, it may be well advanced at two hours but usually is not complete till twenty-four hours; the diluting fluid is somewhat deficient in protein, and some of it passes into the red cells. Not infrequently overdilution occurs. Generally speaking, dilution after bleeding is a slow process in man. There is no evidence that any significant number of red cells is added to the circulation (Ebert et al., 1941). When a litre of blood or rather more is withdrawn completion of the diluting process is still further delayed. The right auricular pressure falls but no other change is found unless the subject faints; and fainting is common with such losses. A faint is initiated by sudden vasodilatation in the skeletal muscles, which lowers the peripheral resistance and produces an abrupt fall of arterial blood pressure, but without a corresponding reduction of cardiac output or right auricular pressure (Barcroft, Edholm, McMichael and Sharpey-Schafer, 1944).

Still larger losses have been studied only in cases of accidental injury; here the conditions have been less completely under control but the studies have been very comprehensive (Cournand, Riley, Bradley, Breed, Noble, Lauson, Gregersen and Richards, 1943). We are dealing now with the condition of hæmorrhagic “shock”
when 30 to 50 per cent. of the blood volume has been lost. Presumably there has been no fainting, or bleeding has continued in spite of fainting or been renewed after recovery from fainting. The peripheral resistance is raised by widespread vasoconstriction, the cardiac output, right auricular and arterial pressures are low and the arteriovenous oxygen difference is increased. Failing transfusion, profound and progressive changes in tissue oxidation and in oxygen consumption, severe acidosis and other features of stagnant anoxia supervene. It is now generally agreed that the central feature of traumatic “shock” is a reduced blood volume, that the reduction is due entirely to haemorrhage, that there is no generalised increase of capillary permeability, that haemoconcentration appears only when plasma is lost, as in burns, and that such plasma loss is confined to the site of injury; further that the dye method is not invalidated by the circulatory changes during “shock.” Whether prolongation of the period of anoxia can produce a state irremediable by transfusion—the so-called “irreversible shock”—is undecided. In clinical practice it is extremely difficult to find examples of injury which have proved fatal despite adequate transfusion and when all causes of death other than prolonged anoxia can be excluded. In passing, mention may be made of some recent observations on “vasomotion” and on the responses of the small blood vessels to haemorrhage (Chambers, 1948). In the early stages of haemorrhage a vasoexcitor substance is produced in the kidney, but later a vasodepressor substance is elaborated in the liver and elsewhere; this has now been identified as ferritin or apoferritin (Mazur and Shorr, 1948). And Frank, Seligman and Fine (1946) have suggested that transfusion through the liver itself is necessary for recovery from advanced haemorrhagic “shock.” However tempting it may be to relate such observations to “irreversible shock” some results by Reinhard, Glasser and Page (1948) indicate the need for caution.

Severe trauma, of course, often proves fatal although haemorrhage is controlled and the blood volume is fully restored and maintained; common examples are injuries to special organs, such as the brain and lungs, and injuries complicated by massive bacterial infection or fat embolism. Abdominal injury, too, may be followed by complex circulatory disturbances. Chute, Cleghorn and others of the Canadian Army Shock Research Team (Canadian Reports, 1945) have found that this injury may be fatal within a few hours, more often within the first twenty-four hours after operation, and with a peculiar type of circulatory collapse, despite adequate transfusion and a normal or high blood volume. The majority of fatalities, however, are due to renal failure several days later.

Recent investigations have directed particular attention to the effects of haemorrhage and oligæmia on the renal circulation. We shall not deal here with the striking renal lesions of crush injury and the much discussed “lower nephron nephrosis,” but apparently injury
involving a large reduction of blood volume is followed by active renal vasoconstriction which persists long after the blood volume and cardiac output are restored (Lauson, Bradley and Cournand, 1944). This conclusion is derived from the study of renal clearances and it is not yet certain that the results of clearances are reliable in the special circumstances. Obviously the kidney can suffer severe damage from prolonged vasoconstriction and anoxia. But the problem is not a simple one. Renal failure is not a common cause of death after battle wounds; in the Canadian experience less than 1 per cent. of the more severely wounded men die from this cause. And renal failure is much commoner after abdominal wounds than after limb wounds although the average blood loss is distinctly greater after limb wounds. How far bacterial infection is responsible for the peculiar circulatory collapse and the later renal failure of abdominal injury is unknown but, as we shall see, similar changes are found in peritonitis.

PERITONITIS

Blood volume and other changes in severe peritonitis have already been published (Theron and Wilson, 1949) and a brief summary only is required here.

Common changes are a reduction of blood volume, mainly of plasma volume, a parallel reduction of total circulating protein and a disproportionate fall of total circulating albumin. Evidence of impaired liver function is found by bromsulphthalein retention and thymol turbidity tests, and of impaired renal function; for instance, in the abnormal relations between plasma and urinary chlorides, in oliguria, azotemia and poor concentrating capacity. In patients who recover the volume and protein deficits are speedily corrected, or overcorrected, by intravenous infusion, except that of total circulating albumin, which may persist for weeks; liver function is quickly restored but kidney function remains disturbed for days. Sometimes the cell volume declines from the fourth day for two weeks or longer. A fairly typical case of recovery from peritonitis is quoted below.

Case Report

James S., 25 years, was admitted with acute appendicitis of about 4 days' duration; he had vomited on only two occasions. At operation gangrenous appendicitis, diffuse peritonitis with copious purulent exudate and mild distension of ileum were found: appendicectomy with drainage was done. Before operation the following reductions were noted: plasma volume 20 per cent., blood volume 16 per cent., total circulating protein 32 per cent., total circulating albumin 20 per cent. Pronounced hypochloraemia was present with chlorides in urine, liver function was impaired. The course is shown in Chart I.

Points. (1) Normal blood pressure and efficient circulation throughout.
(2) After infusion, recovery of volume levels, with overswing of plasma volume, and recovery of total circulating protein (behaviour of albumin atypical).
The causes of the plasma volume reduction of peritonitis are, in all probability, (a) plasma exudation in the zone of inflammation (as in the case quoted), or (b) ileus with large fluid and salt losses; sometimes both are present. The initial disappearance of red cells might be explained by stagnation in some part of the vascular bed, possibly the zone of inflammation; since sometimes, as in the above case, a rise of cell volume follows infusion. The later slow decline of cell volume may be due, in part, to extravasation and loss of cells into the wall and lumen of the inflamed and obstructed bowel. We have found, in fact, that fluid removed by gastric suction may contain iron.
equivalent to 30 ml. blood per litre of fluid; but often it is much less and some other mechanism seems to be acting. Of some interest is our observation that with a sudden development of malignant peritonitis and ascites the plasma volume falls, and rises during infusion above the normal level, while the cell volume remains unchanged.

There is a strong suggestion of adaptation to a reduced blood volume. When peritonitis develops slowly over several days the plasma volume may be reduced by 30 per cent. or more, without a fall of blood pressure or other indication of serious circulatory insufficiency; we have found a reduction of at least 40 per cent. in a case of protracted bile peritonitis. Such falls developing in a matter of hours would produce profound collapse. The adaptation is decidedly less striking than in severe anaemia where total blood volumes of 2 litres or less have been recorded (McMichael, Sharpey-Schafer, Mollison and Vaughan, 1943).

In fatal peritonitis the normal level of blood volume is often not restored by infusion. The signs of a grave illness and of progressive deterioration are; of course, manifest but the blood pressure level is usually maintained till a few hours before death. No doubt oligemia, or a failure of adaptation to it, is sometimes responsible for the final collapse, but not always; the blood volume may be normal shortly before death. Bacterial intoxication probably plays an important part.

The renal disturbances of peritonitis are much accentuated in fatal cases especially if oligemia persists. Renal clearance measurements are then difficult and unreliable. But in some surviving cases the clearances of thiosulphate and para-aminohippurate are greatly reduced and for long periods. It is difficult to believe that vasoconstriction could be so protracted; tubular damage must be suspected. The kidney evidently suffers injury in peritonitis but how far the injury is produced by renal vasoconstriction during oligemia and how far by bacterial intoxication is undecided. Simple fluid depletion, however, can be followed by striking circulatory and renal disturbances and a remarkable example seen in surgical practice is quoted below.

**Case Report**

Mrs A., 66 years, was operated on for chronic cholecystitis 23 days before the investigation began; the gallbladder was removed and the common bile duct drained. Progress was at first fairly satisfactory. The average daily loss of bile was 350 ml.; the average daily urinary output was 800 ml. There was no sign of peritonitis but from the 16th day the patient became depressed and apathetic, and ate and drank very little. On the 23rd day the blood pressure fell to 70/40 mm. Hg. In spite of this fall she passed in the next 7 hours about 700 ml. urine (S.G. 1.012) before infusion was begun. The reductions were: plasma volume 34 per cent., blood volume 26 per cent., total circulating protein 31 per cent. Infusion was started with a litre of plasma. The course is shown in Chart 2.

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Points. (1) Prompt response of blood pressure (70/40 to 105/60 in 4 hours), plasma volume, total circulating protein, azotæmia and hæmocoagulation to the large infusion. Some fall of cell volume during the next 11 days.

(2) Prolonged impairment of renal function. Clearances were still low and the urine of fixed low specific gravity 11 days after infusion begun.

(3) Seven months later there had been a large gain of body weight, increases of cell volume and total circulating protein, and the clearances were nearly normal for her age.

Interesting features are the pronounced reduction of plasma volume and the disappearance of circulating protein without, apparently, great loss of fluid. No cause could be found except restricted intake. The low clearances eleven days after beginning infusion are more likely due to tubular damage than to persistent vasoconstriction.
ACUTE INTESTINAL OBSTRUCTION

Simple occlusion of the bowel and strangulation of small segments may be associated with a fall of plasma volume, but only when fluid and salt losses have been large. Strangulation of larger segments, when considerable quantities of blood are trapped in the bowel and mesentery, is followed by pronounced reductions of plasma and cell volumes. In the early stages the fall is easily corrected by transfusion of blood but in late strangulation, when the bowel has lost, or is losing, its viability, the circulatory disturbance and the response to treatment are similar to those in very severe peritonitis. In our experience it is always better to resect doubtfully viable bowel, even if the patient is desperately ill, than to return it to the peritoneal cavity.

SURGICAL OPERATIONS

Blood Loss

It is an instructive and salutary experience for an operating surgeon to measure the blood lost during operations. The usual method is to extract the Hb. from all bloodstained material by washing it in a measured volume of water, to estimate the Hb. concentration of the stained fluid and of samples of the patient's blood and to calculate the blood loss according to the formula:

$$\text{Blood loss} = \frac{V_F \times Hb_F}{Hb_p}$$

where $V_F =$ volume of fluid, $Hb_F =$ Hb. of fluid, $Hb_p =$ Hb. of patient's blood. The result is always an underestimate because extraction is incomplete; also, an unknown quantity of blood is left in the wound and no account can be taken of bleeding after the wound is closed. But with care and accurate haemoglobinometry the error is probably not large. To allow for the underestimate we add 10 per cent. of the figure obtained. Losses during some operations are shown in Table I.

These correspond fairly well with those quoted by Coller, Crook and Iob (1944) and by others in the literature.

The loss during any one type of operation varies greatly. In one case of partial gastrectomy a loss of 1273 ml. is incurred largely by a slipped ligature which remains undetected for some time. In another case the loss is only 157 ml. because the blood pressure falls at the beginning of operation, and remains at about 50 mm. Hg. (systolic) throughout, returning to normal afterwards without transfusion. Similar events explain the small loss of 323 ml. in an operation involving removal of the whole stomach, the spleen and greater part of the pancreas. The exceptionally large loss of 1023 ml. during cholecystectomy is due to prolonged bleeding from the gallbladder bed of
the liver in a case of portal hypertension. The largest average losses, in our experience, are found in abdomino-perineal excision of the rectum. We have found that the loss of a litre or more of blood (20 to 30 per cent. of the blood volume) in a prolonged operation produces intense "shock," and when the loss reaches 1200 ml. the blood pressure often becomes unrecordable and the radial pulse impalpable. How often fainting occurs during these operations is difficult to say; a slow pulse is rare but this sign might be annulled by pre-operative atropine.

**TABLE I**

*Blood Loss in Operations*

| Operations                        | Cases | Blood Loss in ml. |
|-----------------------------------|-------|-------------------|
|                                   |       | Max.   | Min.   | Av.   |
| Herniotomy                        | 4     | 40     | 15     | 27    |
| Gastro-jejunoscopy                 | 2     | 100    | 62     | 81    |
| Lumbar sympathectomy              | 4     | 122    | 78     | 94    |
| Resection of intestine or colon    | 4     | 420    | 80     | 230   |
| Total gastrectomy, partial         | 1     | 323    | ...    | ...   |
| pancreatetectomy                  | 5     | 1023   | 45     | 381   |
| On bile passages                  | 10    | 968    | 374    | 546   |
| Brain—acoustic neuroma            | 9     | 1273   | 157    | 559   |
| Radical mastectomy                | 3     | 923    | 280    | 614   |
| Partial gastrectomy               | 3     | 865    | 500    | 730   |
| Splenectomy                       | 2     | 1090   | 948    | 1019  |
| Bone tumours                      | 10    | 1748   | 581    | 1140  |
| Perineal excision of rectum       |       | ...    | ...    | ...   |
| Abdomino-perineal excision of rectum, etc. | 58 |       |       |       |

**Blood Loss and Blood Volume Fall**

The blood loss during operation has been compared with the blood volume fall. The blood volume is measured immediately before and immediately after operation. But when the loss has been 1200 ml. and more the patient's condition often appears so grave and alarming that the volume has to be estimated before the operation is completed (but not, as far as can be managed, during active bleeding) and by a single ten- or fifteen-minute sample instead of the usual three samples. Mixing time is undetermined when a single sample is used and is likely to be delayed when the circulation is so severely depressed. Once or twice a slow transfusion of a measured amount of blood has been started before sampling. For these reasons the volume estimations after large blood losses are not entirely reliable and may be too low. The figures for volume fall would then be too great but, on the other hand, the volume fall is measured before the end of the operation in these cases while the blood loss figure is for the entire duration. The results of seven comparisons are shown in Table II.
TABLE II

Blood Loss and Blood Volume

| Case | Sex and Age | Operation                          | Duration min. | B.P. fall | Blood Loss.   | Volume Changes. |
|------|-------------|-----------------------------------|---------------|-----------|---------------|-----------------|
|      |             |                                   |               |           | ml.           | Per cent. B. V. | Plasma.         | Blood.         |
| A    | F. 60       | Laparotomy                        | 30            | Nil       | 55            | 2               | +163            | +157           |
| B    | F. 47       | Cholecystectomy                   | 80            | Nil       | 45            | 1               | +408            | +506           |
| C    | F. 64       | Radical mastectomy                | 90            | Small     | 477           | 14              | -321            | -433           |
| D    | M. 51       | Partial gastrectomy               | 120           | Large     | 877           | 18              | -875            | -1091          |
| E    | M. 67       | Abdomino-perineal excision of rectum | 167       | Large     | 965           | 24              | -317            | -639           |
| F    | M. 71       | Abdomino-perineal excision of rectum | 150      | Large     | 1125          | 20              | -900            | -1607          |
| G    | M. 69       | Abdomino-perineal excision of rectum | 135      | Large     | 1514          | 27              | -1270           | -2510          |

* Figs. in brackets = time of blood volume estimation.

These examples are selected from more than thirty estimations to illustrate certain features and especially some discrepancies between blood loss and blood volume fall; in many cases the correspondence is closer than in the examples. It is clear that in the majority there is a reasonably good correspondence between blood loss and blood volume fall within the experimental errors of the methods. In some cases of small blood loss (see Case B) there is a considerable gain of plasma, which is probably significant, presumably from fluid passing into the circulation. The trend is very distinct and appears in 6 of 8 cases. With large blood losses the volume fall tends to be greater than the blood loss (case F). The discrepancy here may be barely outside experimental error, but in case G the discrepancy is large; here the post-operative volume estimation is done with a single fifteen-minute sample and during a slow transfusion so that, as already explained, the experimental conditions are not quite satisfactory. But the trend appears in nearly all operations with large losses. The discrepancy is mentioned also by Stewart and Rourke (1938) and seems to have been more frequent in their experience than in ours.

If the discrepancy between blood loss and blood volume fall is a real one it would indicate that, during severe operations, a fraction of the blood volume stagnates and passes out of effective circulation. Anoxia and the danger to life would then be disproportionate to the quantity of blood lost. The point is of some theoretical interest, but not now of much practical importance since the practice of transfusing throughout operations of this kind has become general.

**Effects of Hemorrhage**

We may compare the effects of hemorrhage during surgical operation with those recorded in the conscious patient (Wallace and Sharpey-Schafer, 1941; Ebert et al., 1941). It is evident that hemorrhage during operation is more serious. In our experience
transfusion always seems desirable after the loss of 800 ml. to a litre of blood (18 to 24 per cent. of the blood volume) and it becomes imperative and urgent after the loss of 1200 ml. or more (23 to 28 per cent. of the blood volume). By contrast, bleeding the conscious individual up to 1150 or 1200 ml. of blood may produce fainting (and unpleasant features such as unconsciousness and muscular twitchings are recorded) but resuscitation is apparently not required. Surgical operation, of course, introduces many factors which might render the patient sensitive to the effects of haemorrhage. Available evidence certainly implicates anaesthetic drugs, particularly ether and the barbiturates. The rate of bleeding may be important, since repeated small bleedings are less well tolerated than a single, large bleeding of the same total volume. And the influence of trauma itself is still remarkably obscure. The mechanism of sensitisation to haemorrhage is not yet known but there are many indications that the responses of the smallest blood vessels are altered, whereby the flow of blood in the peripheral circulation is seriously retarded. Whether the effective circulating blood volume is reduced by stagnation to the degree suggested by our observation remains to be determined.

I have no time to deal with the examples of increased blood volume we have found in surgical conditions. It is possible that in these conditions we might learn something of the control of blood volume, perhaps some facts which have escaped notice in the study of low volume.

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