# Neonatal Respiratory Care

*Second Edition*

Waldemar A. Carlo
Robert L. Chatburn

SECOND EDITION

# NEONATAL RESPIRATORY CARE

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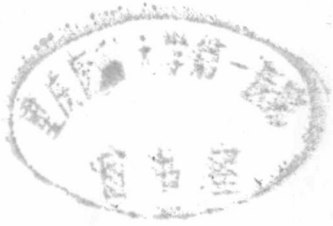
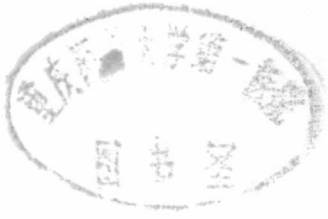


*This book is dedicated to neonatal patients, their parents, and caretakers; Eugenia, Wally, Enrique, Julian, and Maria Carlo, and DEE and Maya Chatburn for their support, understanding, and encouragement; and to Marvin Lough, R.R.T., and Doctors Avroy A. Fanaroff and Richard J. Martin, who taught us neonatal care.*



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# PREFACE

In the 9 years since the first edition there have been tremendous changes in the field of neonatal respiratory care. This book has been revised and updated to reflect this evolution, and every effort has been made to include the latest developments. Sections on high-frequency ventilation, extracorporeal membrane oxygenation, pulmonary function, gas exchange, and complications of assisted ventilation have been added to reflect the enhanced perspective gained from extensive research and experience.

Advances in respiratory care have led to the increased survival of critically ill neonates. Unfortunately, there has been an associated increased incidence of complications. The intent of this book is to guide postgraduate health care professionals and students, including respiratory therapists, nurses, and physicians, in the care of critically ill neonates. It is our firm hope that the information provided in this text will improve neonatal respiratory care and continue to further reduce both morbidity and mortality in this patient population. With thoughtful care, these ill neonates will survive to lead full and productive lives.

*Waldemar A. Carlo, M.D.*
*Robert L. Chatburn, R.R.T.*

# CONTENTS

# 1

# Development of the Respiratory System

Joseph F. Tomashefski, Jr., M.D.
Bradford J. Richmond, M.D., C.R.T.T.

For those involved in the care of the neonate, the newborn lung represents the dynamic interaction of two simultaneous processes: adaptation to extrauterine life and response to injury. The lung in utero develops according to a relatively fixed schedule. After birth, alveolar multiplication continues for at least 8 years. Knowledge of the intrauterine and extrauterine timetables of lung development is essential for an understanding of normal and abnormal neonatal respiratory physiology. It is also fundamental to an understanding of the response of the lung to various interventions to support respiratory function or stimulate lung growth. The selection of respiratory support modalities and the type of equipment used is often dependent on the gestational age of the neonate. It is unlikely that the lungs of the infant born prematurely maintain the intrauterine schedule of development, but the extent to which this schedule is modified in adapting to a new and often hostile environment is unknown. The spectrum of congenital abnormalities of the lung is likewise best understood in terms of the developmental stage at which interference with growth occurs.

In this chapter, we will review the anatomical and biochemical development of the upper and lower fetal respiratory tracts. Since pulmonary development and function are intimately associated with that of the heart, we will also briefly consider cardiac development. Finally, we will discuss the dramatic structural and functional remodeling of the cardiorespiratory system that occurs in the newborn period as the infant adapts to extrauterine life.

## EMBRYOLOGICAL GERM CELL LAYERS

It is not our intention to discuss embryogenesis in detail; for this the reader is referred to standard texts.[1–4] To understand lung development, however, it is important to be familiar with the embryonic germ cell layers and their derivatives. Shortly after conception, the fertilized ovum undergoes rapid cellular proliferation and subsequent internal cavitation to form the *blastocyst*. The cells of the blastocyst reorganize to form a bilaminar germ disk, which is converted to a trilaminar germ disk by the third week of embryonic life. The three germ layers, *endoderm*, *ectoderm*, and *mesoderm*, each give rise to specific body parts. The endoderm ultimately evolves into the lining epithelium of the entire digestive tract and lung, as well as the parenchyma of the liver and pancreas. The ectoderm gives rise to the central and peripheral nervous systems; sensory epithelium of the nose, ears, and eyes; and the skin and its appendages. The mesoderm, the last germ layer to form, establishes the cardiovascular, genitourinary, and lymphoid systems and also develops into a primitive form of connective tissue called *mesenchyme*. Mesenchymal cells have the potential to differentiate into fibrous tissue (fibroblasts), smooth and skeletal muscle (myoblasts), bone (osteoblasts), cartilage (chondroblasts), and blood vessels (angioblasts). The mesoderm also gives rise to *mesothelial cells* that line the serous cavities, i.e., pleura, peritoneum, and pericardium.

## DEVELOPMENT OF THE RESPIRATORY TRACT

In humans, completion of the development of the respiratory system occurs late in fetal life, and as a result, the lung is considered a nonfunctional organ until near term. Thus, in utero, the respiratory system develops independently of the functional demands of the growing embryo and fetus. Physiologic lung activity prior to birth is limited to some respiratory movements, growth, and secretion of various substances during specific times in development. At birth, the fetus is expelled from its aquatic surroundings, and the partially collapsed, fluid-filled lung must be prepared to adapt immediately to air breathing, thus facilitating the oxygen and carbon dioxide diffusion necessary for extrauterine life. The schedule of intrauterine respiratory tract development is summarized in Table 1–1. A list of important congenital malformations of the tracheobronchial tree is provided in Table 1–2. Congenital malformations of the respiratory tract are further discussed in Chapters 4 and 10.

**TABLE 1–1.**
Summary of Respiratory Tract Development

| Approximate Time of Occurrence | Developmental Event |
|---|---|
| 20 days | Foregut established |
| 24 days | Laryngotracheal groove develops |
| 26–28 days | Bronchial buds form |
| 2 wk | Intraembryonic coeloms form |
| 3 wk | Diaphragm development begins |
| 4 wk | Primitive nasal cavities develop; tongue develops; pharynx formation begins; phrenic nerves originate |
| 5 wk | Pseudoglandular phase begins; lobar bronchi are present; pulmonary artery develops; pulmonary vein develops; lung bud migrates into pleural canals |
| 6 wk | Arytenoid swellings (lead to formation of larynx) develop |
| 7 wk | Oropharynx develops; tracheal cartilage is present; smooth muscle of bronchi develops |
| 8 wk | Vocal cords develop |
| 9 wk | Bronchial arteries develop |
| 10 wk | Secondary palate forms; cilia develop; mucous glands appear; cartilaginous rings of trachea develop |
| 11 wk | Lymphatic tissue appears |
| 13 wk | Goblet cells are present |
| 16 wk | Canalicular phase begins; preacinar bronchial branches are complete |
| 22 wk | Methyltransferase system for lecithin synthesis is present; lecithin appears |
| 24 wk | Terminal saccular (alveolar) phase begins; respiratory bronchioles develop; terminal sacs develop |
| 26–28 wk | Alveolar-capillary surface area of respiratory system developed sufficiently to support extrauterine life |
| 35 wk | Phosphocholine transferase system for lecithin synthesis is present |
| 36 wk | Mature alveoli are present |

**TABLE 1–2.**
Congenital Malformations of the Lower Respiratory Tract

| Congenital Malformation | Embryological Origin | Remarks |
|---|---|---|
| Tracheoesophageal fistula (four different varieties) | Results from incomplete division of the foregut into respiratory and digestive portions during the fourth and fifth weeks | Occurs in about 1 of 2,500 births, predominantly in males |
| Tracheal stenosis; tracheal atresia | Probably results from unequal partitioning of the foregut into the esophagus and trachea | Rare |
| Laryngeal web | A membranous web forms around the vocal cords, causing airway obstruction; results from the incomplete | Rare |

(*Continued.*)

**TABLE 1–2 (cont.).**

| | | |
|---|---|---|
| | recanalization of the larynx during the tenth week | |
| Congenital bronchial cysts | Cysts may develop when abnormal saccular enlargements occur in the terminal bronchioles | Rare |
| Agenesis of the lung (absence of the lung) | Results from failure of the lung bud(s) to develop | Unilateral more frequent than bilateral; however, both are rare |
| Hypoplasia of the lung | Lungs unable to develop normally because they are compressed by abnormally positioned abdominal viscera | Rare; seen in infants with posterolateral diaphragmatic hernia |

### The Upper Respiratory Tract

In the fourth week of gestation, the buccopharyngeal (oropharyngeal) membrane ruptures, allowing communication between the ectoderm of the primitive oral cavity and the endoderm of the foregut. The primitive nasal cavities (nasal sacs) originate in the fourth week as two ectodermal thickenings (Fig 1–1) separated by mesenchymal cells destined to become the nasal septum and primary palate. An oronasal membrane separates the growing nasal sacs from the oropharynx. The disintegration of this membrane occurs during the seventh week, allowing the primitive nasal choana to form. Connection of the nasal cavities to the anterior oropharynx then is complete. At this time, lateral sheets of tissue begin to form the secondary palate while the nasal septum develops in continuity with the primary palate. The secondary palate is completed at 10 to 12 weeks of gestation. The anterior palate undergoes membranous ossification; the posterior portions do not become ossified but extend beyond the nasal septum as the soft palate and uvula. The nasopharynx is the region that communicates with bilateral nasal cavities and is roughly separated inferiorly from the oropharynx by the soft palate. Posteriorly the nasopharynx communicates with the oropharynx via the choana. Occasionally, the choana becomes sealed by membranous tissue that occludes the nasal passage. This condition, known as choanal atresia, can result in death of the nose-breathing neonate if medical intervention is not prompt. The tongue grows along the floor of the oral cavity during the fourth to seventh week.

The pharynx arises from the proximal foregut at 4 weeks. The laryngotracheal groove along the floor of the pharynx will give rise to the lower respiratory tract (Fig 1–2). The cranial portion of the tube forming

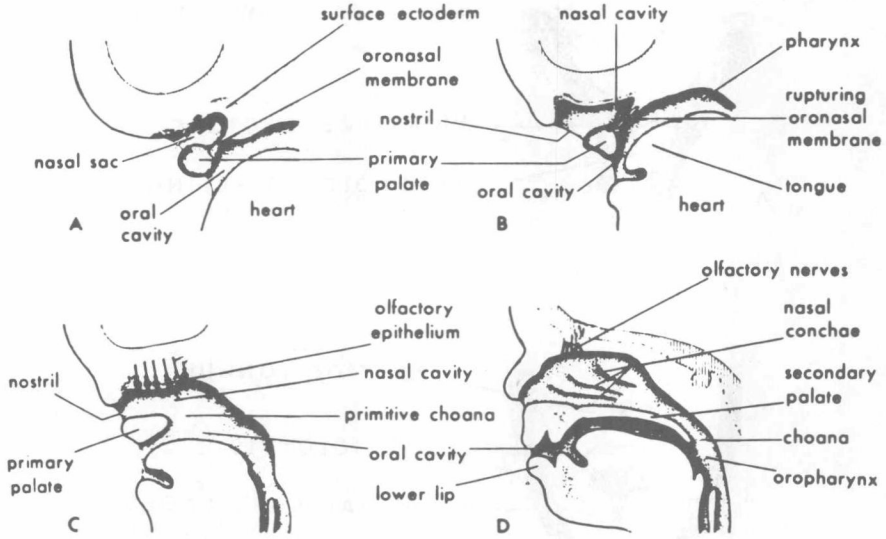


**FIG 1–1.**
Development of the nose. **A,** buccopharyngeal membrane separating nasal sac and oral cavity. **B** and **C,** buccopharyngeal membrane disintegrates, forming communication between oral and nasal cavities. **D,** nasal development at 12 weeks. (From Moore KL: *The Developing Human,* ed 2. Philadelphia, WB Saunders Co, 1977. Used by permission.)

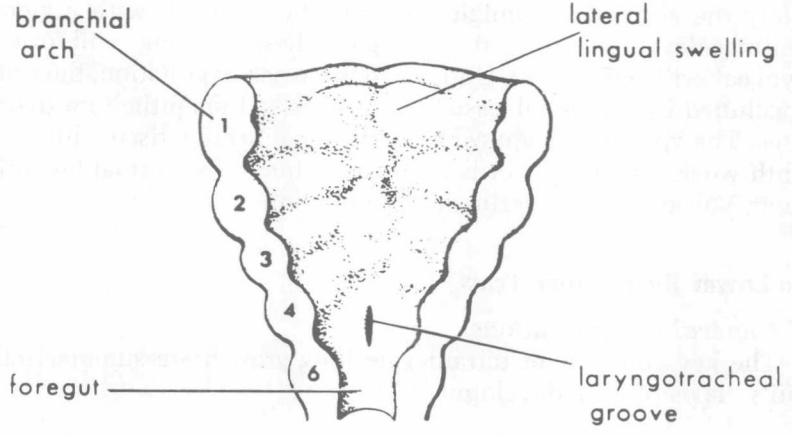


**FIG 1–2.**
The laryngotracheal groove. Precursor of the respiratory tract. (Modified from Moore KL: *The Developing Human,* ed 2. Philadelphia, WB Saunders Co, 1977.)

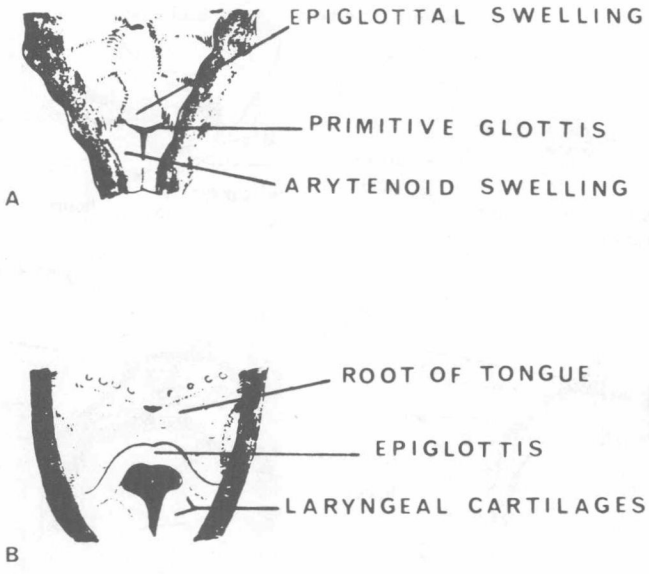


**FIG 1–3.**
Formation of the laryngeal orifice by arytenoid swellings. **A,** laryngeal orifice occluded by epithelial tissue at 6 weeks. **B,** epithelial tissue disintegrates, forming patent laryngeal orifice.

the primordial respiratory tract will become the larynx. At approximately the sixth week, epiglottal tissue has formed, with arytenoid swellings developing toward the tongue. These swellings will form the laryngeal orifice (Fig 1–3). Until the tenth week of gestation, the orifice is occluded by epithelial tissue. At 10 weeks, the epithelium disintegrates. The vocal cords appear as folds of connective tissue during the eighth week. The vocal cords act as a sphincter for normal breathing, cough, Valsalva maneuvering, and intonation.

## The Lower Respiratory Tract

### *General Considerations*

The key concepts of intrauterine lung growth are summarized in Reid's "laws of lung development"[5]:

*Law 1*: The number of preacinar airway branches is complete by the 16th week of intrauterine life.

*Law 2*: Alveolar development begins only after airway development is complete and occurs mainly after birth. Alveoli increase in number until about the age of 8 years and increase in size until growth of the chest wall ceases in early adulthood.