CE Examination
Category 3

Fetal Lung Development

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INTRODUCTION

The 27th Annual Congress of Anesthetists, a joint meeting of the International Anesthesia Research Society and the International College of Anesthetists, was held in Virginia Beach, Va, on September 22-25, 1952. A member of the Department of Anesthesiology, Columbia University, College of Physicians and Surgeons and the Anesthesia Service and the Presbyterian Hospital presented a remarkable paper. The article began:

> Resuscitation of infants at birth has been the subject of many articles. Seldom have there been such imaginative ideas, such enthusiasms, and dislikes, and such unscientific observations and study about one clinical picture. There are outstanding exceptions to these statements, but the poor quality and lack of precise data of the majority of papers concerned with infant resuscitation are interesting.[1,9]

The presenter, then, set forth the results of a careful scientific study and established a grading system for clinical evaluation of the neonate that both revolutionized and stabilized the field. That scoring system remains in effect today, The presenter was Virginia Apgar, MD.[1,9]

Apgar scores are assigned to all infants born in hospital settings in the USA. Values of 0-2 are assigned to five categories: heart rate, respiratory effort, muscle tone, reflex irritability and color. The scores for each item are totaled for the Apgar score. The maximum score is 10. Higher scores are associated with greater health. Scores are assigned at one minute and five minutes post partum. Scores continue to be assigned at five minutes intervals as long as the score is less than seven (See Table 1.)[7]

The Apgar scoring system provides the clinician with a quick and easy tool for evaluation of the neonate. It provides insight into each of the key indicators of health: cardiac, respiratory, muscle tone, nervous system and oxygenation. This article will focus on development related to one of these, namely lung development.

FETAL LUNG DEVELOPMENT[3,4,7]

There are five stages to human lung development, which are summarized in Table 2. An abbreviated but more detailed description follows.

TABLE 1. Apgar Scoring

ITEM SCORED	SCORE = 0	SCORE = 1	SCORE = 2
Heart Rate	Absent heart rate	Heart rate < 100	Heart rate > 100
Respiratory Effort	Absent	Weak, irregular or gasping	Good effort, crying
Muscle Tone	Flaccid	Some flexion of extremities	Well flexed, or active movements of extremities
Reflex Irritability	No reflex response	Grimace or weak cry	Good cry
Color	Blue all over or pale	Acrocyanosis (Raynaud's sign)	Pink all over

At about three weeks gestational age, a ventral epithelial evagination of the foregut forms the respiratory diverticulum. The groove elongates caudally and is separated from the foregut by the tracheo-esophageal septum. At about four weeks, a single lung bud forms at the end of the respiratory diverticulum. The lung bud then divides into right and left primary bronchial buds. Branching occurs rapidly. Three main branches form in the right lung bud and two in the left. These initial branches correspond to the lobar bronchi of the adult lungs. The lung buds grow caudally and laterally, entering the pericardioperitoneal canals. The interaction between splanchnic mesoderm and the respiratory diverticulum is essential to pulmonary development.

The respiratory diverticulum is of endodermal origin, and it forms the epithelial lining of the respiratory system. The splanchnic mesoderm is carried with the growing lung buds after they enter the pericardioperitoneal canals. Splanchnic mesoderm forms connective tissue, cartilage, smooth muscle and blood vessels, all surrounding the epithelium. In the distal development of the respiratory tract, the epithelium of the respiratory diverticulum forms the type I and type II epithelial cells lining the alveolar airways. The splanchnic mesoderm forms connective tissue, blood vessels and lymphatics in the pulmonary alveoli.

During the rapid lateral growth of the lung buds, the pericardioperitoneal canals are progressively obliterated. These canals are lined with mesothelium, the same type that lines the pericardial and peritoneal cavities. As it develops, the lung becomes coated with a visceral pleura that is reflected on the parietal pleura at the mediastinum.

The 17^{th} to 28^{th} weeks are noted for acinar development. During this period, the portion of the lungs that will function for gas exchange is formed and vascularized. The initial respiratory bronchioles appear about the 17^{th} week. The number of connected capillaries continues to increase for some time. These capillaries connect to pulmonary instead of bronchial arteries. The saccules elongate with growth of the acini increasing the distance between terminal bronchioles and the pleura.

Remarkable changes in lung appearance begin about the 28th week of gestation. There is a significant decrease in interstitial tissue, and the airspace walls narrow and become more compact. Lung volume and surface area increase rapidly. In

TABLE 2. Summary of Fetal Lung Development

STAGE	TIME FRAME	DISTINGUISHING CHARACTERISTIC	RELATED PROBLEMS
Embryonic Phase	4^{th} – 6^{th} week of gestation	Initiation: Formation of laryngotracheal groove Termination: Formation of bronchopulmonary segments	Structural abnormalities difficult to establish; developmental errors at the point usually result in death
Pseudoglandular Period	6^{th} – 16^{th} week of gestation	All conducting airways formed by branching of the bronchial buds; Pleural membranes and pulmonary lymphatics develop during weeks 8 – 10	Developmental errors result in abnormalities of bronchial connection, position and number
Canalicular Period	17^{th} – 28^{th} week of gestation	Acinar development, the basic structure of the portion of the lung responsible for gas exchange is formed and vascularized; airways lined by cuboidal epithelium; parenchyma of lungs becomes highly vascularized	Developmental errors result in deficiencies of the components of the lung responsible for gas exchange
Saccular Period	28^{th} – 36^{th} week of gestation	Increase in lung volume and surface area; prenatal phase of alveolar development; squamous type I cells develop; Surfactant-secreting type II cells develop	Developmental errors result in deficiencies of the components of the lung responsible for gas exchange
Alveolar Period	36^{th} week of gestation to 3 years post-term	Surface area expansion continues; 50 million alveoli present at birth and reaching 300 million by age 3	Developmental errors result in deficiencies of the components of the lung responsible for gas exchange

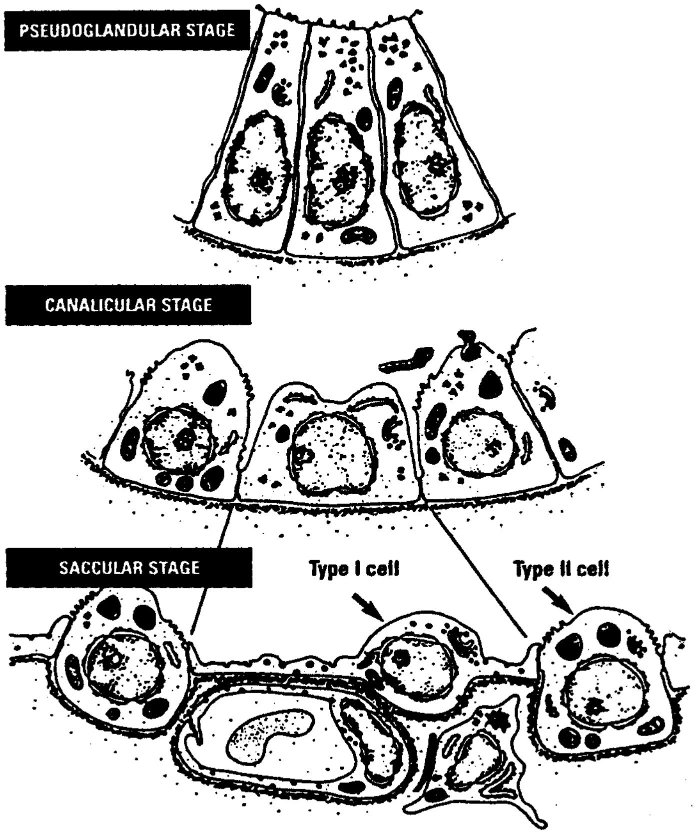

FIGURE 1—Key steps of pulmonary development.

humans, alveoli may appear by week 32 and are always present by week 36. During the saccular stage, the great alveolar cells or surfactant-secreting type II cells are formed. Surfactant forms a thin, continuous film of phospholipid and protein that reduces surface tension at the interface of the fluid-filled alveolus and the alveolar epithelium. The surfactant allows for easy inflation of the lungs. Once a sufficient amount of surfactant-secreting type II cells are formed, the fetus is viable outside the uterine environment. Prior to this time, the incidence of respiratory distress syndrome is greatly increased. Surfactant secretion can be used clinically to evaluate fetal lung maturity.

LUNG LIQUID

The airways are open to contact with amniotic fluid when the glottis is open. The lungs, buccal cavities and nasopharynx contribute to the tracheal effluent. Except in instances of fetal distress, however, amniotic fluid rarely enters the lung proper. The lungs are filled with fluid, but it differs from both amniotic fluid and plasma. Lung liquid is high in chloride with small amounts of bicarbonate and little protein. Potassium levels are similar to plasma until levels increase near term in response to the presence of surfactant. Lung liquid is secreted at 4-6 cc/kg/hr.

The lungs must be cleared of fluid in order to transition from the intrauterine to extrauterine environment. This process begins about three days prior to birth with a drop in secretion rate. The process begins in earnest with the onset of labor. Post partum liquid moves from the air spaces to loose connective tissue in the extra-alveolar interstitium as the lungs expand. Water is removed by lymphatic action and resorption into the vascular compartment.

DIAGNOSTIC INDICATIONS

Respiratory distress syndrome affects many neonates. Respiratory distress syndrome is related to premature birth and inadequate surfactant production. Normal signs of respiratory distress in the infant include flared nares and grunting during respiratory effort and cyanosis. Treatment for respiratory distress syndrome, hyaline membrane disease, continues to develop.

CONCLUSION

The Apgar score is a clinician's tool. Other tests specifically focused on fetal lung maturity have been developed, and modern science has refined our understanding of the factors that contribute to normal and pathologic conditions.[2,3,4,5,6,7,8]

RESOURCES

1. Apgar, V. A Proposal for a New Method of Evaluation of the Newborn Infant. *Current Researches in Anesthesia and Analgesia*. Jul-Aug, 1953, 260. (See also, Internet resources.)
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4. Johnson, KE. *Human Developmental Anatomy: National Medical Series for Independent Study*. Malvern, PA: Harwal Pub. Co; 1988.
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INTERNET RESOURCES

7. Duncan@cerf.net (Webmaster). Pulmonary Function in the Newborn, Contribution from Division of Neonatology, Cedars-Sinai Medical Center, Los Angeles, CA. www.neonatology.org/syllabus/pulmonary.html.
8. Tulane Medical School. Fetal Lung Maturity Testing. www.mcl.tulane.edu/classware/pathology/medical_pathology/pren.../08FLM.html.
9. Apgar, V. A Proposal for a New Method of Evaluation of the Newborn Infant. *Current Researches in Anesthesia and Analgesia*. July-Aug, 1953, 260. Available on-line at Neonatology on the Web. www.neonatology.org/classics/apgar.html.