Blood Volume: Not one Single Volume but the Sum of Two Volumes with Various Mixing in Different Parts of the Circulation

M.		Hatter
U.		Finsterer

München

Dr. med. Mathias Haller, Prof. Dr. med. Udo Finsterer, Institut für Anaesthesiologie, Ludwig-Maximilians-Universität, Klinikum Großhadern, D-81366 München (FRG)

The earliest attempts to determine blood volume date from the 18th century. The tracer dilution method was introduced in 1915 by Keith et al. [1]. Since then, circulating volume has been repeatedly claimed to be an important clinical parameter, with potential relevance in the monitoring of critically ill patients. Up to now, however, there has been no method available which is both easy to use and accurate. Furthermore, there is still considerable debate as to whether plasma or red cell markers should be used as determinants of blood volume. Various studies have attempted to establish standardized values for blood, plasma or red cell volumes. The volumes are mostly standardized to body weight or body surface area but nevertheless there remain considerable interindividual variations. As with many new or not widely used diagnostic parameters it is not clear whether this standardized 'normal' volume represents the optimal volume in the individual clinical situation in the critically ill patient. In intensive care medicine and during anesthesia the intravascular volume is mostly estimated using blood pressure and heart rate, the central venous pressure or the pulmonary occlusion pressure. These pressures may reflect cardiac function rather than the actual volume state of the patient [2].

Tracers for volume determinations are either markers of the plasma or of red cells. In recent years, radioactive isotopes were most commonly used with radioactively labeled human serum albumin for plasma volume and radiochromate tagged red cells for red cell volume determinations [3]. These tracers are difficult to handle in clinical routine and are contraindicated for repeated measurements because of radioactive contamination. Dyes used as tracers in plasma volume estimation are Evans blue [4-7] and indocyanine green [8-12]. These dyes seem to combine accuracy with lack of toxicity. But for repeated measurements, the half-life of Evans blue is too long (corresponding to the half-life of serum albumin) and, as an azo dye, Evans blue may possess a mutagenic potential as indicated in a few in vitro studies [13, 14]. A suitable non-radioactive tracer for red cells is still lacking.

In this issue of INFUSIONSTHERAPIE und TRANSFUSIONSMEDIZIN Lauer et al. [pp 138] report a new method of labeling red cells with sodium fluorescein, a substance widely used in ophthalmology. After the first report of red cell volume measurements with fluorescein (using fluorescein-sulfonate which is more stable than sodium fluorescein) in animals by Hansen [15] and a preliminary study by Lauer et al. [16] the method is compared with radiochromate labeled red cell volume determination as a criterion standard in Lauer et al.'s study. The results demonstrate good correlation between the two methods. The applicability of the method in the

clinical settings may be jeopardized by its complexity. However, sodium fluorescein is to our knowledge the only nonradioactive and readily available red cell marker for use in humans. However, to suggest as these authors do that total blood volume can be estimated by tagging of red cells is misleading. There is considerable evidence from microvascular studies [17], tracer dilution studies in animals [18], and from human studies [19,20] that the hematocrit in large vessels is not representative of the entire circulation. In other words, the hematocrit in peripheral venous or arterial blood may only in some circumstances be the same as the average hematocrit of the total circulating blood. Studies in humans revealed that the ratio of whole body to large vessel hematocrit (the so-called f-cell ratio) may vary between 0.6 and 1.1 [19], thus indicating that there may be a substantial difference between the hematocrit measured in large vessels and the average hematocrit of the entire circulation. Hence, calculating blood volume from the concentration of either a red cell or a plasma marker in a peripheral blood sample may lead to erroneous results. For these reasons, the method of obtaining the whole body hematocrit by applying a fixed f-cell ratio correction factor to the measured peripheral hematocrit – as is done in many studies [2, 20, 21] – is not satisfactory. The only way to measure blood volume using indicator dilution techniques is to use separate markers for each compartment of blood, i.e. red cells and plasma, and to summate these values [22].

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In situations where red cell volume is unlikely to change, as in some physiologic studies or in nonsurgical patients, plasma volume may be the focus of interest. On the other hand, in surgical patients the volume of oxygen carrying cells may be of more relevance than plasma volume. From a theoretical point of view, in certain clinical situations, e. g. acute bleeding, volume replacement therapy or after 'isovolemic' hemodilution, the peripheral hematocrit may not reflect the actual number of circulating red cells.

The volume actually measured in the study of Lauermaun et al. was the red cell volume, calculated from the concentration of the two tracers (sodium fluorescein and radiochromate) in the red cells of the drawn blood samples. Red cell volume is thus calculated as the quotient of the injected tracer amount and the tracer concentration in the drawn blood specimen multiplied by the hematocrit of the same blood sample. Lauermaun et al. have successfully developed a readily avail-

able method for red cell tagging without the use of radioactivity. The authors conclude that their method measures total blood volume and indeed they showed a good agreement between this new method and the standard one using radiochromate. However, we would suggest that while both methods are measuring the same volume and are in good agreement neither is actually measuring total blood volume. With the reintroduction of blood sparing techniques such as perioperative isovolemic hemodilution, methods for the determination of red cell and plasma volume will become more and more important. In the practice of anesthesiology and intensive care medicine, the alterations in the constitution of blood induced by therapeutic interventions such as intentional hemodilution are not yet well understood. Red cell and plasma volume measurements may be important tools for future investigations. So this editorial ends as many of its kind: further studies are needed.

References

Keith NM, Rowntree LG, Geraghty JT: A method for the determination of plasma and blood volume. Arch Int Med 1915;16:547-576.

Shippy CR, Appel PL, Shoemaker WC: Reliability of clinical monitoring to assess blood volume in critically ill patients. Crit Care Med 1984;12:107-112.

International Committee for Standardization in Haematology (Pettit JE, Panel Secretary): Recommended methods for measurement of red-cell and plasma volume. J Nucl Med 1980;21:793-800.

Finsterer U, Kapser S, Reiser-Zimre E, Fottner I: Das Verhältnis von Hämatokrit und Plasmaproteinkonzentration prä- und postoperativ unter «isotoner» Hämodilution und Hämokonzentration und während Laparotomie. Anaesthesist 1981;30:383-389.

Gregersen MI, Gibson JG, Stead EA: Plasma volume determination with dyes, errors in colorimetry; use of the blue dye T-1824. Am J Physiol 1935;113:54-55.

Linderkamp O, Mader T, Butenandt O, Riegel KP: Plasma volume estimation in severely ill infants and children using a simplified Evans blue method. Eur J Pediatr 1977;125:135-141.

Johansen LB, Foldager N, Stadeager C, Kristensen MS, Bie P, Warberg J, Kamegai M, Norsk P: Plasma volume, fluid shifts, and renal responses in humans during 12 h of head-out water immersion. J Appl Physiol 1992;73:539-544.

Schad H, Haider M, Brechtelsbauer H: Bestimmung des Plasmavolumens mit Indocyaningrün. Anaesthesist 1987;36:608-614.

Bradley EC, Barr JW: Determination of blood volume using indocyanine green (Cardio green) dye. Life Sci 1968;7:1001-1007.

Haneda K, Horiuchi T: A method for measurement of total circulating blood volume using indocyanine green. Tohoku J Exp Med 1986;148:49-56.

Busse MW, Zisowsky S, Henschen S, Panning B, Piepenbrock S: Plasma volume estimation using indocyanine green. Anaesthesia 1993;48:41-43.

Haller M, Akbulut C, Brechtelsbauer H, Fett W, Briegel J, Finsterer U, Peter K: Determination of plasma volume with indocyanine green in man. Life Sci 1993;53:1597-1604.

Nakane H, Balzarini J, De Clercq E, Ono K: Differential inhibition of various deoxyribonucleic acid polymerases by Evans blue and aurintricarboxylic acid. Eur J Biochem 1988;177:91-96.

Kornbrust DJ, Barfknecht TR: Comparison of 7 azo dyes and their azo reduction products in the rat and hamster hepatocyte primary culture/DNA-repair assays. Mutat Res 1984;136:255-266.

Hansen E: Blutvolumenmessung mit fluoreszenz-markierten Erythrozyten. Anaesthesist 1985;34 (suppl):89.

Lauermann I: Eine neue Methode zur Bestimmung des zirkulierenden Blutvolumens – Erythrozyten-markierung mit Fluorescein-Natrium. Infusions-therapie 1991;18:130-136.

Mirhashemi S, Messmer K, Arfors K-E, Intaglietta M: Microcirculatory effects of normovolemic hemodilution in skeletal muscle. Int J Microcirc Clin Exp 1987;6:359-369.

Barbee RW, Perry BD, Ré RN, Murgu JP: Micro-sphere and dilution techniques for the determination of blood flows and volumes in conscious mice. Am J Physiol Regul Integr Comp Physiol 1992;263: R728-R733.

Wright RR, Tono M, Pollycove M: Blood volume. Semin Nucl Med 1975;5:63-78.

Sawka MN, Young AJ, Pandolf KB, Dennis RC, Valeri CR: Erythrocyte, plasma, and blood volume of healthy young men. Med Sci Sports Exerc 1992;24:447-453.

Busse MW, Zisowsky S, Henschen S, Panning B, Reilmann L: Determination of circulating blood volume by measurement of indocyanine green dye in hemolysate: A preliminary study. Life Sci 1990; 46:647-652.

International Committee for Standardization in Hematology (ICSH): Panel on Diagnostic Applications of Radioisotopes in Haematology: Standard techniques for the measurement of red-cell and plasma volume. Br J Haematol 1973;25:801-814.