experimental haemorrhage, but in each instance blood loss was complicated by anaesthesia. Wigger (1950) observed the changes of arterial oxygen *content* after haemorrhage, and stated that the reduction of arterial oxygen was never great at the end of oligaemic shock. A diminution of arterial oxygen content occurred after bleeding in some of his dogs in which the haematocrit remained unchanged.

Marked arterial desaturation is incompatible with the survival of severely bled subjects because of the reduction of cardiac output. This may well account for the paucity of reports of central cyanosis after haemorrhage.

BLOOD VOLUME IN CHILDREN

by

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KNOWLEDGE OF A patient's blood volume is of value in clinical practice because a normal circulating blood volume is one of the prerequisites of a normal cardiac output. If blood volume is significantly reduced, cardiac output will fall, although compensatory mechanisms may minimize the degree of this fall; while an acute increase in blood volume (over-transfusion) may cause heart failure, especially in a diseased heart. Because of the relationship which exists between blood volume (considered as a static quantity) and circulatory performance, certain pertinent features of the circulation of the child will be discussed first.

CIRCULATION AND BLOOD VOLUME

At birth, the profound adjustments which occur when the circulation changes from a foetal to a neonatal design are associated with two important alterations in blood volume: (1) separation of the foetal or newborn circulation from the placental one; and (2) an increase in the size of the total vascular bed of the newborn when the lungs expand with the onset of breathing.

1. The role of placental blood

During or soon after normal delivery, whether *per vaginam* (Gunther, 1957) or by section (Secher and Karlberg, 1962), an average of about 80 ml. of blood is transferred from placenta to the newborn infant before pulsation of the cord ceases (even without " milking " of the cord), provided the placenta is held high enough above the child's body to provide a satisfactory head of pressure. This volume represents about 25 per cent. of an average infant's total blood volume (assuming such an infant to weigh 4 kg.). However, this sudden increase in blood volume is not accommo-

dated permanently in the vascular bed. In fact, there is at first a sudden rise in haematocrit as plasma volume decreases to maintain the total blood volume relatively constant: the net gain to the circulation is therefore probably not as great as the total amount infused from the placenta.

2. Increase in intrathoracic blood volume

With the first breath of life, thoracic blood volume almost instantaneously increases to an amount which, once equilibrium is established, represents about 20 per cent. of total blood volume.

Following these rapid changes at birth, the development from the neonatal to the mature circulation is one of gradual transition: the adult pattern differs only quantitatively from that of the older child. In the first year of life, the cardiovascular system is characterized by a state of " centralization ", in which most of the blood circulates within an inner core, at the neglect of the peripheral circulation, in particular the extremities. While the normal blood pressure of the infant is only a little below that of a young adult, there is a high peripheral vascular resistance (partly anatomical in nature), the heart rate is rapid and the stroke volume relatively small. The overall effect of this state is to provide relatively little latitude for circulatory regulation. For example, heart rate being already rapid, further increase—the usual means of increasing cardiac output as in exercise—is restricted, because it would only further shorten the diastolic period required for adequate filling of the heart. The amount of residual volume in the heart (end-systolic volume) is also relatively small and prevents a significant increase in stroke volume. Peripheral vascular resistance already being high, the usual compensatory mechanism of the more mature circulation, i.e. peripheral vasoconstriction, cannot be called into action to nearly the same extent. Within a few months, however, this pattern of centralization gradually changes into the mature one, characterized by a relatively larger stroke volume and cardiac output, and lower peripheral vascular resistance.

For the stated reasons, relatively small changes in blood volume may be difficult to compensate for in infancy. Furthermore, the harmful effects of losing relatively small amounts of blood may easily be underestimated. As a corollary, it must be remembered that seemingly small amounts of blood loss, which are of no consequence to the older child or adult, may be of profound significance to an infant. Obversely, only rather small amounts of blood will be required to correct for losses and the dangers of overtransfusion must not be ignored. It is for the latter reason that severe anaemia in infants is treated often by infusion of packed cells, which provides the needed haemoglobin without unduly expanding blood volume.

In evaluating the infant's capacity of compensating for blood loss it

should also be borne in mind that during the newborn period there is increased red cell destruction and for the first few months of life there is a definitely decreased production of red cells.

Methods of measuring blood volume*

There is no fundamental difference in the procedures employed for measuring blood volume in children from those used in adults. All determinations of blood volume are based on the dilution principle: one measures the degree to which an identifiable substance, which is evenly distributed in the total plasma or RBC pool, is diluted within it. Blood volume is then calculated by multiplying the obtained value for plasma or red cell volume by the haematocrit, the latter corrected for differences between venous and total body haematocrit. To obtain the most accurate results, red cell and plasma volumes are measured simultaneously.

Red cell volume

Red cells may be labelled either with ^{51}Cr (emitting gamma rays) or ^{32}P (emitting beta rays). A known amount of red blood cells emitting a known amount of radiation is injected into the circulation and, after allowing for mixing, a measured quantity of blood is withdrawn from a different site of the vascular system and its radioactivity measured. The chromium method has the advantage that any scintillation counter may be employed and that the labelling of cells is an easy procedure. Measurement of beta rays, as is the case when ^{32}P is used, requires rather less commonly employed counters, but it has the advantage that the biological half-life of ^{32}P is short, because phosphorus is rapidly eluted from the RBC: most of it is excreted in urine within the first 24 hours. It is thus possible to repeat daily blood volume measurements without significantly increasing the amount of radioactivity injected with each subsequent dose. If ^{51}Cr-labelled red blood cells are used, repeated blood volume measurements can be made, but because of the persistent radiation background the dose has to be increased to ensure accuracy.

We found that a dose of 0.1 microcurie per kg. of bodyweight gave accurate results in children. This is a dose well below the accepted limit of 0.5 microcurie per kg. bodyweight, and it may thus be used for repeated blood volume studies. We have found that adequate mixing occurs within five minutes of injection and rapid determination of blood volume is thus possible.

Plasma volume

For many years, before the ready availability of radioactive substances, the dilution of various dyes has been used for the estimation of plasma volume. Evans blue (T–1824) has been the most popular, but other dyes have also been successfully employed. The disadvantage of dyes is that

* Details are given in Mollison (1961) or Veall and Vetter (1958).

all of them leave the vascular compartment at a greater or lesser rate. In the case of T–1824, 10 per cent. of the injected dose passes from the vascular compartment during the first hour and 50 per cent. will have disappeared from it after the first 24 hours. In practice, however, it is adequate to use a one-sample technique in which the concentration of T–1824 is measured in the sample drawn 10 minutes after injection of a known quantity. The result is higher by only 1–2 per cent. than that using multiple samples and extrapolating to zero time, i.e. the moment of injection.

^{131}Iodine or ^{132}I-labelled albumin has been extensively used as a preferred alternative to dye dilution. Using labelled albumin has the advantage that one need not allow for disappearance of the injected albumin from the vascular compartment. ^{132}I has a short half-life and may be used for quickly repeated blood volume measurements, but it requires more complicated procedures and apparatus.

Haematocrit

If blood is spun at low revolutions, error is introduced into the calculation because a significant amount of plasma will be trapped between the red blood cells, and the haematocrit will be falsely high. High relative centrifugal force, achieved by 11,000 r.p.m., prevents this error.

Because the space in which plasma circulates is greater than that within which the red blood corpuscles circulate, a correction must be made from venous haematocrit (or, for that matter, arterial haematocrit) to body haematocrit. The generally accepted correction by which venous haematocrit is multiplied is between 0.91 and 0.95.

Calculation of blood volume

Plasma volume (in ml.) is obtained according to the formula:

$$\frac{\text{Volume of solution injected} \times \text{concentration of dye}}{\text{Concentration of dye in plasma at time of injection}}$$

Red cell volume, using labelled red cells, is obtained from the corresponding formula:

$$\frac{\text{Total counts of injected red cell suspension}}{\text{counts/min./ml. of withdrawn blood} \times \frac{100}{\text{haematocrit}}}$$

Blood volume is the sum of the two, if measured independently. Where only one is measured, blood volume is calculated from the formula:

$$\text{Blood volume} = \text{red cell volume} \times \frac{100}{\text{body haematocrit}}$$

or

$$= \text{plasma volume} \times \frac{100}{100 - \text{body haematocrit}}$$

NORMAL VALUES OF BLOOD VOLUME IN CHILDREN (Table I)

The blood volume of the newborn was found to be higher than that of the adult, about 85 ml. per kg. (at a haematocrit of 60) (Mollison *et al.*, 1950). However, when only those infants were selected whose haematocrits were similar to those of adults (i.e. haematocrit of about 42), blood volume was 77 ml. per kg., i.e. very close to the adult figure (Mollison *et al.*, 1950). Considered per kg. of bodyweight, the blood volume of the premature infant is higher than that of the full-term one.

TABLE I

BLOOD VOLUME OF NEWBORN INFANTS AND ADULTS, AS CALCULATED FROM SEPARATE MEASUREMENTS OF PLASMA VOLUME AND RED CELL VOLUME

Subjects	*Average venous haematocrit* (× 0.95)	*Blood volume* (*ml./kg.*)
Newborn infants: Normal ..	59.7	84.7
Selected* ..	42.6	77.1
(Mollison *et al.*, 1950)		
Normal adults	42.5	76.6
(Mollison, 1961) ..		
Children (10–30 kg.)	43	75.4
Infants	38.2	71.5
(Russell, 1949)		

* Infants with haematocrit values within the normal adult range.

Most calculations of blood volume are derived from a measurement of either plasma or red cell volume multiplied by venous haematocrit (corrected for deviations from body haematocrit). It is therefore worth stating that while there is a generally linear relationship between red cell volume (ml./kg.) and haematocrit, this is not the case at all haematocrit values. Plasma volume tends to increase as haematocrit falls below 55 per cent., but the rate of increase in plasma volume is less than the rate of decrease in red cell volume. As a result, blood volume tends to fall slightly as the haematocrit falls. Conversely, for haematocrit values above 55 per cent. the red cell volume rises more rapidly than the haematocrit, while plasma volume decreases linearly: blood volume thus rises (Mollison, 1961).

BLOOD VOLUME IN CHILDREN WITH CONGENITAL HEART DISEASE*

There is little information available on the changes, if any, of blood volume in congenital heart disease. The profound alterations in haemodynamics that occur with many of these lesions, as well as the cyanosis associated with some of them, suggested that blood volume might be significantly affected. The availability of surgical correction of many of the anomalies made it advisable to determine the resting blood volume

* This study has been conducted jointly with Dr. R. Sephton Smith, Lecturer in Haematology, Institute of Child Health, and will be published in detail elsewhere.

in a large number of infants and children with congenital heart disease, particularly as regards the effect of large intracardiac shunt on total blood volume.

Blood volume was measured by means of red cells labelled by radioactive chromium, which was injected into the inferior vena cava or right atrium via a catheter or polythene tube in sedated children as part of the procedure of cardiac catheterization. Preliminary investigation had shown that only 0.1 microcurie per kg. of bodyweight needed to be injected for satisfactory counting and that the withdrawal of 5 ml. of blood five minutes after injection of the labelled cells gave accurate and reliable results. Packed cell volume was obtained by a micro-haematocrit method. The results are shown in Figures 1–3.

Figure 1 shows the relationship between total blood volume and bodyweight per kg., for the group as a whole. The scatter of results was no greater than was to be expected in blood volume determinations of large groups of unselected normal subjects, and the line of best fit gave an average blood volume of about 75 ml. per kg. bodyweight.

When the values of blood volume were plotted against age in years (Fig. 2), the scatter of points was of course much greater, but the resulting graph shows the rapid rise in blood volume during the first two years of life, followed by a smaller rate of increase for the next five or six years. Age also influenced red cell volume significantly in our material: it was 28 ml. per kg. for those over two years and 23 ml. per kg. for those under two years of age.

Figure 3 relates red cell volume to arterial saturation measured simultaneously. The graph illustrates the wide range of red cell volumes (in ml./kg.), but fails to reveal any significant correlation between arterial saturation and red cell volume, other than a trend towards elevation of the latter in the presence of severe desaturation. Even when cases with a large left-to-right shunt (atrial septal defect, ventricular septal defect, or patent ductus arteriosus) as a group were compared with those cases, as a group, with a large right-to-left shunt (Fallot's tetralogy, transposition of the great vessels or pulmonary stenosis with atrial septal defect), no significant difference in blood volume or red cell volume was demonstrated.

In this our results differ from those reported by others. Prader *et al.* (1949) had found red cell volume markedly increased and plasma volume reduced (from 47 ml./kg. to 39 ml./kg.) in children with cyanotic heart disease. Similarly, in a small group (14) of cyanotic children, Cassels and Morse (1962) found a significant increase in blood volume. The discrepancies may well be due to a difference in the patient material. Other factors may also play a role. But it is our impression that infants and children under the age of 2–3 years (who made up a large proportion of the

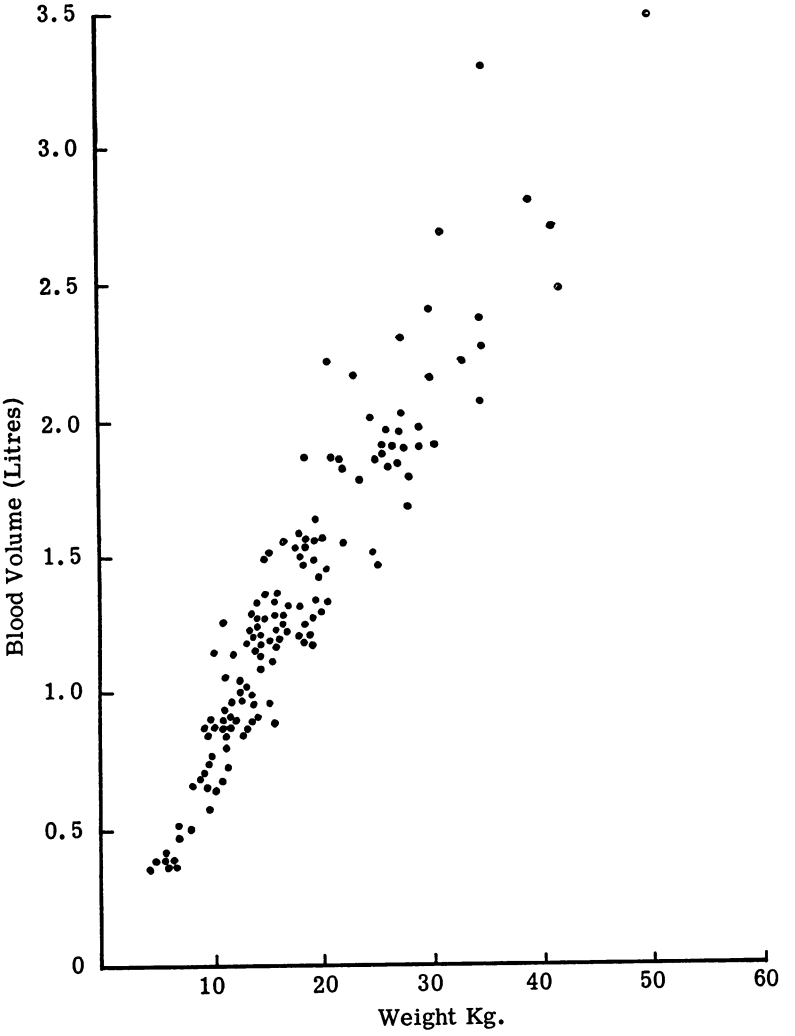

Fig. 1. Relationship between blood volume (in litres) and weight (in kg.) in 130 children with congenital heart disease.

cyanotic cases) behave differently, as far as blood volume and red cell volume is concerned, from older children and adults. Their apparent failure to increase red cell volume (and, secondly, blood volume) needs further investigation.

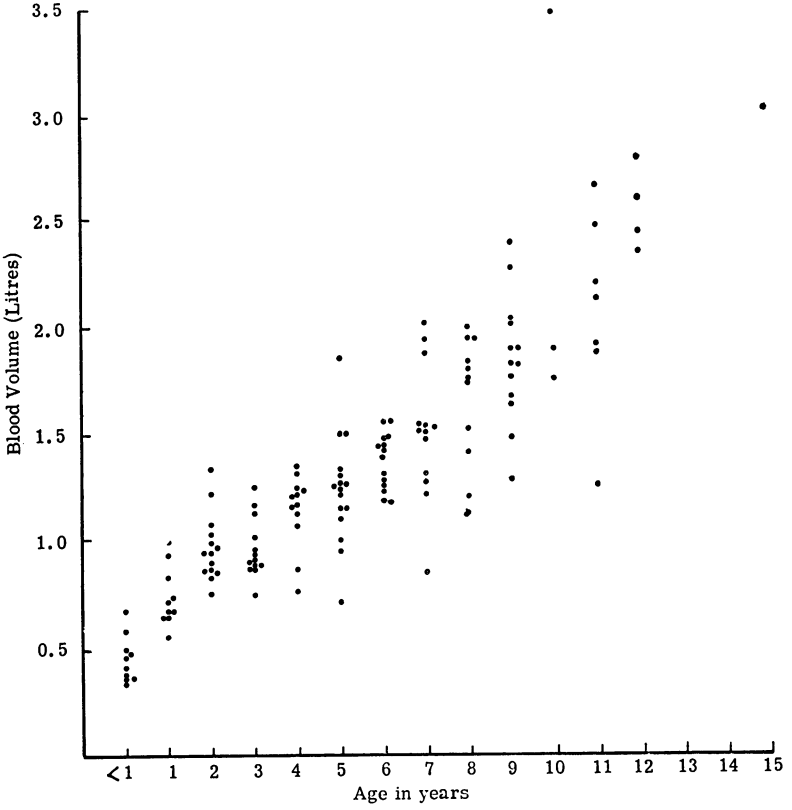

Fig. 2. Relationship between blood volume (in litres) and age (in years) in children with congenital heart disease (same material as in Figure 1).

SUMMARY AND CONCLUSIONS

The measurement of blood volume in children does not differ significantly from that in adults and the values obtained, expressed in ml. per kg. of bodyweight, do not differ significantly from adult values, except for the newborn period where high haematocrit readings cause a deviation. Blood volume averages about 75 ml. per kg., but there is a wide scatter of individual values.

In a personal study of some 130 children, including infants, with various types of congenital heart disease no correlation could be established between type of heart disease and abnormalities of blood volume. This

was true even for a group of cyanotic children. It is not at present known whether the failure of the latter group of patients to increase their red cell volume significantly is a general failure in the younger age group to respond to the stimulus of arterial desaturation or whether it is due to the type of patient included in this study: many were severely handicapped and ill children.

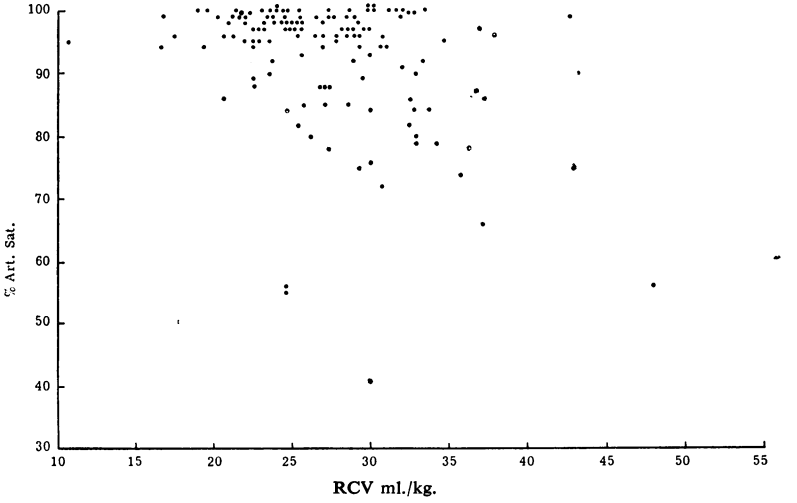

Fig. 3. Relationship between arterial saturation and red cell volume (in ml./kg.) in 130 children with congenital heart disease (same material as in Figures 1 and 2).

While there was relatively little scatter when blood volume was plotted against bodyweight, it was considerable with regard to the values for red cell volume, also expressed in ml. per kg. It would seem that within considerable limits, plasma volume expands or decreases in such a way as to keep the blood volume relatively constant.

A knowledge of blood volume is of particular clinical importance in children, because seemingly small amounts of blood loss may represent a significant proportion of the child's total blood volume.

The various methods of measuring blood volume which are widely employed for adults are equally and as easily applicable to children. In particular, those methods using radioactive red cells or plasma albumin may be safely used in children, even infants, because the radiation dose required for accurate determination is well within accepted limits.

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BLOOD LOSS IN TRAUMA

by

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THE CONCENTRATION OF large numbers of civilian injuries at the Birmingham Accident Hospital has encouraged the application and extension of the lessons learned from the treatment of large-scale wartime casualties (e.g. Grant and Reeve, 1951; Prentice *et al.*, 1954). These lessons are all too often forgotten when, as is common, severely injured patients are thinly distributed amongst many hospitals, none of whose staff acquires adequate clinical experience of major trauma.

SPECIAL FEATURES OF TRAUMATIC BLEEDING

Multiple sources of bleeding

Blood loss in trauma commonly presents clinical features differing markedly from those seen in experimental bleeding and those arising in the course of disease. Severe traumatic oligaemia rarely arises from one area of bleeding as it does in, say, haematemesis or experimental work. In most cases multiple foci of haemorrhage in soft tissues or into body cavities exist, many of them not amenable to surgical haemostasis; this feature greatly alters the clinical picture and increases the difficulty of assessment of blood loss. Difficulties of diagnosis in trauma are frequently caused by the obscuration of signs of one injury by those of another (particularly in cranial or thoracic trauma) and by the development of complications, such as fat embolism or tension pneumothorax, in the course of resuscitation.

Progressive nature of bleeding

Bleeding into the tissues, other than that which can be staunched operatively, frequently continues for at least 24 hours after injury and the blood loss is thus progressive, even after operation, and the circulatory balance is constantly changing.