Pathophysiology of Birth Asphyxia

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KEYWORDS

• Neonate • Birth asphyxia • Perinatal • Fetal acidemia
• Hypoxic–ischemic encephalopathy • Cerebral palsy

KEY POINTS

- The pathophysiology of birth asphyxia centers on the interruption of placental blood flow.
- The goal of the fetus is to preserve blood flow to the brain, heart, and adrenal glands during asphyxia.
- Blood flow to noncritical organs is sacrificed to preserve critical organ blood flow.
- Circulatory and noncirculatory adaptive mechanisms allow the fetus to cope with interruption of placental blood flow.
- The most severe consequence of asphyxia is permanent brain injury. Cerebral injury begins with an initial insult and continues during the reperfusion period.

INTRODUCTION

The term asphyxia can be defined as a condition of impaired gas exchange in a subject, which leads to progressive hypoxia, hypercarbia, and acidosis depending on the extent and duration of this interruption. Birth asphyxia, or impaired gas exchange during the perinatal period, does not have precise biochemical criteria. As such, caution must be exercised in labeling a neonate with "asphyxia." Unfortunately, this term is often inappropriately linked with poor neurodevelopmental outcome, commonly referred to as cerebral palsy. Before a potential causal relationship between an acute intrapartum interruption of placental blood flow and a later case of cerebral palsy can be established, the American Congress of Obstetricians and Gynecologists Task Force on Neonatal Encephalopathy and Cerebral Palsy require 4 essential criteria[1]: (1) evidence of a metabolic acidosis in fetal umbilical cord arterial blood obtained at delivery (pH <7.00 and base deficit $\geq$ 12 mmol/L), (2) early onset of severe or moderate neonatal encephalopathy in infants born at 34 weeks or more of

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gestation, (3) cerebral palsy of the spastic quadriplegic or dyskinetic type, and (4) exclusion of other identifiable etiologies such as trauma, coagulation disorders, infectious conditions, or genetic disorders.

Asphyxia may occur before, during, or after delivery. Its pathophysiology is extremely complex and can be a result of factors related to the mother, the placenta, and/or the fetus and neonate. This section focuses predominantly on the interruption of placental blood flow and the fetal adaptive mechanisms that occur around the time of birth.

The goals of this article are to (1) review the fetal and neonatal circulations and how transition can be disrupted with asphyxia, (2) describe the adaptive responses, both circulatory and noncirculatory that are protective against asphyxia, (3) review the biochemical processes regulating gas exchange in the placenta, and (4) define the mechanisms of cell death after asphyxia and discuss pathologic brain injury as it relates to the asphyxial insult.

NORMAL FETAL CIRCULATION

The human fetus exists in a hypoxemic, but not a pathologically hypoxic state. A number of remarkable mechanisms allow the fetus to thrive under these conditions. Oxygen diffuses readily from the maternal to fetal circulation to bind high-affinity fetal hemoglobin. This blood from the placenta returns through the umbilical vein to the fetus and the majority enters the ductus venosus. The blood has a P_{O_2} of approximately 40 to 50 mm Hg[2] before joining less oxygenated blood from the inferior vena cava en route to the right atrium. Interestingly, the more oxygenated blood from the umbilical vein is directed through the foramen ovale to the left side of the heart. This blood goes on to exit the left ventricle via the aorta to the carotid and coronary arteries.[3] Thus, the fetus preferentially supplies more oxygenated blood to the brain and heart. Less oxygenated blood from the inferior vena cava remains in the right side of the heart to exit via the pulmonary trunk. The majority of this blood bypasses the lungs via the ductus arteriosus[3] and enters the aorta distal to the carotid and coronary pathways. This mixture of blood has a P_{O_2} of 15 to 25 mm Hg,[3] and a portion travels out the umbilical arteries to the placenta.

Additional factors unique to the fetus ensure adequate oxygen delivery to meet tissue demand. Hemoglobin levels are higher in the fetus compared with adults and children.[4] Fetal hemoglobin has a high affinity for oxygen and shifts the oxygen–hemoglobin dissociation curve to the left. This facilitates transfer of oxygen from the mother to the fetus across a smaller concentration gradient. These factors increase the oxygen-carrying capacity of fetal blood. The rate of tissue perfusion is higher in the fetus than the adult.[3] Thus, increased delivery of blood counteracts relatively low oxygen saturation. Additionally, the fetus expends less energy on thermoregulation and respiratory effort than the neonate.

CIRCULATORY CHANGES DURING LABOR AND NEONATAL TRANSITION

Uterine contractions lead to decreased uterine arterial blood flow[5] and decreased flow into the intervillous spaces. Transplacental gas exchange may be impaired transiently,[6] but this is generally inconsequential during normal labor.[7] When the fetal side of the circulation is examined, uterine contractions do not seem to affect umbilical blood flow. This was shown by Malcus and colleagues,[8] who measured umbilical artery flow velocity waveforms via Doppler ultrasonography and found no differences before or during contractions. However, it was noted that fetuses with an arterial