Changes in the Blood Volume During Pregnancy and Delivery

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CHARACTERISTIC of normal pregnancy are profound changes in the maternal circulatory system. These include a considerably expanded blood volume, an increased cardiac output, and an augmented blood flow to several regions of the body.

For the past decade some of us in the Department of Obstetrics and Gynecology of The University of Texas Southwestern Medical School have continued to study several aspects of the changes in the contents of the maternal intravascular compartment during normal and abnormal pregnancies. The observations made during the course of several of the studies of pregnancy-induced changes in blood and red cell volumes, part of which have been previously published while others have not, will be presented in this Review.

Measurement of Maternal Blood Volume

We have measured the apparent maternal blood volume and the red blood cell volume during the last two trimesters of pregnancy, before and after delivery, at the end of the first week postpartum, and again two months or more after delivery using each subject's red blood cells labeled with [51]Cr.[1] The advantages of this method are that the cells are rather easily labeled, the isotope does not readily escape from the intravascular compartment, and the isotope is easy to count. Fortunately no detectable ^{51}Cr crosses the placenta. While the circulating red blood cell volume can be precisely measured with this technic the volume of distribution of the labeled red blood cells, or the apparent blood volume, might be slightly less than the true blood volume. There is somewhat uneven distribution of red blood

cells and plasma throughout the circulatory system and, as a consequence, the red blood cell fraction or the hematocrit of blood in very small blood vessels is lower than in larger ones.[2] Ideally another labeled substance which would allow precise quantitation of the plasma volume should also be used. The availability of such a substance is debated. Although Evans blue dye and iodinated human albumin (RISA) are commonly accepted as ideal agents for measuring plasma volume, there is evidence that the "plasma" volume is somewhat smaller when measured using iodinated proteins with a considerably larger molecular weight than albumin, or with high molecular weight dextran, than when Evans blue or RISA is used.[3] This suggests that the volume of distribution of RISA and Evans blue might be somewhat larger than the true plasma volume.

From the practical standpoint the difference between the apparent blood volume measured with ^{51}Cr-labeled red blood cells and the volume determined by measuring the red blood cell volume with ^{51}Cr plus the volume of distribution of Evans blue or RISA is rather inconsequential. The blood volume measured with ^{51}Cr-labeled red cells averages only about 11 per cent less than when Evans blue or RISA is also used. This means that the ratio of the whole body hematocrit (the red blood cell volume divided by the sum of the red blood cell and plasma volumes) to that of the hematocrit of blood from a large vessel averages 0.89. The whole body-large vessel hematocrit ratio is not altered significantly by pregnancy or parturition.[4-6] Therefore the pattern of the change in blood volume during pregnancy determined with ^{51}Cr-labeled red blood cells is not distorted by any simultaneous induced changes by pregnancy in the whole body-large vessel hematocrit ratio. If one accepts the sum of the red blood cell volume and the Evans blue or RISA "plasma" volume as the "true" blood volume, the volume of distribution of

TABLE 1. Blood and Red Cell Volumes in Normal Women Late in Pregnancy and Again when Not Pregnant

Single Fetus (50)

	Late Pregnant	Non-pregnant	Increase ml.	Increase %
Blood volume	4,820	3,250	1,570	48
RBC volume	1,790	1,355	430	32
Hematocrit	37.0	41.7		

Twins (30)

	Late Pregnant	Non-pregnant	Increase ml.	Increase %
Blood volume	5,820	3,865	1,960	51
RBC volume	2,065	1,580	485	31
Hematocrit	35.5	41.0		

[51]Cr-labeled cells can be converted to a "true" blood volume simply by dividing by 0.89. The relative constancy of the whole body-large vessel hematocrit ratio during pregnancy also means that the red blood cell volume can be calculated from the volume of distribution of Evans blue dye or RISA and the large vessel hematocrit ratio, with the same degree of accuracy as in the nonpregnant state.

Magnitude of Pregnancy Hypervolemia

The blood volumes of 50 normal women pregnant with a single fetus were measured at or very near term but prior to active labor and again two months or more after delivery. Supplemental iron was provided during pregnancy and after delivery. As shown in table 1 the average blood volume of this group of 50 women was 1,570 ml. more (+48 per cent) than when nonpregnant. Slightly greater increases in both blood and red cell volumes were noted in 30 cases of twin pregnancy similarly studied.

The degree of hypervolemia induced by pregnancy varied considerably from subject to subject, ranging from as little as 20 per cent to nearly 100 per cent of the nonpregnant volume. The actual increases in milliliters as well as the percentage increases in blood volume also varied greatly. While there was considerable variation in the intensity of the hypervolemia from subject to subject, the same subject usually developed the same degree of hypervolemia with subsequent pregnancies. The average increase and the range noted by us in women pregnant with a single fetus are similar to those found by Caton and his associates, Berlin and his associates, and by Dahlstrom and Ihrman.[7-9] In several of the studies of earlier investigators somewhat smaller increases were found.

In many of the normal subjects one or two blood volume measurements were also made sometime during the second and third trimesters. The typical pattern of change demonstrated during pregnancy was a moderate increase in blood volume by the end of the first trimester, a more marked increase during the second trimester, and finally a slight rise throughout the third trimester. Initially the increase in blood volume was relatively greater than the increase in red blood cell volume. Late in pregnancy the reverse was usually true.

It has been stated by Burwell and Metcalfe[10] that it is the opinion of most observers in this field that the curve showing the relation of total blood volume to the duration of pregnancy follows the same course as that of cardiac output, reaching a maximum about the eighth month and declining in the last weeks of pregnancy.[11] A few investigators, including ourselves, have questioned the validity of this pattern of change in blood volume so often described for late pregnancy. McLennin and Thouin several years ago noted that not only did their own prior studies not confirm a significant fall in maternal blood volume as term approached but careful evaluation of the published results of some of the proponents also failed to demonstrate any real decrease late in pregnancy.[12] *No distinct decrease in blood volume has been noted by us during the last several weeks of pregnancy.* In fact we have observed a slight rise right up to term.

Mechanisms Responsible for Hypervolemia

The hypervolemia induced by pregnancy serves to meet the metabolic demands of the enlarged uterus with its greatly enlarged vascular system, to protect the mother and, in turn, the fetus against the deleterious effects of impaired venous return and reduced cardiac output when in the supine and the erect positions. It is also of considerable importance, as illustrated below, in safeguarding the mother against the adverse effects of hemorrhage during parturition and the early puerperium.

The actual mechanisms are poorly understood which bring about the addition, on the average, of about one and one half liters of blood including a half liter of red blood cells to the maternal circulation. Aldosterone production is greatly elevated compared to that in the nonpregnant state, but whether this hormone contributes to the hypervolemia is not known. Hypervolemia accompanies other conditions in which there is an increased production of aldosterone including primary hyperaldosteronism.[13] The production of estrogens and progesterone also is markedly increased. A very modest increase in blood volume has been achieved by giving large amounts of estrogens to normal adults but the increase was nowhere near as great as that accompanying normal pregnancy.[14, 15] It is possible that the growth hormone-like substance in the placenta described by Josimovich and by Kaplan and Grumbach contributes to the hypervolemia.[16, 17] Finally, blood flow through the placental implantation site has been considered by some to be akin to that through an arteriovenous fistula.[10] Hypervolemia can be induced experimentally by creating a large arteriovenous shunt.

There is considerable enlargement of many of the blood vessels during pregnancy especially in the region of the pelvis. Cumulatively, the increased capacity of the uterine and associated pelvic blood vessels, the increased filling of all the veins which are below the large pregnant uterus and therefore obstructed by it, and the increased vascularity of the breasts would seem sufficient to contain all or most of the added volume of blood. Certainly during normal pregnancy there is no evidence of circulatory overload even though the degree of hypervolemia is obviously marked. Venous congestion exists only below the level of the uterus.

A fetus is not essential for the development of hypervolemia. In some but not all cases of hydatidiform mole the blood volume has been found to be as much as 50 per cent greater than in the nonpregnant state.[18]

Blood Loss Associated with Delivery

The changes in maternal blood volume associated with parturition often are rather marked. Typically they consist of considerable

TABLE 2. Maternal Blood Loss Associated with Delivery

Method	RBC Loss	Hematocrit	Blood Loss
Vaginal delivery			
Single fetus (75)	190	37.5	505
Twins (20)	320	35.5	905
Repeat cesarean			
Section (40)	340	36.5	930
Repeat cesarean			
section hyst. (35)	425	36.5	1435

reduction in plasma volume accompanied by an appreciable but not as great reduction in red blood cell volume. The measurement of the difference between maternal red blood cell volumes before and after delivery has been utilized by us to estimate the red blood cell loss and in turn maternal blood loss associated with delivery (after it had been demonstrated that there was little difference between the volume of shed red blood cells that were recovered during and soon after delivery and the volume that disappeared from the circulation).[1] The mysterious disappearance or sequestration of rather large volumes of maternal red blood cells during labor and delivery previously described by others could not be demonstrated.

One hundred and fifty women who were without evidence of toxemia, infection, severe anemia, or abnormal bleeding prior to the onset of the third stage of labor were selected for study. Seventy-five underwent spontaneous labor followed by vaginal delivery.[19] Forty women who previously had been delivered by cesarean section were again delivered by cesarean section. Thirty-five other women were delivered by cesarean section followed by total hysterectomy done primarily for sterilization. The measured quantities of blood lost are shown in table 2.

In the 75 patients studied before vaginal delivery and again about 3 hours after delivery an average of 190 ml. of red blood cells was lost from the circulation. Since the average predelivery hematocrit was 37.5, this volume of red blood cells equaled 505 ml. of predelivery whole blood. Seven per cent of the women lost 1,000 ml. or more of blood. In 54 instances, from the first hour following delivery until 3 days later, the blood lost via the

TABLE 3. Average Blood Volume, Red Cell Volume, and Hematocrit Changes in Six Nonpregnant Women Who Underwent Vaginal Hysterectomy and Colporrhaphy

	Blood Volume	Change %	RBC Volume	Change %	Hematocrit	Change %
Preoperative	3325		1405		42.0	
Postoperative						
2–10 hours	2750	−17	1010	−28	36.5	−13
5–6 days	3155	−5	985	−30	31.0	−26

vagina was also quantitated by direct recovery of labeled red cells. The average blood loss was only 80 ml. and practically all of this occurred during the first 24 hours.

The average red blood cell loss during elective repeat cesarean section from the beginning of the operation until 3 hours (on the average) after delivery was 340 ml., equivalent to 930 ml. of predelivery whole blood. Twenty-three per cent of the patients lost between 1,000 ml. and 1,500 ml. of blood, and 8 per cent (3 out of 40) lost a greater amount. If total hysterectomy was also performed the mean blood loss increased to 1,435 ml.

Blood loss associated with the vaginal delivery of 20 cases of twins was similarly measured. Red blood cells equivalent to 905 ml. of predelivery maternal whole blood or nearly twice the amount associated with the delivery of a single fetus was lost during and very soon after delivery.

Newton and his associates measured the blood lost by 100 women during the period from delivery to one hour postpartum by collecting the shed hemoglobin.[20] The average blood loss noted by them also was about 500 ml. including the maternal blood contained in the placenta and corrected for an estimated fraction which was not recovered. Wilcox and his associates similarly measured blood loss during cesarean section by recovery of shed hemoglobin and noted an average loss equivalent to almost exactly 1,000 ml. of maternal whole blood.[21] All these results indicate that the usually quoted values for average blood loss associated with delivery are much too low. Furthermore visual estimates of blood loss not infrequently differ markedly from the actual blood loss: on the average they are only about one-half the amount actually shed.

Delivery and Blood Volume Changes

The response to blood loss at and very soon after delivery is quite different from what it is in nonpregnant women. If healthy nonpregnant women are subjected to a single rapid blood loss, the blood volume falls immediately but expands within 24 hours to approach the volume present before hemorrhage. The fall in hematocrit and hemoglobin levels soon reflect quite accurately the blood loss. This pattern of response is demonstrated in table 3. Premenopausal women in good general health underwent vaginal hysterectomy and colporrhaphy and as a result lost 30 per cent of their red blood cells from the circulation. Blood transfusions were withheld; instead Ringerslactate solution was infused liberally. The hematocrit decrease in a few days was almost identical to the decrease in circulating red blood cells. In other words isovolemia with anemia proportional to the amount of blood shed was the net effect of the hemorrhage.

The pattern of response differs grossly from

TABLE 4. Average Changes in Blood Volume, Red Cell Volume, and Hematocrit in Eight Women Who Underwent Cesarean Section or Cesarean Section Plus Hysterectomy

	Blood Volume	Change %	RBC Volume	Change %	Hematocrit	Change %
Predelivery	4985		1745		35.0	
Postpartum						
+2 to 10 hours	3530	−29	1255	−28	35.5	+1
+6 to 7 days	3525	−29	1180	−32	33.5	−4
Nonpregnant	3220	−35	1320		41.0	

TABLE 5. Serial Observations of Blood Volume Changes in a Case of Twins with Considerable Hypervolemia of Pregnancy (+59 Per Cent) and Very Little Blood Loss During and After Delivery

	Blood Volume	Change %	RBC Volume	Change %	Hematocrit	Change %
Predelivery	4960		1785		36.0	
Postpartum						
+2½ hours	4020	−19	1730	−3	43.0	+19
+1 day					39.0	
+3 days					41.0	
+6 days					44.0	
+7 days	3875	−22	1705	−4	44.0	+22
Nonpregnant	3115	−37	1275		41.0	

this in women with the normal hypervolemia of pregnancy who hemorrhage at the time of delivery. Serial studies of 8 cases of either cesarean section or cesarean section plus hysterectomy in which there was an average loss of red blood cells equal to 1,400 ml. of predelivery whole blood during and soon after delivery, are summarized in table 4. In spite of the loss of 30 per cent of the circulating red blood cells the hematocrit a few hours after delivery and again 6 to 7 days after delivery was the same as the predelivery value. In response to hemorrhage the blood volume dropped to approach the normal nonpregnant level while the hematocrit changed very little (table 4).

Occasionally a pregnant woman with rather marked hypervolemia but little blood loss at delivery will be encountered. Such a case is presented in table 5. The patient, normally pregnant with twins, at the onset of labor had a blood volume which was 1,845 ml. or 59 per cent larger than when nonpregnant. Blood loss by inspection as well as by measured difference in red blood cell volumes was negligible. The hematocrit two and one-half hours after delivery was 43.0 compared to 36.0 antepartum. It dropped to 39.0 the day after de-

livery and then rose to 44.0 by the sixth postpartum day. At the same time the red cell volume decreased but 80 ml. while the blood volume decreased 1,085 ml. accounting for the rise in hematocrit. In a few other similar instances studied to date the hematocrit 5 to 7 days after delivery was noted to increase from the high thirties to nearly 50.

Such sizeable increases in hematocrit postpartum are not the rule with vaginal delivery. The pattern of change for 8 vaginal deliveries with pregnancy-induced hypervolemia of 1,545 ml. and an average delivery blood loss of 450 ml. is demonstrated in table 6. A few hours after delivery two-thirds of the pregnancy hypervolemia remained. This reduction could be accounted for almost completely by blood loss at and soon after delivery. One week later the pregnancy-induced hypervolemia had been further reduced by another one-third. This resulted primarily from hemoconcentration. During the next several weeks the blood volume returned to the normal nonpregnant level with further hemoconcentration. The red blood cells added to the circulation during pregnancy but not lost as the result of delivery presumably disappeared through the process of normal red cell senescence. No evidence has been

TABLE 6. Changes in Blood Volume, Red Blood Cell Volume, and Hematocrit in Eight Normal Women Delivered Vaginally

	Blood Volume	Change %	RBC Volume	Change %	Hematocrit	Change %
Predelivery	5035		1905		38.0	
Postpartum						
+1 to 8 hours	4510	−10	1735	−9	39.0	+3
+6 to 7 days	4180	−17	1705	−10	41.0	+8
Nonpregnant	3505	−30	1470		42.0	

TABLE 7. Blood Volume, Red Blood Cell Volume, and Hematocrit Changes
in a Small Woman with Eclampsia

	Blood Volume	Change %	RBC Volume	Change %	Hematocrit	Change %
Predelivery	2190		825		37.0	
Postpartum						
+8 hours	—		—		28.5	
+3 days					23.0	
+8 days	2060	−6	565	−32	26.0	−30
Nonpregnant	2485	+13	1010		40.5	

found of increased red cell destruction during the puerperium. As the red cell volume fell back to the normal nonpregnant level the production of new erythrocytes by the bone marrow undoubtedly was reduced.

It is apparent from these studies that if the hematocrit or hemoglobin concentration 5 to 7 days after delivery is appreciably less than the predelivery value either the amount of blood lost was quite large or the pregnancy-induced hypervolemia was negligible, or both. During the first 3 or 4 days after delivery, however, the hematocrit and "plasma" volume may fluctuate considerably. A common pattern is a moderate decrease in hematocrit after the day of delivery until day 3 or 4 when it again rises.[20] Such a response is demonstrated in table 5. Undoubtedly a number of factors contribute to these early variations including the magnitude of the hypervolemia induced by pregnancy, the degree of hemoconcentration caused by labor, and the amount and rate of blood loss associated with parturition.

Women with normal pregnancy-induced hypervolemia can usually tolerate considerable blood loss at the time of delivery. They can effectively utilize much or all of that volume added during pregnancy as a buffer; consequently two liters or more of blood may be lost without causing death or even overt shock. Undoubtedly pregnancy-induced hypervolemia has played a major role in allowing the human race to survive, especially prior to the advent of blood banks.

Unfortunately not all women can tolerate blood loss of this magnitude during parturition. Women with a small body mass when not pregnant have small blood volumes and, in general, the actual volume of blood added to their circulation during pregnancy is less than that added by women with a larger body mass.

It should be obvious that they are much less capable of withstanding the same volume of blood loss as the larger women. This important point that smaller women have small blood volumes is sometimes forgotten by physicians caring for these women. Furthermore the protective hypervolemia of normal pregnancy is markedly diminished or absent in some abnormal pregnancies. Classic examples of this are found in our experience with eclampsia. A case of eclampsia in a small woman which demonstrates the absence of normal pregnancy hypervolemia as well as a small nonpregnant blood volume owing to her relatively small size is summarized in table 7. Her height was 60 inches and the nonpregnant weight 95 pounds. The hematocrit changes associated with delivery and the loss of 260 ml. of red blood cells equivalent to 700 ml. of predelivery whole blood are similar to those which would occur in a nonpregnant subject of similar size rather than those of a normally pregnant woman. Women with pregnancy-induced severe megaloblastic anemia also may have blood volumes no greater than or even less than when not pregnant. Obviously they would tolerate hemorrhage poorly.

The fact that most pregnant women can tolerate much more blood loss than nonpregnant women should not lessen the physician's concern for the parturient who is bleeding. While whole blood is being obtained, an intravenous infusion of Ringers-lactate solution or normal saline should be started using a large calibre needle well placed in a vein, and efforts directed toward establishing the cause of the bleeding and achieving hemostasis. Any evidence of distressing hypovolemia should be combatted promptly with whole blood transfusion.

Summary

The volume of circulating blood in normal pregnant women usually is considerably greater than when nonpregnant. There is a moderate increase in blood volume during the first trimester, a more marked rise during the second trimester, and a slight increase throughout the third trimester. No late decrease in blood volume during pregnancy has been demonstrated by us.

Blood loss associated with delivery is appreciable, averaging about 500 ml. with the vaginal delivery of a single fetus and nearly twice this amount with the vaginal delivery of twins, or during repeat cesarean section.

The pregnant woman tolerates hemorrhage at the time of delivery much better than she would a similar hemorrhage when not pregnant.

The normal pregnant woman can usually withstand hemorrhage equal to the volume of blood added to the circulation during pregnancy without gross physiologic embarrassment.

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