Interpreting Umbilical Cord Blood Gases: Section 7: Fetal Circulatory Failure

Jeffrey Pomerance, MD, MPH

"The most common mechanisms responsible for fetal asphyxia at delivery are umbilical cord occlusion and uteroplacental insufficiency. Rarely, however, some other problem in the fetus, such as severe anemia or hypovolemia, becomes the operative mechanism."

The most common mechanisms responsible for fetal asphyxia at delivery are umbilical cord occlusion and uteroplacental insufficiency. Rarely, however, some other problem in the fetus, such as severe anemia or hypovolemia, becomes the operative mechanism. The following case is such an example.

Case 19: Chronic Fetal-Maternal Transfusion

The mother was a 32-year-old, blood type A positive, gravida 1, para 0, aborta 0, with an intrauterine pregnancy at 36 weeks gestation. Several weeks earlier, an ultrasound to rule out fetal growth restriction was reported as normal. The mother now complained of absent fetal movement from the previous evening. She was not in labor. At the hospital, the FHR tracing demonstrated a rate of 130 bpm but with absent variability. Maternal supplemental oxygen was administered. After 10 minutes, there began a slow decline in FHR to 65 bpm. The infant was delivered approximately 10 minutes later by "crash" cesarean section and was observed to be very pale. Amniotic fluid was clear. Apgar scores were 0, 0, 0, and 0 at one, five, 10, and 13 minutes, respectively.

Cord blood gas results were as follows:

	Umbilical Vein	Umbilical Artery
pH	7.24	6.85
Pco_2 (mmHg) ***(kPa)***	48 *6.40*	97 *12.93*
Po_2 (mmHg) ***(kPa)***	43 *5.73*	10 *1.33*
BD_{ecf} (mmol/L)	7	17

Resuscitation included intubation, ventilation with 100% oxygen, chest compressions, and ETT epinephrine. Chest movement was good. The ETT was suctioned and was clear. Resuscitation efforts were discontinued at 13 minutes of life when there was no response. The infant's birth weight was appropriate for gestational age at 3125 g. No edema was detected. An autopsy was not performed, although placental pathology was said to be normal except for numerous nucleated fetal RBCs and a very pale maternal side of the placenta (representing fetal blood). (1)

A hematocrit obtained from the umbilical cord at the same time as cord gases was 6% (hemoglobin 2.0 g/dL). A maternal Kleihauer-Betke test was positive for 3.4% fetal RBCs. There was no history of maternal trauma.

Although it was not mentioned, an enlarged liver was almost certainly present.

"Slowed circulation allows a normal placenta to have prolonged transit time and subsequently increased oxygen diffusion across the intervillous space. (3) The application of maternal supplemental oxygen would enhance this effect. (4,5) The umbilical arterial blood gas is extremely acidotic with combined severe respiratory acidosis and very severe metabolic acidosis."

Interpretation

The umbilical venous blood gas is normal, except for a minimally decreased pH, a slightly elevated Po_2, and a slightly elevated base deficit in a fetus who had not been exposed to labor. Minor increases in fetal base deficit normally occur during the second stage of labor. (2) The mildly elevated Po_2 can be explained based on slowed fetal circulation typically seen during heart failure. Slowed circulation allows a normal placenta to have prolonged transit time and subsequently increased oxygen diffusion across the intervillous space. (3)The application of maternal supplemental oxygen would enhance this effect. (4,5) The umbilical arterial blood gas is extremely acidotic with combined severe respiratory acidosis and very severe metabolic acidosis. The umbilical venoarterial pH, Pco_2, and base deficit differences are all much widened.

It is important to realize that a default value of 15.0 g/dL (or 14.3 g/dL) is assumed unless an alternate hemoglobin value is entered into the blood gas analyzer. A corrected hemoglobin value may be entered into the analyzer after a blood gas is analyzed, but it must be before any subsequent blood gas has been run. As an extra-cellular base deficit has no entry for hemoglobin, a blood base deficit will be reported.The corrected cord blood gas base deficits are as follows:

	Umbilical Vein	Umbilical Artery
pH	7.24	6.85
Pco_2 (mmHg) ***(kPa)***	48 *6.40*	97 *12.93*
Po_2 (mmHg) ***(kPa)***	43 *5.73*	10 *1.33*
BD_b (mmol/L)	6	13

The newly estimated (corrected) base deficit values demonstrate an insignificant change in calculated metabolic acidosis in the umbilical venous sample but a much larger change in the arterial sample. Hemoglobin, oxyhemoglobin, and erythrocyte bicarbonate contained in RBCs are themselves buffers. Indeed, about 53% of the total buffering capacity in whole blood comes from the contents of RBCs (hemoglobin and oxyhemoglobin, 35%; erythrocyte bicarbonate, 18%). (6) As the number of red blood cells and hemoglobin decreases, there is a decreased amount of bicarbonate present. In other words, had the amount of hemoglobin been normal, the pH would have been better.

Why then was this newborn dead with a base deficit of "only" 13? There are at least two likely answers to this question. First, normal placental exchange functions to help maintain normal blood gas values in the fetus until the circulation fails. While carbon dioxide (the respiratory component) equilibrates rapidly across an intact placenta, lactic acid and electrically charged bicarbonate or buffer base can cross the intervillous space relatively slowly. (7)To the extent that these components cross the placenta at all, a fetal umbilical venous blood sample would underestimate the degree of metabolic acidosis present at the fetal tissue level. However, as fetal circulation fails and placental function deteriorates because of inadequate fetal circulation, oxygen debt increases, and metabolic acidosis develops. The fetal kidneys appear to play no role in regulating acid-base balance. (7) Second, as fetal circulation fails, fetal blood pressure falls, eventually approaching zero, and blood ceases flowing in the umbilical arteries. Therefore, an umbilical arterial blood gas only reflects the situation prior to the cessation of arterial blood flow.

"Second, as fetal circulation fails, fetal blood pressure falls, eventually approaching zero, and blood ceases flowing in the umbilical arteries. Therefore, an umbilical arterial blood gas only reflects the situation prior to the cessation of arterial blood flow."

As the fetus is dying, rapidly increasing respiratory and metabolic acidoses occur at the fetal tissue level. Following the complete fetal circulatory failure, tissue status becomes progressively less well represented by the umbilical artery blood gas sample. It is important to appreciate that compensated heart failure is not associated with metabolic acidosis, and it is as compensation fails only, and death is approaching that metabolic acidosis appears. It then will progress rapidly.

In the patient presented above, the umbilical venoarterial blood gas differences are extremely wide. The pH difference is 0.39 (7.24 minus 6.85). Anything wider than 0.10 is abnormal (8, 9) and suggests the umbilical cord blood samples either came from an infant with cord occlusion with terminal fetal bradycardia (common) or, as in this case, chronic fetal heart failure. The perinatologist who delivered this infant found no evidence of umbilical cord occlusion. There was no knot in the cord, nor was the cord around the fetal neck or any other body part. Furthermore, the mother was not in labor. Therefore, the descent of the fetus could not entrap an occult cord or put a stretch on a short cord. Additionally, we have a ready explanation for the infant's demise, namely the extraordinarily severe anemia leading to fetal heart failure. We do not need a cord problem in addition to explain the outcome. The principle of abiding by the simplest solution (Occam's razor) should apply. Widened pH differences have been reported in an *in utero* study of severe fetal anemia secondary to isoimmunization (10) and in a twin with congestive heart failure, possibly secondary to viral myocarditis leading to fibroelastosis. (11)

In severe chronic fetal anemia, initially, the fetus can compensate for the anemia by increasing cardiac output. However, as the anemia worsens, the heart fails, and there is a period of low cardiac output before fetal demise. The dying process is likely more prolonged in a fetus than in a child or adult because the placenta will clear lactic acid (although more slowly than oxygen or carbon dioxide) being produced at the tissue level secondary to hypoxia. (7, 12) In severe fetal anemia, fetal hemoglobin carries the usual amount of oxygen per gram of hemoglobin; however, the hemoglobin level is so critically low that the amount of oxygen delivered to the tissues becomes inadequate to support normal metabolism. When death occurs, it may be quite sudden.

When heart failure occurs in the child or adult, there is also a widening of the pH and Pco_2 differences between arterial and venous blood. However, the differences are in the opposite direction compared with umbilical venous and arterial blood. (13) As heart failure progresses, cardiac output decreases, blood flow slows further, and tissues extract an increasing percentage of oxygen from the blood. Therefore, blood leaving the tissues carries a decreased amount of oxygen and increased carbon dioxide per mL of blood. In other words, the venoarterial difference widens. This phenomenon is explained by the Fick (14) principle, which states, "The amount of a substance taken up or released by an organ is the product of its blood flow rate (referred to as blood flow) and the difference in the concentration of the substance between the organ's arterial and venous blood." (15)

$$\text{Cardiac output (liter/min)} = \frac{O_2 \text{ consumption (mL/min)}}{\text{A-V } O_2 \text{ difference (vol \%)} \times 10}$$

From this equation we can see that if cardiac output decreases and tissue oxygen consumption remains constant, then the venoarterial oxygen difference must increase. Likewise, using the same equation for carbon dioxide production, if cardiac output decreases and carbon dioxide production remains constant, then the venoarterial carbon dioxide difference must also widen. In the absence of a change in the metabolic component of the blood gas, if carbon dioxide increases, pH will fall. Vascular accumulation of lactic acid occurs only in the terminal stage of heart failure, after all other compensation methods have been utilized. What makes this clear is the finding of an absence of metabolic acidosis in the umbilical vein. However, once the tipping point of lactic acid accumulation occurs, death is near. As blood flow from the umbilical arteries through the placenta to the umbilical vein remains intact, one would not expect a widened base deficit between the umbilical vein and the umbilical arteries.

Finding a widened base deficit difference between the umbilical vein and arteries is explained by the following. In the fetus, the pulmonary bed receives less than 10 percent of cardiac output. (16, 17) Therefore, when fetal cardiac failure occurs, essentially, it is right heart failure. Fetal right heart failure leads to increased central venous pressure which, in turn, causes decreased umbilical venous blood flow and, terminally, to complete cessation of blood flow. (18)

This complete cessation of umbilical venous blood flow must occur prior to complete cessation of umbilical arterial flow in order for a substantial base deficit difference to exist, just as typically occurs in cord occlusion with terminal bradycardia. This is precisely why umbilical cord blood gases of newborns with umbilical cord occlusion and terminal bradycardia look so similar to cord blood gases of newborns with chronic fetal heart failure and terminal

bradycardia (see Table 1 below).

Chronic Fetal Heart Failure with Terminal Fetal Bradycardia: Pathophysiology, Duration and Effect on Cord Gases			
Condition	**Changes in Cord Blood Flow**	**Duration**	**Effect on Cord Gases**
Chronic Fetal Heart Failure (compensated)	UV: Slowed UAs: Slowed (↑ time for down/uploading O_2/CO_2 across placenta and at tissue level)	Days to Weeks	UV: ↑ Po_2, ↓ Pco_2, normal BD UA: ↓ Po_2, ↑ Pco_2, normal BD
Chronic Fetal Heart Failure (uncompensated)	UV: Stops (2° ↑ing CVP) UAs: Slows further → Stops	Minutes	UV: No further change UA: ↑ing respiratory and metabolic acidoses

Table 1: Chronic fetal heart failure with terminal fetal bradycardia: Pathophysiology, duration, and effect on umbilical cord blood gases

UV, umbilical vein; UA, umbilical artery; ↑, increased; ↓, decreased; 2°, secondary to

A fetus with cord occlusion and terminal fetal bradycardia has a mechanical obstruction of the umbilical cord followed by a period in which the fetal arterial blood pressure briefly overcomes the obstruction. In contrast, umbilical venous blood flow remains occluded. On the other hand, a fetus with heart failure and terminal bradycardia has right heart failure and elevation of umbilical venous pressure that results in cessation of umbilical venous blood flow while umbilical arterial blood flow continues briefly. Both have a common pathophysiology: a period of cessation of umbilical venous blood flow, but temporarily continuing umbilical arterial blood flow. At birth, how can one distinguish between a newborn with cord occlusion and terminal bradycardia and one with chronic fetal heart failure and terminal fetal bradycardia (see Table 2, this section)?

"A fetus with cord occlusion and terminal fetal bradycardia has a mechanical obstruction of the umbilical cord followed by a period in which the fetal arterial blood pressure briefly overcomes the obstruction. In contrast, umbilical venous blood flow remains occluded."

Why did this infant *not* have any discernable edema? Certainly, with a hematocrit of 6%, hydrops fetalis would be anticipated. Nicolaides et al. (19) studied seven hydropic and ten nonhydropic fetuses at 18 to 25 weeks gestation. All fetuses with sonographic evidence of hydrops had hemoglobin values of 3.8 g/dL (hematocrit approximately 11.4%) or less. All but one nonhydropic fetus had a hemoglobin value greater than 4.0 g/dL (hematocrit approximately 12.0%). Hypoalbuminemia was found in six of the seven hydropic fetuses and in two of the nonhydropic fetuses.

These data suggest that the infant described above had both a chronic and an acute phase of fetal-maternal transfusion. If there had been only an acute phase of blood loss from the fetus to the mother, the infant would have died quite before a hematocrit of 6% was reached. If there had only been a chronic phase of blood loss from the fetus to the mother, hydrops would have been expected. Perhaps the chronic phase brought the fetal hematocrit down to the 12-15% range, a range in which fetal hydrops may not be present, and a superimposed acute phase completed the decrease to six percent. Kohlenberg and Ellwood (20) have reported intermittent fetal-maternal hemorrhage. Asphyxia is not associated with chronic fetal blood loss without superimposed labor until the fetus' hemoglobin falls to less than 4.0 g/dL. (21) During labor, the fetus may deteriorate quickly. When the fetus' hemoglobin is even lower, as in this case, labor does not need to occur for the fetus to be asphyxiated or die.

How can one estimate the extent of fetal blood loss? Conventional methods for calculating fetal blood loss provide only approximations and tend to underestimate. In addition, these methods are more appropriate for calculating acute rather than chronic blood loss.

A look at the issue from the maternal side estimates how much fetal blood is in the maternal circulation. This approach does not consider the fact that fetal RBCs are destroyed gradually (or sometimes not so gradually if the mother is type O and the fetus type A, for example) in the mother's circulation. Therefore, the Kleihauer-Betke test itself also underestimates the amount of fetal-maternal transfer. In the premature between 24 and 28 weeks, fetal hemoglobin (HbF) accounts for more than 90% of fetal blood, while at term, only approximately 75% of hemoglobin is HbF. (22) Fetal RBCs that contain adult hemoglobin rather than HbF are omitted from the estimate.

Assuming a maternal total blood volume of five liters and a maternal hematocrit of 36%, 3.4% fetal RBCs represent approximately 61 mL of packed fetal RBCs in the maternal circulation (5000 x 0.36 x 0.034 = 61). At term, the fetal-placental unit contains approximately 125 mL of blood per kg of infant weight. (23,24) Assuming an initially normal fetal hematocrit of 50% in a 3125 g infant, the total fetal-placental blood volume is 391 mL (125 x 3.125 = 391) with a packed cell volume of 196 mL (391 x 0.50 = 196). Thus, over time, the fetal-placental unit is calculated to have lost approximately 31% (61/196 = 0.31) of the normal, calculated fetal-placental blood volume at term. This assumes that there was no ABO incompatibility between the mother and the fetus, as this would result in a more rapid loss of fetal RBCs from the maternal circulation. (25) In this case, the infant's blood type is unknown, although the mother's A+ blood type makes ABO incompatibility unlikely.

A second approach to estimating the volume of fetal blood loss looks at the issue from the fetal side. This approach does not consider the fact that the fetus continues to produce RBCs, sometimes at a prodigious rate. The placenta demonstrated fetal response (NRBCs) to chronic blood loss. Again, assuming an initial fetal-placental hematocrit of 50%, a hematocrit of 6% at the time of birth suggests a loss of 88% of the fetal-placental blood volume over time (initial Hct minus final Hct, divided by initial hematocrit

((50-6)/50 = 0.88).

These two approaches to estimating fetal-placental blood loss into the mother provide very different estimates. This suggests ABO incompatibility, resulting in more rapid destruction of fetal RBCs in the maternal circulation, although the mother's blood type (A+) argues against this.

These methods of calculating fetal blood loss should be taken with a grain of salt, as results exceeding 100% of fetal blood volume occur fairly often. This points out the problem of differentiating termal fetal bradycardia secondary to cord compression from chronic fetal heart failure secondary to severe fetal anemia.

Differentiating Terminal Fetal Bradycardia Secondary to Cord Compression from Chronic Fetal Heart Failure Secondary to Severe Fetal Anemia

Findings	Cord Compression	Fetal Heart Failure
Abnormal FHR tracing from the time of maternal admission	No	Yes
Preceding late FHR decels	Unlikely	Likely
Cord blood gases with widened pH, Pco_2, and possibly base deficits	Yes	Yes
Maternal placental surface very pale	No	Yes (severe anemia – most common cause of chronic fetal heart failure)
Slow neonatal recovery from metabolic acidosis	Atypical	Common

Table 2 *Differentiating cord compression from chronic fetal heart failure using methods designed for calculating acute blood loss to calculate chronic blood loss.*

It is also of note that this infant had a recorded FHR of approximately 65 bpm 10 minutes prior to delivery. Why was it then that there was no discernable heart rate at the time of birth? Please see discussion of this issue under fetal heart rate present, neonatal heart rate absent, in a prior section.

Key Points

- Cord occlusion and uteroplacental insufficiency account for the great majority of abnormal FHR tracings and abnormal umbilical cord blood gas results.
- Although widened differences between umbilical veno-arterial pH and Pco_2 suggest cord occlusion, they also are typical of a much rarer event, fetal heart failure.
- Cord blood gases of newborns with umbilical cord occlusion and terminal bradycardia look very similar to cord blood gases of newborns with chronic fetal heart failure and terminal bradycardia because they have a common pathophysiology — a period of cessation of umbilical venous blood flow, but with temporarily continuing umbilical arterial blood flow.
- A mildly elevated umbilical venous Po_2 suggests slowed circulation and therefore increased time for oxygen to cross the placenta from the mother to the fetus, prior to the terminal event.
- Widened arterial-venous pH and Pco_2 differences are associated with heart failure in both children and adults, as well as heart failure in the fetus.
- Typically, chronic fetal heart failure is not associated with ongoing metabolic acidosis. What makes this clear is the finding of an absence of metabolic acidosis in the umbilical vein. Therefore, umbilical venous cord gases tend to be normal or near-normal.
- As fetal heart failure becomes terminal, elevated right heart pressures are transmitted to the umbilical vein, resulting in interruption of umbilical venous blood flow prior to cessation of umbilical arterial blood flow and, hence, widened base deficits.
- Once fetal blood pressure falls to a critical level, blood will no longer perfuse the umbilical arteries. After this time, umbilical artery blood no longer reflects continuing change at the fetal tissue level.

References:

1. *Benirschke K, Kaufmann P. Patholgy of the human placenta, 2nd edition, New York, Springer-Verlag; 1990, p361.*
2. *Weiner, CP. The relationship between the umbilical artery systolic/diastolic ratio and umbilical blood gas measurements in specimens obtained by cordocentesis. Am J Obstet Gynecol 1990;162:1198-1202.*
3. *Johnson JWC, Richards DS. The etiology of fetal acidosis as determined by umbilical cord acid-base studies. Am J Obstet Gynecol 1997;177:274-81.*
4. *Edelstone DI, Peticca BB, Goldblum LJ. Effects of maternal oxygen administration on fetal oxygenation during reductions in umbilical blood flow in fetal lambs. Am J Obstet Gynecol 1985;152:351-8.*
5. *Haruta M, Funato T, Sumida T, Shinkai T. The influence of oxygen inhalation for 30 to 60 minutes on fetal oxygenation. Nippon Sanka Fujinka Gakkai Zasshi 1984;36:1921-9*
6. *Winters RW, Dell RB. Regulation of acid-base equilibrium. In: Yamamoto WS, Brobeck JR (eds): Physiological controls and regulations. Philadelphia, WB Saunders Co; 1965, pp181-238.*
7. *Blechner JN. Maternal-fetal acid-base physiology. Clin Obstet Gynecol 1993;36:3-12.*
8. *Bear M. Personal communication, 2011.*
9. *Edwards AL. Experimental design in psychological research, 4th ed. New York, Holt Rinehart Winston; 1972, p274-5.*
10. *Vandenbussche FP, Van Kamp IL, Oeples D, Hermans J, et al. Blood gas and pH in the human fetus with severe anemia. Fetal Diagn Ther 1998;13: 115-22.*
11. *Brar HS, Wong MK, Kirschbaum TH, Paul RH. Umbilical cord acid base changes associated with perinatal cardiac failure. Am J Obstet Gynecol 1988; 158:511-8.*
12. *Friedman EA, Gray MJ, Grynfogel M, Hutchinson DL, et al. The distribution and metabolism of C14-labeled lactic acid and bicarbonate in pregnant primates. J Clin Invest 1960;39:227-35.*
13. *Adrogué HJ, Rashad MN, Gorin AB, Yacoub J, et al. Assessing acid-base status in circulatory failure. Differences between arterial and central venous blood. N Engl J Med*

1989;321:1611-3.
14. *Fick A. Über die messung des blutquantums in den herzventrikeln. SB Physmed Ges, Wurzbürg, 1870, p16.*
15. *Yang SS, Bentivoglio LG, Maranhão V, Goldberg H. Cardiac output. In: Cardiac Catheterization Data to Hemodynamic Parameters, 3rd ed. Philadelphia, FA Davis Co; 1988, p42-66.*
16. *Holzgreve W, Curry CJ, Golbus MS, Callen PW, et al. Investigation of nonimmune hydrops fetalis. Am J Obstet Gynecol 1984;150:805-12.*
17. *Teitel DF. Physiologic development of the cardiovascular system in the fetus. In Polin RA, Fox WW (eds): Fetal and Neonatal Physiology, Vol I. Philadelphia, Saunders; 1992, p 609*
18. *Ojala TH, Hornberger LK. Fetal heart failure. Front Biosci (Schol Ed) 2010;2:891-906.*
19. *Nicolaides KH, Warenski JC, Rodeck CH. The relationship of fetal plasma protein concentration and hemoglobin level to the development of hydrops in rhesus isoimmunization. Am J Obstet Gynecol 1985;152:341-4.*
20. *Kohlenberg CF, Ellwood DA. Fetomaternal haemorrhage treated with intravascular transfusion: A late complication of amniocentesis? Brit J Obstet Gynaecol 1994;101:912-3.*
21. *Kecskes Z. Large fetomaternal hemorrhage: Clinical presentation and outcome. J Matern Fetal Neonatal Med 2003;13:128-32.*
22. *Fagan DG, Lancashire RJ, Walker A, Sorahan T. Determinants of fetal haemoglobin in newborn infants. Arch Dis Child, Fetal-Neonatol ed. 1995;72:F111-4.*
23. *Usher R, Shephard M, Lind J. The blood volume of the newborn infant and placental transfusion. Acta Paediatr 1963;52: 497-512.*
24. *Gruenwald P. Growth of the human foetus. In: McLaren A (ed): Advances in reproductive physiology. New York, Academic Press, 1967, p279.*
25. *Fraser ID, Raper AB. Observation of compatible* and incompatible foetal red cells in the maternal circulation. Br Med J 1962;2:303-4.

Disclosure: The author has no disclosures.

NT

Corresponding Author

Jeffrey Pomerance, MD
Emeritus Professor of Pediatrics,
UCLA
Former Director of Neonatology,
Cedars-Sinai Medical Center, Los Angeles
Email: jpomerance@msn.com