BLOOD AND PLASMA VOLUME IN PREGNANCY

by

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It is generally considered that the plasma and blood volumes are increased during pregnancy. There is perhaps some disagreement as to the degree of increase and whether there is a decrease during the last month of pregnancy corresponding to the reported decrease in cardiac output.

Thomson et al (1938) have shown that the plasma volume increases progressively until the ninth lunar month. They found an average normal non-pregnant value. During the tenth lunar month there is a definite decrease, the plasma volume falling by this time to some 50 per cent above normal. The same workers showed that the total blood volume shows similar changes, increasing by the ninth lunar month to an average of 45.5 per cent above normal.

Wintrobe mentioned that the blood and plasma volumes increase, most of this occurring before the 24th week. At term, the increase in plasma volume may amount to 40 per cent and the increment in total blood volume may be 32 per cent, but the individual variations are very great. This explains why losses of blood volume are borne so well by the parturient woman. Post-partum, the blood volume returns to normal within a week.

Current procedures for the determination of plasma volume utilize the dilution principle. A substance easily determined by chemical or physical methods is injected into the circulatory system where, after a certain time required for mixing, it presumably becomes evenly distributed in the plasma or the red blood cells. If the disappearance of this substance from the vascular system is negligible, then from the amount injected and one or more blood samples obtained after mixing, plasma or red cell volume may be determined. Knowing the simultaneous haematocrit value, total blood volume may also be calculated easily.

Dawson, Evans and Whipple in 1920 found that Evans blue dye by virtue of its blue colour was easily read colorimetrically, and that haemolysis did not interfere with the reading. It is a diazo dye and has been shown to be practically non-diffusible when it is in protein combination. The rate of disappearance was found by Dawson, Evans and Whipple and others to be approximately 5 to 8 per cent per hour.

Dawson and others have shown

that Evans blue dye is bound selectively in a complex to the plasma proteins. It is the strength of this bound dye that determines the rate of disappearance of the dye. The dye is eliminated from the blood stream by phagocytosis, by the reticuloendothelial system, and to a much less marked degree by diffusion and excretion by the liver. It will not appear in the urine if the kidneys are normal and will not appear in oedema or ascitic fluid. It will not pass the placenta or appear in the amniotic fluid.

Hueper and Ichniowski concluded that the dye was not toxic in doses ordinarily used for hemodynamic determinations; however, repeated doses may produce slight nausea and vomiting. Ordinary doses will not dicolour the skin or mucous membranes. The dye method for the determination of plasma volume has been verified by radioactive iron methods. More recently the dye method and the iodinated albumin method of measuring plasma volume have been found to correspond closely.

The validity of the dye dilution method has been questioned. It is beyond the scope of this report to review the evidence in its favour, and it should suffice to state that in recent years an overwhelming body of evidence has been accumulated to indicate that the simultaneous use of Evans blue (T-1824) and some of the more complex reagents, e.g. iodinated human serum albumin or polysaccharide S III, give estimates of plasma volume which are for all intents and purposes identical.

The subject was first brought to the attention of workers in this field by Cruickshank and Whitfield, who presented evidence that a significant portion of the initially injected Evans blue (T-1824) is phagocytized by the reticuloendothelial system. A portion of the solute (dye) is thus immobilized and would lead to erroneously high values if the dilution of the dye were taken as a measure of the volume.

Evans blue (T-1824) containing large amounts of a red impurity gives high results when used for blood volume determinations; this is due, in part, to rapid disappearance from the circulating plasma of the impurity which absorbs light in the region of maximum absorption of the main blue component.

The Ilford 607 (spectrum orange) filters are considered to be more satisfactory than the 608 (spectrum red) for blood volume determinations using T-1824.

In an effort to render these measurements more accurate, use has been made in the past few years of a variety of radio-isotopes as tracer substances. For the determination of the cell volume by use of the dilution principle, a certain amount of red blood cells is labelled by means of either radioactive iron (Fe^{55}, Fe^{59}), radioactive chromium (Cr^{51}), radioactive phosphorus (P^{32}) or radioactive potassium (K^{42}) and then injected into the circulation following the method described above. Radio-isotope-labelled cell methods have been found to be more accurate than plasma dye methods. According to Reid and Orr, these methods, although much easier to handle than earlier procedures, do not yet have

the simplicity and precision needed for routine clinical application.

Methods for Determination of Plasma Volume (T-1824)

1. Blood samples are taken usually early in the morning on an empty stomach.
2. Evans Blue dye gets oxidised if exposed and it may contribute to some extent to the total percentage of error of 15%. Hence it is essential to keep samples sealed and to complete the estimation colorimetrically within 30 minutes of receiving the samples.
3. While taking blood samples no pressure on the arm be put as it may not allow free circulation of the dye.
4. If a reestimation is contemplated, it is essential to repeat the test only after one month as the dye injected during the previous experiment may still be found in the tissues for at least 3 weeks.
5. Ilford 607 (spectrum orange) filters are considered to be more satisfactory than the 608 (spectrum red) for blood volume determinations using (T-1824).

Observations

We have chosen three groups of patients:

(1) Patients with 32-36 weeks pregnancy: Total cases 29
(2) Patients with 32-34 weeks pregnancy (suffering from pre-eclamptic toxaemia) : Total cases 10
(3) Gynaec. cases to compare the difference in blood volume: Total cases 18.

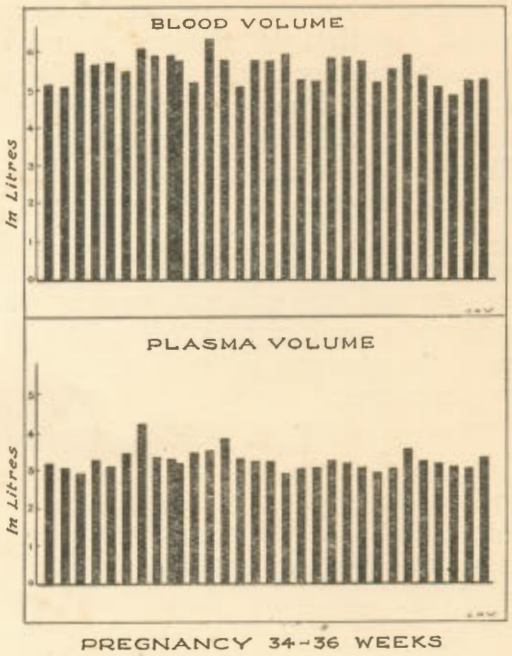

Fig. 1

1. On tabulating the results of plasma volume and blood volume it is found that the average rise of plasma volume is 3.5 litres, 15 per cent more than the normal.
2. The average blood volume was found to be 5.7 litres. It denotes a rise in blood volume by 25%.
3. It is noticed that in the group of toxaemia of pregnancy, the average plasma volume was 3 litres, which is found to be definitely less than that in average normal adult female and it shows a similar trend of fall in blood volume to about 4.15 litres.

Plasma volume and blood volume in the normal human adults which

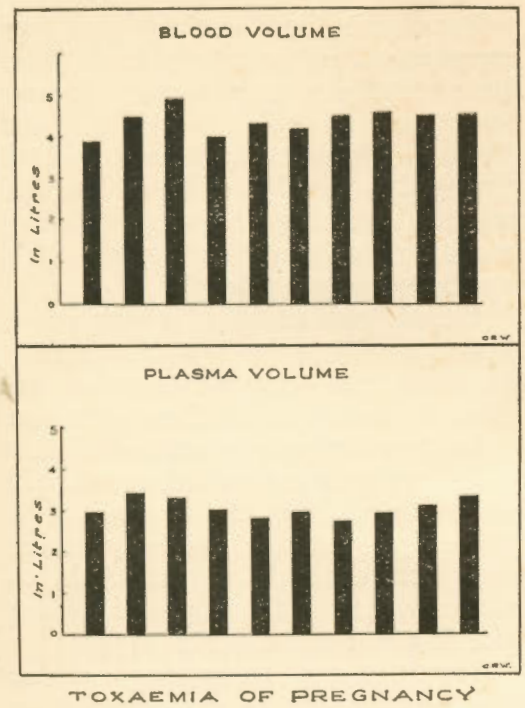

Fig. 2

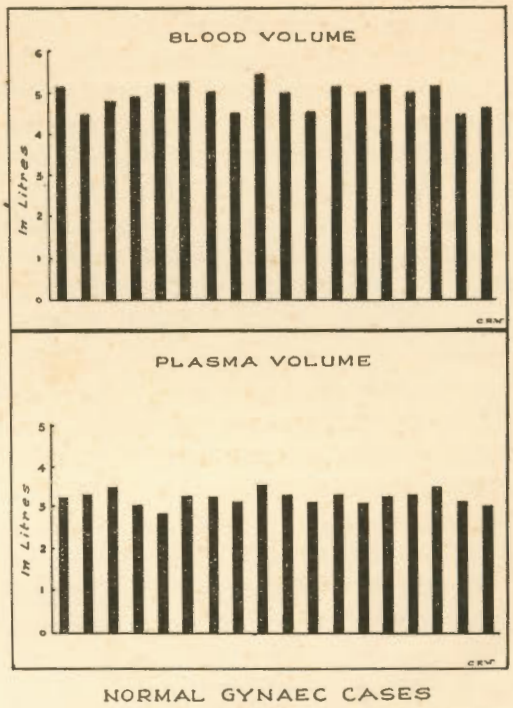

Fig. 3

were admitted for treatment in gynaecological ward were respectively 3.2 and 4.6 litres.

Discussion

In western countries, the various authors who contributed to the determination of plasma volume and blood valume have all suggested that the average rise was by 30% and 40% respectively whereas the average rise in our series in plasma volume and blood volume was by 15% and 25% respectively. These results were based on a group of 29 patients whose haemograms denoted that a few were suffering from microcytic hypocromic anaemia and hypo-proteinaemia. This rise did not quite correspond to that suggested by western countries because of the differences in the weight of the two groups of patients. Plasma proteins estimation might in each case bring to light definite relations with blood volume and plasma volume in pregnancy. It is universally accepted that women with pregnancy suffer from hypoproteinaemia and physiological anaemia. Blood volume deter-

	Plasma volume litres	Blood volume litres
(1) Normal adult female	3.2	4.6
(2) Pregnancy 32 to 36 weeks (patients) ..	3.5	5.7
(3) Toxaemia of pregnancy	3.0	4.15

minations with Evans blue technique can be further improved by using the spectro-photometer instead of the ordinary colorimeter as suggested by Gregerson and Gibbson. This dye method for determination has been verified by radioactive iron methods. More recently, the dye method and iodinated albumin technique of measuring plasma volume have been found to correspond closely.

In our observations we found that women suffering from pre-eclamptic toxaemia have considerably lowered plasma volume and blood volume when compared to normal levels.

Myron I. Buchmen of Cornell University stated that such patients with toxaemia of pregnancy possessed lowered blood volume. These patients therefore suffered easily from shock with regard to operative obstetrics and postpartum haemorrhage. The hazard was doubled when these patients of pre-eclamptic toxaemia suffered from hypoproteinaemia and low blood volume. The average blood volume in nulliparous adult female is 4.5 litres and the plasma volume is 3.2 litres which is definitely lower than those recorded in western countries. The main contributing factor may be the average weight and the nourishment of the patient.

Many gynaecologic patients enter the hospital with a diminished blood volume. Patients who are admitted for vaginal repairs have a deficit in both plasma volume and in blood cell mass, roughly proportionate to the reduction in total blood volume. These deficits in blood volumes are the results of bleeding from fibroids, adenomyosis, or carcinoma or derangements in haemoglobin metabolism secondary to systemic diseases such as tuberculosis. Rendall and Beling and associates have reported that 65% to 75% of their general surgical patients required one or more transfusions to replace preoperative volume deficits.

Shock can usually be averted if patients with a history of excessive bleeding for several months are given a transfusion before operation.

In conclusion, we reiterate that blood volume estimation should be an important item of investigation in obstetrical patients specially suffering from anaemia and toxaemia to clinically assess the degree of deficit and to treat them accordingly.

The values of measuring circulating blood volume are important in the following circumstances:

(1) Undiagnosed pre-operative hypovolaemia resulting in cardiac arrest.

(2) Hypotension due to overhydration.

(3) Unsuspected internal postoperative haemorrhage.

(4) Operative and post-operative hypotension with proper blood replacement.

To stimulate further studies it is suggested that

1. The relation of the plasma proteins to the blood volume be estimated.
2. The relation of the weight gained in toxaemia of pregnancy to deficits of blood volume and the plasma volume be estimated.

3. To estimate the plasma volume and the blood volume by the use of spectrophotometer rather than colorimeter.

Summary

1. Review of literature regarding the methods chosen for the determination of plasma and blood volumes.
2. Methods chosen were Evans blue technique, iodinated human serum, radioisotopes. The first method was utilised in our series.
3. Three groups of cases were chosen:
   (a) Pregnancy 32 to 34 weeks.
   (b) Toxaemia of pregnancy 34 weeks.
   (c) Normal female adults.
4. Observations regarding the results denote that the average rise in plasma volume and blood volume is relatively less than that mentioned in the western countries.
5. In toxaemia of pregnancy the blood volume and plasma have been found to be lowered as compared to the normal.

In the end it is my duty to express my thanks to Dr. B. N. Jungalwalla, Professor of Obstetrics and Gynaecology, for permitting me to choose cases from the Department and to Dr. B. C. Bose, Principal, M.G.M. Medical College, Indore, for encouragement in Research Problems. It is also my duty to thank Mr. Amrit Modi of Unichem Laboratories for his liberal supply of .5% Evans Blue and Dr. D. P. Mukerji (R.M.O.) from haematology department for his assistance.

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