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Anemia and Polycythemia in the Newborn

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Red blood cell (RBC) mass in the newborn is highly variable. As an infant makes the transition from the intrauterine to the extrauterine environment, a change occurs in both the mass and the composition of RBCs. The range of normal, while clearly defined, is wide because of the many fluctuating variables involved in the physiology of the peripartum period.

In utero, fetal hemoglobin predominates. When compared with adult hemoglobin, fetal hemoglobin has enhanced oxygen-binding capacity, a characteristic that allows sufficient oxygen transfer to the fetus in the absence of gas exchange with the external environment. Even with fetal hemoglobin’s increased affinity for oxygen, the intrauterine environment is relatively hypoxic. As a result, the hemoglobin level in a near-term fetus or term infant is relatively high. The normal hemoglobin concentration for a term newborn is 19.3±2.2 g/dL (193±220 g/L), with a hematocrit of 61%±7.4% (0.61±0.074), values that continue to rise until they reach a maximum at about 2 hours after birth.

Within the first week after delivery, hemoglobin and hematocrit values begin to drop in response to the higher ambient oxygen concentration ex utero. It is postulated that this increase in oxygen concentration, combined with a rising percentage of adult hemoglobin, downregulates production of erythropoietin in the neonate, in turn leading to a decrease in hemoglobin. The hemoglobin and hematocrit values continue to decrease until they reach the physiologic nadir, which usually occurs at 8 to 12 weeks after birth in the term neonate. Normal values for hemoglobin at this point range from 9 to 11 g/dL (90 to 110 g/L). The nadir is termed “physiologic anemia of infancy,” although it actually is not truly anemia, which is defined by a deviation from age-specific norms.

Physiology in the preterm infant is distinctive. The bulk of fetal iron stores is not transferred from maternal blood until late in the third trimester. Therefore, preterm neonates begin with lower baseline hemoglobin and hematocrit values as well as lower iron stores. The discrepancy widens with decreasing gestational age at delivery. After delivery, the breakdown of hemoglobin leads to storage of the iron byproduct for future erythrocyte production. Because they begin with a lower amount of hemoglobin, preterm infants store less iron, predisposing them to iron deficiency anemia in addition to a physiologic nadir that is lower than that in term infants and that occurs as early as 3 to 8 weeks of age. With immature hematopoietic systems, preterm infants also have lower erythropoietin levels, leading to underproduction of erythrocytes. Excessive phlebotomy in preterm infants exacerbates the condition.

Other causes of anemia in the newborn period affect both term and preterm infants and are classified into three basic categories: blood loss, decreased production of RBCs, and decreased destruction of RBCs.

Blood loss can occur before, during, or after delivery. In utero, fetal-maternal transfusion or twin-twin transfusion can cause moderate-to-severe fetal anemia. Placental abruption can cause blood loss before and during delivery. Other intrapartum causes of blood loss include delayed cord clamping (as in an unattended delivery), damage to the cord or placenta, and internal hemorrhage, either from trauma or another cause.

Decreased production of erythrocytes is associated most commonly with iron deficiency, although other factors, such as bone marrow disorders, TORCH infections (toxoplasmosis, rubella, cytomegalovirus, herpesvirus), congenital leukemia, and nutritional deficiencies other than iron, also can be responsible.

Immune hemolytic anemias, such as Rh disease and ABO incompatibility, are responsible for a large proportion of cases of anemia that are caused by...
increased destruction of RBCs. When no risk factor for an immune hemolytic anemia is known, other causes of hemolysis must be considered, including the RBC enzyme defects (eg, glucose-6-phosphate dehydrogenase deficiency), RBC membrane defects (eg, spherocytosis, elliptocytosis), thalassemia, unstable hemoglobinopathies, sepsis, metabolic disorders, and even some nutritional factors (such as vitamin E deficiency).

The treatment of anemia in the newborn depends on the underlying cause. Many infants are asymptomatic and require only observation. Preterm infants or those who have known iron deficiency may be treated with oral or parenteral iron therapy. The use of erythropoietin in preterm infants remains controversial. Although its efficacy in inducing erythropoiesis has been demonstrated consistently, it has yet to be shown to reduce the need for RBC transfusion substantially. For the subgroup of patients who have clinical signs of anemia, such as tachycardia and respiratory distress, the mainstay of treatment is transfusion of packed RBCs.

Polycythemia is another important clinical problem in the newborn period and is defined as a hemoglobin or hematocrit value greater than 2 standard deviations above the mean for gestational and postgestational age in a venous blood sample. Many hemoglobin and hematocrit measurements in the newborn period, whether alone or as part of a complete blood count, are drawn by capillary venous sampling from a heel stick. Commonly, hemoglobin and hematocrit values from capillary samples are as much as 15% higher than those from venous samples. Therefore, when considering a diagnosis of polycythemia, it is important to obtain a venous measurement, either from a peripheral vein or the umbilical vein.

The incidence of polycythemia is 1% to 5% in healthy term newborns. The maximum hematocrit is found at 2 hours of age, so blood drawn at this time is more likely to show a higher count than blood drawn earlier or later. Polycythemia can lead to many secondary complications, including hyperviscosity, hyperbilirubinemia (from increased hemoglobin breakdown), and hypoglycemia (from unknown mechanisms). Although not all polycythemic blood is hyperviscous, a direct linear relationship becomes exponential when the hematocrit is greater than 65% (0.65). Hyperviscosity has been linked to decreased blood flow to vital organs, most notably the brain, but also to the lungs, liver, heart, bowel, and kidneys. Polycythemia itself may cause decreased blood flow, even in the absence of hyperviscosity, purportedly from a direct vascular response to the increased oxygen content of the blood.

There are two basic physiologic causes of polycythemia in the newborn: RBC transfusion and increased intrauterine erythropoietin production. In the first category, the most common cause is delayed cord clamping, which can lead to increased placental transfusion of blood to the neonate. Other causes include twin-twin transfusion, maternal-fetal transfusion, and iatrogenic causes, such as administration of an inappropriately large volume of RBCs during transfusion.

The two major factors leading to increased intrauterine erythropoietin production are placental insufficiency (such as that seen in long-standing diabetes or in renal or vascular disease) and chronic intrauterine hypoxia (from maternal hypoxia or poor oxygen transfer).

Symptoms of polycythemia may involve the neurologic (irritability, jitters), pulmonary (respiratory distress/hypoxemia), gastrointestinal (poor feeding, signs and symptoms of necrotizing enterocolitis), and genitourinary (hematuria, oliguria) systems. Of note, cyanosis may be exaggerated in infants who have polycythemia from the larger ratio of deoxygenated RBCs to oxygenated RBCs.

Treatment is aimed at minimizing the risk of hyperviscosity. Because the hemoglobin concentration decreases rapidly in most newborns, observation is appropriate in most asymptomatic infants. However, in symptomatic newborns whose hemoglobin does not decrease quickly enough, partial exchange transfusion is the mainstay of treatment, enabling the reduction of hemoglobin while maintaining blood volume, because dehydration worsens the risks associated with hyperviscosity. Infusion of a crystalloid solution may be used to reduce viscosity temporarily until partial exchange transfusion can be performed. In addition, care must be taken to screen all infants who have polycythemia for hyperbilirubinemia and hypoglycemia, two common complications.

Interestingly, polycythemia itself does not necessarily lead to worse long-term neurologic outcomes. When documented hyperviscosity is present, there is an increased risk of neurologic morbidity, whether or not the infant is treated with partial exchange transfusion. Because there is no readily available and reliable test for hyperviscosity itself and because the two phenomena are so closely linked, it is appropriate to treat all infants who have symptomatic polycythemia.

In summary, an understanding of normal RBC physiology in newborns supports the need to screen at-risk infants for anemia, polycythemia, and their complications.
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