The Fetal Physiology and Birth Transition

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The Fetal Pulmonary System
The Fetal Circulatory System
Cardiopulmonary Changes at Birth
Persistent Pulmonary Hypertension of the Newborn

We begin this journey into pediatric anesthesia by looking at fetal cardiopulmonary physiology and the changes that occur during the birth process. Knowledge of these changes is important for understanding a variety of pathophysiologic conditions of the neonate. For purposes of clarity and consistency, the term “neonate” will henceforth refer to an infant in the first 28 days of life, regardless of the gestational age. The term “infant” will refer to a child in the first year of life. The “gestational” age refers to the number of weeks between conception and birth; the normal term gestational age is between 38 and 42 weeks of pregnancy.

Newborn infants can be classified by their size relative to their gestational age:
• **Appropriate for gestational age (AGA)** describes an infant whose birthweight is between the 10th and 90th percentiles.
• **Small for gestational age (SGA)** describes an infant whose birthweight is below the 10th percentile.
• **Large for gestational age (LGA)** describes an infant whose birthweight is above the 90th percentile.

**Intrauterine growth restriction** (or **retardation**) (IUGR) is an abnormal pattern of restricted fetal growth for gestational age. An easy way to think of the distinction between IUGR and SGA is that IUGR is a term used by obstetricians to describe a pattern of growth over a period of time, whereas SGA is a term used by pediatricians to describe a single point on a growth curve.

**THE FETAL PULMONARY SYSTEM**

As the lungs grow and develop during fetal life, they do not function in the capacity of oxygen and carbon dioxide exchange, for this role is carried out by the placenta. Rather, the lungs are fluid-filled organs that grow terminal bronchioles and alveoli in preparation for the air-breathing that is required after birth.

Fetal lung development is divided into four stages of progressive lower airway and alveolar growth (Table 1-1). During the last or saccular stage, the fetal lung finalizes the physiologic processes that will allow respiration in an extraterine environment. This includes maturation of the alveolar-vascular interface and development of a full complement of surfactant, which will reduce surface tension within the alveoli and prevent their collapse. The fetal airways and alveoli are distended by secreted lung fluid, which becomes a component of the amniotic fluid.

As the peripheral chemoreceptors and the respiratory center of the brain mature, the fetus develops stronger and more regular breathing patterns throughout development. After the 30th week of gestation, the fetus is noted to “practice” breathing at about 60 times per minute, approximately 40% of the time.

**THE FETAL CIRCULATORY SYSTEM**

The overall goal of fetal circulation is to distribute oxygen, glucose, and other nutrients from the placenta to the developing brain and vital organs (Fig. 1-1), and is outlined in the following steps.

In the placenta, the organ of fetal respiration, fetal blood picks up oxygen and releases carbon dioxide. Fetal-type hemoglobin (Hgb F) is characterized by its leftward shift of the oxyhemoglobin dissociation curve. Therefore, fetal blood has a greater affinity for oxygen than does maternal blood, and oxygen is transferred to fetal hemoglobin in the placenta. Release of oxygen from Hgb F to fetal tissues is facilitated by the relatively increased temperature and lower pH of the fetus, both of which shift the oxyhemoglobin dissociation curve to the right.
Table 1-1 Stages of Fetal Lung Development

<table>
<thead>
<tr>
<th>Stage</th>
<th>Gestational Weeks</th>
<th>Noteworthy Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryonic</td>
<td>4–7</td>
<td>Initial formation of primitive lung tissue and vascular connections</td>
</tr>
<tr>
<td>Pseudoglandular</td>
<td>5–17</td>
<td>Development of a bronchial tree that begins to form lumens</td>
</tr>
<tr>
<td>Canalicular</td>
<td>16–26</td>
<td>Alveoli begin to form Vascular and lymphatic systems develop alongside the bronchial tree Differentiation of type 1 and type 2 pneumocytes with beginning of surfactant production Extrauterine life possible at later weeks</td>
</tr>
<tr>
<td>Saccular</td>
<td>24th–birth</td>
<td>Peripheral bronchiola branching Maturation of surfactant system Breathing efforts begin Alveoli at birth number 30–50 million</td>
</tr>
<tr>
<td>Alveolar</td>
<td>Birth–3 years</td>
<td>Continued alveolar growth to adult level of 300 million Reduction of interstitial tissues</td>
</tr>
</tbody>
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Figure 1-1 Anatomy of the fetal circulation. AO = aorta; DA = ductus arteriosus; DV = ductus venosus; FO = foramen ovale; IVC = inferior vena cava; L = liver; LA = left atrium; LB = lower body; LV = left ventricle; PL = placenta; RA = right atrium; RV = right ventricle; PA = pulmonary artery; SVC = superior vena cava; UA = umbilical artery; UV = umbilical vein. (Redrawn with permission from Bell C, Kain ZN, Hughes C. The Pediatric Anesthesia Handbook, 2nd edn, Mosby, Philadelphia, 1997.)
Oxygenated blood travels to the fetus in a single umbilical vein (contained within the umbilical cord). The maximal $P_{O_2}$ in the umbilical vein measures only 30–35 mmHg. The umbilical vein travels through the liver, where approximately half the blood flow joins the hepatic circulation, while the other half bypasses the liver through the ductus venosus, a structure present only in fetal life. The ductus venosus carries the oxygenated blood from the umbilical vein into the inferior vena cava (IVC), where it mixes with poorly oxygenated blood from the fetal lower extremities and then travels to the right atrium.

Inside the fetal right atrium the relatively oxygenated blood from the IVC is preferentially directed across the foramen ovale and into the left atrium, while deoxygenated blood from the head via the superior vena cava (SVC) is preferentially directed through the tricuspid valve into the right ventricle.

The deoxygenated blood that enters the right ventricle is ejected into the pulmonary artery; but owing to high pulmonary vascular resistance, only a small portion (about 10%) flows into the pulmonary arterial system. The remainder is directed across the ductus arteriosus and into the aorta, where it joins aortic blood flow returning to the placenta via the umbilical arteries. The ductus arteriosus usually enters the aorta just proximal to the origin of the left subclavian artery.

The oxygenated blood that has crossed into the left atrium passes through the mitral valve into the left ventricle, and is ejected out the ascending aorta where it provides oxygen and glucose to the developing brain via the carotid arteries. The $P_{O_2}$ is now about 26-28 mmHg, but provides sufficient oxygen for fetal organ growth.

**CARDIOPULMONARY CHANGES AT BIRTH**

The birth process entails a number of simultaneous and dramatic cardiopulmonary changes that allow fetal transition to extraterine life. The lung becomes the organ of respiration, and the cardiovascular system undergoes conversion from two parallel circulations to two circulations in series. These changes include the following important processes.

During the newborn’s first breaths, air is drawn into the lungs, and lung fluid is absorbed or expelled. Intrathoracic distending pressures are estimated to reach $-60 \text{ cmH}_2\text{O}$, and facilitate opening of fluid-filled alveoli. The pressure required for lung expansion becomes increasingly less negative over several breaths. These initial breaths will establish the residual volume (RV) and functional residual capacity (FRC) of the newborn’s lungs, and will facilitate the absorption of lung fluid and the spread of surfactant.

The umbilical cord (containing the umbilical vein and arteries) is severed and clamped, which results in a dramatic increase in systemic vascular resistance (SVR). The umbilical arteries form a portion of the internal iliac and superior vesical arteries, and the ductus venosus (previously supplied by the umbilical vein) will atrophy and form a remnant known as the ligamentum venosum.

Pulmonary vascular resistance (PVR) decreases secondary to the establishment of negative intrathoracic pressure during inspiration, the increase in blood $P_{O_2}$, decrease in $P_{CO_2}$, and correction of fetal acidosis. Pulmonary blood flow is established, and arterial blood gas values normalize within the first 24 hours of life (Fig. 1-2).

The combined increase in SVR and decrease in PVR no longer allow blood to flow through the ductus arteriosus. Left atrial pressure increases causing the “flap-valve” foramen ovale to close, thus establishing for the first time a circulation in series.

Over the first several hours of life, the ductus arteriosus functionally closes as a result of constriction of specialized contractile tissue within its arterial wall. This constriction is caused by a number of factors, including

![Figure 1-2](image-url)
withdrawal from placenta-derived prostaglandin E₂, an increase in arterial oxygen tension, and a decrease in blood acidosis. Over several weeks the ductus arteriosus becomes anatomically closed; its remnant is called the ligamentum arteriosum.

**PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN**

During the first several days of life, a number of pathological conditions of the newborn prevent the normal decrease in PVR and closure of the ductus arteriosus. These conditions include processes that cause hypoxemia, hypercarbia, and/or acidosis. Examples include respiratory distress syndrome of the premature infant and meconium aspiration syndrome, as well as hypothermia and congenital heart disease, among others. In the past, this condition was referred to as “persistent fetal circulation” (PFC); it is now referred to as “persistent pulmonary hypertension of the newborn” (PPHN). The lower the gestational age, the more likely that PPHN will occur.

Because of the abnormally high PVR, the fetal pattern of circulation continues: blood flows through the patent ductus arteriosus (PDA) or foramen ovale in a right-to-left direction and hypoxemia worsens, thus creating a vicious cycle that can be overcome only by aggressive therapy for the underlying disorder as well as correction of hypoxemia, hypercarbia, and acidosis. Selective pulmonary vascular dilatation using inhaled nitric oxide is a promising future therapeutic option.