Assessment of Anemia in Newborn Infants

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The approach to the study of anemia that I shall discuss has developed over the past 20 years; during this period I have been directly involved in the study and management of newborn infants with anemia.

When I began, I found that there were remarkable features of the nature of anemia and its investigation that were unique to the newborn and particularly to the premature infant. I often found it very difficult to understand what was happening using the criteria I had applied previously to older children or adults.

For example, I could not understand why hemoglobin levels fluctuated so greatly from day to day. The explanation I was usually given was that of "a fluid shift." I also could not understand why so many transfusions were required in the newborn period without gross evidence of hemorrhage or severe hemolytic disease. And when I was faced with the problem of studying the anemia of a newborn infant, the usual criteria for the diagnosis of hemolysis (e.g., increased reticulocyte count, depressed haptoglobin levels, increased bilirubin levels, etc.) did not apply or were not readily interpretable.

We therefore began our studies which attempted to define these problems more clearly. This chapter describes the results of those studies (1).

THE DEFINITION OF NORMAL

This seemed to be a reasonable place to start. We therefore initiated a study of normal hemoglobin levels during the first 5 days of life in a population of normal newborn infants. This study was carried out by Dr. Ted Hui, a fellow who was working with me at that time. He examined 164 newborn infants, and the results were graphed as shown in Fig. 1. These charts, which included other hematologic data, are called by us, "hematology of the unborn and infant" (HUI) charts. The cord blood level is shown, as well as the values from day 1 demonstrating the characteristic rise that occurs during the first 24 hours of life due in part to the placental transfusion. We also did reticulocyte counts on these patients and they are shown in Fig. 1 as well. With these two techniques, it was remarkable how easy it was to
assess anemia. This is shown in Fig. 1, which demonstrates the changes in hemoglobin and reticulocyte counts which are seen as a result of fetal anemia due to transplacental hemorrhage (Fig. 1a), bleeding immediately prior to delivery (Fig. 1b), anemia due to blood loss after delivery (Fig. 1c), and finally fetal anemia due to failure of red cell production (Diamond–Blackfan anemia) (Fig. 1d). These simple techniques, when used in an organized way with an understanding of normal values, make the diagnosis and the understanding of anemia in newborn infants much easier.

We also determined the number of nucleated red blood cells found in the blood of normal infants and found a mean value of 850 mm$^3$ (SD = 850). An increase in normoblast numbers in newborn infants is seen in severe hemolysis or other conditions causing an increase in red cell production. This unfortunately is not a specific test because other conditions causing stress (e.g., acute fetal or neonatal hypoxia) will cause increased numbers of normoblasts to enter the blood acutely. An increase in the number of normoblasts is also not a sensitive test because mild increases in red cell production may not be accompanied by an increase in normoblast numbers.
Therefore "erythroblastosis" is neither a sensitive nor a specific test of increased red cell production in newborn infants.

**DAY-TO-DAY VARIATIONS IN HEMOGLOBIN LEVELS IN NEWBORN INFANTS**

It was generally believed that the variations in hemoglobin levels that are seen from time to time in individual newborn infants resulted from fluid shifts in the patients or perhaps from some other unknown cause. Clearly, the first thing we had to establish was the error of hemoglobin testing. We studied 25 infants to determine this. We found that the error of multiple testing of a single blood sample in an automatic counter was 0.2 g/dl. In our study, we also examined the error of capillary

![Graph showing simultaneous capillary and venous hematocrits](image)

**FIG. 2.** Simultaneous capillary and venous hematocrits in 45 premature infants (birth weight 1000–1500 g) taken during the first 6 weeks of life. The difference between the two horizontal lines represents the average differences of the two techniques (1).
sampling. For this we performed duplicate heel punctures—one from the left foot and one from the right foot—and compared the differences. The standard deviation of the error of this technique was 0.8 g/dl. Thus, for example, in a baby with a true hemoglobin of 11 g/dl, 95% of the samples would fall between 9.4 and 12.6 g/dl. This range is quite large and certainly explains some of the day-to-day variations that had puzzled us previously.

The well-known difference between venous and capillary hematocrit or hemoglobin values shown in Fig. 2 also explains some of the variations from day to day. The data in Fig. 2 include not only newborn infants, a previously reported observation, but also premature infants in whom the venous capillary differences persisted to 6 weeks of age.

IS THE BLOOD HEMOGLOBIN CONCENTRATION AN ACCURATE REFLECTION OF THE TOTAL BODY HEMOGLOBIN CONCENTRATION?

In assessing anemia, it is customary to believe that the hemoglobin concentration in a blood specimen is a good estimate of the total body hemoglobin content. That is the case in adults. We wondered whether the traditional capillary hemoglobin of the newborn bears a close relationship to the total red cell mass. Dr. Victor Blanchette, a colleague of mine, was working with me as a fellow and studied the red cell mass in a series of premature infants at birth and at 6 weeks of age. The results of those studies (1) are shown in Fig. 3 and indicate that the correlation is very poor; this must be borne in mind when anemia is considered in newborns.

![FIG. 3. Simultaneous capillary hematocrit and circulating red cell mass values in 135 premature infants (birth weight < 1500 g) studied during the first week of life (correlation coefficient r = 0.48) (1).](image-url)
Parenthetically, I should mention the importance of total body hemoglobin in the assessment of anemia and, in particular, anemia in premature infants. This is considered in Fig. 4 which is a diagrammatic representation of the anemia of prematurity (2). It shows that after birth there is a steady drop in hemoglobin concentration associated with a decline in erythropoiesis as evidenced by the falling reticulocyte count. At about 5–6 weeks of age erythropoiesis increases, however, despite the fact that the case in Fig. 4 shows no rise in hemoglobin concentration. Traditionally, evidence of increased red cell production (reticulocytosis) with a falling or even stable blood hemoglobin concentration means either hemolysis or hemorrhage. But in the premature infant it may mean something else, namely growth. This is reflected in the diagram (Fig. 4) by the rising total body hemoglobin concentration associated with an increase in body size. It must be stated therefore that anemia in premature infants cannot be assessed without considering the changes in body size and indirectly thereby the total body hemoglobin concentration.

WHY DO PREMATURE INFANTS REQUIRE BLOOD TRANSFUSIONS?

Dr. Victor Blanchette, Dr. Ed Bell, and I studied this question with reference to the amount of blood taken from these infants for studies.
FIG. 5. Cumulative blood losses through sampling in premature infants expressed as a percentage of their red cell mass at birth. Infants were studied during the first 6 weeks of life, and each vertical bar represents a single infant (1).

FIG. 6. Relationship between the cumulative volumes of blood sampled from and transfused into 57 premature infants (birth weight < 1500 g) during the first 6 weeks of life ($r = 0.82$) (1).
In Fig. 5, results of studies on 57 premature infants are shown. All blood taken from these infants during the first 6 weeks of life is documented in this figure and expressed as a percentage of the baby's total blood volume. I should add that most of this blood was taken during the first 2 weeks of life. Clearly, many infants had more than 100% of their total blood volume taken, and some reached as high as 300%! It is of interest that, when the amount of blood taken from these babies was compared to the amount transfused (Fig. 6), the relationship appeared to be a straight line one with an origin near zero, which means that if no blood had been taken, none need have been given. From this we can conclude that the major cause of anemia in premature infants is blood sampling and that anemia in newborn infants cannot be assessed without detailed information concerning the amounts of blood sampled and transfused.

One of my fellows, Dr. Ami Ballin, addressed himself to this problem several years ago. We reasoned that most, if not all, blood sampling was done in order to carry out tests which could and would be done on plasma. The red cells were usually discarded and therefore our "anemia of intensive care" might be better described as the "anemia of the laboratory sink." In a series of experiments on rabbits (2) he showed that most laboratory tests used in newborns could be done on plasma and
that those animals who received their red cells back did not develop anemia as rapidly as those who did not (Fig. 7). We can therefore prevent the anemia of intensive care in rabbits but have not yet done so in humans. When one considers the risks and costs of blood transfusions, such a step might represent a major contribution to neonatal care.

HEMOLYTIC DISEASE IN NEWBORN INFANTS

This is very difficult to study in newborns because the usual laboratory evidence of hemolysis that we employ in adults or older children does not apply to newborns. Consider that in adults hemolysis is indicated by (a) a stable or falling hemoglobin level associated with reticulocytosis, (b) low serum haptoglobin levels, and (c) raised serum bilirubin levels. We have already discussed the limitations of (a), which are further complicated by the wide range in reticulocyte counts found in the newborn (Fig. 1). Haptoglobin levels are of little value because low levels occur normally in newborns. Elevations of serum bilirubin, of course, are not specific evidence of hemolysis because there are many causes of hyperbilirubinemia other than excessive red cell destruction.

What then are we left with? We have generally regarded anemia with reticulocytosis in the absence of hemorrhage as being evidence of a hemolytic process. One traditional means of assessing this is an examination of the red blood cells themselves.

Several years ago we undertook a study of the effect of vitamin E on the anemia of prematurity and we planned to include an evaluation of red cell morphology because traditionally that is included in the hematologist’s assessment of anemia. I found that I could not quantitate erythrocyte morphology in that way and that variations from film to film and within the same film gave very discrepant results. My colleague, Betty Brown, and I therefore developed a new technique (3) which we believe provides a simple and accurate method of assessing erythrocyte morphology in newborn infants and, indeed, in any patient with anemia.

In Fig. 8, I show the actual shapes of fixed red blood cells using scanning electron microscopy. We adapted that technique to light microscopy, permitting us to view the entire three-dimensional shape of the red blood cell as shown in Fig. 8. Furthermore, we recognized the need to evaluate the types of erythrocyte shapes which occurred in newborn infants. We found that the erythrocytes of premature infants differed greatly from those of adults, and for that reason we established normal values for premature and full-term infants as well as adults (Table 1). We determined also that these shapes, with the exception of echinocytes, were characteristic of the erythrocytes themselves rather than secondary to changes in the plasma because in a series of 11 cases they disappeared after exchange transfusions and did not reappear for the next 7 days of study.

Accordingly, we believe that in the assessment of anemia in newborn infants a quantitative and accurate assessment of erythrocyte morphology is essential.
FIG. 8. Scanning electron microscopy (left) and light microscopy (right) of glutaraldehyde-fixed erythrocytes of a newborn infant. (a, f) discocytes; (b, g) bowls; (c, h) keratocytes; (d, i) schizocytes; (e, j) acanthocytes.
TABLE 1. Erythrocyte differential count in adults and newborn infants

<table>
<thead>
<tr>
<th></th>
<th>Adults</th>
<th>Full-term</th>
<th>Premature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number studied</td>
<td>53</td>
<td>31</td>
<td>52</td>
</tr>
<tr>
<td>Discs</td>
<td>78 (42-94)</td>
<td>43 (18-62)</td>
<td>39.5 (18-57)</td>
</tr>
<tr>
<td>Bowls</td>
<td>18 (4-50)</td>
<td>40 (18-58)</td>
<td>29 (13-53)</td>
</tr>
<tr>
<td>Discs/bowls</td>
<td>2 (0-4)</td>
<td>2 (0-5)</td>
<td>3 (0-10)</td>
</tr>
<tr>
<td>Spherocyte</td>
<td>0 (0-0)</td>
<td>0 (0-1)</td>
<td>0 (0-3)</td>
</tr>
<tr>
<td>Echinocyte</td>
<td>2 (0-3)</td>
<td>1 (0-4)</td>
<td>5.5 (1-23)</td>
</tr>
<tr>
<td>Acanthocyte</td>
<td>0 (0-1)</td>
<td>1 (0-2)</td>
<td>0 (0-2)</td>
</tr>
<tr>
<td>Dacrocyte</td>
<td>2 (0-1)</td>
<td>1 (0-3)</td>
<td>1 (0-5)</td>
</tr>
<tr>
<td>Keratocyte</td>
<td>0 (0-1)</td>
<td>2 (0-5)</td>
<td>3 (0-7)</td>
</tr>
<tr>
<td>Schizocyte</td>
<td>0 (0-1)</td>
<td>0 (0-2)</td>
<td>2 (0-5)</td>
</tr>
<tr>
<td>Knizocyte</td>
<td>1 (0-4)</td>
<td>3 (0-8)</td>
<td>1 (0-6)</td>
</tr>
<tr>
<td>Others</td>
<td>1 (0-4)</td>
<td>3 (0-7)</td>
<td>4 (1-11)</td>
</tr>
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*a All values are expressed as a median plus the 5–95% range because the distribution of most values was non-Gaussian.

*b 29 ABO compatible; 1 AB (mother A); 1 AB (mother B).

*c Includes both ABO-compatible and -incompatible infants.

FIG. 9. Hemoglobin concentration and percent of erythrocytes containing Heinz bodies in a premature infant during the first 9 weeks of life. Multivitamin administration is indicated by the horizontal bars (4).
I shall now describe one case (4) whose study exemplifies our approach to the assessment of anemia in premature infants (Fig. 9). This was a baby of 27 weeks' gestation and birth weight 1190 g. She was doing quite well in the premature unit until 3 weeks of age when, for no apparent reason, jaundice developed. Erythrocyte morphology was abnormal and Heinz bodies were present on special staining. I should add that Heinz bodies are denatured hemoglobin, the result of excessive oxidation, and it is known that erythrocytes of newborn infants are susceptible to such oxidative damage. Nothing unusual had been done to that baby and there was no other evidence of disease. What was noted, however, was that the jaundice and falling hemoglobin had occurred shortly after institution of multivitamin therapy (Fig. 9). Accordingly, we discontinued vitamins following which Heinz body numbers fell, the hemoglobin concentration rose, and jaundice disappeared. The reinstitution of vitamin therapy was associated with a recurrence of the Heinz body hemolytic anemia. Subsequent laboratory and animal studies confirmed that vitamin C can produce oxidative damage of the erythrocytes of the newborn and, in particular, premature infants and that it may represent a significant cause of anemia and hyperbilirubinemia in newborns (4). My colleague, Dr. John Doyle, has developed and is at present conducting a randomized blinded trial of vitamin C therapy and anemia in premature infants.

ANEMIA IN OLDER INFANTS AND CHILDREN

The assessment of anemia in older infants and children requires attention to the same principles which are applied to the newborn, namely knowledge of normal values, the limitations of technology, and specific diseases that are age-related.

Concerning normal values, it is clear that normal hemoglobin levels change with age; this is shown in Fig. 10.

The fall in hemoglobin levels which occurs during the first 6 weeks of life is, like the anemia of prematurity, due both to a decrease in red cell production and to a rapid rate of growth and therefore blood volume expansion. The decrease in red cell formation appears to be secondary to reduced erythropoietin production. This is most evident in those children in whom hemoglobin levels are low at birth (e.g., following a transplacental hemorrhage) or in whom a hemolytic process continues after birth (e.g., anti-D isoimmune disease). Under those conditions the hemoglobin level may fall to 5 or 6 g/dl during the first 6 weeks of life because of failure to mount an adequate erythropoietic response.

Although serum folic acid levels fall during the first 6 weeks of life, there is no evidence that folic acid deficiency plays a role in this "physiologic anemia of infancy." Similarly, this anemia is not a manifestation of iron deficiency.

Hemoglobin levels during the remainder of the first year of life tend to rise slowly, although that rise may be limited by the development of iron deficiency. Through
the remainder of childhood, hemoglobin levels gradually rise but do not achieve adult levels until puberty is completed.

REFERENCES


DISCUSSION

Dr. Dallman: Your curves for hemoglobin values in premature infants were presumably based on infants who were relatively healthy. How different are the values in infants who have had multiple transfusions, where HbF has been replaced by HbA? The studies of Stockman and coworkers suggest that hemoglobin values in such infants should equilibrate at a lower level since HbA is more efficient at unloading oxygen to the tissues.

Dr. Zipursky: I believe that the stimulus to red cell production in the newborn is the hemoglobin level; however, the "thermostat" is set at a different value from that in adults, in whom red cell production increases if the Hb level falls below 13 or 14 g/dl. In full-term infants the set-point level may be 8 g/dl and perhaps lower in the preterm infant. It is true,
however, that the erythropoietin response may vary depending on the type of hemoglobin in the red blood cells. Oski pointed out that during the neonatal period, infants whose erythrocytes contain a relatively high proportion of HbA (mostly as a result of exchange transfusion) have lower erythropoietin levels than do infants whose erythrocytes contain predominantly HbF. They suggested that this was due to better tissue oxygen delivery by HbA-containing red cells, thus reducing the need for additional erythropoiesis. While this may be true, it could also be that infants who have received exchange transfusions were sicker in the neonatal period and this caused suppression of erythropoiesis.

Dr. Bell: I was one of the collaborating neonatologists in Dr. Zipursky’s studies, so I can give Dr. Dallman some of the information he requests. The data on total blood volume were all obtained from babies under 1500 g, most of whom were on ventilators. The ones that had the largest volumes removed all received assisted ventilation over a long period and had blood gases measured every 4–6 hours. Their hemoglobin concentration declined after birth and then plateaued at around 10 g/dl, being kept at that level by transfusion. Hemoglobin concentration was one of the criteria used to assess the need for transfusion.

Dr. Dallman: In theory I agree that it would be desirable to demonstrate abnormalities attributable to impaired oxygen delivery before deciding to transfuse an infant with a low hemoglobin concentration. In practice, this may not be reasonable, bearing in mind that tissue hypoxia may have long-term consequences. Transfusions are typically given when there is suboptimal growth, bradycardia, or apneic spells, or if there is concern that the Hb value is abnormally low. It seems hard to draw firm rules about transfusions in this age group.

Dr. Zipursky: I should like to see a controlled trial to determine the indications for transfusion. There have been a few attempts, but the results have not been clear. There are risks to transfusion, and we should know whether the benefits of transfusions outweigh the problems they might impose in such infants.

Dr. Bell: Two small clinical trials on the criteria for transfusing preterm infants have provided incomplete information. One of them suggests that you can decrease the severity of idiopathic apnea of prematurity if you keep the hematocrit above a certain level. The real issue of course is the adequacy of oxygen delivery to the tissues; knowing the Hb or even the red cell mass is only part of the answer. We also need to know the cardiac output and the oxygenation status. We should like to be able to transfuse these babies before their physiologic mechanisms for compensating for anemia are overcome. Blood lactate levels have been suggested as a measure of tissue hypoxia, but in the face of lung disease there are confounding factors that make lactate levels hard to use. We have attempted to launch a clinical trial to investigate these issues, but we have been unsuccessful in getting funding. Thousands of blood transfusions are given to premature babies in North America and presumably elsewhere, but there is very little scientific basis for the decisions about how or when to give them.

Dr. Shaw: Dr. Zipursky has implied, as have others, that the “early anemia of prematurity” associated with Hb levels of 8–9 g/dl is not really an anemia, perhaps because the Hb level is regulated to this value and there is no shortage of substrates necessary for hemoglobin synthesis. Have you any data on whether transfusion benefits infants with hemoglobin values in this range, or are our clinical impressions of benefit based on anecdote?

Dr. Zipursky: Published studies on this are equivocal. I do not think there is evidence clearly establishing either a hemoglobin level or clinical criteria at which a transfusion should or should not be given.

Dr. Shaw: I agree with that. There is, however, one circumstance when it is mandatory to transfuse preterm infants. This is in those babies under 1000 g who require frequent blood
sampling during the first days of life to monitor their management. We record every milliliter of blood taken and replace it when the total (often only 5-7 ml) approaches 10% of the blood volume. The effect of transfusing adult hemoglobin may not be very great. Peter Wimberly (1), working in our department, showed some years ago that the rise in red cell 2,3-DPG following birth was higher in preterm infants than in full-term infants. This shifts the oxygen dissociation curve to the right, tending to reduce the difference between adult and fetal hemoglobin.

**Dr. Doyle:** There is a major problem in defining anemia in these infants which I don’t think has been solved. Perhaps Dr. Zipursky could comment on the question of the “gold standard” for neonatal hemoglobin values.

**Dr. Zipursky:** I believe that the most important gold standard for the need for transfusion is the clinical opinion of a skilled neonatologist. Usually that opinion is supplemented by information on blood hemoglobin. I would emphasize that there is a poor correlation between the hemoglobin level and total red cell mass in babies. Sick babies may have a tiny red cell mass. Techniques for its assessment need to be developed for clinical use in these babies.

**Dr. Cooper:** The body responds to anemia by increased cardiac output, erythropoietin production, hyperventilation, and other reactions. Could one not define whether the level of hemoglobin in a newborn infant is physiological or not by evaluating whether these corrective mechanisms have been activated?

**Dr. Zipursky:** There are some data to support your thesis. For example, premature infants with anemia have a rapid heart rate. When you transfuse them the heart rate comes down. There are also studies showing that lactate levels are raised in children with low Hb levels, suggesting the presence of tissue hypoxia. Lactate levels have been reported to decrease after transfusion.

**Dr. Cooper:** It still seems fair to me to call it “anemia” if the body responds to it. The situation may be unusual in the premature infant since until recently most did not survive. The technology which has enabled many to survive has generated a series of empirical procedures and thresholds for intervention. The point at which a preterm infant receives a transfusion will often be based on these and not on whether the infant requires the additional hemoglobin.

**Dr. Zipursky:** There is a need to establish the hemoglobin range for babies under a variety of conditions; and when the value falls below that established range, then perhaps the level would be considered abnormal. The point I am trying to make, however, is that in the anemia of prematurity or of adolescence, the problem is not the actual hemoglobin level. It is whether or not there are immediate and long-term serious effects of the low hemoglobin level.

**Dr. Shaw:** What matters is oxygen consumption. If oxygen consumption and work done increase because of the anemia, it should perhaps be treated. However, a tachycardia and increased cardiac output do not necessarily mean increased work because in anemia the blood viscosity is reduced.

**Dr. Bell:** I think the situation is even more complex than that. It depends on the balance between oxygen supply and consumption. Now that there are noninvasive methods for measuring cardiac output and oxygen consumption in infants, this area has become subject to investigation in a way that was not possible before.

**Dr. Doyle:** This is all very confusing. Most of the signs and symptoms mentioned are indicators of metabolic rate rather than anemia. I don’t believe you can determine whether one newborn is “anemic” and another not on the basis of hemoglobin concentration. Two infants can both have hemoglobin values of 7 g/dl, and one may be very sick while the other is perfectly well. The whole area is still full of uncertainty.
ASSESSMENT OF ANEMIA IN NEWBORN INFANTS

Dr. Doyle: With regard to vitamin C, it is clear that there is potential here for another disaster of the type we have already seen with other supplements given to preterm infants. Very large amounts of vitamin C are given to these babies, partly because manufacturers make use of the property of vitamin C to stabilize other ingredients in the preparations, and also because, since the vitamin is known to be unstable and subject to degradation, an excess is provided deliberately. Some babies may get in excess of 60–70 mg/kg body weight, in a setting in which little is known of the real daily requirement. Our studies with Dr. Zipursky have shown that plasma vitamin C can reach values in these infants that are quite capable of causing denaturation of hemoglobin in neonatal erythrocytes.

Dr. Koletzko: The example given by Dr. Zipursky was a graphic one. It emphasizes again the question raised with respect to malnourished children about the possible harmful effects of a combination of iron and ascorbic acid. In this patient you said you made a systematic search for oxidants and identified vitamin C as a possible cause. Did you also look at antioxidant status? I would suspect that the major problem in this baby was tocopherol deficiency.

Dr. Zipursky: I do not agree with this, and I do not believe that vitamin E deficiency is responsible for the development of anemia in newborn infants.

Dr. Viteri: Are there methods for measuring red cell mass that are less invasive than chromium-51 labeling?

Dr. Bell: There are several methods of assessing circulating red cell mass or volume. The biotin method has been used successfully by Cavill and coworkers in the United Kingdom. This method is not easy to use, but it has promise. Another method published by Wimberly some years ago (1) makes use of the decline in fetal hemoglobin after transfusion of adult blood to estimate red cell mass.

Dr. Dallman: Can you envisage a practical way of returning red cells left from blood that has been used for laboratory studies? Bacterial contamination must be a major problem.

Dr. Zipursky: It would mean devising a closed system, which would require a lot of planning. However, I believe that if such a system were to be established it would remove the need for most blood transfusions in neonates.

Dr. Brabin: I want to focus on the rise in hemoglobin in the first 24 hours rather than on the fall we see subsequently. You said this is due to the transfusion of blood at the time of placenta separation. I don’t understand this explanation. The transfusion of blood from the placenta should increase the intravascular volume, but I do not see why it should increase the hemoglobin. It is important, however, because it is relevant to the time of cord clamping and it is clearly possible that late clamping would be beneficial.

Dr. Zipursky: There have been several studies on hemoglobin levels following early versus late clamping. It is clear that early clamping will result in substantially lower Hb levels in the early days of life. It has been estimated that one-quarter to one-third of a neonate’s blood volume may be received as a placental transfusion after delivery.

Dr. Bell: Twenty-five years ago it was recommended that cord clamping be delayed to provide the extra transfusion. It was then recognized that hyperviscosity could occur, so most of the time now the aim is to neither increase nor limit the transfusion; hence the cord is clamped fairly soon after delivery.

Dr. Zlotkin: Do you think the time of cord clamping has any effect on the ferritin level at 6 months?

Dr. Doyle: I don’t believe this has been looked at. Another aspect of cord clamping is in relation to hypovolemia. Usher’s group showed that if you clamp the cord immediately, especially in the preterm infant, you have increased mortality and morbidity (2). These investigators were able to show by measurement of red cell volume that infants with the smallest
red cell volumes were most at risk. It seems desirable to aim for an intermediate time for clamping the cord.

REFERENCES