BLOOD VOLUME DETERMINATIONS IN SURGICAL PATIENTS

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by

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PREFACE:

The work presented in this manuscript was performed during the tenure of a Hosmer Teaching Fellowship in the Department of Experimental Surgery of McGill University from July, 1954 to June, 1955. Experience with the T-1824 method of blood volume determinations as used at the New York Hospital - Cornell Medical Center in 1952-1953 awakened the author's interest in the potentialities of a Blood Volume Laboratory in a teaching hospital with a surgical service which dealt with complicated problems of water and electrolyte metabolism and blood volume homeostasis in poor-risk patients and patients subjected to extensive operative procedures. Over the past several years, Dr. James R. McCorriston of the Department of Surgery of the Royal Victoria Hospital has been interested in the radioactive iodinated human serum albumin (RIHSA) method of determining blood volume and the application of the method to surgical patients of the Royal Victoria Hospital.

Dr. McCorriston suggested this project as a thesis subject and supervised the details of its execution.

It has been a pleasure and a beneficial experience to work with Dr. McCorriston over the past year. Dr. McCorriston has been generous in the time which he has allowed to discussing problems of fluid and electrolyte balance and the thesis subject with the author. Dr. McCorriston's enthusiasm and advice have made this project a stimulating introduction to clinical r esearch.

In the summer of 1954, this project was discussed with Dr. Louis Lowenstein of the Hematology Service of the Royal Victoria Hospital. Dr. Lowenstein was interested in initiating a program of radioactive isotope studies of hematologic disorders for the Hematology Service. It was decided to make this investigation and the developement of a Blood Volume Laboratory, a joint project of the Department of Surgery and the Hematology Service. Under the direction of Dr. Lowenstein, Dr. Maurice R. Dufresne, Clinical Fellow in Medicine of the Royal Victoria Hospital, and the author commenced the work presented in this thesis. It was a pleasure to work with Dr. Dufresne throughout the year. The development of the method used, and the

results presented are the result as much of Dr. Dufresne's work as the author's. Dr. Dufresne has completed an equal number of blood volume determinations in medical patients and it is hoped that our combined data in 500-600 determinations of blood volume may be the subject of publication in the future under the auspices of the Hematology Service and the Department of Surgery of the Royal Victoria Hospital.

Appreciation is due to Dr. Donald R. Webster, Director of the Department of Experimental Surgery and Surgeon-In-Chief of the Royal Victoria Hospital. This project was commenced with Dr. Webster's approval and encouragement and discussed with him throughout the year.

Dr. Carleton B. Peirce, Chairman of the Department of Radiology of the Royal Victoria Hospital, obtained permission from the Atomic Energy Commission for use of the radioactive iodine, approved the proposed project and encouraged the investigation. Dr. Peirce's guidance was most valuable in suggesting details of

safe radiation dosage for adults and children and precautions in the use of the I^{131}.

Dr. Lloyd Stephens-Newsham, Physicist of the Department of Radiology of the Royal Victoria Hospital, provided the counter used and instructed Dr. Dufresne and the author in use of the scaler and the techniques of standardization of equipment. Dr. Stephens-Newsham was kind enough to order the radioactive iodine as required.

Dr. Darrell D. Munro, Surgeon of the Royal Edward Laurentian Hospital, Montreal, invited the author to study the blood volume of patients with tuberculosis at that hospital. Over one month (May-June, 1955) Dr. Munro supervised the investigation and allowed the pre- and post-operative studies and measurements in the operating room to be made.

Dr. David R. Murphy of the Montreal Children's Hospital was kind enough to allow an investigation of blood volume in childhood to be performed on patients of the Surgical Service.

Miss Jeanne M. Wirth, Secretary of the Department of Experimental Surgery, McGill University has typed this manuscript, the tables and the charts. Miss Wirth has been most helpful during the entire year, has facilitated the work of each of the members of the Surgical Diploma Course and has been responsible for scheduling lectures, arranging Seminars, correspondence and innumerable details which have contributed to the value of the year for all of us.

Mr. Paul Roustan has prepared the photographs used and Miss Barbara Heward drew the graphs.

Finally, my appreciation is due to my wife and children who were most patient while the material for this thesis was compiled and the actual writing of the thesis done.

Francis R. Coughlin, Jr.,
McGill University,
August, 1955.

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PART I INTRODUCTION

The surgical service of a teaching hospital presents an unique opportunity for the study of the physiological and pathological response of individuals to alterations in circulating blood volume. Surgeons are frequently confronted with problems relating to the management of dehydration, massive hemorrhage, thermal and mechanical trauma and the preparation of elderly, malnourished, chronically ill patients for major operative procedures. The hemodynamic response of patients to anaesthesia and operation is an important factor determining operative mortality and morbidity rates.

Progress in the developement of new operative techniques of organ resection, vascular anastomosis and cardiac surgery has been associated pari passu with improved pre- and post-operative care, safer anaesthetic techniques, the use of antibiotics and the availability of whole blood for transfusion. At the same time, extensive operative

procedures have been made available to and have even been designed for patients who are poor operative risks. Massive resection procedures such as radical pelvic exenteration are performed for malignant disease which occurs more commonly in patients of advanced age, many suffering from concurrent chronic cardiovascular, renal or pulmonary disease.

Many operative procedures are potentially associated with operative blood loss and replacement which may amount to exchange transfusion (92, 104). Blood loss and replacement of this magnitude can present a serious challenge to the debilitated patient's ability to maintain circulatory homeostasis and equilibrium of circulatory dynamics. The experience of three major wars in the past forty years has focussed the attention of surgeons on the role of the transfusion of blood and plasma expanders in the treatment of hemorrhage and the prevention of the clinical state of shock (134).

The efficacy of the transfusion of whole human blood in cases of acute hemorrhage was noted in the nineteenth century. Blundell (2,5) in 1829 transfused a patient who had had a post-partum hemorrhage. William Stewart Halsted (185) performed a transfusion using a syringe in 1881. Blum (24) stated in 1876 that "hemorrhage was shock and shock, hemorrhage". However, the measurement of blood volume in the casualties of World War I promoted the idea of shock as a problem of acute blood volume deficiency. This concept has been consistently maintained. Stored plasma became available in large quantities during World War II. Although plasma by expanding the total blood volume was efficacious in the treatment of casualties who had sustained wound trauma and hemorrhage, Churchill (32) was of the opinion that whole blood when available appeared to be preferable in restoring blood volume deficits due to whole blood loss. The availability of large quantites of blood, plasma and synthetic plasma expanders during

the Korean War permitted a comparative trial of these agents in the resuscitation of severely wounded casualties. Though plasma volume expanders were satisfactory and eliminated the problem of homologous serum hepatitis, whole blood in large quantities was recommended by Prentice (129,130), Artz (7,8), and Howard (86,87) for the treatment of blood volume deficits due to wound trauma and hemorrhage.

Since 1915, when Keith, Rowntree and Geraghty (94) described the vital red dye method of the measurement of the blood volume in living human subjects a complex and almost incomprehensible literature has developed on the subject of blood volume measurement. The principle expounded by these authors in 1915 continues to be used today although a variety of test substances, modifications of sampling procedure, and technical methods have subsequently been reported.

Practically, surgeons are interested in the blood volume determination as a means of approaching a more rational prescription of transfusion therapy conducive to lowered patient mortality and morbidity. The laboratory determination of blood volume gives information precisely ascertainable in no other way. A laboratory test of blood volume which can be performed simply and provides reliable data in a short period of time can be of great value in guiding transfusion therapy in surgical patients.

Recent reviews (74, 135, 136) of the literature on blood volume determinations emphasize that fairly precise estimates of blood volume can be made with the methods available at present despite the controversy as to which is the better method. However, no ideal method of blood volume determination has yet been developed. The dye T-1824 has been used most widely for the clinical determination of blood volume and has been recommended for the simplicity, rapidity and precision with which determinations may be made.

In 1950 Storaasli, Krieger, Freidell and Holden (166) described the use of radioactive iodinated human serum albumin, known as RIHSA, for the measurement of blood volume clinically. This method offers simplicity, rapidity and precision in the performance of routine blood volume studies. The scintillation counting technique permits tracer doses of radioactivity to be used. Successive determinations are not affected by increasing concentrations of the radio-isotope in the patient's blood, hemolysis or lipemia. Moreover the blue discoloration of the skin which occurs when serial T-1824 studies are performed is eliminated. Time consuming in vitro labeling of blood elements such as is done with the recent red cell tagging methods is eliminated. Thus the RIHSA method was chosen for use in this investigation of blood volume in surgical patients.

It was desired to study the RIHSA method itself initially in order to develop a practical technique applicable for routine use in a hospital such as the Royal Victoria Hospital, Montreal, Quebec,

where it was intended to establish a Blood Volume Laboratory which would be at the disposal of the clinical staff. This necessitated an appraisal of the various methods described for the performance of the RIHSA determination and modification of the procedure to the available scintillation counting apparatus. Following a standardization of the equipment and technique used, it was then proposed to study the blood volume in various groups of patients.

Normal adult male and female subjects were found amoung personnel and patients of the Royal Victoria Hospital. These subjects provided a basis for the comparison of the blood volumes of subjects who had clinical evidence of abnormal hemodynamics or abnormal blood volume. Individual and serial blood volume determinations were performed on subjects who had abnormalities of electrolyte balance or who had large blood losses and were being treated for these conditions. Emphasis was placed on elderly and poor-risk patients.

In order to ascertain the relationship of age to blood volume a group of normal subjects in early childhood was studied at the Montreal Children's Hospital.

The effect of chronic illness on blood volume was studied in a group of pre-operative patients with tuberculosis at the Royal Edward Laurentian Hospital, Montreal, Quebec. A detailed study of the measurement of operative blood loss in the surgery of pulmonary tuberculosis was conducted at this institution.

In general, it was hoped to learn something about: the general principles of the measurement of blood volume by the RIHSA method; the factors involved in the maintenance of the blood volume hemostasis in surgical patients; the rational rules of transfusion therapy in surgical patients.

During the period from the summer of 1954 until late spring of 1955 a method for the

performance of RIHSA blood volume determinations was evolved and over 300 determinations performed on human subjects,

PART II REVIEW OF THE LITERATURE

1 - DILUTION PRINCIPLE:

The measurement of blood volume in living human beings has since 1915 been performed by the injection of test substances into the circulating blood, allowing a period of time to elapse for mixing and then measuring the concentration of test substance in the plasma or red cells (94). From the dilution of the test substance can be calculated the plasma volume or the red cell volume. Total blood volume is measured by the simultaneous performance of plasma volume and red cell volume determinations or by the performance of either plasma volume or red cell volume determination and the venous hematocrit. (The venous hematocrit is considered as an indicator of the ratio of plasma or red cell volume to whole blood volume). Gregersen (75) has commented that the techniques devised for

blood volume determination in living man depend on the volume distribution of a known amount of some suitable test substance in the volume to be measured. This dilution principle has been phrased in other words by Edelman (48): "the extent to which a substance is diluted in a solvent constitutes a measure of the volume of the solvent". The method assumes that a definite compartment is measured in the case of plasma volume measurements. This compartment is really the circulating albumin pool - which Fox (61) states may be larger than the true plasma volume, and in the case of red cell volume measurements the compartment is that of the active circulating red cell mass which may or may not represent the true red cell volume. The test substances used, then, are divided into two categories: the substances used to measure plasma volume directly and the substances used to measure red cell volume directly. The test substances

most widely used clinically have been the dye vital red (94), T-1824 (67), radioactive iodinated human serum albumin (166), and labelled red cells. The red cells may be labelled in vivo by the inhalation of CO (6), or labelled in vitro by the isotopes, P^{32} (84), Cr^{51} (163), (using the patient's own cells), or labelled in a donor by his ingestion of Fe^{59} (79), or labelled by being of a different serological type (Ashby technique (9) -- depending upon differential agglutination).

2 - IDEAL TEST SUBSTANCE:

For clinical use the characteristics of an ideal test substance for blood volume determination must be considered under the classifications of:

1) precision desired
2) convenience and rapidity with which the determination may be performed and results known
3) the expense of having the laboratory facilities for the test available.

Test substances must, of course, be non-toxic in the dosage used, have no pharmacological action on the circulatory system for a long enough period to allow thorough mixing and representative sampling, must mix readily with the normal constituents of the blood and must be easily identified and measured (136). For practical clinical purposes a method which is precise within two units of blood (1000 cc.)

is a minimum standard; actually a method of blood volume measurement precise within one unit if blood is desired. Beling (15) states that the outside limits of error of routine T-1824 blood volume determinations is probably 10%, that is, 500-600 cc. in a normal 70 Kgm male adult, but that a reproducibility within 5% error, an entirely satisfactory standard of biological measurement, is claimed for successive T-1824 blood volume determinations. Brady (27) found a reproducibility of 3% for serial I^{131} - RIHSA blood volume measurements. Royster (145) found that T-1824 method of determining plasma volume plus the hematocrit was accurate to plus or minus 250 cc. in estimating changes in blood volume associated with operative blood loss and transfusion replacement. Frank (62) found Cr^{51} measurements to be reproducible within 3%. Thus it appears that clinically satisfactory measurements can be obtained with care in the technique using the T-1824, I^{131}, Cr^{51}, or P^{32} methods. The reproducibility does

not mean that the true blood volume is measured, but that the volume in which the test substance has mixed, the active circulatory volume, has been measured with precision.

Serial samples with the Cr^{51} method can vary less than 5% over a one hour period according to Prentice (129) and the mixing curve of I^{131} RIHSA according to Storaasli (166) is logarithmic at a rate not inconsistent with simple removal of the tagged albumin from the circulatory system rather than "slow mixing" with a non-actively circulating volume of blood. These facts provide good evidence that the I^{131} - RIHSA measurement approximates the plasma volume or at least the albumin pool and depots of plasma or cells do not exist under normal circulatory conditions. For surgical purposes, when rapid measurements may be necessary, the dye (T-1824) or I^{131} - RIHSA methods are inherently less complicated, more rapid, less elaborate, requiring only one injection and a blood sample. The removal of blood, tagging of cells at room temperature

with isotope (P^{32} or Cr^{51}) and reinjection and sampling do not commend themselves for use when part of the value of results consist in the rapidity and simplicity with which the results may be obtained. At such times, accurate rapid information may be required in the interests of the patient's well-being and, in general, greater simplicity of performance of a laboratory test may be rewarded with fewer errors. If blood volume determinations were as readily performed, facilities for performing the determination would undoubtedly be present wherever hemoglobinometry is performed. Blood volume determinations are reported by McInnes (104) as being of great value in instances of radical pelvic exenteration when a complete change of circulatory blood volume may occur during the operative period. Berlin (20), McInnes (104), Beling (15) have established blood volume laboratories for the performance of these determinations on a routine basis in chest surgery (20), radical pelvic surgery (104) and general surgery (15).

3 - NORMAL BLOOD VOLUME AND ITS EXPRESSION IN RELATION TO PHYSICAL MEASUREMENTS:

A) - Values reported:

Blood volume has been related to weight, height and surface area. Blood volume has been stated in percentage of body weight; cubic centimeters per kilogram of body weight, per centimeter of height, per square meter of surface area. Average normal values for the various methods may be found in Wintrobe's textbook (192). Average normal values have varied with the method used but there is fairly good agreement. Hence Bischoff's (23) direct method of exsanguination gave a normal value of 7.7% of the body weight or 73 cc/Kgm. In 1915, Keith, Rowntree and Geraghty (94), using vital red in 18 males, reported: Plasma volume 49 cc/Kgm, 1764 cc/m^2; total blood volume 85.8 cc/Kgm. In 1937, Gibson and Evans (68) using T-1824 in 41 females reported: plasma volume

41.5 cc/Kgm, 1520 cc/m^2; total blood volume 46.1 cc/Kgm, 2523 cc/m^2; cell volume 24.6 cc/Kgm. In 1950, Berlin (18) using P^{32} - tagged red cells reported values in 71 males; total blood volume 69.0 cc/Kgm; red cell volume 29.9 cc/Kgm; plasma volume 38.7 cc/Kgm. In 1951, Berlin (16) using P^{32} - tagged red cells reported values in 16 females: total blood volume 64.4 cc/Kgm; red cell volume 27.0 cc/Kgm; plasma volume 37.0 cc/Kgm. In 1950, Storaasli, (166) using RIHSA reported values in 31 males: plasma volume 40.3 cc/Kgm; total blood volume 73.0 cc/Kgm. In 1953, Brady (27) in a comparative study of the RIHSA, P^{32} and T-1824 methods reported in 25 subjects: RIHSA plasma volume 43.6 cc/Kgm; RIHSA total blood volume 71.8 cc/Kgm; T-1824 plasma volume 45.4 cc/Kgm; T-1824 total blood volume 81.3 cc/Kgm; P^{32} red cell volume 30.1 cc/Kgm. In 1953, Gray and Frank (72) in a comparative study of radioactive chromic chloride and radioactive sodium chromate in 10 adults

performance of routine blood volume determinations.

The values reported by various means of blood volume determination as stated in terms of the relation of blood volume to body weight, height and surface area, do not completely agree. When the same parameter of physical measurement is used (e.g. weight in kilograms), some variation in the reported values for blood volume may be attributed to such factors as:

1) Differences in test substances employed. Specifically, the volume distribution of the test substances employed differs during the period allowed for mixing. Thus Mollison (107) states that the carbon monoxide red cell method may give an artifactitiously higher value for red cell mass than the later isotope methods of tagging red cells.

2) Differences in time of collection of the post-injection blood sample. If, for example, dye has begun to leave the circulation

in significant amounts, collection of a "delayed" blood sample will result in over-estimate of the plasma volume because the volume distribution of the dye is larger.

3) Differences in the criteria for sampling of the normal population. For example, the inclusion of values obtained from individuals recovering from acute illness as done by Schreiber (50), may introduce a bias so that the mean value is not truly representative of the normal.

4) Differences in the mode of calculation of total blood volume when the dilution - hematocrit method is used. Systematic error may occur in the calculation when trapped plasma differs from the factor used and when body-venous hematocrit difference is neglected as pointed out by Mollison (107).

5) Individual physiological variation in intravascular volume. Though the average volumes

generally agree well when calculated in the same manner and when a satisfactory test substance is used, there is a wide range of values in normal individuals listed by various authors, which may in part be due to individual physiological variation.

B) - Relation of blood volume to body type:

Most commonly and most conviently (107) the blood volume is expressed in terms of cubic centimeters per kilogram of body weight. It is recognized that the average values cannot be rigidly applied in the estimation of deficits because of the wide range of normal values. However, some authors have satisfactorily applied arbitrary standards of excess or deficit based on average normal values for the method which they are using. For example see Berlin's (19) article on blood volume in pulmonary tuberculosis.

Ravdin (135) in a review of the literature on the problem of blood volume maintanence and regulation concludes that effective circulating blood volume is correlated closely with the mass of active metabolizing tissue and that an approximation sufficiently accurate for

average clinical use may be derived by measurement of the patient's height, and the calculation of a theoretically normal blood volume for an individual of average normal weight for the patient's height.

Gibson and Evans (68) in 1937 related estimates of blood volume determinations to weight, height, and surface area. On the whole, plasma volume was more closely related to height and surface area than to weight. They found that predominately muscular individuals tended to have plasma volume above the average for their height and that tall thin individuals had plasma volumes below the average for their height.

Perera (122) reported the effect of significant weight change on predicted plasma volume. A significant volume increase was noted only with an increase in lean body mass.

Gregersen and Nickersen (76) in 1950 studied the relation of blood volume to body type. They noted the satisfactory agreement as far as average normal values were concerned, but that the spread of

data on which the average is based is so wide that the average normal value cannot be applied to all cases. In an attempt to place the relationship of body size to blood volume on a more quantative basis they followed Sheldon's (155) classification of somatotypes. Their results under rigidly standardized determinations, were that computations made in terms of square meters of surface area showed the smallest variation, particularly in the group of extreme body types. It appeared that plasma volume is a function of body type. They found values for plasma volume as follows:

extreme endomophs - 36.9 cc/kgm

student endomophs - 40.5 cc/kgm

student ectomophs - 50.1 cc/kgm

extreme ectomophs - 56.5 cc/kgm

Thus, in general, it has been noted that: the obese have a lower blood volume and the thin a higher blood volume when expressed as cubic centimeters per kilogram body weight (76); the muscular individuals

have a higher blood volume and the thin individuals a lower blood volume when expressed as cubic centimeters per centimeter of height (68). Blood volume correlates best with active metabolic mass (135) and this may be reflected in the somatotype (76). There is a good correlation of blood volume with surface area (68, 76, 91). Reeve (136) and Gregersen (74) have both indicated that it is fortunate that the majority of methods of blood volume estimation in common use do give values sufficiently accurate for clinical use. Expression of normal blood volume in cubic centimeters per kilogram is convenient (107), but one must be aware of wide range of values from which the average is derived in order that rigid application of normal values be avoided in individuals who might represent extremes of the normal. Serial blood volume changes may accurately indicate the trend of change in the blood volume of an abnormal individual. When a single blood volume determination is performed on a patient with an abnormal blood volume (e.g. after hemorrhage or massive transfusion)

one requires a knowledge of the limitation of average values plus some arbitrary standard of normal extremes of blood volume to interpret adequately the laboratory findings.

I^{131} RISA BLOOD VOLUME - 70 kgm NORMAL MALE

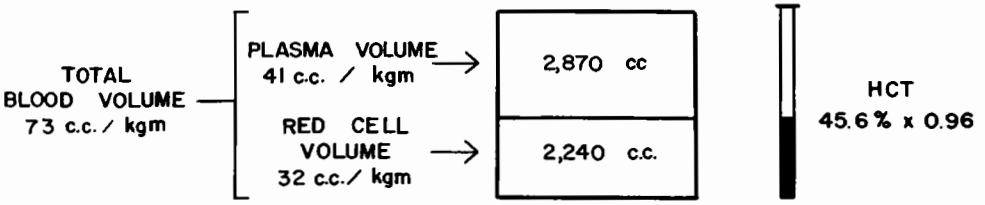

FIGURE 1

Normal blood volume values (male adult) . Values obtained from RIHSA blood volume determination in a normal male subject. Total blood volume, plasma volume and red cell volume are stated in absolute amounts (ML.) and relative to weight (ML/KGM). Venous hematocrit is corrected for 4% trapped plasma.

4 - THE VENOUS HEMATOCRIT AND TRAPPED PLASMA:

The precision with which the hematocrit determination can be performed enters into a consideration of the precision with which total blood volume can be calculated from direct measurements of plasma volume or red cell volume. First, it is of interest to note that several investigators have reported that, whith repeated withdrawal of small samples of blood, the venous hematocrit decreases out of proportion to the quantity of red cells removed. A hemodilution of 3% may occur (29, 67, 82, 115, 175). Rydin and Verney (147) considered this to be due to secretion of the antidiuretic hormone and this view is shared by other investigators interested in the problem of the regulation of oncotic pressure (125).

The term "trapped plasma" refers to the amount of plasma remaining in the packed red cell mass after centrifugation of whole blood. In 1953 Owen and Power (119) reviewed the extensive literature on the subject and performed studies of

their own, using radioactive iodinated-albumin as an indicator of the amount of plasma remaining in packed red cells after centrifugation. They tested heparinized venous samples from 39 human subjects. They concluded that 3.79% plus or minus 0.70%, that is, slightly less than 4% of the cell volume as determined by centrifugation, consists of trapped plasma.

In 1952, Chaplin and Mollison (31) studied the problem using T-1824 as an indicator of the amount of plasma trapped. They concluded that over a range of venous hematocrits from 15-85%, trapped plasma values increased from 1.5 to 5%. Trapped plasma varied inversely with total centrifugal force applied (speed, time, radius of centrifugation) and directly with the magnitude of the hematocrit value. They have a useful chart in their paper, permitting their results to be applied by reference to this chart.

In 1953, Schlenker (149), in a paper on the determination of packed cell volume, states that the completeness of packing depends upon:

a) centrifugal force applied, speed and effective radius
b) duration of centrifugal spin
c) volume concentration of cells in sample
d) anticoagulant used
e) secondary factors, such as bore of tube, state of aggregation, etc.

Centrifugal force may be calculated from the formula CF = RPM X RADIUS X $2/10^6$. Schlenker (149) states that with normal bloods CF 187 (2500 RPM, radius 15 cm) for 15-20 minutes is sufficient to obtain complete packing; a value within 5% of the minimum can be obtained after 10 minutes. When the erythrocyte count is 2.0 to 4.0 million per cubic millimeter CF 120 (2000 RPM, radius 15 cm) for 10 minutes is sufficient.

Berlin (17) does not use any correction for trapped plasma. Beling (15) and Storaasli (166) also omit use of this correction factor. Vazquez (174) corrects all venous hematocrits spun at 3000 RPM for 30 minutes for 2% trapped plasma. Brady (27) corrects all venous hematocrits spun at 3000 RPM for 30 minutes for 4% trapped plasma. Reeve, Gregersen and co-workers (139) routinely correct for 4% trapped plasma. In 1951, Mollison (107) interprets the "hematocrit" to refer to the red cell column only and ignored the layer of white cells on top of the column, correcting for 5% trapped plasma routinely.

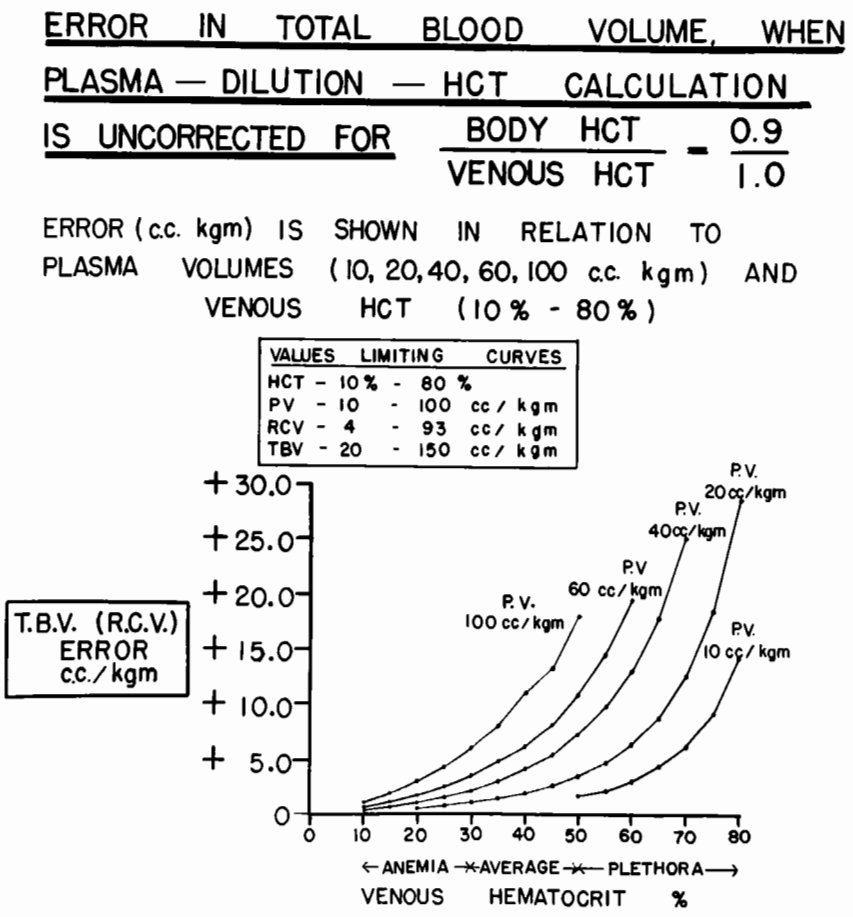

FIGURE 2

Body-venous hematocrit difference. Effect of body-venous hematocrit difference on calculation of total blood volume when using RIHSA method. Error increases as hematocrit % and plasma volume per kilogram increase.

RED CELL VOLUME "OVERESTIMATE" RELATED TO PLASMA VOLUME AND VENOUS HEMATOCRIT

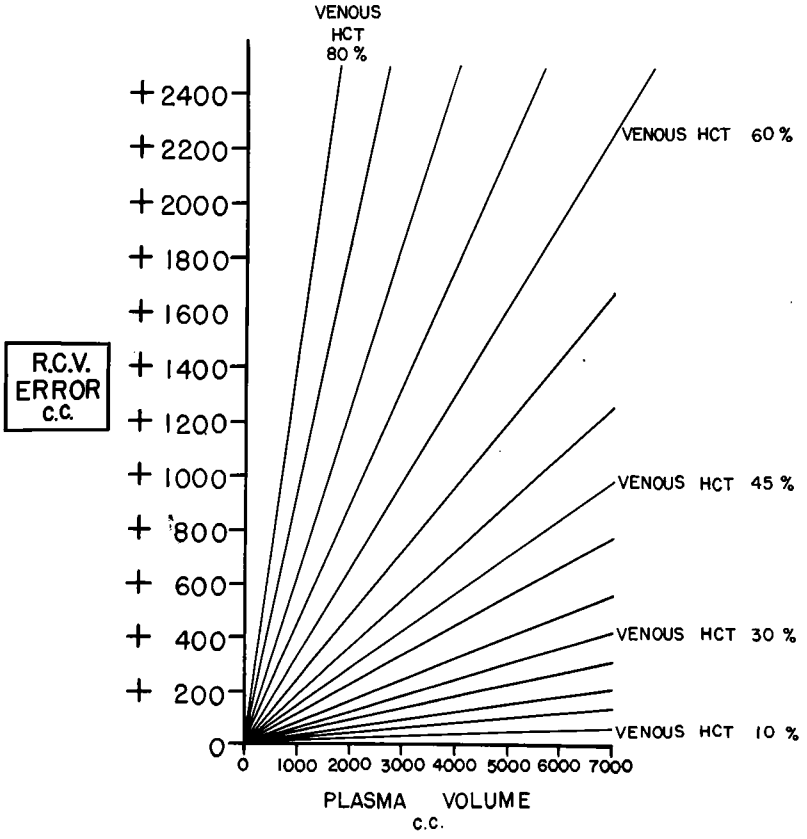

FIGURE 3

Body-venous hematocrit difference. Effect of body-venous hematocrit difference on calculation of total blood volume when using RIHSA method. Error increases as hematocrit % and plasma volume in absolute amounts (ML) increase.

5 - BODY HEMATOCRIT CONCEPT:

The use of a substance such as T-1824 or RIHSA to estimate total blood volume by the dilution hematocrit method assumes:

a) that plasma dilution methods measure absolute plasma volume;
b) that the venous hematocrit is a representative sample of the absolute total blood volume;
c) that the measured plasma volume and venous hematocrit may be used to calculate absolute total blood volume.

A) Definitions:

Absolute plasma volume is the true volume of plasma in the body. Gregersen (75) states that the volume distribution of T-1824 is identical with that of various antigens (77) of albumin (152) tagged with I^{131} and of hemoglobin (4), constituting

strong evidence that the dye method measures the true plasma volume. T-1824 combines with albumin by linkage with the epsilon ammonium radical of lysine (95), I^{131} combines with albumin by linkage with the tyrosyl groups (90). Therefore, T-1824 and RIHSA measure at least the circulating albumin pool which, though slightly larger than the true plasma volume, is at least in rapid equilibrium with it (151). The question of the volume distribution of T-1824 and RIHSA is discussed by Freinkel (63).

Absolute red cell volume is the true volume of red blood cells in the body. Gregersen (75) states that P^{32} and Fe^{55} agree (114) as to the measurement of red cell volume, but that the carbon monoxide method over-estimates red cell volume due to loss of the gas in tissues. Mollison (107) concurs with this statement concerning carbon monoxide.

Absolute total blood volume is the true volume of blood in the body, the sum of the

plasma volume and red cell volume. The sum of the plasma volume by the dilution method (e.g. RIHSA) plus the red cell volume by the dilution method (e.g. Cr^{51} tagged red cells) would be a measurement of the true blood volume within the limits of those methods.

Venous hematocrit is the ratio of red cells to whole blood in the venous blood. A hematocrit of 45% indicates that the blood sample contains 45% red cells and 55% plasma.

Body hematocrit is the ratio of red cells to whole blood in a statistically representative sample of the absolute total blood volume. To obtain this sample one would have to drain all of the blood of the body into a container, agitate the blood well and centrifuge a sample. Practically, the body hematocrit is calculated by simultaneously performed measurement of the plasma volume (e.g. by RIHSA) and the red cell volume (e.g. by Cr^{51} tagged red cells). The calculation is as follows:

$$\text{Body hematocrit} = \frac{(Cr^{51})\ \text{red cell volume}}{(Cr^{51})\ \text{red cell volume plus (RIHSA) plasma volume}}$$

The importance of an understanding of the body hematocrit and venous hematocrit is this: if the body hematocrit is the same as the venous hematocrit, one may calculate total blood volume from the equation:

$$TBV = \frac{\text{RIHSA plasma volume (ml.)}}{1.00 - \frac{\text{Venous hematocrit (\%)}}{100}}$$

If the body hematocrit is smaller than the venous hematocrit the above calculation will result in over-estimating total blood volume (and red cell volume). If the body hematocrit and venous hematocrit differ constantly under all conditions of circulation when using accurate means of simultaneous measurement of plasma volume and red cell volume a correction factor, K, may be used to overcome the error, so that the equation becomes:

$$TBV = \frac{\text{RIHSA plasma volume (ml.)}}{1.00 - \frac{\text{Venous hematocrit (\%)} \times K}{100}}$$

Interest in the concept of body - venous hematocrit difference has arisen from a comparison of total blood volumes calculated from the simultaneous determination of plasma volume using plasma diluents (especially T-1824) and labelled red cells (17). Differences have been noted for example when total blood volume was:

a) calculated from T-1824 plasma volume plus venous hematocrit

b) calculated from P^{32} red cell volume plus venous hematocrit

c) calculated by adding T-1824 plasma volume and P^{32} red cell volume.

To account for these differences, a difference between venous hematocrit and body hematocrit is postulated.

Evaluation of the body - venous hematocrit question involves a review of the opinions regarding:

a) variations in the composition of blood in different sized vessels in the body;

b) the findings of investigators who have employed simultaneous plasma diluent and tagged red cell methods of calculating total blood volume;

c) the opinion of investigators as to the practical significance, the magnitude and nature of the error in calculation of total blood volume from the plasma diluent - hematocrit method, with special reference to the errors which might occur in the RIHSA - hematocrit blood volume measurement.

B) Variations in composition of blood in different sized vessels:

Blood is a suspension of finely particulate matter in a fluid medium, hence cannot be expected from the point of view of viscosity to obey the physical laws governing the behavior of simple fluids such as homogenous solutions (107).

Krogh (97) has described the flow of blood in capillaries with red cells having an axial flow and the plasma forming a cuff about the red cells. Fahraeus (55) demonstrated that the hematocrit of blood passed through fine glass tubes varied with the diameter of the tubes. Thus when the tube diameter was 1.0 mm. the hematocrit was 40%, when the diameter was 0.1 mm. the hematocrit was 34%, when the diameter was 0.05 mm. the hematocrit was 28%. In the smaller vessels, then, the red cell to plasma ratio was 28:72 and in the larger tubes the ratio was 40:60. Mollison (107) states that it is now accepted that "the blood vessels are lined with

a layer of relatively slowly moving plasma and the red cells form an axial stream". Green (73) estimates that in a dog with a total blood volume of 1150 ml. the total capacity of the venous system is about 870 ml. (76% of total); the total capacity of the aorta, arteries and arterioles is of the order of 220 ml. (19%); the capacity of the capillaries is roughly 60 cc. (5%). Bazett (14) estimated that the smaller vessels (arterioles, capillaries, venules) held, at most, only 15% of the blood of the body. From the estimates of Green (73) and Bazett (14) one would conclude that the capacity of the smaller vessels is not large enough to account for the reported differences in body - venous hematocrit. However, Gregersen and co-workers are convinced from studies of the proportion of red cells and plasma to whole blood in various organs (5) and in the eviscerated animal (78) that the "extra plasma" is probably distributed throughout the body and not present as a single large pool in some organ or tissue.

C) Simultaneous plasma volume - red cell volume dilution measurements:

Smith, Arnold and Whipple (159) in 1921 insisted that the true blood volume could be determined only by estimating plasma volume and red cell volume seperately and then adding them together. For the estimation of red cell volume they used the carbon monoxide method and for measuring the plasma volume they used the red dye method. Although both of the methods which they used lead to positive errors which should have negated each other (107, 75), these investigators found a discrepancy between the total blood volume as calculated seperately by the dye - hematocrit and tagged cell - hematocrit methods.

Gregersen (75) in 1953 reported measurements of plasma volume with T-1824 and red cell volume with P^{32} in splenectomized dogs. These studies were intended to elucidate the

problem of body - venous hematocrit difference. He states that in normal human subjects the total blood volume as calculated from the red cell tag substances and the venous cell percentage (i.e. venous hematocrit) has been on the average (137) 10% lower than the total blood volume determined from the sum of the dye dilution plasma volume and the tagged cell dilution red cell volume. On the other hand, the total blood volume as calculated from the dye dilution plasma volume and the venous cell percentage has been higher than the sum of the separate measurements. References cited are: for the T-1824 - P^{32} comparison (83, 140, 111, 21); for the T-1824 - Fe^{55} comparison (70); and for the T-1824 - Ashby marked cell comparison (12).

Gregersen (75) considers that the T-1824 dye method accurately measures the true plasma volume (because of the characteristics of its volume distribution) but over-estimates the total blood volume (because of the body - venous hematocrit difference); the isotopic red cell tag methods

accurately measures the true red cell volume, but under-estimates total blood volume. In splenectomized dogs the ratio of body hematocrit to venous hematocrit was 0.87 to 1.00. Hence in the splenectomized dog the under-estimation of total blood volume by the isotopic red cell tag method would be about 13%; the over-estimation of total blood volume by the plasma dilution method would range from about 2% at venous hematocrit 10% to about 30% over-estimation at venous hematocrit 70%. In other words when using a plasma dilution method (e.g. T-1824 or RIHSA) the larger the venous hematocrit, the larger will be the absolute and relative over-estimation of total blood volume (and red cell volume). Thus use of the equation:

$$TBV = \frac{\text{RIHSA plasma volume (ml.)}}{1.00 - \frac{\text{venous hematocrit (\%)}}{100}}$$

would result in an error of 3 - 30% over the 10 - 70% hematocrit range in splenectomized dogs,

whereas use of the equation:

$$TBV = \frac{\text{RIHSA plasma volume (ml.)}}{1.00 - \frac{\text{venous hematocrit (\%) X 0.87}}{100}}$$

would result in the same estimate for total blood volume as would the sum of the plasma dilution plasma volume plus the red cell dilution red cell volume.

The validity of the correction factor 0.87 in the splenectomized dog was substantiated under the following experimental conditions:

1 - conscious dogs in a normal circulatory state;

2 - immediately after severe hemorrhage and at intervals of days thereafter;

3 - after infusions of dextran into dogs with normal blood volume;

4 - after infusions of concentrated cell suspensions into dogs with normal blood volumes;

5 - after three weeks acclimatization to low oxygen tension;

6 - after "dehydration" with intraperitoneal dialysis or with intravenous infusions of 50% sucrose and again after "rehydration".

However in dogs after hemorrhage followed immediately by infusions of dextran, for unknown reasons, the ratio was not 0.87 but 0.80.

These findings of Gregersen are detailed in the series of papers in the American Journal of Physiology, November, 1953, and present a sound pattern of experimental surgical approach to the clarification of the body - venous hematocrit difference. An outstanding finding was that the 0.87 correction factor could be applied with confidence except in the cases of hemorrhage immediately treated with dextran. As mentioned by Gregersen (75), this latter finding should be studied more intensively.

In the case of the human being Chaplin and Mollison (31), using T-1824 and P^{12}, conclude that

the body - venous hematocrit difference was real, relatively constant and that a correction factor of 0.91 could be applied with confidence. Gray and Frank (72), using radioactive chromic chloride and radioactive sodium chromate, found that a correction factor, of 0.91 could be applied in normal adults. Schreiber (150) using RIHSA and radioactive sodium chromate tagged red cells found that a correction factor of 0.937 was applicable in normal adults but that the body - venous hematocrit ratio was less than 0.937 in congestive failure and altered when cardiac compensation occurred.

D) Significance of the body - venous hematocrit difference in relation to the plasma dilution hematocrit method of blood volume determination:

From the foregoing paragraphs it is probable that a real difference exists in man between the body and venous hematocrits. The correction factor is probably about 0.9 when the RIHSA method is used. If this correction factor is a constant, an over-estimate of total blood volume (and red cell volume) will occur when the correction factor is not used. The following are the opinions regarding the significance, magnitude and nature of this error of over-estimation.

Berlin (17) omits the use of any correction for body - venous hematocrit difference when using the P^{32} method, stating: "This concept (i.e. body - venous hematocrit difference) is based upon the use of Evans blue for the measurement of plasma volume, which we do not regard as satisfactory, and, since theoretical considerations of the hydro-

dynamics of blood flow seem to indicate that a significant change in the hematocrit does not occur in the smallest vessels, we do not believe that the total body hematocrit differs significantly from the venous hematocrit!! If Berlin's position is incorrect and the correction factor is constant at about 0.9 as suggested by Mollison (107), Berlin's calculations of total blood volume would result in under-estimates of total blood volume by about 10%. Berlin (15), Whiting and Hotz (188), McInnes (104) using the T-1824 method; Storaasli (166), Brady (27), Siler and Fultz (157) using the RIHSA method -- have omitted use of the body - venous hematocrit correction factors when reporting use of blood volume determinations. These reports were all made in surgical publications within the past five years and the authors all claimed satisfaction with their particular method of blood volume determination.

Mollison (107) is of the opinion that a correction factor of 0.9 should be used whenever the dilution hematocrit method is used in the estimation of total blood volume. He points out the magnitude of the error which may occur when the hematocrit is elevated and cites examples of serial blood volume determinations where transfused blood was accurately accounted for when the correction factor was used and unsatisfactorily accounted for when the factor was omitted. He illustrated mathematically the large errors which may occur when the hematocrit is elevated and hence is in substantial agreement with Gregersen (75).

6 - CHARACTERISTICS OF RADIOACTIVE IODINATED HUMAN SERUM ALBUMIN (RIHSA):

The period during which detectable amounts of RIHSA remain in the circulatory and lymphatic systems has not been determined precisely. This time has been reported to be perhaps 6 days (141), after intravenous injection, and the time is probably longer. Complete mixing with the circulating blood occurs within 10 minutes according to Aust (10). Within a few minutes after injection radio-activity is detectable in the thoracic duct. This is negligible and amounted to less than 2% in 10 minutes according to Storaasli and co-workers (166, 96). Equilibrium of the activity between blood and lymphatic systems is complete within 7 to 13 hours (182). No activity is found in the spinal fluid up to five days after injection (166, 182). Negligible amounts are found in the bile after intravenous administration (166).

A) Disappearance from serum:

In dogs 91.5% of the activity is located in the plasma one hour after injection, 80% remains at 5 hours, 45% at 24 hours, and 32% at 72 hours (182). In man, Storaasli (166) found that on the basis of 100% being present at 10 minutes, 96% remains at 15 minutes, 95% at 30 minutes, 90% at one hour, 86% at two hours, 81% at three hours, 78% at four hours, 74% at six hours, 69% at eight hours. The five minute sample contains 106% of the activity of the 10 minute sample.

B) Urinary excretion:

The urine is the chief route of elimination of I^{131} following the administration of RIHSA. At the end of the first day after injection, the total urinary excretion may reach from 5 to 20% of the total amount given (10, 166, 161). Apparently RIHSA is gradually metabolized by the body, with the liberation of free I^{131}. Most of the free I^{131} is excreted in the urine (as Na I^{131}), the remainder being taken up by the thyroid gland. Another factor in the disappearance of the RIHSA from the vascular system is due to the diffusion of the iodinated protein from the vascular bed to the extra-vascular spaces as demonstrated in the studies of thoracic duct lymph (166).

C) Thyroid uptake:

Approximately 5% of the injected radioactivity has been found in the thyroid gland within the first 24 hours (166).

Absence of activity in the bile (166) would indicate that the liver does not participate in the excretion of RIHSA. However, it is of interest to note that Sterling (161, 162) has reported that in the hypoalbuminemia associated with Laennec's cirrhosis there is a slower turnover and longer half-time of intravenously administered RIHSA than in other hypoalbuminemic states.

Tyor (173) has studied the serum disappearance rate and urinary excretion rate of I^{131} after RIHSA injection in patients with cirrhosis and has compared it with findings in other diseases. Disappearance from serum was similar, but urinary excretion of I^{131} (inorganic)

was decreased, during the first 24 hours in patients with cirrhosis. Stirrett (165) has successfully employed RIHSA in 300 microcurrie doses in the diagnosis and localization of liver metastases. Chou (34, 34, 126), Farmer (56), Yuhl (194) and Dunbar (45) have employed RIHSA in the diagnosis and localization of intracranial tumours.

7 - BLOOD VOLUME AND CONCENTRATION INDICES:

Performance of the hemoglobin, red blood cell count and hematocrit determinations permits the calculation of volume, color and saturation indices (192) expressed in absolute terms as the mean corpuscular volume, mean corpuscular hemoglobin and the mean corpuscular hemoglobin concentration. These are called the corpuscular constants and are of value in the classification and treatment of anemia. Consideration of the constants in a particular case permits of a diagnosis, e.g., of normocytic, normochromic anemia (in acute hemorrhage), or hypochromic microcytic anemia (iron deficiency or chronic blood loss). Several authors have effectively shown the lack of correlation between laboratory tests of concentration (HGB, RBC and HCT determinations) and the findings of blood volume determinations (192, 36). A moment's

reflection will show that it is possible to have a 90% HGB, 43% HCT and 4.5 million RBC count in a normal male immediately after a hemorrhage of 1000 cc. before fluid shifts into or out of the vascular space have occurred. Hemodilution would occur if fluid shifted into the vascular space and hemoconcentration if fluid shifts out of the vascular space. The stability of circulatory dynamics depends more upon the volume of total blood than upon the composition of the blood as far as red cells or plasma is concerned within wide limits. Howard (87) has stated than an acute 50% deficit in red cell volume is tolerated better than an acute 50% deficit in total blood volume. Moreover, as Mollison (107) points out, a patient with aplastic anemia (chronic red cell volume deficit) may be ambulatory with five gms. % hemoglobin. Also profound hypotension and circulatory depression may occur in severe dehydration due to generalized peritonitis (acute plasma volume -

and total blood volume deficit) in the presence of a higher hematocrit which represents a suprious or relative polycythemia (assuming normal red cell volume).

Recognizing the limitations of concentration indices, but maintaining their value in the absence of blood volume determinations and measurements of operative blood loss in surgery, Thomas (170) has studied the blood changes after intrathoracic operations. Thomas (170) felt that the hematocrit (and hemoglobin) determination was better than the red cell count since the latter often gave erratic results.

8 - PHYSIOLOGICAL VARIATIONS IN BLOOD VOLUME:

Physiological variations in normal individuals may explain some of the discrepancies between different published estimates of normal blood volume (107).

A) Effect of activity:

Plasma volume is affected by posture, exercise and rest in bed (107). Thompson (171) found that 20-30 minutes of standing after 30 minutes in the recumbent position produces a decrease in plasma volume of approximately 300 ml. Conversely, Walters (179) and Widdowson and McCance (189) found that lying down for one to two hours produces a fall in hemoglobin and hematocrit of about 5%. Taylor (169) found that lying in bed for three weeks produces a fall in plasma volume of about 500 ml. in males. This is accompanied by a scarcely significant fall in red cell volume and thus the hematocrit rises.

B) Differences between infants and adults:

Normal newborn infants have a larger blood volume per kilogram than normal adults, the difference depending almost entirely upon the different levels of the venous hematocrit. Mollison (107) using T-1824 and P^{32} tagged red cells, separately found that newborns having a venous hematocrit of 63% had a total blood volume of 84.7 ml/Kgm. Normal adults with a venous hematocrit of 44.7% had a blood volume of 76.6 ml/Kgm. Russell (146) studied a group of 64 infants and young children weighing 10-30 Kgm. Recalculation of his data by Mollison (107) revealed an average blood volume of 75.4 ml/Kgm.

Ely and Sutow (52) studied the growth of thiocyanate space in infancy and childhood and performed T-1824 blood volume determinations on infants and children up to the age of 8 years and weighing 2 to 25 Kgms. They found an increase in blood volume in absolute amounts with age. The

increase was directly related to weight, height, and surface area. The best correlation appeared to be with weight. In 50 subjects, aged 0-9 years, the mean total blood volume was 81.1 ml/Kgm, with a venous hematocrit of 40%. No correction was made for trapped plasma or venous hematocrit-body hematocrit difference. (When recalculated after the manner used by Mollison (107), the total blood volume in this series of 50 children is found to be 74. ml/gm).

Robinow and Hamilton (143), using vital red dye, concluded that the blood volume of children was about 90 ml/gm. The size of the volume may be attributed to: inaccuracy of the vital red method and lack of appropriate correction for trapped plasma and venous hematocrit-body hematocrit difference.

C) Pregnancy:

Mollison (107) remarks on the magnitude of the increase in plasma volume during normal pregnancy while accounting for the observed decrease in venous hematocrit. Berlin (17) using the P^{32} red cell tag method agrees with the findings of increased plasma volume, but maintains that a decrease in red cell volume occurs too, contributing to the fall in hematocrit. The decrease in red cell volume, according to Berlin (17) is apparently due to a failure of production of red cells rather than due to excessive destruction of cells or decreased red cell survival time.

9 - MEDICAL AND SURGICAL CONDITIONS AFFECTING BLOOD VOLUME:

Numerous reports have been made on various medical and surgical conditions affecting blood volume. Berlin's review (17) mentions congestive heart failure, uremia, pulmonary tuberculosis, cirrhosis, cancer, leukemia, polycythemia and pregnancy. Berlin (20) and Albritten (2) have studied changes in blood volume with thoracic surgery; Bonica and Lyter (26) have summarized much of the pertinent literature on blood loss in general surgery.

There has been a great deal of controversy over the findings in specific disease conditions with different results being found by different investigators of the same disease with the same or different methods. In general, congestive heart failure appears to increase the total blood volume, red cell volume and plasma volume and, with compensation, the volumes approach normal.

Uremia, according to Berlin (17) decreases the red cell volume and the plasma volume may be normal, smaller or larger than normal. In pulmonary tuberculosis, blood volume is usually reduced by 15% or so. In hepatic cirrhosis, plasma volume is usually large and red cell volume is usually small, that is, a true anemia exists and hemodilution may be present. In cancer, red cell volume may be small (33) or variable (17). In chronic leukemia, when the spleen is palpable, the plasma volume is usually enlarged but this is variable. With treatment of chronic myelogenous leukemia, the plasma volume may decrease, if previously enlarged. In primary and secondary polycythemia the blood volume is usually enlarged due to an increased red cell volume. Relative polycythemia occurs in patients with obvious fluid loss or shock, an elevated hematocrit being present when there is a normal red cell volume.

In normal pregnancy, using the P^{32} red cell labelling method, Berlin (17) found that

there is a decrease in red cell volume during the first trimester. An increase in total blood volume, red cell volume and plasma volume occurs in the 2nd and 3rd trimesters. Low hematocrit values may be due to a disproportionate increase of plasma volume over red cell volume in the 2nd and 3rd trimesters.

The state of knowledge of the influence of specific disease states on blood volume continues to be in a state of flux pending further knowledge and agreement on the method of determination (e.g. I^{131}, RIHSA or Cr^{51} - tagged red cells), which is best for demonstrating true changes in blood volume in specific conditions, the limitations of each method and the proper mode of expression of results obtained (e.g. on basis of surface area, true body mass, ideal weight, etc). In the interim, serial determinations by the same method and mode of calculation at least reflects changes in blood volume in the same patient.

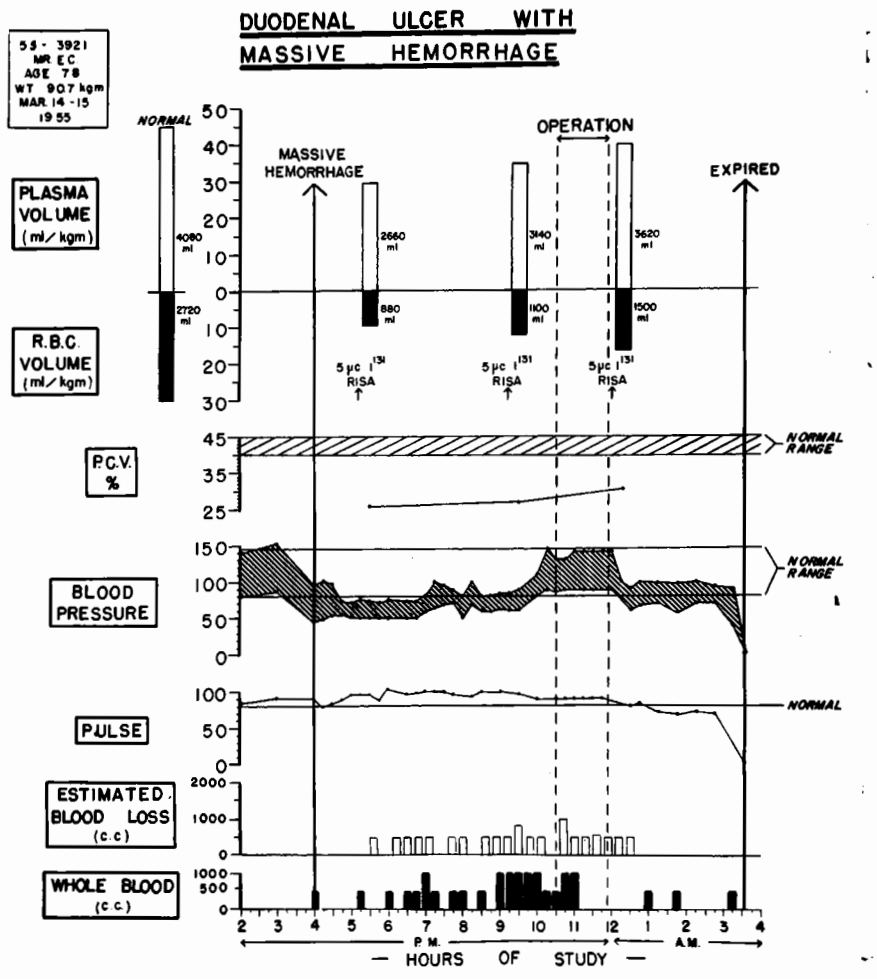

FIGURE 4

Blood volume and hemodynamic response in massive gastrointestinal hemorrhage. Hypotension and tachycardia are not early indices of oligemia. Partial replenishment of deficient blood volume pre-operatively reverted blood pressure to normal. 3500 ML of blood given from 4pm until 11pm. Death was due to hemorrhage post-operatively.

10 - CIRCULATORY DYNAMICS:

Patients who are to undergo anaesthesia and stress of surgery require careful evaluation of the adequacy of their circulatory dynamics. The relationship of the total blood volume to circulatory homeostasis would appear to be more important than the relative volume of the plasma or red cell mass. Three considerations make this apparent:

1) On the basis of a study of 4500 casualties Howard (87) concluded that a rapid loss of 50% of the red cell mass can be tolerated if the total blood volume is maintained, whereas, a 50% reduction of the total blood volume is usually accompanied by hypotension and other signs of decompensation of circulatory dynamics.

2) Profound hypotension and circulatory depression may occur in patients with a normal red cell volume but a low

total blood volume. This occurs in cases of acute peritonitis with internal fluid loss and no concomitant red cell volume loss. Hence, a patient with peritonitis may have a blood pressure of 80 systolic and a hematocrit of 55%.

3) In subjects with chronic anemia, such as pernicious anemia, the hemoglobin may fall as low as 3 gm % before the patient is admitted to hospital. Normal non-strenuous activity may be performed by patients with a hemoglobin level of only 5 gm %.

These facts indicate that the red cell mass is important for its space-occupying function and oxygen transport as emphasized by Moore (109) but that total blood volume is of greater importance when acute stress is applied to the circulatory system.

The following discussion is taken from Elkinton (50). The peripheral arterial blood pressure is a function of the peripheral vascular (mainly arteriolar) resistance, the cardiac output and, to a lesser degree, the elasticity of the larger arteries. Cardiac output is a function of the heart rate, force of systole and the venous return. The venous return is a function of the total circulating blood volume, the propulsive forces (muscle contraction, gravity, changes in thoracic and abdominal body cavity pressure and differences in capillary venous pressure) applied to the blood in the venous system and the tonus of the veins and capillaries. Peripheral resistance is a resultant of local factors (external thermal change, chemical influences) and central regulation by the vasomotor center which is situated in the floor on the fourth ventricle at the level of the calamus scriptorius. Reflex activity of the vasomotor center is under regulation of higher centers (cerebral cortex and hypothalamus), radiation from the respiratory center, afferents from

the pressoreceptors, other afferents, hypercapnia and oxygen lack. (50)

Although a normal blood volume is only one of the variables which determine the adequacy of the circulation, reduction in blood volume or plasma volume always results in impairment of the circulatory dynamics (50). For this reason changes in the volume of blood and plasma associated with various types of dehydration and traumatic shock are of intense practical interest.

11 - PHYSIOLOGICAL REGULATION OF PLASMA VOLUME:

From an analysis of his own and other authors' work, Mollison (107) concluded that:

1) The plasma volume and venous hematocrit have a substantially rectilinear inverse relationship with plasma volume decreasing from 60 to 35 c.c./Kgm over the hematocrit range 10-70% (107, 65, 66, 70, 115, 140, 146, 108).

2) The red cell volume and venous hematocrit have a substantially rectilinear direct relationship with red cell volume increasing from 5 to 40 c.c./Kgm over the hematocrit range 10-55% (140, 108). Above a venous hematocrit of 55% the red cell volume increases disproportionately and above a venous hematocrit of 75%, in congenital heart disease (117), the disproportionate red cell volume increase is even more striking.

3) The total blood volume appears to increase throughout the range of hematocrit values from 10 to 70%, especially above a venous hematocrit of 55% (107, 66, 70, 140, 146, 108).

It shpuld be noted that these conclusions were reached as a result of direct-dilution plasma volume or red cell volume measurements and with the elimination of the error which may be introduced by the difference between venous hematocrit and body hematocrit.

The plasma volume can be altered far more rapidly than the red cell volume. The body has no normal mechanism for destroying excess red cells and red cell volume can be reduced very slowly by diminishing production and waiting for the excess red cells to reach the end of their normal life span (107). By contrast, plasma volume can be rapidly altered and until venous hematocrit values of 55% are exceeded,

plasma volume is readjusted so as to keep the sum (plasma volume plus red cell volume) approximately constant (107). In Mollison's (107) opinion, the factors controlling plasma volume are:

1) red cell volume;
2) serum protein concentration (a reduction in the total amount of circulating protein tends to be accompanied by a reduction in plasma volume and an increase in circulating protein tends to be accompanied by an increase in plasma volume);
3) salt balance (in the presence of deficits of the principal extracellular cation, sodium, extracellular volume decreases. Since plasma cation is in equilibrium with interstitial cation, plasma volume decreases correspondingly).

Mollison (107) is of the opinion that intravascular hydrostatic pressure, protein concentration of the plasma and body salt balance are adequate to explain

control of plasma volume and that it is not necessary to postulate a center for control of the body fluid volume. However, one wonders, in view of the remarkable control of the blood volume, if a center is not present perhaps in the bone marrow similar to the oncorceptors, postulated by Verney (176) which are concerned with the regulation of oncotic pressure or the chemoreceptors and pressoreceptors described by Comroe (37, 38) and Schmidt (38) which reflexly affect respiration, heart rate and blood pressure.

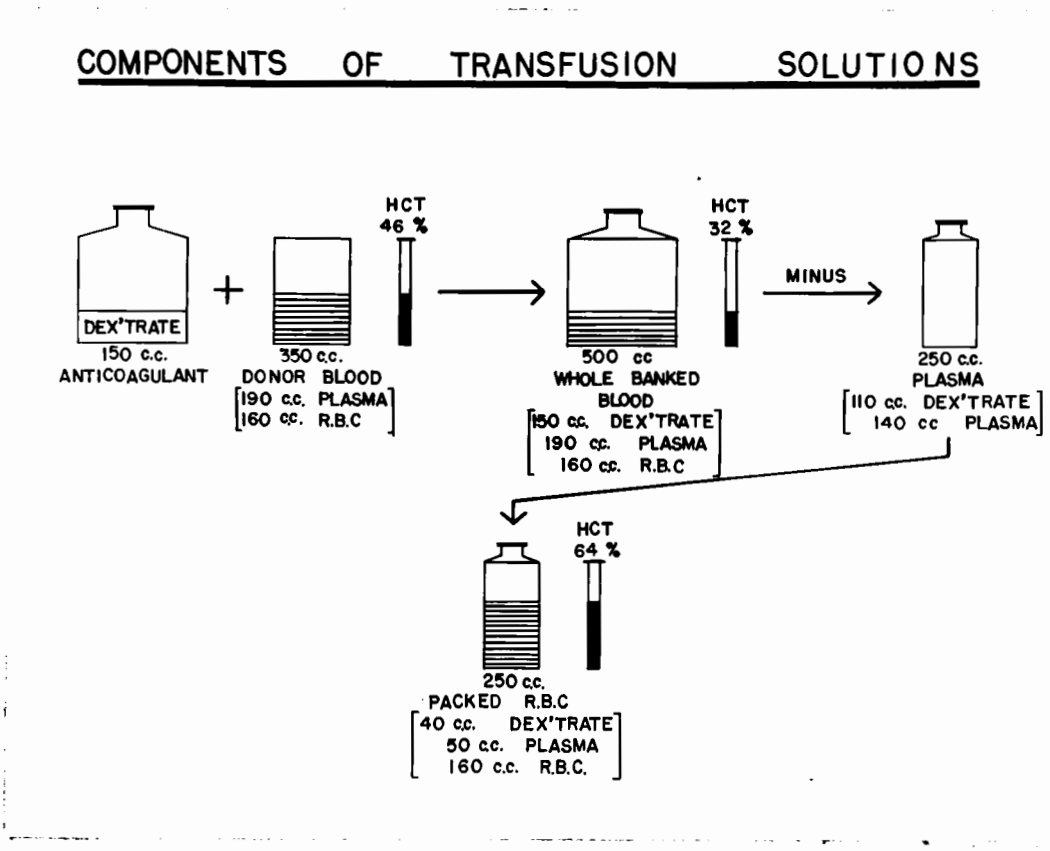

FIGURE 5

Components of transfusion solutions. An approximation is shown of the red cell, plasma and anticoagulant composition of whole blood, stored plasma and packed red blood cells as supplied by the Royal Victoria Hospital Blood Bank.

12 - TRANSFUSION SOLUTIONS:

Transfusion therapy and the use of plasma expanders are indicated for the immediate correction of quantitative and qualitative blood deficits. The substances generally used consist of whole banked blood, concentrated red cell suspensions, plasma, concentrated human serum albumin, synthetic large molecule polysaccharide solutions (PVP or Dextran). Whole blood is stored for a maximum of 21 days under refrigeration, heparinized, citrated or in siliconed containers. Concentrated red cell suspensions are prepared from whole banked blood by removal of supernatant plasma following sedimentation or centrifugation. Red cells may be suspended in a minimum volume of plasma or washed with saline solution and resuspended in saline solution. Plasma is prepared by separation from whole banked blood and may be stored under refrigeration, dehydrated or stored at room temperature, for six months or more. Plasma contains plasma proteins

and electrolytes and has nutritional as well as osmotic properties. The value of the plasma expanders consists mainly in the osmotic properties of their large molecule colloids. Whole blood contains red cells which have space occupying and oxygen carrying capacities (109). Packed red cells contain a larger mass of red cells per unit volume than whole blood. Specific transfusion therapy is always desirable (6). For deficits in total blood volume - whole banked blood; for deficits in plasma volume - plasma; for deficits in red cell volume - packed red cells are indicated. In emergencies, when whole blood is not immediately available, correction of acute total blood volume deficits may be made with plasma or a plasma expander. Artz and Howard (7) were entirely satisfied with these agents in resuscitation of the severely wounded in Korea during 1953. However, it was found that the use of pooled, refrigerated, irradiated plasma was accompanied by a serum hepatitis incidence of 20%. Hence

plasma expanders were used in place of plasma. The most widely used plasma expanders are dextran and PVP. Dextran may be accompanied by evidence of interference with the normal coagulation mechanism (28); as much as 30% of administered PVP is stored in the reticulo-endothelial system, the last being excreted over one week in the urine. Examination 10 years later of German soldiers who received PVP during World War II showed no evidence of abnormality referable to the incomplete excretion of PVP (184). The characteristics of a satisfactory plasma volume expander (49) are : maintenance of satisfactory colloidal osmotic pressure, constant molecular composition, adequate viscosity, stability within a fairly wide range of temperature change, stability in storage for long periods of time, ease of sterilization. It must be non-pyogenic, non-allergenic, non-toxic to tissues (early or delayed), inexpensive and reproducible in adequate quantities for stockpiling. To these qualities might be added non-interference with proper typing and cross-matching of blood and non-interference with normal hemostatic mechanisms.

The use of whole blood or plasma purely for nutritional purposes is inefficient and not economical (158, 3). In 500 cc of donor blood there are but 19 gms of plasma protein. For restoration of the nutrition of malnourished patients quantities of blood would be required of the order sufficient to cause hemosiderosis from deposition of broken-down hemoglobin. The transfusion of whole blood has been recommended in cases of so-called medical (i.e. non-hemorrhagic) shock as may occur in acute infections, myocardial infarction or diabetic acidosis. In the absence of pre-existing red cell volume deficit the hypovolemia which may occur in these conditions is on the basis of a concentrated plasma volume. Plasma volume expansion is effective in restoring circulatory blood volume and circulatory dynamics (107). Sayen (148) has reported success with the vasopressor nor-adrenalin in myocardial infarction. Peters (123) maintains that when hypotension is

present in diabetic acidosis, blood may be indicated and feels that blood has a specific activity in improving circulatory efficiency lacking in plasma or plasma expanders. Peters states (124) that he has not seen complications (thrombosis or dehydration) referable to increasing the red cell volume in patients with diabetic acidosis by whole blood transfusions and notes furthermore that, following reversion of the acidosis, red blood cell counts, hemoglobin and hematocrit determinations are usually reduced. (This may be interpreted not only as a pre-existing red cell volume deficit, but as over-expansion of plasma volume due to therapy).

13 - SPECIFIC TRANSFUSION THERAPY:

Specific transfusion therapy is predicated upon the qualitative and quantitative replacement of blood volume to replace existing deficits (158). The route of administration of transfusion solutions is ordinarily intravenously, although intra-arterial transfusion has been recommended under certain circumstances. Intraperitoneal transfusion of blood has been found to result in some increment of the blood volume as cells and plasma are transported by the abdominal lymphatics and thoracic duct to the systemic circulation (107). The subcutaneous administration of blood has no merits to recommend it (107). The rate of administration of transfusion is conditioned by the severity of the deficit and the rapidity with which the deficit was incurred. In general, in the replacement of acute total blood volume deficits the rate of administration

should be rapid. Replacement of chronic deficits should be undertaken over several days in order to minimize disturbance of compensated circulatory dynamics. The rate of administration of a transfusion appears to be as important as the route of administration (7). The amount of transfusion solution required for the correction of deficits is a matter of controversy. In severe acute blood volume deficits there is an agreement that transfusion should proceed until there is evidence of restoration of normal circulatory dynamics. Specifically, replacement should be titrated against pulse and blood pressure until the latter have been established at normal levels. One authority on the subject of trauma, Sir Reginald Watson-Jones (183), states that transfusion should proceed further until there is no longer evidence of peripheral compensatory vasoconstriction; that is, pallor and coolness of skin should be absent. He suggests that the warmth at the tip of the nose is a reliable clinical indicator of the degree of

peripheral vasoconstriction. Artz (7), Prentice (129), and Howard (87) were more vigorous in the treatment of acute hemorrhagic blood volume deficits. These authors felt that the greatest single difference between the therapy of wounded men in the Korean War and those in World War II was the use of massive quantities of blood administered throughout different treatment periods. They noticed that the greatest single factor in judging the prognosis of the wounded was not the blood pressure on commencement of therapy but the number of transfusions required for resuscitation. (In patients requiring 5-10 pints, the group mortality was 1.6%; inpatients requiring 20-56 pints, the group mortality was 53%). The overall mortality of 138 wounded persons, studied in the last six months of the Korean War was 14.5%. These were patients who required from 5 to 56 pints of blood in the first 24 hours of injury. Evidently as

a minimum standard of adequate treatment Artz (7) states "unless hemorrhage is uncontrolled, the patient should be restored until the systolic blood pressure is 110 mm. of mercury or more and the pulse rate 120 per minute or less before the operation".

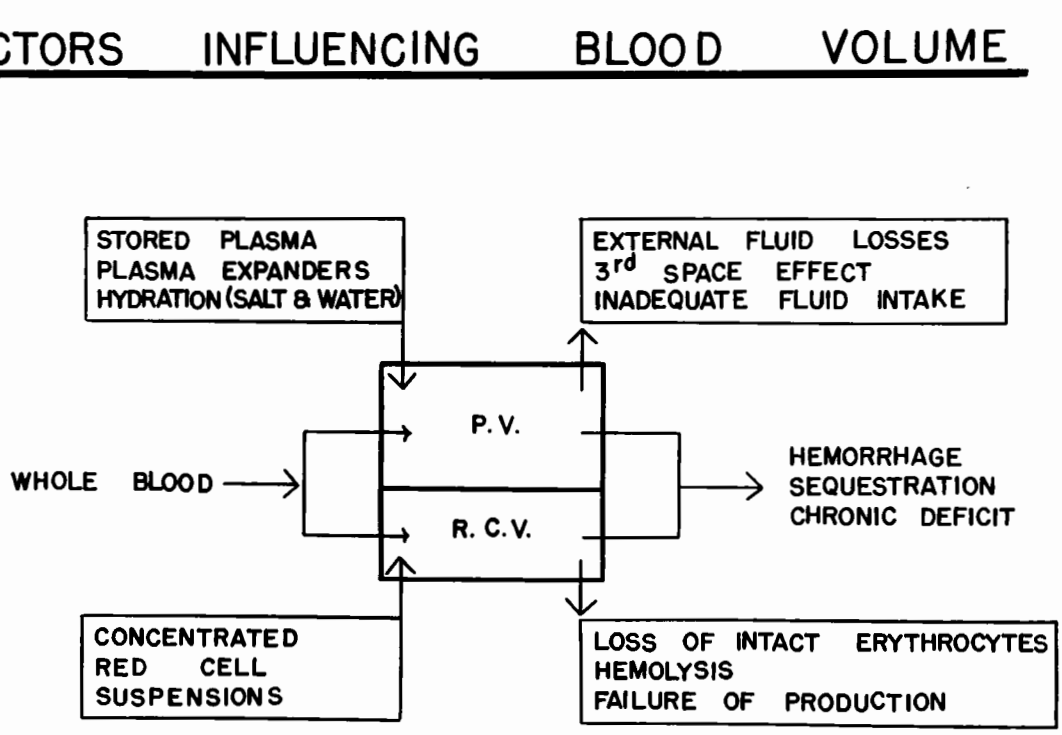

FIGURE 6

Factors influencing blood volume. Volume replacement and loss are shown as being algebraically related. With certain reservations this concept is the basis for the practical management of quantitative and qualitative therapy of circulatory volume abnormalities.

14 - PATHOLOGY OF BLOOD VOLUME REDUCTION:

With respect to circulatory efficiency three entities are of interest surgically:

A) the acute blood volume reduction occurring in the presence of massive hemorrhage or unreplaced operative blood loss;

B) acute plasma volume reduction;

C) the chronic reduction of blood volume occurring in debilitated malnourished individuals with chronic benign or malignant disease.

A) Acute blood volume reduction:

The term shock is ill-defined and in the minds of surgeons has generally been associated with hemorrhage. The statement made by Blum (24)

in 1876, that "hemorrhage is shock and shock, hemorrhage", has played a significant role in the therapy of hemorrhage. Since 1915 (94) blood volume studies have promoted the association of the term shock with hypovolemia according to Ravdin (134). Wiggers (190) has studied the problem of shock intensively in dogs and has standardized a method of producing hemorrhagic shock by reduction of blood volume to such a degree that the arterial systolic pressure is lowered to 50 mm. of mercury. He divides the reactions into oligemic and normovolemic shock. Oligemic shock (following hemorrhage) is described as having three phases: the initial period of stabilized hemorrhagic hypotension, impending or progressive stage of shock and the critical stage. Normovolemic shock (following re-infusion of all of the withdrawn blood) is described as having a compensatory stage, a progressive stage and a terminal stage. He is of the opinion that vasoconstriction has only a negligible effect in maintaining arterial blood

pressure and may actually be detrimental to the survival of the animal by decreasing blood flow when hypotension exists. He is of the opinion that dibenamine and hexamethonium have therefore possible advantages in certain stages of shock. Howard (88) is of the opinion that vasoconstrictors have little or no place in the treatment of shock, but that their place is limited to meeting a deficiency in the autonomic nervous system. In the presence of adequate transfusion, vasoconstrictors were of no value in the treatment of hypotensive shock resulting from traumatic hemorrhage.

Essentially, the results described in Wigger's experiments are those of failure of compensation of circulatory dynamics: reduction in venous pressure, arterial blood pressure, cardiac output, tachycardia (decreased cardiac rate occurring terminally) and increasing peripheral vasoconstriction. That is, if the hemorrhage (blood volume reduction) is of sufficient magnitude

a satisfactory equilibrium of circulatory dynamics is impossible.

The question arises: what must be the magnitude of blood loss in order to produce a new, compensated, equilibrium of circulatory dynamics in a previously normal individual? (Considered from the aspect of blood volume determinations - the residual volume after bleeding as well as the volume of hemorrhage regulates the circulatory response.) In dogs a 40% reduction of blood volume was necessary to lower the arterial pressure to 50 mm. Hg. by Wigger's method (190); a 48% reduction of blood volume was necessary to produce fatal shock by bleeding in Walcott's series (177). Howard (87) and Prentice (130) have reported that 15-25% blood volume reduction in man by hemorrhage and wound trauma may be associated with no hypotension, but that after a loss of 25-30% of the blood volume hypotension will develop pre-operatively (that is, before the emergency surgery necessitated by significant wound trauma).

An interesting reaction to injury is the hypertensive response. Howard (88) studied 52 men who had a sustained systoic blood pressure above 140 mm. Hg. These were individuals who had non-critical wounds associated with a loss of one liter of blood or less and had no previous history of hypertension. The hypertension disappeared following the induction of general or spinal anaesthesia. Hexamethonium abolished and regitine depressed the hypertensive response. The response seemed to be an over-compensation for blood loss and trauma and appeared to be mediated through the sympathetic nervous system. The authors quote the findings of Grant and Reeves (71) who reported similar observations in patients with limb injuries and small or medium sized wounds and blood volumes within 20% of the predicted normal.

B) Acute plasma volume reduction:

Acute plasma volume reduction may result from inadequate salt and water intake; internal redistribution of plasma volume as may occur in burns, paralytic ileus, peritonitis - the third space effect described by Randall (133); excessive gastrointestinal fluid loss from the body by diarrhea, vomiting or nasogastric secretion. Plasma volume reduction results in an increase in the concentration of red blood cells, increased blood viscosity and may be attended by the features of oligemia as described under acute hemorrhage. In addition, compensation for decreased plasma volume cannot proceed effectively when the specific problem features the passage of fluid from the vascular into the interstitial space (i.e., in dehydration and third space effect). When spontaneous restitution of plasma volume is impossible, expansion of plasma volume by fluid

and electrolyte therapy is a prerequisite for survival. Burns are complicated by the fact that there is initial red cell destruction and by the anemia which may occur in the early post-injury period.

C) Chronic blood volume reduction:

Clark (33) studied the blood volumes of chronically-ill patients, using T-1824. They found that, when the blood volume was expressed on the basis of the standard or usual weight prior to illness, marked deficits in total blood volume, total circulatory protein, hemoglobin and red cell mass were present. They maintained that in these patients the operative risk could be reduced by restoration of the blood volume toward normal. Large transfusions were tolerated well and no evidence of hemoconcentration occurred, indicating that the transfusions had replaced a real deficit. Furthermore, serial blood volume studies showed the expected increment due to transfusion. Patients so treated withstood operations well without marked change in blood pressure and pulse rate. These authors considered that the deficiency of hemoglobin was a factor of primary importance

in the problems engendered by depletion of body proteins. They agreed with Whipple and others (186, 103) that in the presence of a deficiency of both hemoglobin and tissue protein, priority is assigned to the fabrication of new hemoglobin.

15 - THE SPONTANEOUS RESTITUTION OF NORMAL BLOOD VOLUME OCCURRING IN HYPOVOLEMIC AND HYPERVOLEMIC STATES:

The immediate effects of hypovelemia due to acute deficits in total blood volume (oligemia) or of hypervolemia due to acute excesses in total blood volume (transfusion hypervolemia) may be reflected in changes in the circulatory dynamics as evidenced by changes in peripheral vascular tonus, venous pressure, heart rate, blood pressure and cardiac output. The restoration of circulatory homeostasis depends largely upon the lability of the plasma volume with fluid shift occurring across the capillary membrane. Starling's hypothesis is the basis of the current concepts on the control of the volume of blood and the distribution of water and electrolytes across capillary and cell membranes (73). The direction of flow between the intravascular and interstitial

space depends upon the effective filtration pressure. The latter is determined by four variables: the intracapillary hydrostatic pressure, the intracapillary colloid osmotic pressure, the interstitial hydrostatic pressure and the interstitial colloid osmotic pressure. Equilibrium is present when there is no net shift of water in either direction.

16 - COMPENSATION FOR ALTERATIONS IN BLOOD VOLUME AND COMPOSITION:

Compensation, that is, reversion toward a normal blood volume, may occur in certain pathological states which decrease a normal blood volume or following therapy which increases a normal blood volume. The compensation referred to is alteration in the abnormal blood volume so that it approaches normal. Confining the discussion to hypovolemia which affects circulatory dynamics, as manifested by a tendency toward hypotension or tachycardia or lowered venous pressure, the usual causes are acute total blood volume deficit or acute plasma volume deficit. Acute red cell volume deficit in massive hemolysis may be found in certain conditions.

A) Acute total blood volume deficit:

Acute total blood volume deficit is encountered in patients with massive hemorrhage (e.g. gastrointestinal tract bleeding) or with unreplaced operative blood loss. Physiological compensation occurs by fluid shift across the vascular membrane from the interstitial space into the vascular space, thus augmenting the plasma volume (51). Removal of 430 cc. of blood in four minutes was observed to decrease venous pressure for thirty minutes without hypotension or,tachycardia (101). Removal of 1050-1150 cc. of blood rapidly, results in no hypotension in some individuals when lying in the supine position but may result in unconsciousness where there is a sudden change of position (178). Removal of 1500-2000 cc. of blood rapidly results in low right auricular pressure and low cardiac output despite some tachycardia (89). These individuals exhibited signs of

pallor, cold, clammy extremities and sometimes, air hunger.

Ebert, Stead and Gibson (47) studied the rate at which restoration of the blood volume occurred spontaneously. After hemorrhage of 1000 cc. adults were found to require 36 hours to restore blood volume. This was judged by noting the rate of fall of the hematocrit, assuming no significant red cell formation within 36 hours.

Berlin (20) noted that, following thoracoplasty procedures in patients studied 2-6 days post-operatively, the average post-operative blood volume deficit was only 865 cc., in contrast to a deficit of 1250 cc. calculated from the change in pre- and post-operative red cell volume measurements. Hence an average of approximately 400 cc. was spontaneously added to the circulation by an increase in plasma volume supplementary to incomplete transfusion replacement of blood of patients sub-

jected to stress of operation, anaesthesia and blood loss.

Royster (145) in comparing estimates of change in pre- and post-operative blood volume with operative blood loss measured by the gravimetric technique of Baronofsky (13) in patients undergoing radical operations for cancer of the head and neck, noted that in 8 out of 17 cases the post-operative blood volume ranged from 0 to 2000 cc. more than expected on the basis of measured loss and replacement. In their interpretation of their results they referred to "changes of an unpredictable nature in the fluid shift and blood constituents following large operations with profuse bleeding". Undoubtedly a shift of fluid into the vascular compartment with expansion of the plasma volume played a significant role in the change noted.

Wiggers' (190) conclusions on the repletion of blood volume following hemorrhage in

the dog are that contraction of the spleen may replace at least 10% of the blood withdrawn, when the hemorrhage was adequate to produce shock. (The hemorrhage usually amounted to 2000 ml. and the splenic contraction increased the circulatory volume 200 ml.) If the spleen of the dog has an open circulation as described by MacKenzie, Whipple and Wintersteiner (102) it would seem that contraction of the spleen would result in a relocation of the contained blood rather than an actual increase of the blood volume. However, this relocation of blood would efficiently contribute to the active circulating blood volume by its redistribution to areas of more active metabolism than the spleen. Wiggers (190) notes the present tendency to question the importance of the spleen as a blood reservoir even in dogs. Wiggers (190) states that a shunting mechanism may be present relocating blood from the capillary bed into larger vessels containing the active circulation. Wiggers' (190) opinion is that fluid

migration into the blood stream through the capillaries is simple and based on reduction of intracapillary hydrostatic pressure while colloid osmotic pressure remains the same. The effective filtration pressure becomes higher in tissue spaces than within the capillaries, hence water and electrolytes enter the blood stream. The rates of plasma replenishment in hemorrhage experiments have been given as 0.25 cc/Kgm/min. (1), 0.154 cc/Kgm/min. (100), 0.101 cc/Kgm/min. (132).

Shortly after hemorrhage the re-expansion of plasma volume is from interstitial fluid only (51). The interstitial fluid is apparently replaced from exogenous sources provided that the intake of water is adequate (101) rather than from intracellular water as concluded earlier by Stewart and Rourke (164) and Lands and Johnson (99).

B) Acute plasma volume deficit:

Acute plasma volume deficit is encountered in states of dehydration (salt and water deficit) which may be due to inadequate fluid and electrolyte intake, or excessive abnormal loss. A normal loss of fluid and electrolytes may be: internal - 3rd space effect described by Randall (133) occurring in burns, ileus, peritonitis, ascities or hydrothorax, or external- with abnormal gastrointestinal tract losses due to vomiting, nasogastric suction, enterocutaneous fistulae or diarrhea.

In fact, in war wounds of the abdomen usually accompanied by peritonitis as opposed to wounds of the extremities where whole blood loss occurs predominately, it has become an axiom that "abdominal wounds hemoconcentrate, extremity wounds hemodilute" (87). Abdominal wounds are accompanied by a much higher

mortality rate than wounds of the extremities (87). This may be partially related to the plasma loss of peritonitis plus whole blood loss and injury to viscera such as the kidneys and liver. In specific deficits of plasma volume one of the factors in compensation for the lowered total blood volume, is absent: The spontaneous restitution of plasma volume by shift of interstitial fluid into the vascular space. Hence, in support of failing hemodynamics (lowered blood pressure, elevated pulse, lowered venous pressure) vasopressors have little value in resuscitation of the patient with hemorrhagic or traumatic shock (86) and prompt fluid, electrolyte or transfusion therapy must be supplied.

17 - TOLERANCE OF BLOOD VOLUME DEFICITS:

Blood volume deficits may be incurred rapidly or slowly. Massive hemorrhage results in the rapid depletion of circulating blood volume. A chronic anemia may gradually decrease the red cell volume when there is interference with the production of red cells and a normal duration of red cell survival (43) or when there is normal production of red cells and decreased duration of red cell survival (41). Clark (33) drew attention to the significance of existing circulating blood volume deficits in debilitated, malnourished patients with chronic benign or malignant disease. These workers considered that the surgically significant feature of reduced blood volume is an increased susceptibility to shock, correctable by transfusion. Clark (33) recommended that debilitated patients in a state of "chronic shock" should have deficits

of total blood volume, circulating hemoglobin and red cell volume corrected pre-operatively by transfusion to the standard value, (T-1824 method) for their usual weight in health. By doing so, it was found that poor-risk patients tolerated major operative procedures better as regards circulatory dynamics and wound healing.

It has been observed that 1000 cc. of blood may be rapidly withdrawn from healthy young adults without ill effects (47) but that occasionally withdrawal of less than 500 cc. of blood from blood donors may result in fainting or a "vaso-vagal response" (107). An individual's hemodynamic response to blood volume depletion is apparently a function of:

1. - the volume removed; Wiggers (190) defines the maximal amount of blood which may be removed from an individual without death resulting the "sublethal bleeding volume");

2. - the volume remaining in the circulatory system;

3. - the functional capacity of the individual to compensate for the discrepancy between the actual remaining and the usual blood volume.

Paquin (121), who has studied 60-80 year old patients with carcinoma who were candidates for radical pelvic surgery, is of the opinion that in such adults the physiological limit of deficit for operative blood loss lies somewhere about 1000 cc. Recalculation of some of Berlin's (20) data on blood volume in thoracic surgery indicates that post-operatively 3 of 27 patients had deficits of 1000 cc. or more and none was in shock at the time of the blood volume study.

Regarding the pre-operative correction of blood volume deficits several empirical rules

have been established for transfusion. Crehan (39) states that 40 ML. per pound of weight loss pre-operatively is a useful "rule of thumb". Crehan (39), in discussing restoration of blood volume in gastrointestinal bleeders, stated a preference for whole blood rather than plasma volume expanders, commenting that his choice is influenced by the superiority of red blood cells in regard to their persistent space-occupying function and oxygen-carrying capacity (109, 153,). Beling (15), using T-1824 and calculating normal values on the basis of normal weight in health, stated that any deficit in total blood volume of 500 cc. or more should be corrected pre-operatively by transfusion. Mollison (107) states that patients should not be subjected to operation with a hemoglobin level of less than 10 gm.%, and quotes the statement of Grant and Reeve (71), that, in patients who have trauma associated with blood loss, the blood volume should be raised to at least 80% of normal before operation is begun.

18- CLINICAL SIGNIFICANCE OF FACTORS AFFECTING THE PRECISION OF BLOOD VOLUME MEASUREMENTS:

The question of the degree of accuracy with which an estimate of the blood volume can be made is of particular interest to the surgeon. As stated by Fox and Lasker (60), the objective of fluid therapy in surgical emergencies, including hemorrhage, loss of gastrointestinal fluids and thermal burns, is "to restore cardiac and renal output and the function of other vital organs so that essential surgical procedures can be performed". Using the terminology of Fox and Lasker (60), there may occur: vascular fluid loss (e.g. hemorrhage), extravascular fluid loss (e.g. vomiting, naso-gastric suction, diarrhea, fistulas or intra-abdominal fluid extravasation due to peritonitis or pancreatitis) or fluid loss primarily as an

internal redistribution caused by tissue trauma (e.g. thermal burns, extensive crushing injury, fractures). These fluid losses decrease the volume of circulating blood and maintenance of circulatory dynamics (as reflected in venous pressure, blood pressure, pulse, state of tonus of skin vessels) is dependent upon the mobilization of physiological mechanisms to compensate for decreased blood volume. Decrease in blood pressure and rise in pulse rate with associated decline in venous pressure and evidence of peripheral vasoconstriction are frequently indications of marked decrease in circulating blood volume. Artz (7) states that hypotension in an individual who has been subjected to trauma or hemorrhage is almost always an indication of the need of further therapy to expand the blood volume. One author (118) recently stated that he used operative hypotension as an indication for blood volume expansion in a study of the

efficacy of plasma volume expanders. The physiologic and biochemical response of the patient are effective guides to therapy (60) and are the usual basis for a practical decision on rates, quantity and type of therapy to be employed when confronted with surgical emergency such as oligemic hypotension. Blood volume determinations, then, should provide the clinician responsible for the management of such an emergency with data which will allow a more exact prescription of transfusion solutions so that the patient's compensatory mechanisms may function more adequately. The precision of blood volume determinations depends upon: the method used, the condition of the patient (with reference to circulatory dynamics and integrity of the vascular membrane enclosing the vascular space) and familiarity with the technique of the method by the technician performing the determination.

When dilution methods of performing blood volume determinations are used it is assumed that a rather well-defined compartment of body fluid is being measured, namely, the intravascular (or blood volume) compartment. However, the vascular compartment consists not of rigid inanimate tubing but of tubing which is capable of contraction, dilatation and distension and which is really a semipermeable protoplasmic membrane separating the intravascular and extravascular fluid spaces of the extracellular fluid space. This concept, as it pertains to distribution of fluid after trauma and the measurement of blood volume, is discussed by Fox (60, 61). RIHSA or T-1824 have the volume distribution of albumin and hence measure the "circulating albumin pool" which may be slightly larger (63) yet in rapid equilibrium with the plasma volume during the 10-15 minutes mixing time usually allowed for a blood volume determination. In hemorrhage fluid shifts occur

into the plasma (51), mixing of the test substance may be altered by an abnormal circulation time and loss of the test substance from an open vessel may increase its apparent distribution. Test substances measure only the volume in which they are mixed hence will not measure stagnant blood in the body. In short, the dilution method measures only circulating blood volume. Prentice (129), Artz and Howard (7) have postulated sequestration of blood as a reason for the deficits existing in casualties treated with massive transfusion. These authors point to damaged muscle as a place where blood may be lost from the active circulation. Alternatively, they suggest hemolysis or bleeding between blood volume studies are responsible for an expansion of the discrepancies.

T-1824 may stain tissues and be taken up by reticulo-endothelial cells (193,

43, 105), thus giving an artifactitiously high blood volume. Inaccuracies of colorimetry are present (107) in higher dye concentration ranges and limit the accuracy of the method.

Under normal conditions of circulation, T-1824 has been reported to give results which are serially reproducible within 3.5-10.0% (15, 27); radioactive chromium - 3% (62, 72), RIHSA - 3% (27). These estimates are for studies done within two hours of each other.

Experiments involving transfusion and hemorrhage of measured amounts of blood have been done in conjunction with blood volume determinations (72, 62) (157). In general, an increase in blood volume has been shown with transfusion and a decrease with hemorrhage. Use of a factor to correct for body-venous hematocrit difference will affect the calculation of the magnitude of blood volume and red cell volume changes when plasma diluent test substances are used. Clark (33),

and McInnes (104) in serial studies of blood volumes of patients noted increases in blood volume when the patients were transfused pre-operatively but did not express any quantitative comparison of the measured amount given and the blood volume increase. Fox (60, 61) notes that not all of the volume of transfusion can be accounted for by blood volume measurements and attributes this to shifts of cells and plasma occuring within the patient rather than to the methods (RIHSA and Cr^{51}) or calculations used. Berlin (20), in calculating "blood turnover" during operations, assumes that satisfactory precision is present in his measurement. (i.e. "turnover" equals difference between post and pre-operative blood volumes plus transfusion.) Correlation of the blood volume "turnover" with gravimetrically measured operative blood loss would have provided a basis for practical evaluation of the assumption which is probably correct since such a correlation

has been made (145) using T-1824 for the same purpose. Siler and Fultz (157) using RIHSA in studying measured hemorrhage in dogs could account for 65% of the measured blood loss. However, there is no mention of their paper as to the circulatory state of the animals when measurements were made and apparently the dogs were not previously splenectomized. Gregersen (75) points out that blood volume measurement is not reproducible precisely in non-splenectomized dogs.

Realizing the inherent limitations of the dilution methods, clinically precise data may nevertheless be obtained. RIHSA has a satisfactory volume distribution (63) during the normal mixing time (10-15 minutes) and reproducible measurements are obtained under normal circulatory conditions (27). A three sample technique (27) may be used to minimize the effect of abnormal mixing in abnormal circulatory states such as congestive heart failure or shock.

In patients subjected to trauma, blood loss and transfusion, Prentice and co-workers (129, 130), using Cr^{51} tagged red cells, obtain multiple blood samples until the samples differ by less than 5% indicating complete mixing. Red cell tag methods, especially those using injected isotopically labelled red cells, have the advantage that the volume distribution of the cells cannot be greater than the vascular compartment unless the vascular membrane is broken (e.g. as in hemorrhage from an open vessel) or injured (permitting diapedesis).

19 - OPERATIVE BLOOD LOSS MEASUREMENT:

The quantitative determination of operation blood loss has been approached in four ways: by the colorimetric method, by the gravimetric method, by blood volume determinations and by measuring changes in weight of the patient.

A) Colorimetric method:

Gatch and Little (64) introduced the acid hematin colorimetric method in 1924. This involves washing all the sponges, linen and instruments free of blood, then adding hydrochloric acid to these washings to make an 0.1 N solution. The acid hematin preparation is then compared colorimeterically with a sample of acid hematin prepared from the blood of the patient before surgery. These authors considered the estimate thus obtained to be a minimum because of the inability to recover all of the

hemoglobin by washing. The error was stated to be at least 5%. Modifications of the procedure have been described (127, 112, 187, 154). Results of the determination are not available until completion of the operation except in the case of transurethral prostatic resection, where blood is washed directly into a container. Transfusion requirements during operation are supplied on the basis of the surgeon's estimate or routine policy for specific procedures. Such estimates based on clinical impression of the amount of blood loss may be seriously in error (36). Dingman (44) used the colorimetric method in a study of blood loss in infant cleft lip and cleft palate surgery. Pre-operative blood volumes of the children were not measured, but estimated at approximately 90 cc/Kgm as given by Robinow (143). The cleft lip patients weighed from 2.5 to 9.2 kilograms and lost from 3 to 13% of their estimated blood volume; the cleft palate patients ranged from 7.6 to 20.1 kilograms and lost from 4 to 7% of their estimated blood volume at operation. The value of a method

of operative blood loss measurement in children is commended by these authors.

B) Gravimetric method:

Wangensteen (180) described the gravimetric method in 1942. The method consists of: the use of dry sponges throughout the operation; blood soaked sponges are weighed frequently during the operation, minimizing loss of weight by evaporation; the gain in weight of the sponges is regarded as blood loss, each gram being considered equivalent to one ml. Moist sponges may be used to cover viscera and minimize fibrin formation; these sponges are not weighed. The gravimetric method (13) was found to give 10% higher values for blood loss than the colorimetric method, and to provide the advantage of a record of the measurement contemporaneous with the loss so that transfusion may be quantitative during operation.

Average values for blood loss by the gravimetric method reported in Wangensteen's paper of 1946 (13) were:

Operation	ML.
appendectomy	25.8
hernia	82.9
gall bladder	179.4
subtotal gastrectomy for ulcer	499.8
subtotal gastrectomy for cancer	455.6
thyroidectomy	405.6
radical mastectomy	415.4
pneumonectomy, lobectomy	1399.

Royster (145) studied operative blood loss in head and neck surgery. Their gravimetric measurement showed the following average losses:

Operation:	ML.
radical maxillary resection	1505.
bilateral jaw - upper neck dissection	1849.
jaw - tongue - neck dissection	2473.

radical neck dissection	2483.
jaw - neck dissection	4068.

Average blood losses for the various groups of operations ranged from 376 to 770 ML. per hour.

Ladd and Gross (98) use this method routinely in operations on children. Barononfsky (13) states that for blood losses of 500 ML. or less, an equivalent amount of plasma is usually adequate; for blood losses in excess of 500 ML. it is best to replace them with an equivalent amount of blood.

C) Blood volume determinations and estimate of operative blood loss:

The performance of blood volume determinations before and after surgery allows an estimate of operative blood loss when the extent of transfusion is known. Royster (145) used the

T-1824 method. Correlation with the gravimetric measurement averaged plus or minus 250 ML. when the difference between pre- and post-operative total blood volume determinations was compared with the measured (gravimetric) loss, the loss on dressings and transfusion.

Berlin (20) used the P^{32} method. Blood turnover was calculated by adding the red cell volume of transfusion (assumed to be 200 ML. per 500 ML. transfusion) to the difference between pre- and post-operative red cell volume measurements. It was noted that the apparent turnover (i.e. loss) of whole blood during operation was less than expected from a calculation of the whole blood loss represented by the red cell loss. This was accounted for by the spontaneous restitution of plasma volume which occurs due to shift of fluid into the vascular compartment from the extravascular fluid compartment.

McInnes (104) used the T-1824 method. Blood volume determinations were performed

in four patients before and after radical surgery. All patients had cancer, were deficient in red cell volume and received transfusions pre-operatively. Low post-operative red cell and total blood volumes were restored to normal values by transfusion.

In an attempt to permit a continuous estimate of the volume of circulating blood during radical surgery Plentl and Gelfand (128) described a method of serial determinations of blood volume using T-1824. A dilute solution of dye was introduced in 3-4 mgm. amounts during operation and repeated determinations made. These authors found satisfactory results with the small concentrations of dye permitting several serial determinations to be performed within the period of operation.

D) Gravimetric body weight method:

Paquin (121) described a method of determining operative blood loss by measuring the weight of the patient immediately before and immediately after operation. The difference in weight is due to the net difference between the weights of materials added or removed during operation. Contributing to weight gain are: transfusion of blood, intravenous fluids; contributing to weight loss are: blood loss, water loss (insensible water loss, urine, intestinal contents, bronchial secretions, ascitic fluid, etc.), specimen removed. Routinely the patient is weighed by the intern on a special scale in the operating suite; the weight of the specimen is measured by the circulating nurse, the volume of blood and water administered are recorded accurately by the anaesthetist. Insensible loss is calculated on the basis on 0.75 gm/Kgm/hour. These data permit calculation of post-operative blood

requirements. Paquin comments that in pelvic exenteration procedures, urine collected in a suction bottle may be measured as blood loss and insinuate an error in the direction of greater loss. The loss of blood in the pelvis may constitute a third space effect in Randall's (133) terminology, and cause an error in the direction of lesser loss. In pelvic exenterations this third space effect may cause a large decrease in circulating blood volume which was illustrated in one case in which the loss amounted to 1500-1700 cc. (The change in circulating blood volume was based on T-1824 determinations pre-operatively and post-operatively and knowledge of transfusion and operative blood loss by the gravimetric method).

PART III MATERIALS AND METHODS

A) MATERIALS:

In this section are described the requirements for a hospital blood volume laboratory in which an average of ten RIHSA blood volume determinations per day may be performed. The description is based on experience in equipping and establishing such a laboratory at the Royal Victoria Hospital, Montreal.

1 - Laboratory space:

Running water, sinks, electrical outlets, vacuumline, water bath and equipment storage space were present in a laboratory which had stainless steel tables. Special shielding is not necessary under ordinary conditions of background radio-activity. Since tracer quantities of radioactivity are used, waste may be poured

down drains which connect with main sewage outlets and further diluted by running water. Contamination of the laboratory would be indicated by an elevation of background count, but should not occur with ordinary care in the handling of RIHSA.

2 - Counting equipment:

A well-type scintillation counter was provided by Dr. Lloyd Stephens-Newsham of the Department of Radiology, of the Royal Victoria Hospital. Similar scintillation counting apparatus is commercially available (e.g. Model D S -3 Scintillation Well Counter, Nuclear Chicago, 223 W. Erie Street, Chicago 10, Illinois). The counter used had an efficiency of 35-40% for gamma disintegrations. The counter consists essentially of a sodium iodide crystal, phototube and preamplifier surrounded by a lead housing. Well counting permits the immediate counting of

liquid specimens (e.g. plasma, urine, gastric aspirate) with maximum sensitivity and favorable background rates so that counting errors of less than 1% may be obtained when using 0.01 microcuries of radioactive iodine.

A scaler with an automatic timing device was used. (Atomic Instrument Company Model 1030A). The background was approximately 500 counts per minute at voltage 800, pulse height selector plus 40, attenuator 2. Two ml. samples of plasma or other solution containing approximately 0.01 μc gave more than 10 times the background activity. Counting was performed for 5 minutes. The scaler, being connected with the counter, automatically registered the counts. The counting apparatus should be turned on at least 15 minutes before counting, as some variation in counting may occur immediately after the counter is turned on. Each counter should be tested periodically for variability in counting.

The optimum setting for voltage, pulse height, and attenuation can be determined by altering these settings and noting the range over which successive counts differ least. For example, by altering the voltage a curve may be constructed with a constant slope, a plateau, and a further slope. Counting should be done at a voltage situated on the plateau of the curve in order to minimize effects on counting due to voltage fluctation occurring in the source of the current.

3 - Centrifuge:

For the determination of the hematocrit a satisfactory centrifuge is absolutely necessary. An angle centrifuge cannot be used. A small laboratory centrifuge (3000 r.p.m.; 15 cm radius) with a mounting for four tubes is satisfactory. A larger centrifuge with a timer (greater than 3000 r.p.m.; 22 cm radius) is superior.

Centrifugation must be standard (e.g. 3000 r.p.m.; 15 cm; 30 minutes) as variation in the packing of red cells due to different durations and amounts of centrifugal force may introduce errors beyond those due to trapped plasma and body-venous hematocrit difference. For a rough estimate of the ratio of red cells to whole blood, 15-20 minutes of spinning (3000 r.p.m.; 15 cm) will probably be within 5 divisions of the final hematocrit reading. For precise results, the importance of standardization of centrifugation conditions cannot be over-emphasized when using the RIHSA-hematocrit method.

4 - RIHSA:

Radioactive Iodinated Human Serum Albumin ("RISA") was obtained from Abbott Laboratories, Department of Radioactive Pharmaceuticals, North Chicago, Illinois. An allocation number and a certificate of compliance was first

obtained from the Atomic Energy Commission by Dr. Carleton B. Peirce, Department of Radiology, Royal Victoria Hospital. The RISA was shipped by air express directly from Oak Ridge, Tennessee. Approximately 5 millicuries per month were used. The RISA, in 10 cc. sterile rubber-capped bottles, contained approximately 10 mgm of human serum albumin and from 0.4 to 1.0 millicuries of I^{131} per cubic centimeter. Not more than one atom of iodine per 6000 molecular weight of albumin is introduced in the preparation of the RISA (141).

The RISA should be stored under refrigeration (2° - 10° C,) and should be used within four weeks after the date of preparation. An assay of the radioactivity at time of shipment is included with each lot. I^{131} has a half-life of eight days. A chart of factors from day 1 to 30 based on the half life is useful in calculating the activity on a specific day.

5 - Heparin:

Five cc. ampules of heparin solution, 10000 u per ML (Connaught Laboratories) were used. Heparin was drawn into the syringe for a blood sample, allowed to thinly coat the barrel and the excess discharged into the ampoule. Actually only 0.25 to 0.5 mgm of heparin is needed to prevent coagulation of 5 ml of blood. Sequestrene (disodium ethylene diamine tetraacetic acid) 5 mgm per 5 ml of blood (80) or evaporated oxalate (81), is suggested as a cheaper alternate and neither anticoagulant should effect the hematocrit determination.

6 - Sterile normal saline:

Sterile normal saline in 100 ml. rubber-capped containers is required for preparation of dilute RIHSA for injection. One bottle is sufficient for 15 determinations on the average.

7 - Laboratory glassware and apparatus:

a) 2000 ml volumetric flask with glass stoppers (2)

b) 1000 ml volumetric flask with glass stoppers (2)

c) 2 ml volumetric pipettes (24)

d) 1 ml volumetric pipettes (12)

e) Wintrobe hematocrit tubes (12)

f) Wintrobe pipettes (12)

g) Round bottom glass test tubes for counting 16 x 75 mm (36)

h) centrifuge tubes, glass (36)

i) suction trap bottle

8 - Decontamination and cleaning of equipment:

a) enameled tray (14" x 18" x 3") - (1 or 2)

b) beakers 1500 ml (3)

c) Kodak automatic tray siphon, (Canadian Kodak Co., Toronto, Ont.) (1)

d) Clay-Adams hematocrit tube cleaner (1)

e) sodium iodide (1 pound) (Merck and Co, Montreal, Quebec)

f) detergent powder

g) Versene (Ethylenediaminetetraautic acid) (5 pounds) (Bersworth Chemical Co., Framingham, Massachusetts)

h) test tube brushes

i) tongs for handling warm glassware

j) rubber gloves

9 - Equipment used in performing test:

a) basket for carrying equipment to patient

b) forms on which to record data pertaining to patient (date, weight, height, diagnosis, reason for examination, time and amount of injection, time of sample) (space for recording results and interpretation)

c) syringes - 5 ml (multi-Fit, Luer-Lok) (20-30)
10 ml (10)
20 ml (20)
1 ml tuberculin (3)

d) covers for syringes

e) needles #20 gauge (36)
#25 gauge (6)

f) containers, glass, 30 ml for blood samples

g) glass marking pencils

h) parafilm for covering sample containers
25 - 20" size (Fisher Scientific, Montreal)

i) alcohol for cleansing skin before veni-puncture

j) sponges (2" x 2")

B) METHODS:

1 - Pattern of investigation:

Isolated single determinations were performed on normal individuals and individuals with conditions thought to affect the volume of circulating blood (e.g. carcinoma, portal cirrhosis, intestinal obstruction, burns, ulcerative colitis, hemorrhage). The majority of the patients studied were from the Royal Victoria Hospital.

Serial studies during treatment were performed on patients of the Royal Victoria Hospital (surgery service) who presented interesting electrolyte and blood volume problems.

Operative blood loss in general surgical and thoracic surgical patients was estimated by pre- and post-operative blood volume determinations plus a record of transfusion at operation. An intensive investigation over a period of one month was conducted at the Royal Edward Laurentian Hospital.

Correlation between gravimetric and RIHSA estimate operative blood loss was studied and determinations were performed on 35 pre-operative patients on the surgical service of the hospital during that month. This study was undertaken to evaluate the adequacy of operative transfusion routine, to ascertain the influence of chronic disease on the blood volume of patients with tuberculosis, and to determine the practicability and usefulness of the RIHSA method in such an institution.

The effect of age on blood volume was the subject of an investigation of the blood volume in early childhood conducted largely at the Montreal Children's Hospital.

The problems related to the establishment of a blood volume laboratory were investigated by a trial in the Royal Victoria Hospital of various methods of RIHSA blood volume determinations. Associated problems of decontamination and re-use of glassware, evaluation of errors in technique,

and the reproducibility of test results were studied.

2 - RIHSA blood volume method:

The method diagrammed in Figure 7 is that evolved in the Blood Volume Laboratory of the Royal Victoria Hospital and is recommended for the performance of routine blood volume studies. The steps in the figure are outlined below:

a) RIHSA solution containing 500-1000 microcuries per milliliter is received from the supplier by air express.

b) Preparation of dilute (2 uc/ml.) RIHSA solution: 200 uc (approximately) is withdrawn (tuberculin syringe; #25 needle) from the concentrated solution and injected into the rubber-capped 100 ml. bottle of sterile normal saline. This dilute solution may be used up to one week after preparation but must be kept under refrigeration.

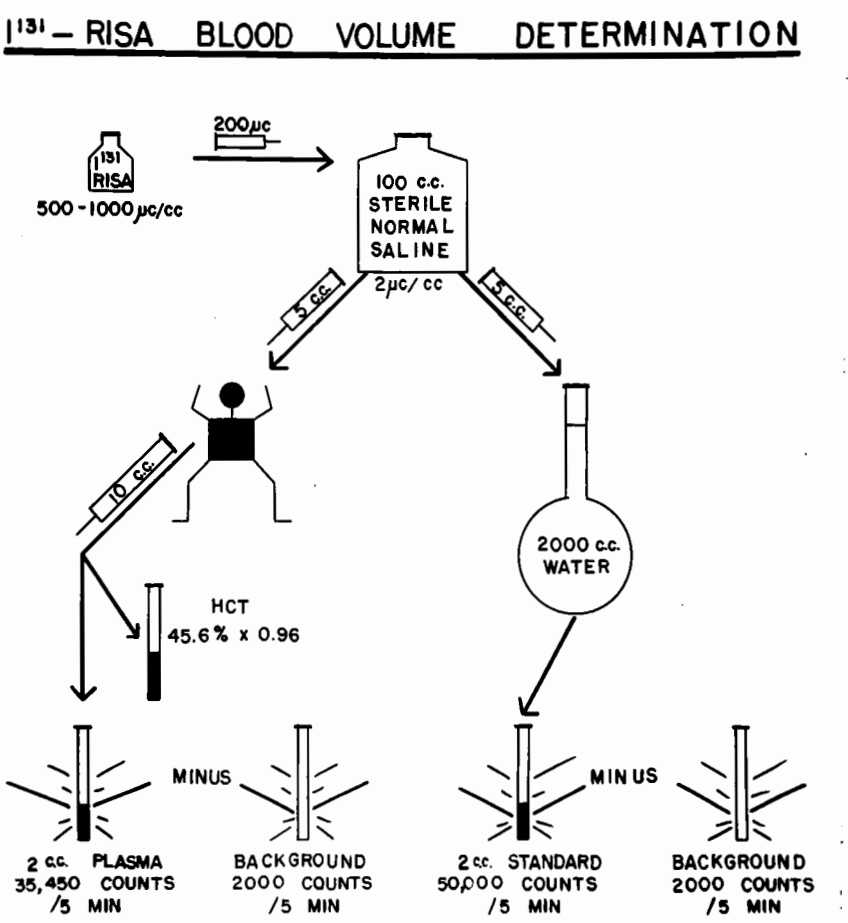

FIGURE 7

RIHSA blood volume method. Diagram illustrates the method employed at the Royal Victoria Hospital, Montreal.

c) Injection: Exactly 5 ml. (Multi-Fit syringe; #20 needle) is withdrawn from the dilute RIHSA solution after the bottle has been shaken well. The 5 ml. are injected into a peripheral vein of the patient; the syringe is not rinsed out with blood. The injection may be made into the rubber tubing of an intravenous infusion set already in place with the solution running.

d) Equilibration time; sampling: Between 10 and 15 minutes are allowed for equilibration under normal circulatory conditions when only a single post-injection sample is to be withdrawn. Under abnormal conditions 10, 20 and 30 minute samples may be used to calculate the RIHSA volume distribution. A 10 ml. blood sample is withdrawn with minimal tourniquet stasis from another vein using a lightly heparinized needle-syringe. When venous pressure is low and peripheral veins are in collapse the blood sample may be obtained from the femoral vein or artery.

e) Preparation of standard: Exactly 5 ml. of dilute RIHSA is placed in a volumetric flask which is filled with tap water up to the 2000 ml. mark. (The volume of dilute RIHSA taken for the standard is critical; it must be exactly 5 ml., the amount injected into the patient.) The flask is inverted ten times for uniform mixing. Tap water may be used in the preparation of the standard as gamma radiation is being counted in the well counter. Beta counting may be affected by the phenomenon of "self-absorption" of radiation in protein solutions. Hence for beta counting, plasma of the same protein concentration as that of the patient's plasma should be used.

f) Hematocrit determination: The patient's blood sample is mixed well and 1 ml. placed in a Wintrobe hematocrit tube. This is spun under standard conditions (i.e. 3000 RPM; 15 cm; 30 minutes) of 167 G. for 30 minutes. Under these conditions the venous hematocrit is multiplied by 0.96 to correct for trapped plasma. Pending

an accurate definition of body-venous hematocrit difference when RIHSA is used, no correction is made for this difference. It must be remembered that such a policy may lead to an over-estimate of red cell mass of 2 to 20% (75). For an appreciation of the magnitude of this error see Figures 2 and 3 of this thesis. The error is partially nullified by noting changes in serial determinations and the accuracy of the RIHSA plasma volume is not affected by the hematocrit. The hematocrit is read to the top of the red cell volume; buffy coat is not included.

g) Preparation of plasma for counting: The remaining whole blood is rapidly centrifuged to obtain the supernatant plasma. Exactly 2 ml. of plasma (2 ml. T.D. volumetric pipette) are placed in a glass counting tube which has already been counted for at least one minute. Background count equals count of empty tube for 5 minutes. Sample plus background count equals count of the same tube containing 2 ml. plasma for 5 minutes.

h) Standard counting: From the well mixed standard exactly 2 ml. are taken and placed in a glass counting tube similar to that used to hold the plasma. Background counting is done with the tube empty. Standard plus background count equals count of tube containing 2 ml. of standard for 5 minutes. Counting of the empty tube eliminates contamination of the counting tube as a source of counting error.

3 - RIHSA Blood volume calculations:

The calculation is predicated upon the assumption that the same total amount (5ml.) of dilute RIHSA is injected a)into the patient, and b)into the 2000 ml. flask. Thus, the concentration in the plasma (plasma counts minus background counts) times the volume of plasma equals the concentration in the standard (standard counts minus background counts) times the volume of the standard (2000 ml.).

Solving the equation for Plasma Volume:

$$PV = \frac{(\text{Plasma Counts} - \text{Background Counts}) \times 2000}{(\text{Standard Counts} - \text{Background Counts})}$$

The Total Blood Volume is calculated from the Plasma Volume and the venous hematocrit times 0.96:

$$TBV = \frac{PV}{1.00 - \frac{HCT\% \times 0.96}{100}}$$

Red Cell Volume is the difference between the Total Blood Volume and the Plasma Volume:

$$RCV = TBV - PV$$

4 - Serial RIHSA blood volume determinations:

In order to perform a second determination, the residual radioactivity from the previous determination must be taken into account. An initial blood sample

is taken and the plasma radioactivity determined. More RIHSA is injected and then the usual post-injection sample is taken. The increment in plasma radioactivity of the second sample is accepted as being due to the RIHSA injected for the second determination. This increment in radioactivity then reflects the volume distribution of the RIHSA during the second determination. Calculation of the second RIHSA blood volume is then similar to the calculations described above. For examples of serial determinations and the protocol of these experiments see Table 6 - Technique Standardization.

5 - Gravimetric measurement of operative blood loss:

The method used was essentially that described by Wangensteen in 1946 (180), in which each gram of weight gain of dry sponges was taken as one ml. of blood loss. In addition the volume of suction was noted during the procedure. At the close of the operation the four to six towels used to drape the operative area were removed and weighed. The large

drape was not weighed but blood on it was estimated. Large sponges weighed 26 gms., small (2" x 2") sponges weighed 6.5 gms., towels (14" x 26") weighed 75 gms. The procedure was simplified and arithmetical errors minimized by:

a) counterbalancing sponges to be weighed with an equal number of dry sponges;

b) placing the sponges in a paper bag immediately after they were discarded from the sterile field. Groups of sponges were then weighed: 6 large sponges in a paper bag (counter-balanced with 6 large dry sponges and a paper bag) or 10-20 small sponges in a paper bag (counterbalanced with an equal number of small sponges in a paper bag).

PART IV RESULTS

The experimental and clinical investigative results are presented in Tables 1 to 19 inclusive; Figures 8 to 11 inclusive; and Charts 1 to 4 inclusive.

Tables 1 to 5 present the data on normal adults and children; Tables 6 to 11 are on technique standardization; Tables 12 and 13 are on counter standardization; Tables 14 to 19 review the data obtained from the investigation of blood volume changes associated with the surgery of pulmonary tuberculosis.

Figures 8 to 11 graphically illustrate representative blood volume problems studied by serial determinations.

Charts 1 to 4 present data obtained by single and serial RIHSA blood volume determinations

in patients presenting problems of abnormal blood volume, fluid and electrolyte abnormalities in elderly and poor-risk patients and a miscellaneous group of patients. Clinical data are appended to the results of the RIHSA blood volume determinations.

RIHSA BLOOD VOLUME DETERMINATIONS
GROUP MEANS

CLASSIFICATION AND NUMBER	MEAN AGE	AGE RANGE	PLASMA VOLUME ML/KGM	RED CELL VOLUME ML/KGM	TOTAL BLOOD VOLUME ML/KGM	HCT %	SURFACE AREA M^2	TOTAL BLOOD VOLUME ML/M^2
NORMAL ADULT MALES (25)	27	15-45	40.8 ± 6.0	32.0 ± 5.4	72.7 ± 8.5	45.6 ± 3.0		
NORMAL ADULT MALES (15)	27	21-41	. . .			45.2 ± 3.5	1.91 ± 0.14	2766 ± 255
NORMAL ADULT FEMALES (18)	30	14-46	43.5 ± 7.5	27.2 ± 5.7	70.7 ± 10.2	40.5 ± 5.5		
NORMAL ADULT FEMALES (11)	28	14-44				40.2 ± 2.7	1.58 ± 0.21	2518 ± 205
NORMAL CHILDREN (27)	6	2-11	49.6 ± 4.5	28.7 ± 2.4	78.5 ± 6.1	38.2 ± 1.9	0.80 ± 0.16	1974 ± 186
PULMONARY TBC MALES-PRE-OP (16)	38	26-60	41.4 ± 7.0	31.9 ± 4.7	73.5 ± 10.4	45.4 ± 5.4		
PULMONARY TBC FEMALES - PRE-OP (16)	35	24-55	40.1 ± 5.5	24.1 ± 2.6	64.2 ± 7.1	39.3 ± 3.3		
PULMONARY TBC MALE- POST-OP (9)	36	26-60	36.4 ± 5.9	26.2 ± 6.6	62.6 ± 11.0	43.2 ± 5.3		
PULMONARY TBC FEMALE- POST-OP (6)	36	29-41	37.9 ± 2.4	22.0 ± 3.2	59.9 ± 5.3	38.0 ± 2.4		

TABLE 1

Composite table of mean values for all groups studied by the RIHSA blood volume method.

PLASMA VOLUME, RED CELL VOLUME, TOTAL BLOOD VOLUME DETERMINATIONS

WITH IODINATED HUMAN SERUM ALBUMIN NORMAL FEMALES AGES 18-46

#	NAME	DATE	DIAGNOSIS	AGE	HT (CM.)	WT	HCT	HCT X 0.96	PLASMA VOLUME ML	PV ML/KGM	RED CELL VOLUME ML	RCV ML/KGM	TOTAL BLOOD VOLUME ML	TBV ML/KGM
1	G.P.	9/25	NORMAL (O.P.D.)	25	150	59.4	38.0	36.5	2152	54.1	1226	31.1	5358	85.2
2	D.P.	9/29	BREAST CYST	17	—	58.2	36.0	34.6	3018	51.9	1597	27.4	4615	79.3
3	L.B.	10/6	NORMAL (R.V.H.)	28	—	60.5	39.5	37.9	2257	37.3	1377	22.8	5634	60.1
4	S.L.	10/14	PSYCHONEUROSIS	46	—	80.5	42.0	40.3	2650	32.7	1776	22.0	4406	54.7
5	J.T.	12/15	LAB. TECH.	28	157	50.3	38.3	36.8	2203	43.8	1285	25.5	3488	69.3
6	R.B.	12/15	LAB. TECH.	37	178	84.0	45.5	43.7	2672	31.8	2074	24.7	4746	56.5
7	J.B.	12/16	LAB. TECH.	29	173	61.2	39.5	37.9	3483	56.9	2126	34.8	5609	91.7
8	C.B.	12/16	PHYSICIAN	30	179	72.6	35.5	34.1	3554	49.0	1839	25.3	5393	74.3
9	B.B.	12/16	LAB. TECH.	22	158	51.2	37.0	35.5	2395	46.8	1318	25.7	3713	72.5
10	T.J.	12/26	PSYCHONEUROSIS	19	155	45.4	41.5	39.8	2244	49.4	1484	32.7	3728	82.1
11	A.C.	—	NORMAL (R.V.H.)	40	155	45.4	42.0	40.3	1929	42.5	1302	28.7	3231	71.2
12	J.A.	1/18	APHERESTORY (P.O.#6)	14	165	59.5	41.5	39.8	2190	36.8	1448	24.3	3638	61.1
13	U.S.	3/4	NORMAL (R.V.H.)	44	165	58.0	42.0	40.3	2319	40.0	1565	27.0	3884	67.0
14	L.O.	5/12	BREAST CYST	42	—	41.8	44.0	42.2	1960	46.9	1408	33.7	3368	80.6
15	E.M.	5/25	LAB. TECH.	29	—	61.4	36.0	34.6	2960	48.2	1566	25.5	4526	73.7
16	U.O.	5/25	LAB. TECH.	29	—	75.0	47.5	45.6	2480	33.1	2079	27.7	4559	60.8
17	E.B.	5/27	SECRETARY	39	—	62.5	38.0	36.5	2405	38.6	1582	22.2	5787	60.8
18	L.T.	5/27	SECRETARY	25	159	43.6	41.0	39.4	1900	43.6	1255	28.3	3155	71.8
AVERAGE (18 FEMALE SUBJECTS)							HCT 40.5%			PV 45.5		RCV 27.2		TBV 70.7
S.D.							±5.3			± 7.3		±5.7		±10.2

TABLE 2

Normal female subjects studied by RIHSA method. Plasma volume 45.5 ML/KGM, red cell volume 27.2 ML/KGM, total blood volume 70.7 ML/KGM. (HCT 40.3%)

PLASMA VOLUME, RED CELL VOLUME, TOTAL BLOOD VOLUME DETERMINATIONS

WITH IODINATED HUMAN SERUM ALBUMIN NORMAL MALES - AGES 15-45

#	NAME	DATE	DIAGNOSIS	AGE	HT	WT	HCT	HCT x 0.96	PLASMA VOLUME ML	PLASMA VOLUME ML/KGM	RED CELL VOLUME ML	RED CELL VOLUME ML/KGM	TOTAL BLOOD VOLUME ML	TOTAL BLOOD VOLUME ML/KGM
1	K.C.	9/15	BIL. HERNIOPLASTY (P.O. #4)	19	--	73.0	43.5	41.8	3610	49.5	2993	35.5	6203	85.0
2	A.B.	9/16	DUODENAL ULCER	33	--	65.7	49.5	47.5	2281	34.7	2064	31.4	4345	66.1
3	A.S.	10/12	HERNIOPLASTY (P.O. # 7)	29	72	66.4	37.5	36.0	3123	47.0	1757	26.5	4880	73.5
4	R.M.	10/13	APPENDECTOMY (P.O. # 8)	29	--	65.0	43.0	41.3	3440	52.9	2420	37.2	5860	90.2
5	R.D.	10/23	SCAR	20	--	78.2	46.0	44.2	3420	43.7	2705	34.6	6129	78.4
6	V.M.	10/29	HERNIA	30	--	90.0	47.5	45.6	2960	32.9	2481	27.6	5441	60.5
7	J.P.	12/1	MED. STUDENT (R.V.H.)	24	--	79.4	47.0	45.1	3312	41.7	2721	34.3	6033	76.0
8	M.M.	12/8	NORMAL (R.V.H.)	35	--	102.0	46.3	44.4	3727	36.5	2976	29.2	6703	65.7
9	F.S.	1/26	MED. STUDENT (R.V.H.)	22	68	70.1	45.6	43.8	2508	35.8	1955	27.9	4463	63.7
10	E.B.	2/1	FRACT. HALLUX (6 DAYS)	30	66	80.8	45.0	43.2	2700	33.4	2054	25.4	4754	58.8
11	P.G.	2/3	MASTOIDECTOMY (P.O. # 4)	22	74	72.6	42.2	40.5	3790	52.2	2580	35.5	6370	87.8
12	A.D.	2/3	MASTOIDECTOMY (P.O. # 3)	41	61	57.7	45.0	43.2	2340	40.6	1780	30.8	4120	71.4
13	J.J.	2/3	MED. STUDENT	24	74	88.0	42.5	40.8	4180	47.5	2881	32.7	7061	80.2
14	D.L.	2/3	PILONIDAL SINUS	24	70	80.0	42.7	41.0	2990	37.4	2359	29.5	5349	66.9
15	M.B.	3/2	APPENDECTOMY (P.O. # 7)	21	69	63.0	47.0	45.1	2750	43.7	2259	35.9	5009	79.5
16	B.M.	3/12	NORMAL (R.V.H.)	15	--	57.2	51.0	49.0	2055	35.9	1974	34.5	4029	70.4
17	M.M.	3/25	VARICOSE VEINS	45	--	100.0	46.5	44.6	3660	36.6	2946	29.5	6606	66.1
18	I.M.	5/25	PHYSICIAN	25	--	77.2	45.0	43.2	3670	47.5	2791	36.2	6461	83.7
19	F.C.	5/25	PHYSICIAN	28	71	77.2	51.0	49.0	2840	36.8	2729	35.3	5569	72.1
20	J.M.	5/25	PHYSICIAN	36	72	81.0	45.5	43.7	3160	39.0	2453	30.3	5613	69.3
21	M.S.	5/27	MED. STUDENT	24	74	88.6	48.5	46.6	3020	34.1	2635	29.7	5655	63.8
22	M.S.	5/27	MED. STUDENT	23	68	70.4	46.0	44.2	2700	38.4	2139	30.4	4839	68.7
23	B.P.	5/27	MED. STUDENT	23	70	75.0	48.7	46.8	3010	40.1	2648	35.3	5658	75.4

TABLE 3

Normal male subjects studied by RIHSA method. Plasma volume 40.8±6.0 ML/KGM, red cell volume 32.0±3.4 ML/KGM. Total blood volume 72.7±8.5 ML/KGM (HCT 54.8%).

NORMAL FEMALE AND MALE SUBJECTS

TOTAL BLOOD VOLUME IN RELATION TO SURFACE AREA AND HEMATOCRIT:

NO.	AGE	M^2	TBV-ML.	TBV-ML./M^2	HCT %
F 1	23	1.29	3358	2603	38.0
F 5	28	1.49	3468	2328	38.3
F 6	37	2.00	4746	2373	45.5
F 7	29	1.72	5609	3261	39.5
F 8	30	1.90	5393	2838	35.5
F 9	22	1.50	3713	2475	37.0
F 10	19	1.41	3728	2643	41.5
F 11	40	1.41	3231	2299	42.0
F 12	14	1.62	3638	2245	41.5
F 13	44	1.61	3884	2412	42.0
F 18	25	1.41	3135	2223	41.0
FEMALE ADULT MEAN:		1.58 M^2		2518 ML.	40.2 %
S.D.		± 0.21		± 295	± 2.7
M 3	29	1.87	4880	2610	37.5
M 9	22	1.83	4463	2439	45.6
M 10	30	1.90	4754	2502	45.0
M 11	22	1.96	6370	3250	42.2
M 12	41	1.55	4120	2658	45.0
M 13	24	2.12	7061	3330	42.5
M 14	24	1.97	5349	2715	42.7
M 15	21	1.77	5009	2830	47.0
M 19	28	1.95	5569	2856	51.0
M 20	36	2.01	5613	2793	45.5
M 21	24	2.12	5655	2668	48.5
M 22	23	1.85	4839	2644	46.0
M 23	23	1.92	5658	2947	48.7
MALE ADULT MEAN:		1.91 M^2		2788 ML.	45.2%
S.D.		± 0.14		± 253	± 3.3

TABLE 4

RIHSA blood volume measurements of normal male and female subjects in relation to surface area. Male subjects averaged 2788 ML/M^2; female subjects averaged 2518 ML/M^2.

AGES 2 - 11 years
WEIGHT 11 - 37 KGM.
HEIGHT 90 - 147 CM.
SURFACE AREA 0.5 - 1.25 M^2.

RIHSA BLOOD VOLUME DETERMINATIONS

NORMAL CHILDREN

#	NAME	DATE	ADMISSION - DIAGNOSIS	MONTHS AGE	CM HT	KGM. WT.	M^2 S.A.	HCT	HCT X 0.96	PV ML	BCV ML	TBV ML	PV ML/KGM	BCV ML/KGM	TBV ML/KGM	PV ML/M^2	BCV ML/M^2	TBV ML/M^2	PV ML/CM	BCV ML/CM	TBV ML/CM
1	B.E.	2/17	EAR DEFORMITY	132	147	37.3	1.25	42.0	40.3	1446	916	2422	38.8	26.1	64.9	1157	780	1937	9.8	6.7	16.5
2	S.P.	3/17	T. and A.	84	131	30.9	1.05	37.0	35.5	1521	837	2358	49.2	27.1	76.3	1449	797	2246	11.6	6.4	18.0
3	J.C.*	1/6	APPENDECTOMY (P.O.#5)	108	134	29.1	1.05	38.0	36.5	1281	736	2017	44.0	25.3	69.3	1220	701	1921	9.6	5.5	15.1
4	M.A.*	6/16	T. and A.	102	128	24.5	0.94	37.5	36.0	1165	655	1820	47.6	26.7	74.3	1239	697	1936	9.1	5.1	14.2
5	J.F.	3/9	RECTAL POLIP.	96	130	24.1	0.94	40.5	38.9	1098	698	1797	45.6	29.0	74.6	1168	744	1912	8.4	5.4	13.8
6	K.D.	6/19	T. and A.	122	122	26.3	0.93	38.0	36.5	1284	738	2022	48.8	28.1	76.9	1381	793	2174	10.5	6.1	16.6
7	P.D.	6/16	T. and A.	82	127	22.9	0.90	37.3	35.8	1215	678	1893	53.1	29.6	82.7	1350	753	2103	9.6	5.3	14.9
8	S.T.*	6/16	T. and A.	94	126	22.2	0.90	39.0	37.4	1189	710	1899	53.6	31.9	85.5	1321	789	2110	9.4	5.7	15.1
9	M.A.*	6/26	T. and A.	107	126	22.8	0.90	37.4	35.9	1179	660	1839	51.7	28.9	80.6	1310	733	2043	9.4	5.2	14.6
10	T.H.	6/23	T. and A.	103	125	22.4	0.89	41.0	39.4	1103	717	1820	49.3	32.0	81.3	1239	806	2045	8.8	5.8	14.6
11	F.H.*	6/26	T. and A.	83	115	23.5	0.86	41.2	39.6	990	649	1639	41.2	27.6	69.7	1151	755	1906	8.6	5.6	14.2
12	R.C.	6/23	T. and A.	73	113	22.5	0.83	38.3	36.8	1083	631	1714	48.1	28.1	76.2	1305	760	2065	9.6	5.6	15.2
13	R.B.	6/19	T. and A.	78	113	21.9	0.82	39.0	37.4	1117	667	1784	51.0	30.5	81.5	1362	814	2176	9.9	5.9	15.8
14	S.L.	3/10	CAST CHANGE (P.F. #60)	77	117	20.5	0.81	37.2	35.7	1033	574	1607	50.4	28.0	78.4	1275	709	1984	8.8	4.9	13.7
15	L.D.	6/16	T. and A.	72	117	19.8	0.80	39.0	37.4	965	578	1542	48.7	29.2	77.9	1206	722	1928	8.2	5.0	13.2
16	S.B.	5/31	T. and A.	44	108	20.9	0.78	38.0	36.5	1187	682	1869	56.8	32.6	89.4	1522	874	2396	11.0	6.3	17.3
17	J.F.	6/23	T. and A.	58	112	17.7	0.74	38.4	36.9	994	581	1575	56.2	32.8	89.0	1343	785	2128	8.9	5.2	14.1
18	S.B.*	6/19	T. and A.	62	104	18.3	0.71	37.7	36.2	990	539	1489	52.1	29.5	81.6	1338	759	2097	9.1	5.2	14.3
19	D.H.*	6/19	T. and A.	62	110	15.0	0.68	36.0	34.6	799	402	1161	50.6	26.8	77.4	1116	591	1707	6.9	3.7	10.6
20	C.A.*	6/26	T. and A.	49	102	15.4	0.65	37.5	36.0	816	459	1275	53.0	29.8	82.8	1255	707	1962	8.0	4.5	12.5
21	B.B.	5/30	HYPOSPADIAS	48	99	15.5	0.65	34.5	33.1	828	410	1238	53.4	26.5	79.9	1274	631	1905	8.4	4.3	12.5
22	H.B.	3/27	CLEFT PALATE	36	101	15.2	0.65	37.5	36.0	795	444	1239	52.3	29.2	81.5	1223	683	1906	7.9	4.4	12.3
23	J.B.	6/29	HERNIA	79	102	15.0	0.65	39.0	37.4	813	486	1299	54.2	32.4	86.6	1251	747	1998	8.0	4.7	12.7
24	P.O.	6/16	T. and A.	46	95	13.9	0.59	39.7	38.1	671	445	1116	49.7	30.6	80.3	1171	721	1892	7.3	4.4	11.7
25	C.L.*	4/1	POST-PHEMORITIS	33	93	13.6	0.58	37.3	35.8	607	338	945	44.6	24.9	69.5	1047	582	1629	6.5	3.7	10.2
26	B.B.*	5/16	CLEFT PALATE (P.O. #11)	24	91	12.5	0.55	41.0	39.4	515	335	850	41.2	26.8	68.0	936	609	1545	5.7	3.7	9.4
27	W.L.	5/31	T. and A.	36	90	11.1	0.52	32.2	30.9	593	265	858	53.4	23.9	77.3	1140	510	1650	6.6	2.9	9.5

* = FEMALE CHILD

	S.A.	HCT	PV ML/KGM	BCV ML/KGM	TBV ML/KGM	PV ML/M^2	BCV M^2	PV ML/CM	TBV M^2	BCV ML/CM	TBV ML/CM
MEAN VALUES	0.80	38.25	49.6	28.7	78.3	1250	724	8.7	1974	5.1	13.8
STANDARD DEVIATION	±0.16	±1.9	±4.5	±2.4	±6.1	±130	±80		±186		

TABLE 5

RIHSA blood volume in normal children

TECHNIQUE STANDARDIZATION

REPRODUCIBILITY OF CLOSELY SPACED RIHSA BLOOD VOLUME DETERMINATIONS:

NO.	NAME	DATE	TIME	PROCEDURE	PLASMA ACTIVITY c.p.m. 5 m.	PLASMA ACTIVITY INCREMENT	STANDARD ACTIVITY c.p.m. 5 M.	PLASMA VOLUME ML	PV COEFFICIENT OF VARIATION %	HCT % XO.96	TOTAL BLOOD VOLUME ML	TBV COEFFICIENT OF VARIATION %	REMARKS
1.	A.B. 64 M. CA. STOM. R.V.H.	12/4	1450 1505 1506 1517	INJECT 5 ML SAMPLE 1 INJECT 5 ML SAMPLE 2	32349 62049	32349 30600	52552 52552	2000 2115	2.79	42.2 42.2	5460 5659	2.80	RESTING IN BED
2.	A.B. 64 M. CA. STOM. R.V.H.	12/6	1420 1421 1432 1433 1445	SAMPLE 1 INJECT 5 ML SAMPLE 2 INJECT 5 ML SAMPLE 3	16939 65285 109621	46344 46338	49567 49567	2130 2131	0.00	45.4 45.1	5901 5882	0.24	RESTING IN BED-HAD 2 UNITS WHOLE BLOOD OVER PRECEDING 48 HRS
3.	D.B. 77 M. DUOD. ULCER R.V.H.	12/7	1146 1147 1158 1159 1210	SAMPLE 1 INJECT 5 ML SAMPLE 2 INJECT 5 ML SAMPLE 3	9549 39257 67029	29688 27785	46019 46019	5100 5515	5.32	55.3 56.0	4791 5177	5.67	RESTING IN BED
4.	J.G. 26 M. TBO BELH	5/12	1505 1506 1517 1519 1520	SAMPLE 1 INJECT 5 ML SAMPLE 2 INJECT 5 ML SAMPLE 3	1965 27494 52426	25531 24932	55376 55376	2615 2677	1.17	58.6 58.6	4259 4360	1.17	IMMEDIATELY POST-OP (LT. LOWER LOBECTOMY) NOT IN SHOCK
5.	Z.P. 51 M. TBO BELH	5/15	1807 1808 1826 1827 1839	SAMPLE 1 INJECT 5 ML SAMPLE 2 INJECT 5 ML SAMPLE 3	1805 21135 38892	19330 17757	29950 29950	3099 3375	4.25	44.2 44.2	5554 6045	4.25	IMMEDIATELY POST-OP (LT. LOWER LOBECTOMY) NOT IN SHOCK
6.	A.P. 56 F. TBO BELH	5/19	1526 1527 1537 1538 1539	SAMPLE 1 INJECT 5 ML SAMPLE 2 INJECT 5 ML SAMPLE 3	2859 59853 114219	56994 54366	48800 48800	1712 1795	2.57	56.8 56.5	2709 2827	2.15	5 HOURS POST-OP (PHEOCHROMOCYTOMA) HYPOTENSIVE (BP 86/65; P 96)
7.	L.W. 30 F. TBO BELH	6/1	1027 1042 1045 1055	INJECT 5 ML SAMPLE 1 INJECT 5 ML SAMPLE 2	28504 56873	28504 28369	55515 55515	2510 2486	0.48	54.6 56.5	5858 5915	0.99	RESTING IN BED

MEAN COEFFICIENT — PLASMA VOLUME: 2.09%

MEAN COEFFICIENT — TOTAL BLOOD VOLUME : 2.20%

TABLE 6

Technique standardization. The reproducibility of RIHSA blood volume measurements was ±2.2%.

TECHNIQUE STANDARDIZATION

PRECISION OF SYRINGE MEASUREMENTS

(AUGUST 26, 1954)

SYRINGE NUMBER	2 ML VOLUME CM	COEFFICIENT OF VARIATION %	5 ML VOLUME CM	COEFFICIENT OF VARIATION %
1	1.996	1.09	5.002	0.30
2	2.034	0.79	5.047	0.60
2	2.046	1.39		
3	2.011	0.35	5.028	0.22
4	2.031	0.64	5.025	0.16
5	2.042	1.19	5.043	0.52
5			5.041	0.48
6	2.015	0.15	5.006	0.22
7	2.002	0.79	5.011	0.12
8	2.027	0.45	5.033	0.32
9	2.025	0.35	5.027	0.20
10	1.989	1.44	4.979	0.76
11	2.015	0.15	5.014	0.06
12	2.034	0.79	5.041	0.28
13	2.011	0.35	4.994	0.46
14	2.000	0.89	5.013	0.08
15	2.010	0.40	5.025	0.16
15			5.004	0.26
16	2.003	0.74	4.992	0.50
17	2.019	0.05	5.009	0.16
17	2.006	0.59		
18	2.012	0.30	5.013	0.08
19	2.020	0.10	5.020	0.06
20	2.037	0.94	5.025	0.16
MEAN	2.018	0.63 %	5.017	0.28 %
S.D.	± 0.015		± 0.015	
EXTREMES	1.989	1.44 %	4.979	0.76 %
	2.046	1.39 %	5.047	0.60 %
RANGE	0.057		0.068	
TESTS	22		22	

TABLE 7

Technique standardization. Syringe precision test. When 5 ml. volume was delivered, mean coefficient of variation was 0.28%.

COUNTING ERROR

SAMPLE MORE THAN TEN TIMES BACKGROUND.

SUCCESSIVE 5 MINUTE COUNTS OF 2ML. SAMPLE OF PLASMA CONTAINING LESS THAN 0.01 μc I^{131}. BACKGROUND EQUALS LESS THAN 2500 COUNTS PER 5 MINUTES. RADIOACTIVE DECAY IS NEGLECTED.

DATE	FEBRUARY 7, 1955	FEBRUARY 25, 1955	FEBRUARY 26, 1955
PERIODS	COUNTS/5 MIN.	COUNTS/ 5 MIN.	COUNTS/5 MIN.
1	29031	43590	39403
2	28838	43457	39328
3	28829	43656	39205
4	28920	43548	38949
5	28779	43649	38957
6	29082	43679	39240
7	29086	43808	39219
8	29179	43522	39235
9	28878	43535	38984
10		43542	39116
11		43183	39068
12		43433	39104
13		43550	39104
14			39104
15			39109
MEAN	28958	43550	39147
S.D.	± 140	± 142	± 131
S.D.%	± 0.48%	± 0.33%	± 0.33%
EXTREMES	28779 29179	43808 43183	38949 39403
RANGE	400	625	454
TESTS	9	13	15

TABLE 8

Technique standardization. Counting error due to variation in counting apparatus is less than 1% (S.D.O. 48 - 0.33%).

TECHNIQUE STANDARDIZATION

VARIATION IN COUNTING REPLICATE PLASMA SAMPLES.

#	NAME	AGE	PL. ML.	DATE	PLASMA + TUBE BACKGROUND	TUBE BACKGROUND	PLASMA ACTIVITY	MEAN PLASMA ACTIVITY	% VARIATION FROM MEAN
1	CORBETT		2	2/1	53141	1965	51176	50904.5	0.53%
			2		52598	1965	50633		
2	CORBETT		2	2/1	49624	2040	47584	47921	0.65%
			2		50163	1905	48258		
3	HAWKINS		2	1/21	17689	1745	15944	15881	0.40%
			2		17603	1785	15818		
4	VUKELICH		2	1/31	4881	1845	3036	3060	0.78%
			2		4819	1735	3084		
5	VUKELICH		2	1/31	17670	1865	15805	15812	0.04%
			2		17534	1715	15819		
6	VUKELICH		2	1/24	6774	2160	4614	45475	1.47%
			2		6611	2150	4481		
7	VUKELICH		2	1/24	22451	1895	20556	20383.5	0.85%
			2		22371	2160	20211		
8	MANDELOORN	59	2	12/15	28455	1935	26520	26644.5	0.47%
			2		28624	1855	26769		
9	MANDELOORN	59	2	12/15	27969	1840	26129	26107	0.08%
			2		27955	1870	26085		
						MEAN COEFFICIENT OF VARIATION			0.58%

NET VARIATION DUE TO:

VOLUMETRIC TECHNIQUE (PIPETTING 2 ML.; PIPETTE DIFFERENCES)

BACKGROUND VARIATION

COUNTING (COUNTER. TIMER. GEOMETRY).

TABLE 9

Technique standardization. Replicate plasma samples showed a mean coefficient of variation of 0.58%.

TECHNIQUE STANDARDIZATION

VARIATION BETWEEN COUNTS OF UNEQUAL PLASMA SAMPLE VOLUMES.

NAME	DATE	VOLUME	PLASMA + TUBE BACKGROUND	TUBE BGD	PLASMA ACTIVITY	PLASMA ACTIVITY CORRECTED TO 2 ML	MEAN PLASMA ACTIVITY
GIROUX	11/22	2	65160	1960	63200	63200	99.0%
		1	33752	1830	31922	63844	100%
GIROUX	11/22	2	7040	2010	5030	5030	98.3%
		1	4482	1923	2559	5118	100%
GIROUX	11/22	2	28153	1880	26273	26273	95.9%
		1	15522	1826	13696	27392	100%
DURELLE	11/18	2	44280	1770	42510	42510	99.1%
		1	23342	1897	21445	42890	100%

NET VARIATION DUE TO:

DIFFERENT GEOMETRY OF 1 ML. AND 2 ML. SAMPLES, VOLUMETRIC TECHNIQUE, BACKGROUND VARIATION, COUNTING ERRORS.

TABLE 10

Technique standardization . The comparison of one and two ML. Sample counts shows the lack of counter variation when counting these volumes.

TECHNIQUE STANDARDIZATION

EFFECT OF DILUTING VOLUME OF SAMPLE CONTAINING 0.01 μC RIHSA.

	DATE	VOLUME ML.	c.p.m. 0.01 μC TUBE+BGD	c.p.m. BGD	c.p.m. 0.01 μC ACTIVITY	
APPROXIMATELY 0.01 μC	2/24	2	9732	450	9282	100%
I^{131} RISA IN TAP	2/24	3	9597	450	9147	99%
WATER.	2/24	4	9031	450	8581	92%
	2/24	5	8516	450	8066	87%
	2/24	6	7856	450	7406	80%

NET VARIATION DUE TO:

ALTERATION IN GEOMETRY OF 2ML TEST SOLUTION BY FURTHER DILUTION

VOLUMETRIC TECHNIQUE ERRORS IN ADDITION OF DILUENT

BACKGROUND VARIATION, COUNTING ERROR.

TABLE 11

Technique standardization. Precision of counting is relatively independent of geometrical relationship of crystal to solution when 2 ml. is counted but changes with dilution.

COUNTER STANDARDIZATION

EFFECT OF VOLTAGE VARIATIONS

FEBRUARY 23, 1955

VOLTAGE	C.P.M. I^{131} + BGD	C.P.M. BGD	C.P.M. I^{131}
400	16		
450	16		
500	31		
550	140	111	29
600	2750	214	2536
650	11164	322	10842
700	13682	394	13288
750	15564	466	15098
800	* 16272	600	15672
850	17755	1002	16753
900	33029	13503	19526

ATTENUATOR SETTING : 2

PULSE HEIGHT SELECTOR : +40

COUNTING PERIODS : ONE MINUTE

RADIOACTIVE DECAY NEGLECTED.

* SETTING CHOSEN : VOLTAGE 800

TABLE 12

Counter standardization. Optimal voltage (800) setting was chosen by variation of voltage over a wide range. Fluctuations in counter input voltage result in minimal counting variation when voltage is set at 800.

COUNTER STANDARDIZATION

EFFECT OF VOLTAGE AND PULSE HEIGHT SELECTOR VARIATIONS

FEBRUARY 23, 1955

P.H.S.	VOLTAGE: 600		VOLTAGE: 700		VOLTAGE: 800	
	c.p.m. I^{131} + BGD	c.p.m. BGD	c.p.m. I^{131} + BGD	c.p.m. BGD	c.p.m. I^{131} + BGD	c.p.m. B.G.D.
0	—	—	—	—	—	—
+5	17925	456	21347	908	—	—
+10	14745	345	19728	433	29752	6714
+15	12615	272	18823	435	21961	1452
+20	9132	232	17861	432	20679	601
+25	1429	153	16164	416	19919	552
+30	681		15962	376	19432	465
+35			15270	344	18777	478
+40			14148	321	*18691	447
+45			13307	301	18225	431
+50			12939	265	17954	440
+55			12046	229	17247	
+60			10824	251	16822	382
+65			6818	223	16474	
+70			1920	193	15479	348
+75			806	158	14959	
+80					13896	288
+85					12756	
+90					1474	178

ATTENUATOR SETTING: 2.

TEST SUBSTANCE: 2ML. - Less than 0.2μC I^{131} (RIHSA).

COUNTING PERIODS: ONE MINUTE.

RADIOACTIVE DECAY NEGLECTED.

* SETTING CHOSEN: ATTENUATOR, 2 - PULSE HEIGHT SELECTOR, + 40.

TABLE 13

Counter standardization. Optimal pulse height selector (+40) - Setting was chosen from settings for voltage (800) and attenuator (2) settings.

RIHSA BLOOD VOLUME
PULMONARY TUBERCULOSIS (PRE-OPERATIVE)

NO.	AGE	WT. KGM	P.V. ML/KGM	ROV ML/KGM	TBV ML/KGM	HCT %	NO.	AGE	WT KGM.	PV ML/KGM	ROV ML/KGM	TBV ML/KGM	HCT %
1 TEL	27	64.5	44.8	39.7	84.5	49.0	*17 ELL	29	52.7	40.7	24.9	65.6	39.5
2 LEB	32	57.5	41.9	34.4	76.3	47.0	*18 PAT	39	46.8	44.4	23.9	68.3	36.5
3 GEN	26	75.0	39.7	28.4	68.1	43.5	*19 CAM	36	48.2	41.8	26.1	67.9	40.0
4 POD	31	76.8	41.4	36.1	77.5	48.5	*20 CAL	41	47.7	42.4	23.4	65.8	37.0
5 KAC	60	71.8	34.5	28.9	63.4	47.5	*21 DUP	38	56.8	48.6	26.8	75.4	37.0
6 HOF	33	69.1	32.5	27.9	60.4	48.0	*22 PAL	30	51.8	37.3	26.5	63.8	45.3
7 FOR	41	58.2	42.1	32.1	74.2	45.0	*23 BIC	53	65.0	33.6	23.1	56.7	42.5
8 TUC	57	73.6	33.3	24.9	58.2	44.6	*24 DES	24	53.5	36.4	23.9	60.3	41.2
9 PRE	36	64.5	35.5	30.8	66.3	48.3	*25 SHA	26	63.0	34.8	21.7	56.5	40.0
10 LAW	60	47.7	49.4	32.5	81.9	41.3	*26 PAR	26	55.2	37.7	24.5	62.2	41.0
11 OTT	33	107.	30.3	26.4	56.7	48.5	*27 BAR	37	56.4	39.5	24.9	64.4	40.3
12 TAL	32	50.0	48.9	30.2	79.1	39.7	*28 LIV	34	58.4	50.2	30.0	80.2	39.0
13 WRI	39	59.8	49.1	39.0	88.1	46.0	*29 DIZ	43	63.6	44.7	18.9	63.6	31.0
14 DUC	32	63.6	55.8	31.0	86.8	37.2	*30 LIE	27	64.5	28.4	22.1	50.5	45.5
15 DAL	50	40.8	45.7	40.6	86.3	49.0	*31 KEN	47	58.2	36.6	20.5	57.1	37.5
16 CRO	44	79.3	38.1	26.8	64.9	43.0	*32 WHI	32	56.1	44.5	24.5	69.0	37.0

	PV	ROV	TBV	HCT
AVERAGE TBC (16 MALES)	41.4	31.9	73.3	45.4%
	±7.0	±4.7	±10.4	±3.4
NORMAL AVERAGE (23 MALES)	40.8	32.0	72.7	45.8%
	± 6.0	± 3.4	± 8.5	± 3.0

	PV	ROV	TBV	HCT
AVERAGE TBC (16 FEMALES *)	40.1	24.1	64.2	39.3%
	±5.5	±2.6	±7.1	±3.3
NORMAL AVERAGE (18 FEMALES)	43.5	27.2	70.7	40.3%
	±7.3	±3.7	±10.2	±3.3

TABLE 14

Pulmonary tuberculosis surgery. RIHSA blood volume in pre-operative patients. There is no statistically significant difference between the tuberculosis group averages and the normal group averages.

RIHSA ESTIMATE, MEASURED OPERATIVE BLOOD LOSS, REPLACEMENT AND POST-OPERATIVE RIHSA TOTAL BLOOD VOLUME (PULMONARY TUBERCULOSIS)

NO.	BLOOD LOSS RIHSA ESTIMATE	BLOOD LOSS TOTAL MEASURED	REPLACEMENT (BLOOD + PVP)	POST-OPERATIVE RIHSA TOTAL BLOOD VOLUME REPORT
1 TEL	2370	1953	1550	TBV DECREASED 861 ML.
2 LEB	865	1461	1325	TBV INCREASED 73 ML.
3 GEN	3258	2694	2165	TBV DECREASED 851 ML.
4 POD	1627	1847	1400	TBV INCREASED 92 ML.
5 KAC	5561	5554	4517	TBV DECREASED 1231 ML.
6 HOF	2072	2091	1450	TBV DECREASED 568 ML.
7 FOR	2365	2185	1945	TBV DECREASED 568 ML.
8 TUC	1593	1491	1400	TBV DECREASED 462 ML.
9 PRE	727	954	500	TBV DECREASED 133 ML.
17 ELL*	2306	2596	2175	TBV DECREASED 241 ML.
18 PAT*	1322	1534	1100	TBV DECREASED 426 ML.
19 CAM*	1136	709	636	TBV DECREASED 485 ML.
20 CAL*	1492	1697	1550	TBV DECREASED 494 ML.
21 DUP*	2716	2639	2180	TBV DECREASED 1108 ML.
22 PAL*	1318	1217	1900	TBV INCREASED 316 ML.

SUMMARY:

POSTOPERATIVELY PATIENTS HAD AVERAGE NET DECREASE OF 436 ML. TOTAL BLOOD VOLUME, RIHSA ESTIMATE AND TOTAL MEASURED LOSS VARIED 243 ML. ON THE AVERAGE. (MAXIMUM VARIATIONS WERE ± 600 ML).
PATIENTS' MEASURED LOSS EXCEEDED REPLACEMENT BY 325 ML. (AVERAGE).
VOLUME OF TRANSFUSION AND PVP ADMINISTERED COULD BE SATISFACTORILY ACCOUNTED FOR WHEN LOSS WAS MEASURED, REPLACEMENT NOTED AND RIHSA BLOOD VOLUME DETERMINATIONS PERFORMED BEFORE AND AFTER OPERATION.
POSTOPERATIVE BLOOD VOLUME DEFICIT OF 1000 ML. IS AN INDICATION FOR TRANSFUSION.

TABLE 15

Pulmonary tuberculosis surgery. Summary of blood volume changes associated with pulmonary tuberculosis surgery. RIHSA estimate and gravimetric measurement of operative loss correlate well. The post-operative RIHSA blood volume test indicates the adequacy of replacement of operative blood loss.

POST OPERATIVE

CHANGE IN RIHSA TOTAL BLOOD VOLUME (PULMONARY TUBERCULOSIS)

NO.	AGE	OPERATION	POST-OPERATIVE TBV (ML.)
1 TEL	27	L.U.L.	- 861
2 LEB	32	L.U.L.	+ 73
3 GEN	26	L.L.L. + D.	- 851
4 POD	31	L.U.L.	+ 92
5 KAO	60	R.U.L.	- 1231
6 HOF	33	L.U.L.	- 568
7 FOR	41	L.U.L.	- 568
8 TUC	37	R.U. + L.L.	- 462
9 PRE	36	T.	- 133
17 ELL*	29	R.L.L.	- 241
18 PAT*	39	R.P.	- 426
19 CAM*	36	R.P.	- 485
20 CAL*	41	R.U.L.	- 494
21 DUP*	38	L.U.L.	- 1108
22 PAL*	30	R.U.L.	+ 316

AVERAGE NET CHANGE: 463 ML. DEFICIT
TRANSFUSION IN RECOVERY ROOM RECOMMENDED IN CASES 5 KAO and 21 DUP* (5 KAO REMAINED NORMOTENSIVE; 21 DUP* BECAME HYPOTENSIVE IN RECOVERY ROOM).
OVER REPLACEMENT RECOGNIZED IN O.R. IN CASE 22 PAL*. OPERATIVE AND FOUR HOUR POST-OPERATIVE HYPOTENSION - PROBABLY RELATED TO DIFFICULTY IN MAINTAINING PROPER VENTILATORY EXCHANGE.

TABLE 16

Pulmonary tuberculosis surgery. Change in total blood volume associated with surgery. Post-operatively 15 subjects had an average deficit of 463 ml.

RIHSA ESTIMATE** OF OPERATIVE BLOOD LOSS

BASED ON COMPARISON OF PRE- AND POSTOPERATIVE BLOOD VOLUME DETERMINATIONS.
(PULMONARY TUBERCULOSIS)

NO.	Δ ROV (ML)	BLOOD TRANSFUSED ML	Δ WB	RIHSA ESTIMATE
1 TEL	- 594	1050	1320	2370
2 LEB	+ 207	1325	- 460	865
3 GEW	- 492	2165	1093	3258
4 POD	- 102	1400	227	1627
5 KAO	- 920	3517	2044	5561
6 HOF	- 280	1450	622	2072
7 FOR	- 639	945	1420	2365
8 TUO	- 87	1400	193	1593
9 PRE	- 327	NIL	727	727
17 ELL*	- 59	2175	131	2306
18 PAT*	- 102	1100	227	1322
19 CAM*	- 225	636	500	1136
21 DUP*	- 466	1680	1036	2716
22 FAL*	+ 37	1400	- 82	1318
20 CAL*	- 199	1050	442	1492

**CALCULATION:
RIHSA ESTIMATE EQUALS BLOOD TRANSFUSED PLUS NET GAIN OR LOSS OR WHOLE BLOOD (Δ WB). Δ WB IS CALCULATED FROM NET CHANGE IN RED CELL VOLUME (Δ ROV). ΔROV IS THE INCREASE IN POSTOPERATIVE ROV (PLUS Δ ROV) OR DECREASE IN POSTOPERATIVE ROV (- ΔROV).

FOR CALCULATION ASSUME:
1. 500 ML. BLOOD TRANSFUSION REPRESENTS AN AVERAGE OF 225 ML. RED CELLS.
2. NET CHANGE (GAIN + OR LOSS-) OF 225 ML. OF RED CELL VOLUME (ΔROV) REPRESENTS A NET CHANGE OF 500 ML. OF WHOLE BLOOD (Δ WB). IF Δ WB IS AN INCREASE DUE TO OVERTRANSFUSION, SUBTRACT Δ WB FROM BLOOD TRANSFUSED; IF Δ WB IS A DECREASE DUE TO UNDERTRANSFUSION, SUBTRACT Δ WB FROM BLOOD TRANSFUSED. ANSWER IS RIHSA ESTIMATE OF OPERATIVE BLOOD LOSS.

TABLE 17

Pulmonary tuberculosis surgery. Estimate of operative blood loss as calculated from pre- and post-operative RIHSA blood volume measurements.

MEASUREMENT OF OPERATIVE BLOOD LOSS AND REPLACEMENT

(PULMONARY TUBERCULOSIS)

NO.	AGE	WT	OPERATION	SPONGES	DRAPES	SUCTION	CHEST TUBE	TOTAL	BLOOD	PVP	REPLACEMENT TOTAL
1 TEL	27	64.5	L.U. LOBECTOMY	1656	317			1955	1050	500	1550
2 LEE	32	57.5	L.U. LOBECTOMY	1224	87		150	1461	1325		1325
3 GEN	26	75.0	L.L. LOBECTOMY-DECORTICATION	1797	197	300	400	2694	2165		2165
4 POD	31	76.8	L.U. LOBECTOMY	1367	280		200	1847	1400		1400
5 KAO	60	71.8	R.U. LOBECTOMY-THROUGH THORACOPLASTY	4784	220	200	350	5554	3517	1000	4517
6 HOF	33	69.1	L.U. LOBECTOMY	1480	211	200	200	2091	1450		1450
7 FOR	41	58.2	L.U. LOBECTOMY	1485	200	150	350	2185	945	1000	1945
8 TUC	37	73.6	R.U. AND L. LOBECTOMY	1249	82	160		1491	1400		1400
9 PRE	36	64.5	THORACOPLASTY	797	102	5	50	954		500	500
17 ELL*	29	52.7	R.L. LOBECTOMY	2211	85	100	200	2596	2175		2175
18 PAT*	39	46.8	R. PNEUMONECTOMY	1184	350			1534	1100		1100
19 CAM*	36	48.2	R. PNEUMONECTOMY	552	87	90		709	656		656
20 CAL*	41	47.7	R.U. LOBECTOMY	1357	110	30	200	1697	1050	500	1550
21 DUP*	38	56.8	L.U. LOBECTOMY	1689	565	185	200	2639	1680	500	2180
22 PAL*	30	51.8	R.U. LOBECTOMY	972	165	60	20	1217	1400	500	1000

* FEMALE PATIENTS

AVERAGE BLOOD LOSS IN O.R. (SPONGES, DRAPES, SUCTION):

1-THORACOPLASTY 904 ML.
2-PNEUMONECTOMY 1121 ML.
11-LOBECTOMY (EXCLUDING 5 KAO)1814 ML.

AVERAGE DISCREPANCY BETWEEN TOTAL MEASURED LOSS AND REPLACEMENT:

REPLACEMENT AVERAGED 325 ML. LESS THAN LOSS.

TABLE 18

Pulmonary tuberculosis surgery. Measurement of operative blood loss and replacement. Summary of 15 cases. These patients had replacement of blood loss averaging 325 ml. under-transfusion. Maximal blood losses were encountered when procedures such as lobectomy required extensive dissection.

RISSA BLOOD VOLUME

PULMONARY TUBERCULOSIS (POST-OPERATIVE)

NO	AGE	WT KGM	PV ML/KGM	BCV ML/KGM	TBV ML/KGM	HCT %	NO	AGE	WT	PV ML/KGM	BCV ML/KGM	TBV ML/KGM	HCT %
1 - TEL	27	64.5	40.6	30.5	71.1	44.7	17 - ELL[X]	29	52.7	37.3	23.7	61.0	40.5
2 - LEB	32	57.5	39.5	38.0	77.5	51.0	18 - PAT[X]	39	46.8	37.5	21.7	59.2	38.2
3 - GEH	26	75.0	34.9	21.9	56.8	40.2	19 - CAH[X]	36	48.2	36.4	21.4	57.8	38.5
4 - POD	31	76.8	43.9	34.8	78.7	46.0	20 - CAL[X]	41	47.7	36.2	19.2	55.4	36.9
5 - HAC	60	71.8	30.2	16.1	46.3	36.3	21 - DUP[X]	38	56.8	37.3	18.6	55.9	34.7
6 - HOF	33	69.1	28.4	23.8	52.1	47.5	22 - PAL[X]	30	51.8	42.7	27.2	69.9	40.6
7 - FOR	41	58.2	43.4	21.0	64.4	34.0							
8 - TUC	37	73.6	28.2	23.7	51.9	47.6							
9 - FRE	36	64.5	38.5	25.7	64.2	41.7							

	PV	BCV	TBV	HCT%		PV	BCV	TBV	HCT%
POST-OP TBC AVERAGE (9 MALES)	36.4 ± 5.9	26.2 ± 6.6	62.6 ± 11.0	43.2 ± 5.3	POST-OP TBC AVERAGE (6 FEMALES)	37.9 ± 2.4	22.0 ± 3.2	59.9 ± 5.3	38.0 ± 2.4
PRE-OP AVERAGE (16 MALES)	41.4 ± 7.0	31.9 ± 4.7	73.3 ± 10.4	45.4 ± 3.4	PRE-OP AVERAGE (16 FEMALES)	40.1 ± 5.5	24.1 ± 2.6	64.2 ± 7.1	39.3 ± 3.3
NORMAL AVERAGE (23 MALES)	40.8 ± 6.0	32.0 ± 3.4	72.7 ± 8.5	45.8 ± 3.0	NORMAL AVERAGE (18 FEMALES)	43.5 ± 7.3	27.2 ± 3.7	70.7 ± 10.2	40.3 ± 3.3

TABLE 19

Pulmonary tuberculosis surgery. Post-operative blood volume studies. (Within four hours after operation).

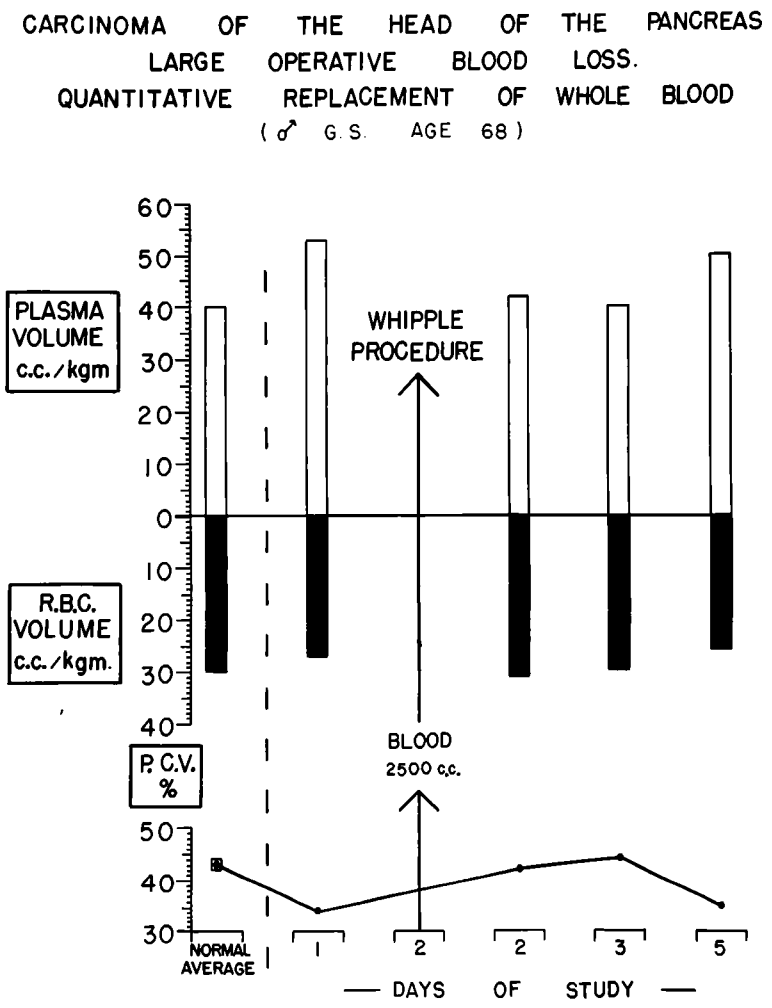

FIGURE 8

Replacement of whole blood loss; blood volume changes associated with a major operative procedure. The pre-operative hematocrit (PCV%) of 34% was low due to a large plasma volume. Operative transfusion was adequate.

DUODENAL ULCER.
MASSIVE HEMORRHAGE.
QUANTITATIVE REPLACEMENT OF WHOLE BLOOD.
(♂ S.C. AGE 77)

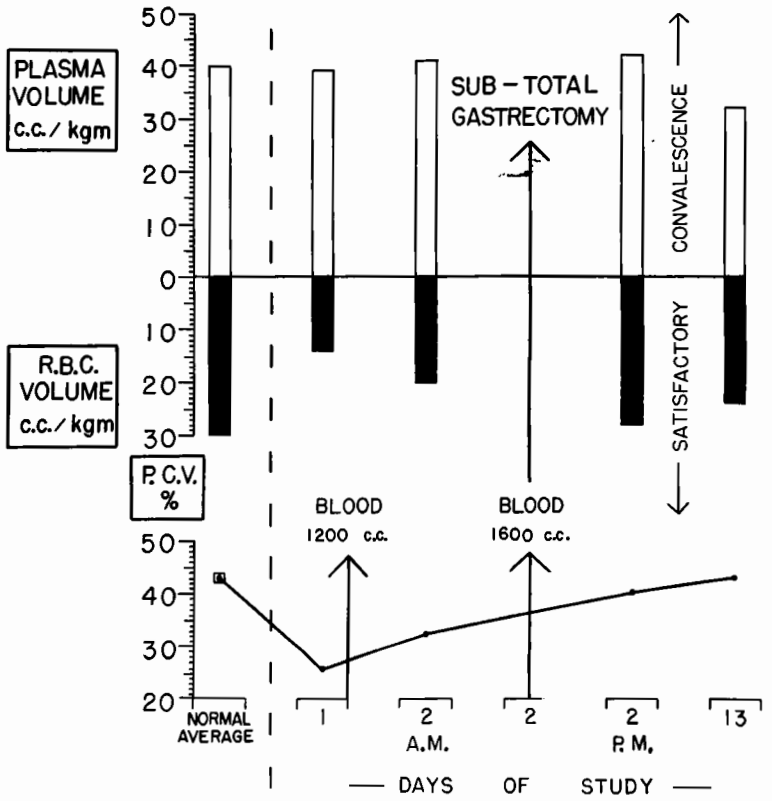

FIGURE 9

Replacement of whole blood loss in the surgical treatment of hemorrhage from a duodenal ulcer. Though the hematocrit (PCV%) on day 13 was normal there was a true anemia (red cell deficit).

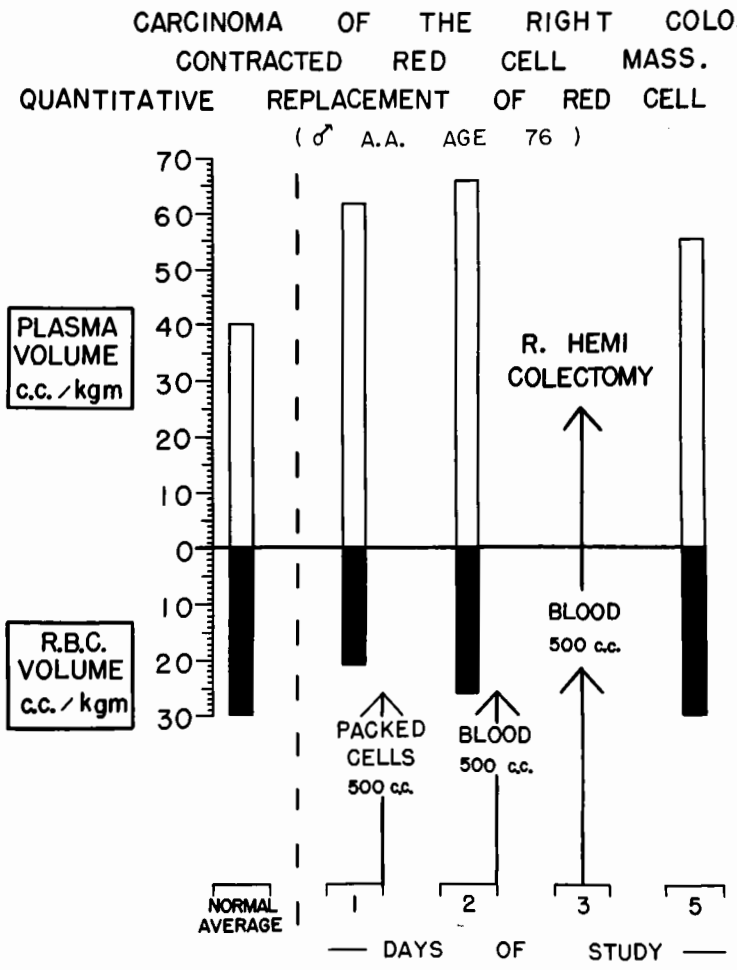

FIGURE 10

Replacement of red cell deficit. Packed red cells were given pre-operatively because of the large total blood volume and chronic anemia. Operative blood loss was minimal.

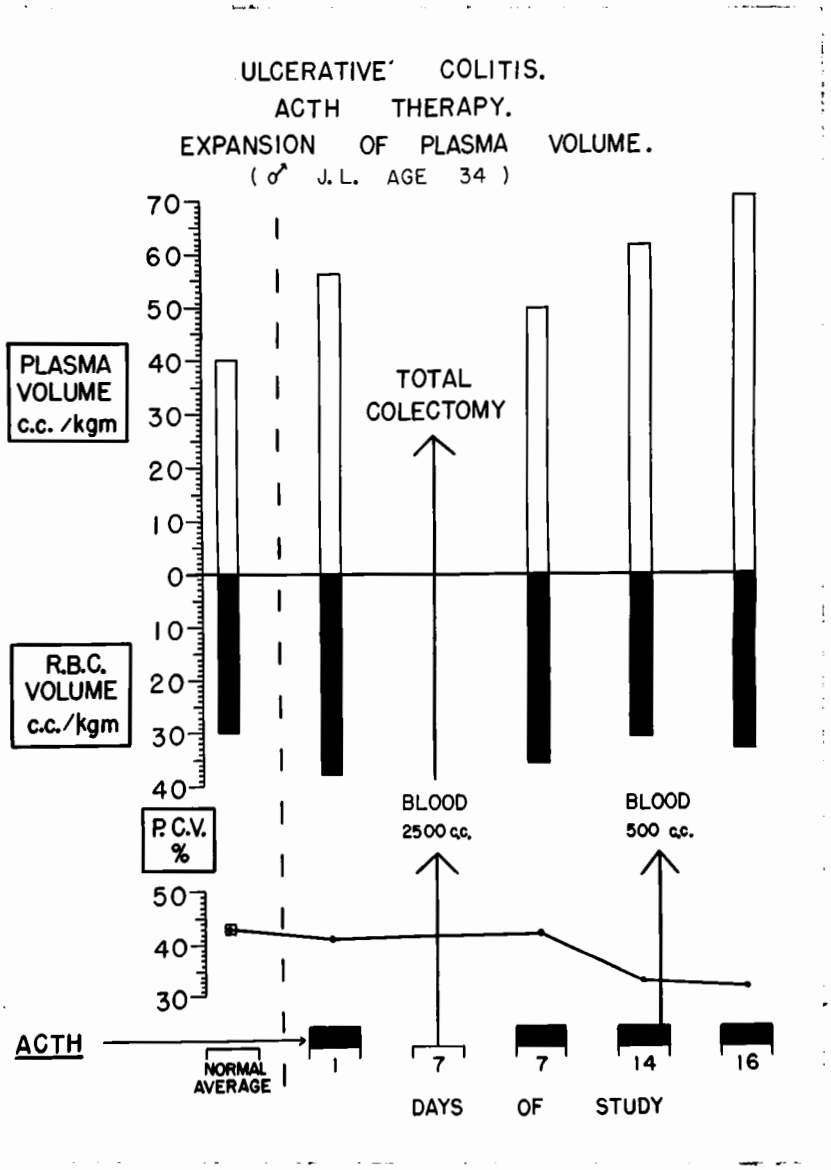

FIGURE 11

Expansion of plasma volume occurring during ACTH therapy. Hematocrit (PCV%) changes are shown and illustrate the genesis of a spurious anemia.

CHART I

RIHSA BLOOD VOLUME DETERMINATIONS IN SURGICAL CONDITIONS

ASSOCIATED WITH: a) total blood volume deficit
b) red cell volume deficit

REQUIRING REPLACEMENT THERAPY: a) total blood volume expansion
b) red cell volume expansion

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT	Remarks
4-20	S.C.	77	9/25	78.6	Duodenal ulcer - massive hemorrhage	3112	1038	4150	39.6	13.2	52.8	26.0	Pale; pulse 92; actively bleeding
4-21	S.C.	77	9/26	78.6	Duodenal ulcer - massive hemorrhage	3333	1477	4810	42.4	18.8	61.2	32.0	1200 ML blood since yesterday; bleeding stopped
4-22	S.C.	77	9/26	78.6	Duodenal ulcer - massive hemorrhage	3357	2093	5450	42.7	26.6	69.3	40.0	1600 ML blood plus gastrectomy since last test. Immediate post-op.
4-37	S.C.	77	10/7	78.6	Duodenal ulcer - massive hemorrhage	2178	1532	3710	27.7	19.5	47.2	43.0	P.O. #11; eating poorly
4-64	A.A.	76	11/30	69.8	CA. ascending colon - anemia	4290	1460	5750	61.5	20.9	82.4	26.5	Hemorrhage 1 month ago; 1000 ML blood over past 48 hours
4-69	A.A.	76	12/1	69.8	CA. ascending colon - anemia	4560	1780	6340	65.5	25.5	91.0	29.0	500 ML packed cells yesterday

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CHART I

RIHSA BLOOD VOLUME DETERMINATIONS IN SURGICAL CONDITIONS

ASSOCIATED WITH: a) total blood volume deficit
b) red cell volume deficit

REQUIRING REPLACEMENT THERAPY: a) total blood volume expansion
b) red cell volume expansion

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT	Remarks
4-20	S.C.	77	9/25	78.6	Duodenal ulcer - massive hemorrhage	3112	1038	4150	39.6	13.2	52.8	26.0	Pale; pulse 92; actively bleeding
4-21	S.C.	77	9/26	78.6	Duodenal ulcer - massive hemorrhage	3333	1477	4810	42.4	18.8	61.2	32.0	1200 ML blood since yesterday; bleeding stopped
4-22	S.C.	77	9/26	78.6	Duodenal ulcer - massive hemorrhage	3357	2093	5450	42.7	26.6	69.3	40.0	1600 ML blood plus gastrectomy since last test. Immediate post-op.
4-37	S.C.	77	10/7	78.6	Duodenal ulcer - massive hemorrhage	2178	1532	3710	27.7	19.5	47.2	43.0	P.O. #11; eating poorly
4-64	A.A.	76	11/30	69.8	CA. ascending colon - anemia	4290	1460	5750	61.5	20.9	82.4	26.5	Hemorrhage 1 month ago; 1000 ML blood over past 48 hours
4-69	A.A.	76	12/1	69.8	CA. ascending colon - anemia	4560	1780	6340	65.5	25.5	91.0	29.0	500 ML packed cells yesterday

(continued, next page)

CHART I

[redacted]

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT	Remarks
4-72	A.A.	76	12/4	69.8	CA. ascending colon - anemia	3780	2120	5900	54.3	30.4	84.6	37.5	500 ML blood 12/1; Rt. hemicolectomy with 500 ML blood 12/2; P.O.#2
5-A	J.S.	55	5/9	55.5	CA. stomach - massive hemorrhage	3220	775	3995	58.0	14.0	72.0	20.0	Has been transfused; actively bleeding
5-55	W.S.	79	3/10	59.0	Gastric ulcer - massive hemorrhage	2700	1060	3760	45.7	18.0	63.7	29.3	Has been transfused; actively bleeding
5-45	C.P.[x]	68	3/7	57.2	CA. colon - anemia	2115	1320	3435	36.9	23.1	60.0	40.0	Has been transfused; pre-op hemicolectomy; HGB was 39% 3/1
5-10	A.S.	74	1/31	81.0	Duodenal ulcer - massive hemorrhage	3200	1300	4500	39.5	16.0	55.5	30.2	Hemorr. 48 hours ago; 1500 ML blood since; choledocholithotomy 16 days ago
4-32	S.G.	61	10/1	73.4	Esophageal varices - bleeding	3030	1210	4240	41.3	16.5	57.8	28.5	Has had: 7000 ML blood, 500 ML packed cells, 700 ML PVP
4-35	S.G.	61	10/4	73.4	Esophageal varices - bleeding	3900	1920	5820	53.2	26.2	79.4	33.0	Has had: 1000 ML blood, 500 ML packed cells, developed hepatic failure, died
5-3	R.H.	16	1/18	52.7	Esophageal varices - bleeding	2880	1560	4440	54.5	29.8	84.3	36.6	Hemorrhage 2 weeks ago; Has had 2000 ML blood

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CHART I (continued)

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT	Remarks
4-34	L.R.[X]	32	10/4	50.0	Esophageal varices	3104	2450	5570	62.1	49.0	101.1	44.0	Hemorrhage 1 month ago; now pre-op
4-36	L.R.[X]	32	10/5	50.0	Esophageal varices	2489	1563	4052	49.8	31.2	81.0	38.5	Post-op; shunt impossible; 3500 ML blood in OR (hemorrhage)
4-38	L.R.[X]	32	10/7	50.0	Esophageal varices	1993	1027	3020	38.9	20.5	60.4	34.0	P.O.#2; wound bleeding; has had 1000 ML blood since 10/5
5-19	M.R.[X]	29	2/8	54.5	Ulcerative Colitis - bleeding	3240	1570	4810	59.5	28.8	88.3	34.0	Pre-op
4-41	L.R.[X]	32	10/8	50.0	Esophageal varices	2246	1264	3510	44.9	13.3	70.2	36.0	P.O.#3; 500 ML blood yesterday
5-25	M.R.[X]	29	2/14	54.5	Ulcerative colitis - bleeding	2410	1770	4180	44.3	32.4	76.7	44.0	Post-op colectomy plus transfusion
5-5	A.H.	39	1/21	52.7	Post-gastrectomy bleeding	4360	810	5170	82.7	15.4	98.1	16.3	Operation 1949, HGB 10% 1/20 before 1000 ML blood plus 75 ML packed cells
4-74	A.B.	64	12/4	44.5	CA. stomach	2075	1015	3090	46.6	22.8	69.4	44.0	Pre-op
4-76	A.B.	64	12/6	44.5	CA. stomach	2130	1750	3880	47.9	39.3	87.2	47.3	Had 1000 ML blood over 48 hours pre-op
4-81	A.B.	64	12/2	44.5	CA. stomach	1925	1575	3500	43.3	35.4	78.7	47.0	Post-op.; laparotomy (non-resectable)
5/B	J.D.	70	5/19	65.9	Post-prostatectomy hemorrhage	3820	1730	5550	58.0	26.3	84.2	32.5	Hemorrhage; massive transfusion; cardiac failure

(continued next page)

CHART I (continued)

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT	Remarks
5-14	E.S.[X]	65	2/5	79.3	Post-cholecystectomy hemorrhage	2680	1080	3760	33.7	13.7	47.4	30.0	Bleeding 72 hours; transfused; pale
5-15	E.S.[X]	65	2/6	79.3	Post-cholecystectomy hemorrhage	2560	1410	3970	32.3	17.8	50.1	37.0	Has had 1300 ML blood since 2/5; continues to bleed
5-18	E.S.[X]	65	2/7	79.3	Post-cholecystectomy hemorrhage	2620	1730	4350	33.1	21.8	54.9	41.5	Has had 500 ML blood since 2/6; bleeding stopped
5-24	R.S.[X]	44	2/14	71.8	Ulcerative colitis - acute	2160	2416	4576	30.1	33.6	63.7	55.0	P.O.#3 laparotomy; had 1000 ML blood in OR; now bleeding. Died 2/6 gangrene of colon
4-50	M.R.	61	10/28	69.0	CA. Stomach - post-op	2720	3330	6050	39.4	48.2	87.6	55.0	Esophagogastrectomy today ; hemorr. and 3500 ML blood in OR; in pulmonary edema
4-51	M.R.	61	10/29	69.0	Ca. stomach - post-op	1900	2910	4810	27.5	42.2	69.7	60.5	Phlebotomy 300 ML 10/28; congestive failure; hypotension. Died.
5-55	J.L.[X]	44	2/17	70.8	Post-op abdomino-perineal resection	2645	1715	4360	37.4	24.2	61.6	41.0	Unstable B.P. (100/); pulse 120. Stablized after 1000 ML blood
5-26	G.V.[X]	50	2/14	57.2	Post-colectomy hypotension	2250	1770	4020	39.3	30.9	70.2	46.0	BP 96/64; P. 120, P.O.#1; 1000 ML blood in OR
5-C	E.C.	78	3/14	90.7	Duodenal ulcer - massive hemorrhage	2660	880	3540	29.7	9.7	39.4	26.0	1720 hours. bleeding actively. 5000 ML blood after this study

(continued next page)

CHART I (continued)

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT	Remarks
5-D	E.C.	78	3/14	90.7	Duodenal ulcer - massive hemorrhage	3140	1100	4240	34.6	12.1	46.7	27.0	2110 Hrs. given 7000 ML blood after this; operation
5-E	E.C.	78	3/14	90.7	Duodenal ulcer - massive hemorrhage	3620	1355	4975	39.9	14.9	54.8	30.7	2400 hrs. post-op given 1500 ML blood more. Bled again. Died 3/15-0330
5-F	E.E.	53	3/22	75.7	Post-op hypotension (neosynephrine used) internal mammary transplant	2000	1630	3630	26.4	21.4	47.8	46.8	P.O.#1 400 ML blood in OR; 500 ML blood today. Neosynephrine maintain in GBP 120/80
5-G	E.E.	53	3/23	75.7	Post-op hypotension (neosynephrine used) internal mammary transplant	2190	1635	3825	29.0	21.6	50.6	44.5	P.O.#2 decreasing neosynephrine. skin cold, pale, clammy since 3/22
5/H	E.E.	53	3/24	75.7	Post-op hypotension (neosynephrine used) internal mammary transplant	2720	1600	4320	35.9	21.1	57.0	38.7	P.O.#3 Warm, dry. Urine S.G. 1.027
5-I	E.E.	53	3/25	75.7	Post-op hypotension (neosynephrine used) internal mammary transplant	2700	1630	4330	35.7	21.5	57.2	39.0	P.O.#4 Warm, dry
5-J	E.E.	53	3/26	75.7	Post-op hypotension (neosynephrine used) internal mammary transplant	2840	1640	4480	37.5	21.7	59.2	38.3	P.O. #5 Warm, dry
5-K	E.E.	53	3/28	75.7	Post-op hypotension (neosynephrine used) internal mammary transplant	2760	1640	4400	36.4	21.0	58.0	38.7	P.O. #7 normotensive; no vasoconstriction (total I^{131} used approximately 50 μC.
5-L	C.P.[X]	29	5/28	58.2	Mitral stenosis	2121	1364	3485	36.4	23.5	59.9	39.0	Pre-op study. Commissurotomy done 6/6: 750 ML loss; 500 ML blood given

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CHART I (continued)

File No.	Name	Age	Date	WT	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT	Remarks
5-M	C.P.[x]	29	6/6	58.2	Post-op wound hemorrhage	1500	860	2360	25.8	14.7	40.5	37.0	Bled 1200 ML into chest bottle; BP 80/ ; given 1000 ML before study, 1000 ML blood after study
5-N	M.R.[x]	60	3/28	70.5	Strangulated hernia	2330	2520	4850	33.1	35.7	68.8	52.0	50% of small bowel strangulat rehydrated and given 1000 ML plasma pre-op
5-O	M.R.[x]	60	3/28	70.5	Strangulated hernia	3140	2090	5230	44.5	29.6	74.1	40.0	Before this study: bowel resection; 1000 ML blood; 500 ML PVP. Died 3/29
4-73	D.B.[x]	45	11/2	48.0	Post-op radical mastectomy	1755	1122	2877	36.6	24.3	59.9	41.0	P.O. #1 was transfused in OR
4-79	S.C.[x]	19	12/10	46.2	Post-op ligation P.D.A.	1720	1110	2830	37.2	24.0	61.2	40.7	P.O. #4 was transfused less than loss measured in OR
5-P	D.I.[x]	34	5/55	51.8	Post-op pulmonary resection	2130	1110	3240	41.1	21.4	62.5	35.6	Immediate post-op hypotensive 3500 ML blood in OR
4-19	H.A.	58	9/24	54.5	CA. sigmoid	3494	1223	4717	64.1	22.4	86.5	27.0	Pre-op before transfusion
5-27	B.T.[x]	3 1/4	2/16	14.3	10% burn (1/1) operative hypotension (2/15)	538	349	887	37.6	24.4	62.0	41.0	Post-op study. Had 250 ML blood for hypotension at time of grafting
5-9	A.P.	63	5/15	57.6	Duodenal ulcer. Hemorrhage	2230	1000	3230	38.7	17.4	56.1	32.4	500 cc hematemesis 8 hours ago; transfused; pre-op

(continued next page)

CHART I (continued)

File No.	Name	Age	Date	WT	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT	Remarks
4-75	D.R.	77	12/4	45.5	Duodenal ulcer - chronic obstruction, bleeding	3980	1540	5520	87.5	33.8	121.3	29.2	Pre-op. lost 36 pounds in 3 years
4-77	D.R.	77	12/7	45.5	Duodenal ulcer - chronic obstruction, bleeding	3205	1755	4960	70.4	38.6	109.0	36.8	Pre-op had 500 ML packed cells 500 ML blood since 12/4

CHART I (continued)

[redacted]

CHART II

RIHSA BLOOD VOLUME DETERMINATIONS

Conditions associated with abnormalities of body water and electrolyte metabolism in geriatric and poor-risk patients.

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT %	Remarks
4-43	A.K.	59	10/9	75.0	Spontaneous rupture of esophagus; Lt. hydrothoray	2180	2820	5000	29.1	37.6	66.7	56.5	Hypotensive; oliguric; poor skin turgor rehydration begun
4-44	A.K.	59	10/11	75.0	Spontaneous rupture of esophagus; Lt. hydrothoray	3140	2900	6040	41.8	38.7	80.5	48.0	Chest drainage plus 500 ML blood 10/9; normal urine output and B.P.
5-34	J.L.	59	3/5	75.0	20% burn (2/4)	3070	1850	4920	41.0	24.5	65.5	39.1	Given 1000 ML blood after this
5-50	J.L.	59	3/10	75.0	20% burn (2/4)	2690	2080	4770	35.8	27.7	63.5	45.4	Poor skin turgor; disorientation; given tube feeding
5-53	J.L.	59	3/12	75.0	20% burn (2/4)	2640	1900	4540	35.3	25.3	60.6	44.2	Intermittently disoriented; burn healing
5-AA	J.L.	59	4/6	75.0	20% burn (2/4)	2830	1690	4520	37.7	22.6	60.3	39.0	Skin graft 4/1 plus 500 ML blood; normal hydration; improved affect
4-66	J.L.	34	12/1	58.6	Ulcerative colitis; took ACTH 6 weeks	3190	2060	5250	54.5	35.0	89.5	41.0	Pre-op (no ACTH-2 weeks); diuresis and 31 pound weight loss-3 weeks

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CHART II

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File No.	Name	Age	Date	WT.	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT%	Remarks
4-78	J.L.	34	12/7	58.6	Ulcerative colitis; took ACTH 6 weeks	2930	1970	4900	50.0	33.6	83.6	41.7	Post-op. 2500 ML blood in OR (all volumes calculated on 58.6 KGM dry weight)
4-80	J.L.	34	12/14	58.6	Ulcerative colitis; took ACTH 6 weeks	4060	1900	5960	69.3	32.4	101.7	33.0	P.O.#7; ACTH being given; gained 4 pounds since 12/1; 500 ML blood started
4-83	J.L.	34	12/16	58.6	Ulcerative colitis; took ACTH 6 weeks	4320	2040	6360	73.7	34.8	108.5	33.3	P.O.#9; Na 132; K 2.7; CL 96; CO_2 27.2; continues weight gain and ACTH
5-AB	J.L.	34	3/12	58.6	Ulcerative colitis; took ACTH 6 weeks	4320	2000	6320	73.7	34.1	107.8	33.0	ACTH has been stopped; had 1500 ML blood since last test; has lost weight over past two months
5-38	J.B.	73	3/5	61.4	Pemphigus; hydrocortone q.d. 6 months	2930	2270	5200	47.7	37.0	84.7	45.5	650 MGM hydrocortone q.d.; losing weight
5-AC	J.B.	73	3/22	61.4	Pemphigus; hydrocortone q.d. 6 months	3020	2010	5030	49.2	32.7	81.9	41.7	Decreasing hydrocortone; lost 10 pounds, 17 days
5-AD	S.D.[x]	74	3/20	52.5	Pneumonia; paralytic ileus	1150	1460	2610	21.6	27.6	49.2	56.0	Oligoric; poor skin turgor; HGB 118%; NPN 118; Na 128; being hydrated
5-AE	S.D.[x]	74	3/22	52.5	Pneumonia; paralytic ileus	1520	1410	2930	29.0	26.8	55.8	50.0	Somnolent; fair skin turgor; urine output 1300 ML 3/21
5-AF	S.D.[x]	74	3/24	52.5	Pneumonia; paralytic ileus	1780	1180	2960	33.9	22.5	56.4	41.6	Had 500 ML plasma for hypotensi 3/23; 500 ML blood started now

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CHART II (continued)

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT%	Remarks
5-AG	S.D.[x]	74	3/27	52.5	Pneumonia; paralytic ileus	1715	1395	3110	32.6	26.6	59.3	46.8	Was unconscious 2 days; now alert; K falling
5-AH	S.D.[x]	74	4/7	52.5	Pneumonia; paralytic ileus	1620	1300	2920	30.6	24.7	55.6	46.5	Hypotension (70/44) reversed with 325 ML plasma, oliguric. Died
4-65	P.L.[x]	87	11/30	36.4	CA. ampulla of vater	1670	1244	2914	45.9	34.2	80.1	44.5	P.O.#3 cholecystjejunostomy letaargi icteric. Na 120; NPN 50
5-16	B.R.[x]	65	2/6	46.5	Perforated duodenal ulcer	1685	2375	4060	36.2	51.2	87.4	60.0	P.O.#1 Plication of perforation; dehydrated Na - 119; oliguric; transfused in OR
5-17	B.R.[x]	65	2/7	46.5	Perforated duodenal ulcer	2460	2240	4700	52.9	48.1	101.0	49.7	Had 500 ML 3% NaCL; better hydration Na-131; adequate urine output
5-21	B.R.[x]	65	2/9	46.5	Perforated duodenal ulcer	2185	2240	4430	47.4	48.1	95.3	52.7	NPN 24; Na 137; out of oxygen tent
5-AI	G.M.	55	4/1	84.2	Acute renal failure-post-op.	3260	1950	5210	38.7	23.2	61.9	39.0	Post-op colostomy; psuedomyxoma peritone 11
5-AJ	B.P.[x]	69	3/25	61.4	Post-op Rt. hemicolectomy	3110	1350	4460	50.7	21.9	70.6	31.5	P.O.#1; dehydration; olicuria
5-AK	B.W.[x]	62	4/24	40.0	Post-op abdomino-perineal resection	1855	1520	3375	45.8	37.5	83.3	47.0	P.O.#3; dehydration; poor skin turgo Na-126; 500 ML blood given; rehydrat
5-AL	B.W.[x]	62	4/27	40.0	Post-op abdomino-perineal resection	2020	1550	3570	49.9	38.3	87.2	45.2	P.O.#6; better skin turgor; Na-130; Bleeding from G-I tract

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CHART II (continued)

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT%	Remarks
5-12	C.	60	2/1	50.0	Post-op prostatectomy	2440	1130	3570	48.2	22.6	71.4	33.5	Na 97.5 on 1/31; rehydrated since then. Died 2/3. Renal failure
5-AM	H.S.	60	4/11	74.1	Appendectomy 4/6	2000	2100	4100	27.0	28.3	55.3	53.5	Hypotensive; oliguric; Na 146.5; Given 1000 ML plasma later
5-AN	H.S.	60	4/17	74.1	Appendectomy 4/6	3570	1800	5370	48.2	24.3	72.5	35.0	Better hydrated; NPN 139; oliguric
5-AO	H.S.	60	4/18	74.1	Appendectomy 4/6	4160	2330	6490	56.1	31.4	87.5	37.5	Poor skin turgor; transfused. Died. ? Renal failure
5-AP	I.L.	57	4/27	39.5	Gastrostomy 4/23 - CA	2340	1345	3685	59.2	34.1	93.3	38.0	Dehydrated; poor skin turgor; cachectic
5-9	B.R.	33	1/27	48.6	Mitral stenosis; congestive failure (therapy: digitoxin, diuretics, phlebotomy; surgery: mitral commissurotomy total RIHSA dose: less than 80 UC over 60 days).	3240	2260	5500	70.3	49.2	119.8	43.0	Failure: dyspnea; pulmonary congestion; distended neck veins
5-13	B.R.	33	2/4	46.4	Mitral stenosis; congestive failure (therapy: digitoxin, diuretics, phlebotomy; surgery: mitral commissurotomy total RIHSA dose: less than 80 UC over 60 days).	3070	2270	5340	66.9	49.5	116.3	42.5	Essentially similar to 1/27. Enlarged TBV. (volumes calculated on basis of dry weight 45/KGM)
5-20	B.R.	33	2/9	45.4	Mitral stenosis; congestive failure (therapy: digitoxin, diuretics, phlebotomy; surgery: mitral commissurotomy total RIHSA dose: less than 80 UC over 60 days).	2840	2040	4880	61.9	44.4	106.3	43.5	Phlebotomy 350 ML 2/6

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CHART II (continued)

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File No.	Name	Age	Date	WT..	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT%	Remarks
5-23	B.R.	33	2/13	45.0	Mitral stenosis; congestive failure (therapy: digitoxin, diuretics, phlebotomy; surgery: mitral commissurotomy; Total RIHSA dose: less than 80 UC over 60 days).	2950	1730	4680	64.3	37.7	102.0	38.6	Phlebotomy 350 ML 2/11. Clinically improved
5-31	B.R.	33	3/3	45.9	Mitral stenosis; congestive failure (therapy: digitoxin, diuretics, phlebotomy; surgery: mitral commissurotomy; total RIHSA dose: less than 80 UC over 60 days).	3450	1680	5130	75.2	36.6	111.8	37.9	Plasma volume enlarged; weight gain; diuretics giv 3/4
5-48	B.R.	33	3/9	45.9	Mitral stenosis; congestive failure (therapy: digitoxin, diuretics, phlebotomy; surgery: mitral commissurotomy; total RIHSA dose: less than 80 UC over 60 days).	2790	1870	4660	60.8	40.7	101.5	41.7	Commissurotomy 3/7,750 ML measured loss; 750 ML bloo 3/7; 250 ML blood 3/9
5-AP	B.R.	33	3/14	45.4	Mitral stenosis; congestive failure (therapy: digitoxin, diuretics, phlebotomy; surgery: mitral commissurotomy; total RIHSA dose: less than 80 UC over 60 days).	3030	1810	4840	66.0	39.4	105.4	39.0	P.O.#7; NPN-59 3/9 (P.O.#2 NPN-28 3/17 (P.O.#10), nor post-op course
5-AR	B.R.	33	3/30	44.4	Mitral stenosis; congestive failure (therapy: digitoxin, diuretics, phlebotomy; surgery: mitral commissurotomy; total RIHSA dose: less than 80 UC over 60 days).	2670	1530	4200	55.2	33.3	91.5	38.0	P.O.#23; discharged from hospital; no signs of fai ure; digitoxin maintenanc

CHART II (continued)

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CHART III

RIHSA BLOOD VOLUME DETERMINATIONS IN MISCELLANEOUS SURGICAL CONDITIONS

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML/KGM	RCV-ML/KGM	TBV-ML/KGM	HCT %	Remarks
5-7	J.F.	27	1/25	65.8	Fracture Rt. Femur	45.4	24.0	69.4	36.0	Fracture few hours ago; 500 ML blood given pre-op
5-35	L.L.	70	3/5	70.5	Fracture Lt. Humerus and Leg	36.1	20.2	56.3	37.5	Fractures 3/4; casts applied
4-58	H.W.	53	11/25	71.1	CA. stomach	43.1	26.9	70.0	40.0	Lost 30 pounds - 8 weeks; pre-op, transfused after test
4-23	W.P.	56	9/29	51.0	Gastric ulcer	67.0	33.2	100.0	34.6	Pre-op
4-13	V.L.[x]	51	9/17	75.5	Duodenal ulcer	35.8	18.3	56.1	34.0	Obese, no weight change; pre-op
4-12	E.C.	57	9/17	77.3	Duodenal ulcer	36.1	26.4	62.5	44.0	Pre-op; slightly obese
4-3	J.M.	52	9/15	71.0	Duodenal ulcer	38.1	27.8	65.9	44.0	Medical regime - 3 weeks treatment before test
5-39	H.T.	65	3/5	88.7	Duodenal ulcer	34.7	29.7	64.4	48.0	Obese, pre-op
5-B1	K.G.[x]	41	3/23	61.4	Acute cholecystitis	41.4	24.8	66.2	39.0	Also has mitral stenosis
5-46	L.G.	53	3/9	65.9	CA. cecum	41.8	25.1	66.9	39.0	Pre-op

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CHART III

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File No.	Name	Age	Date	WT.	Diagnosis	PV-ML/KGM	RCV-ML/KGM	TBV-ML/KGM	HCT %	Remarks
5-30	L.B.[x]	52	2/18	62.2	CA. rectum	61.8	34.6	95.8	37.5	Lost 25 pounds - one year
4-24	A.L.	69	9/29	68.2	ABD. aneurysm	55.4	24.9	80.4	36.0	Lost 30 pounds - 3 months
4-28	U.R.[x]	37	9/29	51.0	Hyperthyroidism	51.0	32.8	83.8	40.0	BMR minus 32; on medication 6 months
5-32	E.L.	39	3/4	51.4	Mitral stenosis	56.7	31.1	87.8	37.0	6 months pregnant
5-29	A.L.	46	2/17	63.6	Mitral stenosis	39.5	38.1	77.4	51.0	Pre-op commissurotomy
5-36	F.N.	67	3/5	91.0	Fracture Lt. Rt. legs	36.7	24.6	61.3	41.8	Fracture 12/13; in casts; bed rest
4-52	A.D.[x]	49	11/18	34.0	CA. hypopharynx	62.3	40.0	102.3	45.0	Cachectic; post-gastrostomy
5-40	J.M.	63	3/5	77.2	CA. stomach	51.8	29.5	81.3	37.8	Post-gastrostomy and transfusion
4-10	L.D.	50	9/17	61.4	Duodenal ulcer	34.2	31.6	65.8	50.0	P.O. #2 Gastrectomy
4-2	L.H.	24	9/15	55.5	Duodenal ulcer	47.3	32.0	79.3	42.0	P.O. #12 Plication of perforation

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CHART III (continued)

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML/KGM	RCV-ML/KGM	TBV-ML/KGM	HCT %	Remarks
5-6	J.V.	54	1/21	67.7	Duodenal ulcer	50.8	14.9	65.7	23.8	P.O.#28 gastrectomy; disruption of duodenal stump; transfused
5-8	J.V.	54	1/24	67.7	Duodenal ulcer	47.0	16.1	63.1	26.6	P.O.#31, transfused since last test. melena
5-11	J.V.	54	1/31	67.7	Duodenal ulcer	51.8	23.4	75.2	32.5	P.O.#38 given 1000 ML blood since last test
5-22	J.V.	54	2/10	67.1	Duodenal ulcer	54.1	22.8	76.9	33.0	P.O.#48 Given 1500 ML blood since last test; entero-cutaneous fistula
5-45	J.V.	54	3/9	67.1	Duodenal ulcer	50.4	28.0	78.4	37.0	Developed bowel obstruction today; pre-op
4-70	Y.M.[x]	31	11/2	57.0	Hypotension post-op	38.1	34.8	72.9	49.0	P.O.#1 cholecystectomy; transfused; ECG showed ? myocardial infarct
4-6	T.B.[x]	48	9/16	69.0	Wound infection	28.9	20.8	49.5	42.0	P.O.#6 cholecystectomy; pale
4-29	T.B.[x]	48	9/29	69.0	Wound infection	53.6	23.4	77.0	30.5	P.O. #19
5-B2	M.L.[x]	41	4/4	142.	Wound hematoma	34.2	19.0	53.2	37.3	Marked obesity
4-1	J.M.[x]	69	9/14	55.0	CA. sigmoid	41.2	29.8	71.0	42.0	P.O.#3 sigmoid resection

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CHART III (continued)

File No.	Name	Age	Date	WT.	Diagnosis	PV-ML/KGM	RCV-ML/KGM	TBV-ML/KGM	HCT %	Remarks
5-B3	P.S.[x]	70	3/16	89.5	CA rectum	25.9	20.6	46.5	46.0	P.O.#1 A-P resection; marked obesity
5-B4	P.S.[x]	70	3/18	89.5	CA rectum	29.6	20.4	50.0	41.0	P.O.#3 not transfused
4-8	I.G.[x]	54	9/16	35.6	Bowel obstruction	61.1	21.6	82.7	26.0	Adhesions; P.O.#2; extremely thin; CA colon, 1948
5-43	G.K.[x]	70	3/6	45.9	Bowel obstruction	47.9	25.5	73.4	36.3	P.O.#10; Richter's femoral hernia; CA rectum, 1947
5-2	F.F.[x]	60	1/18	67.7	Hypersplenism	38.4	19.6	58.0	33.8	P.O.#5 Splenectomy
5-41	E.A.[x]	74	3/6	51.0	Varicose veins	45.1	20.6	65.7	32.5	Diabetic; undergoing skin grafting
5-B5	E.R.[x]	46	5/9	68.2	Lymphoma	45.4	28.7	74.1	40.5	Pre-op
5-4	H.M.	64	1/18	70.0	Emphysema	39.6	32.6	72.2	47.0	----------
4-9	B.K.[x]	40	9/16	64.0	CA. breast	47.6	21.4	69.0	31.0	Post-op mastectomy

CHART III (continued)

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CHART IV

RIHSA BLOOD VOLUME DETERMINATIONS (PRE- AND POST-OPERATIVE)

File No.	Age	Date	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT%	WT.	Remarks
1-HT	58X	3/27	Parotid Tumor	2250	1650	3900	34.4	25.2	59.6	44.0	65.5	Pre-op
2-HT	58x	3/28	Parotid tumor	1880	1430	3310	28.7	21.8	50.5	45.0	65.5	Post-op excision-parotid tumor, radical neck dissection; 2385 gravimetric loss; 2500 blood replacement
3-HT	58x	3/29	Parotid tumor	1745	1655	3400	26.6	25.3	51.9	50.7	65.5	P.O.#1 had 500 ML blood before this study
4-HT	58x	4/4	Parotid tumor	2560	1710	4270	39.1	26.1	65.2	41.7	62.0	P.O.#7
1-MF	68x	9/28	CA - colon (ascending)	2364	1210	3574	47.6	24.2	71.8	34.0	49.8	Pre-op; diabetic; lost 80 pounds-several years
2-MF	68x	9/30	CA - colon (ascending)	1977	1163	3140	39.6	23.4	63.0	37.0	49.8	Post-op. Rt. hemicolectomy; no transfusion in OR
3-MF	68x	10/7	CA - colon (ascending)	1877	843	2720	37.7	16.9	54.6	31.0	54.3	P.O. #7
1-ES	42x	4/6	Mediastinal tumor	2295	1205	3500	34.8	18.3	53.1	35.8	66.0	Pre-op; not transfused
2-ES	42x	4/7	Mediastinal tumor	1950	1100	3050	29.6	16.4	45.2	37.6	66.0	Post-op thoracotomy and excision of tumor; 500 blood in OR; BP-98, unstable; given 1250 ML blood; BP-120; 500 blood given 4/8

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CHART IV

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File No.	Age	Date	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT%	WT.	Remarks
1-AM	42x	11/28	Mitral stenosis	2150	1830	3980	33.4	28.4	61.8	48.0	64.5	Pre-op; commissurotomy 11/29
2-AM	42x	11/29	Mitral stenosis	2040	1710	3750	31.6	26.5	58.1	47.5	64.5	Post-op. 100 blood given in OR
1-FT	59	10/7	Unresolved pneumonia	2050	1460	3510	37.3	26.5	63.8	41.5	55.0	Pre-op wedge resection Lt. upper lobe 10/7. Post-op 500 blood in OR
2-FT	59	10/7	Unresolved pneumonia	2006	1514	3520	36.5	27.5	64.0	43.0	55.0	Post-op 500 blood in OR
3-FT	59	10/3	Unresolved pneumonia	2510	1860	4370	45.7	33.8	79.5	42.5	55.0	P.O. #5
1-LM	35x	11/23	Bowel obstruction (CA. ceruix)	2110	1660	3770	33.8	26.6	60.4	46.0	62.5	Pre-op colostomy
2-LM	35x	11/23	Bowel obstruction (CA. ceruix)	2360	1690	4050	37.8	27.0	64.8	43.5	62.5	Post-op (no blood in OR) minimal blood loss.
1-LC	32	5/16	Mitral stenosis	2600	2070	4670	46.2	36.8	83.0	46.3	56.3	Pre-op commissorotomy 5/18
2-LC	32	5/18	Mitral stenosis	1880	1576	3456	33.4	28.0	61.4	47.5	56.3	Post-op 888 gravimetric loss; 500 blood in OR
1-SH	19x	5/31	Bronchiectasis (Rt. M.L. and Rt. L.L.)	2018	1180	3198	48.0	28.1	76.1	38.5	42.0	Pre-op R.M.L. and R.L.L. segmental 6/1
2-SH	19x	6/1	Bronchiectasis (Rt. M.L. and Rt. L.L.)	1761	965	2726	41.9	23.0	64.9	36.9	42.0	Post-op 1500 blood given in OR
1-PN	67x	4/9	Jaundice-obstructive (P.O. hepatitis)	2470	1540	4010	39.4	24.5	63.9	40.0	62.7	Pre-op choledochotomy, liver biopsy 4/10

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CHART IV (continued)

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File No.	Age	Date	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT%	WT.	Remarks
2-PN	67x	4/10	Janndice-obstructive (P.O. hepatitis)	1650	1310	2960	26.3	20.9	47.2	46.2	62.7	Post-op; transfused in O.R.
3-PN	67x	4/11	Jaundice-obstructive (P.O. hepatitis)	2095	1755	3850	33.4	27.9	61.3	47.5	62.7	P.O. #1 Had 1500 ML blood since 4/10 study
1-GS	68	9/20	CA-ampulla vater	3704	1841	5545	53.6	26.6	80.2	33.5	69.1	Pre-op whipple procedure 9/21
2-GS	68	9/21	CA-ampulla vater	2992	2019	5011	43.3	29.2	72.5	42.0	69.1	Post-op 2500 ML estimated loss (surgeon); 2300 ML blood in OR
3-GS	68	9/22	CA-ampulla vater	2802	2013	4815	40.5	29.2	69.7	43.5	69.1	P.O. #1
4-GS	68	9/24	CA-ampulla vater	3475	1759	5234	50.3	25.4	75.7	35.0	69.1	P.O.#3 slightly dehydrated
1-AP	62	3/16	Peptic esophagitis (stricture)	2730	1880	4610	42.1	28.9	71.0	43.0	64.8	Pre-op thoraco-abdominal esophago-gastrectomy 3/25
2-AP	62	3/24	Peptic esophagitis (stricture)	3335	1915	5250	51.4	29.4	80.8	37.9	65.0	Pre-op
3-AP	62	3/25	Peptic esophagitis (stricture)	2740	1870	4610	42.1	28.7	71.0	42.2	65.0	Post-op 2764 gravimetric loss; 4000 ML blood in OR (2700 donor blood)
4-AP	62	3/26	Peptic esophagitis (stricture)	2510	1960	4480	38.6	30.1	68.7	45.7	65.0	P.O.#1
5-AP	62	3/27	Peptic esophagitis (stricture)	3095	1945	5040	47.6	29.9	77.5	40.8	65.0	P.O.#2
6-AP	62	3/28	Peptic esophagitis (stricture)	3180	1760	4940	48.8	27.1	75.9	37.2	65.0	P.O. #3 Mild icterus-skin
7-AP	62	4/7	Peptic esophagitis (stricture)	3025	1735	4760	46.6	26.7	73.5	37.9	60.9	P.O.#13 No post-op transfusions

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CHART IV (continued)

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File No.	Age	Date	Diagnosis	PV-ML	RCV-ML	TBV-ML	PV	RCV	TBV	HCT%	WT.	Remarks
1-MH	45	3/25	Varicose veins	3660	2950	6610	36.6	29.5	66.1	46.5	100.	Pre-op bilateral vein stripping
2-MH	45	3/25	Varicose veins	3530	2960	6490	35.3	29.6	64.9	47.5	100.	Post-op minimal blood loss
1-TF	57	9/28	CA esophagus	3480	1590	5070	72.2	33.0	105.2	37.0	48.2	Pre-op gastrostomy 10/13 cachectic; lost 16 pounds in 3 months
2-TF	57	10/13	CA esophagus	2820	2610	5430	58.5	54.2	112.7	48.0	48.2	Post-op transfused pre-op; 1500 ML blood

CHART IV (continued)

PART V DISCUSSION OF RESULTS

A - RESULTS IN NORMAL SUBJECTS: (Tables 1 to 5)

Although there is a tendency for the total blood volume of children to be larger and of the normal female adults to be smaller in ml./Kgm. than the total blood volume of normal male adults, no statistically significant difference of two standard deviations is seen between the group means. The normal males had a higher average hematocrit than the normal female adults and normal children accounting for the slightly higher red cell volume in ml./Kgm. in the normal male adults. Total blood volume results expressed as milliliters per square meter of surface area, however, show that children have a smaller blood volume than the adult males and females. (Statistically significant difference is seen in comparison of the children with the adult males). This latter fact was pointed out by Rowntree, Brown and Roth (144) in their red dye studies reported in 1929 and later by Robinow (143). Inspection of the

results of Ely and Sutow (52) shows that with T-1824 blood volume studies, larger children have relatively larger total blood volumes expressed as milliliters per square meter of surface area. The wide range of normal values is noted in our series as in the other reported series when results are expressed as Ml./Kgm. The children's group is more homogenous than the adult groups as can be ascertained by the standard deviation of 6.1 for a total blood volume of 78.3 ML./Kgm. Our values for adults agree well with those reported by Storaasli (166) and Brady (27). No normal RIHSA values have appeared in the literature for children. Our values for children's total blood volume is markedly different from Robinow's (143) value of 90 ML./Kgm. which Dingman (44), for example, has accepted. Because children have a larger body surface area to height relationship then adults, it would appear to be more satisfactory to use weight as a basis of prediction of blood volume in children. Ely and Sutow (52) and Inkley (91) found weight and surface area to be satisfactory in the prediction of blood volume in children (52) and adults (91).

B - TECHNIQUE AND COUNTER STANDARDIZATION:

(Tables 6 to 13)

Serial RIHSA blood volume determinations by the method described in the section on Materials and Methods shows a reproducibility of plus or minus 2% (Table 6). This is acceptable for a biological measurement and agrees with the findings of Brady (27) who also used RIHSA.

Five ml. of dilute RIHSA could be delivered with a variation of much less than 1% (Table 7); counter variation was less than 1% (Table 8); replicate plasma samples were counted with a variation of less than 1% when counting rates were greater than ten times background (Table 9). Geometrical relationships of sample to counter were satisfactory when 2 ml. samples were counted (Tables 10 and 11).

Variations of voltage, pulse height selector and attenuator settings were made (Tables 12 and 13) so as to establish optimal counting conditions.

C - PULMONARY TUBERCULOSIS SERIES: (Tables 14 to 19)

Pre-operatively the pulmonary tuberculosis patients had approximately the same average hematocrit values as the normal groups of adults, with lower values for females than for males. The variation between the RIHSA estimate of operative blood loss and the gravimetric method of measuring operative blood loss averaged plus or minus 250 ml. in the 15 cases studied with a maximum variation of 600 ml. in two cases (Table 15). RIHSA blood volume studies and gravimetric measurement of operative loss serve complementary functions as laboratory aids in maintaining patients in a state of blood volume equilibrium. Pre-operatively a RIHSA blood volume study will help to uncover unsuspected blood volume deficits correctable by transfusion. This may be helpful in poor-risk patients. During operation the measurement of blood loss by the gravimetric means is simple, practical and permits contemporaneous replacement of blood loss,minimizing the dangers of

hemorrhagic hypotension or circulatory overload and cardiac failure. This is useful where large blood loss is anticipated. Large operative blood loss may occur when lobectomy is done in individuals who have had previous collapse procedures or empyema and may be expected to have numerous vascular adhesions and require protracted dissection. Postoperatively a RIHSA blood volume study is of value in ascertaining the adequacy of replacement of operative blood loss and in the estimation of the degree of abnormality of the blood volume. This information is useful in the differential diagnosis of post-operative hypotension and in guiding transfusion therapy for the prevention of hemorrhagic hypotension.

Familiarity with the information which the RIHSA blood volume determination and the gravimetric measurement potentially offer, will suggest many instances in which either test or both in combination may be of great value in selected patients. The ability to account for blood loss

and transfusion replacement within 250 ml. on the average is highly suggestive that sequestration of blood does not occur under the conditions of our experiments.

In battle casualties large areas of soft tissue damage may contain blood which is extravascular but not extracorporeal. Artz, Howard and Prentice (8) in studies of battle casualties have noted an inability to measure accurately by blood volume techniques the expected increment due to large volumes of transfused blood. This has resulted in their emphasis on sequestration of blood occurring in individuals who require massive transfusion for restoration of normal hemodynamics after injury.

Our findings are of particular interest in connection with recent application of blood volume studies to patients with pulmonary tuberculosis. Berlin (19), Kehne (93) and Albritten (2) have reported the occurrence of blood volume deficits in patients awaiting surgery of pulmonary tuberculosis. The suggestion is made by these authors

that transfusion to normal blood volume at least for present weight be done pre-operatively. Our findings corroborate the lack of correlation of the hematocrit with blood volume findings in pulmonary tuberculosis as reported by these authors.

The decision as to what constitutes a significant deficit in blood volume cannot be made without reference to statistical considerations nor can it be made purely on the grounds of statistics. Clinically a total blood volume deficit of 15 ML/Kgm ($1\frac{1}{2}$ times standard deviation 10) is probably of importance. This would represent a discrepancy from normal average blood volume of about 1050 ml. in the 70 Kgm, male of average physique. Weighing the risk of transfusion against the risk of failure of compensation of circulating dynamics during a major operative procedure when blood loss may amount to more than 1000 ml. and not be replaced contemporaneously, causes us to favor such an arbitrary figure as the limit of pre-operative deficit. It must be recognized that the expression of blood volume in

ml/Kgm. has limitations that affect the interpretation of results. Specifically, obesity affects the percentage of body weight represented by the active metabolic mass, to which blood volume is probably most closely related. Wide physiological variations in blood volume occur so that normal values may not be rigidly applied to individuals. Conversely the blood volume determinations plus clinical evaluation of the extent of the patient's disease, magnitude of operation procedure contemplated, ability to contemporaneously replace operative blood loss by forming an accurate estimate of loss during the operative procedure - these factors will influence the credence placed in a single pre-operative blood volume determination.

Routine pre-operative transfusion of pulmonary tuberculosis patients is as unwarranted as routine failure to transfuse. Normal concentration indices (hemoglobin, red cell count, hematocrit) are not helpful in the selection of patients for pre-operative transfusion. Clinical estimate based on recent weight change, duration of disease and

sanitarium care and roentgenologic estimate of the extent of disease, may at times be misleading. Blood volume determinations may help and at times are extremely useful when related to the clinical picture, especially when performed serially as a means of following changes in blood volume consequent to pre-operative transfusion.

Berlin (19) noted that 2 out of 26 cases studied apparently had a secondary polycythemia due to pulmonary fibrosis. Our results indicate the same findings in some of the male patients. If routine transfusions were given pre-operatively these patients may have developed circulatory overload. Even though the polycythemia may be compensatory for an abnormal pulmonary alveolar-capillary gradient of diffusion of oxygen due to fibrosis of the lung parenchyma, there is no positive reason for administering transfusion which will only increase the polycythemia.

The female patients did have a normal average hematocrit (39%). Among the female patients there were no instances of hypervolemia and they had lower blood volumes on the average than the male patients.

Transfusion might be considered more frequently in the female patients pre-operatively.

Where facilities for blood volume determinations are not available and a large volume of pulmonary tuberculosis surgery is performed, the occurrence of significant pre-operative deficits in certain patients will not be recognized pre-operatively. This emphasizes the necessity for careful estimate of operative blood loss and contemporaneous replacement. Where practical, routine gravimetric measurement of blood loss should be employed in pulmonary tuberculosis surgery. At least, the measurement of operative blood loss should be conducted on those cases recognized clinically as poor risks. A period of two to three weeks trial of the method is educational to surgeons, anaesthetists, operating room nurses and blood bank personnel responsible for supplying properly cross-matched blood for use during operation. Such a trial of the method is an instructive discipline for surgeons who are completely confident of their ability to judge operative

blood loss. Placing the sponges on a rack after weighing permits a valuable correlation between the reported measurement and the visual image of the number and saturation of the gauze sponges used. Improved operative technique prompted by a desire for economy in blood loss may ultimately benefit the patient.

The largest pre-operative deficit of total blood volume was found in male patient #11. Although he had a hematocrit of 48.4%, his pre-operative total blood volume was 22% less than expected. Clinically he was judged a poor risk, having poor pulmonary function studies, a large cyst in the left upper lobe and an immobile emphysematous chest. Following left upper lobectomy (transfusion 1450 cc.; blood loss 2000 cc.) his blood volume was further decreased 550 ml. His post-operative blood volume was 30% sub-normal. Post-operatively this patient was not hypotensive but did have markedly low hemoglobin and hematocrit determinations. From the hemodilution one may infer

rapid re-expansion of the plasma volume by translocation of extracellular fluid. This mechanism for expanding the blood volume would practically explain the absence of oligemic hypotension post-operatively.

D - RESULTS OF SINGLE AND SERIAL STUDIES PRESENTED IN CHARTS 1 TO 4:

Determinations were performed in poor-risk patients with blood volume deficits (Chart 1), electrolyte abnormalities (Chart II), miscellaneous surgical conditions (Chart III), and in patients before and after operation (Chart IV). These studies showed the practicability of the RIHSA blood volume as applied to the problems of surgical patients. Correlation of the laboratory data with the clinical condition of the patient helped to define and elucidate abnormalities of blood homeostasis and fluid balance. The rapid differentiation of plasma volume, red cell volume, and total blood volume deficits was of considerable practical importance in many cases of hemorrhage, dehydration and hypotension in poor-risk patients. In surgical centers to which complicated surgical problems are referred for treatment, maintenance of a blood volume laboratory with scintillation counting equipment for RIHSA blood volume studies

may be compared with maintenance of a metabolism laboratory with flame photometry apparatus for serum cation analysis. The rapid, accurate measurement of blood volume and the rapid, accurate measurement of serum cations may both be indicated in problems of pre- and post-operative management, especially of poor-risk patients or patients subjected to major operative procedures. The interpretation of tests of serum cation analysis and blood volume are best made by an individual who understands the limitations of the laboratory tests and appreciates the relationship of the tests to the clinical conditions of the patient. The interpretation of blood volume tests should ideally be done by the clinician responsible for the surgical management. However the advice of a consultant trained in metabolism, especially as related to surgical problems, and in physiology as related to circulatory dynamics would be of great value to the individuals assigned the responsibility

for the pre- and post-operative care of poor risk surgical patients.

Examination of the data of Charts I to 4 effectively demonstrates the lack of correlation of the hematocrit percent with the total blood volume in ml./Kgm. Most of the authorities on the subject of blood volume from Rowntree (144) in 1929 to Berlin (17) in 1952 have made this observation. However with the data of a recent blood volume study, physical examination of the patient with respect to general state of health and state of hydration and history of fluid intake, state of nutrition, history of transfusions or blood loss and the hematocrit percent or other concentration indices of the blood have some value in ascertaining blood volume excesses or deficits in surgical patients. In a surgical patient, when there is an abnormality of blood volume sufficient to interfere with the maintenance of normal hemodynamics, a rapid blood volume test such as the RIHSA test, is a source of more meaningful information than is an index of concentration such as the hematocrit percent.

Figures 8 to 11 illustrate diagrammatically typical surgical cases in which blood volume studies correlate well with the clinical course of the patient and are more useful than hematocrit determinations.

E - INTERPRETATION OF BLOOD VOLUME DETERMINATIONS; ESTIMATE OF VOLUME DEFICITS:

It has been noted that there is a good general agreement as to normal values of the currently used (i.e. T/1824, RIHSA, P^{32} and Cr^{51} tagged red cell) methods of plasma volume or red cell volume determination and that the methods are clinically satisfactory (74, 135, 136), for determination of total blood volume when used with the venous hematocrit over an average range of 30-50%. However, it has been pointed out that average normal values may not be rigidly applied to individuals because of the wide range of normal values which are included in the average normal value (136). Hence the statistical limitations and the clinical applicability of values must be reconciled in some way. The wide range of average values when expressed as ml/Kgm. probably arises to a great extent from the differences in body density or proportion of lean body mass to body weight in different individuals (68). However, expression of results as ml./Kgm is the most convenient and not the most

inexact way of expressing blood volume (136). When an extreme of body type is encountered (i.e. marked obesity or marked leanness) one must realize the probably effect of body type on the number of ML. of blood per Kgm and then compare the findings in the particular individual with the findings in the average normal. Applying a statistical rule of considering a variation of two standard deviations from the mean as significant, some obese normals will be considered not significantly different from the normal. In our series of 23 male patients: PV = 40.8 plus or minus 6.0; RCV = 32.0 plus or minus 3.4; TBV = 72.7 plus or minus 8.5. The range of values is: PV 32.9 - 52.9; RCV 25.4 - 37.2; TBV 58.8 - 90.2. Hence it can be seen that there is a wide range of normal. Repeated sampling since 1915 (94) with dilution methods of blood volume determination has not succeeded in narrowing the ranges when results are expressed as ml./Kgm. In our series of normal males, one standard deviation represents the following percent of the mean: PV - 14.7%; RCV - 10.6%; TBV - 11.7%. Hence it is quite obvious that, from a statistical point

of view, deviations of 10% from the average are not significant in an isolated determination. (The variation of 10% between successive determinations would probably be significant statistically as well as clinically since the coefficient of variation between serial determinations with RIHSA is of the order of 2 to 3%). Before major surgical procedures the finding of a red cell volume deficit of at least 15% or a total blood volume deficit of at least 15% in a patient who is not extremely obese would suggest that transfusion might be adventageous. (These arbitrary limits are based on approximately $1\frac{1}{2}$ times the standard deviation for red cell volume and $1\frac{1}{2}$ times the standard deviation for total blood volume). Since neither transfusion nor pre-operative anemia are innocuous, the problem must be solved on a basis of an evaluation of the risk of unnecessary transfusion (inconpatibility, allergic reaction, septicemia, circulatory overload, hemosiderosis with multipe transfusions) as opposed to the risk of omitting necessary transfusion (decreased oxygen carrying capacity of blood , hypovolemia

rendering the patient more susceptible to decompensation of circulatory dynamics with anaesthesia and operative blood loss, hypoproteinemia). From the point of view of circulatory dynamics it has been shown that patients with normal blood volume tolerate transfusion well (47), thus transfusion of a patient who had a normal blood volume but a laboratory report of "10% deficit" would not necessarily cause the patient to suffer from an over-expansion of his blood volume. Thus for clinical purposes we are inclined to categorically state that these deficits are not necessarily clinically significant: red cell volume less than 15% below normal, total blood volume less than 15% below normal. Deficits in plasma volume of the order of 15% in a patient with history of extracellular fluid loss or internal redistribution of fluid after mechanical or thermal trauma may suggest the use of plasma or plasma expanders as well as rehydration (salt and water replacement). As applied to a 70 Kgm male, 15% deficits would amount to: PV - 430 cc.; RCV - 330 cc.; TBV - 760 cc. Following such a rule

will prevent the administration of transfusion solutions to patients who may not require transfusion. However, if a patient had a larger blood volume in ml./Kgm than average, lost some of the volume, and a laboratory report of "10% deficit" was made, the patient may have gone from a 115% to a 90% average volume and be in need of transfusion, i.e., he would have lost 22% (22, 115) of his original blood volume. This instance applies particulary to those individuals with whole blood loss. Hence, in a thin individual a 10% volume deficit of total blood should be corrected to average normal for weight by whole blood transfusion. The problem of what constitutes a deficit can probably best be solved by some means of readily relating the volume of blood to the active metabolic mass of the patient, but no practical, simple means of doing this is at hand.

PART VI SUMMARY

A review of the literature of clinical blood volume studies has been made with reference to application of a rapid, reliable, simple method to surgical patients. Problems bearing on the precision and accuracy of blood volume methods have been discussed. The relationship of blood volume to circulatory dynamics and alterations of blood volume in states of health and disease have been mentioned.

The RIHSA method of blood volume determination was chosen as being satisfactory for the purpose of routine clinical blood volume study in surgical patients and as a basis for the establishment of a Blood Volume Laboratory in the Royal Victoria Hospital. A method of using the RIHSA for these purposes was evolved and tested over a period of one year commencing in July, 1954. The technique and counting equipment were standardized. Over 300 determinations performed in human subjects demonstrated the practicability and utility of the method.

Normal values were established for adults and children. A group of patients with pulmonary tuberculosis were studied before, during and after surgery with measurements being made of pre- and post-operative RIHSA blood volume and of operative blood loss. Correlation was made of directly measured operative blood loss and the estimate of operative blood loss made from pre- and post-operative RIHSA blood volume.

Single and serial RIHSA blood volume determinations were performed in poor risk surgical patients, patients subjected to operative procedures and patients who had abnormalities of fluid and electrolyte metabolism.

PART VII CONCLUSIONS

1. - The RIHSA blood volume method is a rapid, simple, reliable method of estimating blood volume, particularly suitable for use in surgical patients.

2. - A Blood Volume Laboratory was inaugurated in the Royal Victoria Hospital and over 300 determinations performed in human subjects.

3. - A modification of the RIHSA blood volume was developed and described for use in the Blood Volume Laboratory of the Royal Victoria Hospital.

4. - The RIHSA blood volume method described was found to give serially reproducible results with plus or minus 2.2% variation.

5. - Normal values in ml./Kgm. were obtained for:

(continued pg. 219)

	Plasma volume	Red Cell volume	Total Blood volume	Hematocrit %
Adult males	40.8 ± 6.0	32.0 ±3.4	72.7 ±8.5	45.8 ±3.0
Adult females	43.5 ± 7.3	27.2 ± 3.7	70.7 ±10.2	40.3 ±3.3
Children	49.6 ±4.5	28.7 ±2.4	78.3 ±6.1	38.2 ±1.9

6. - Children were found to have a smaller blood volume per square meter of body surface than adults (27 children; 11 adult females; 13 adult males):

	Ml. Total Blood Volume per square meter of surface area.
Children	1974 ±186
Female adults	2518 ±295
Male adults	2788 ±253

7. - The mean blood volume of pulmonary tuberculosis patients (32 subjects) was not significantly different from the mean blood volume of the normal subjects.

8. - Routine blood transfusion before surgery for pulmonary tuberculosis is discussed but not recommended.

9. - Gravimetric measurement of operative blood loss during pulmonary tuberculosis surgery (15 patients) agreed well with the estimate made from pre- and post-operative RIHSA blood volume studies. Average variation was 243 ml. and maximum variations were plus or minus 600 ml.

10. - The RIHSA blood volume method provides laboratory data which is of value in the management of problems of water and electrolyte metabolism occurring in surgical patients.

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