

SH Lecture - Respiratory System Development

From Embryology



Introduction

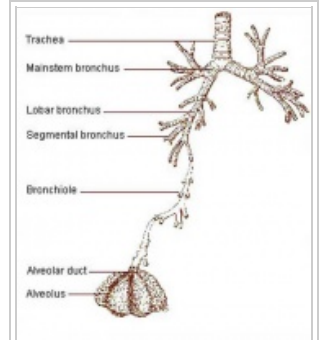


The lecture will introduce the development of the respiratory system and associated structures. The lecture will not cover adult anatomy, physiology of gas exchange and red blood cell function and cardiovascular development.

SH Links: Lymphatic Lecture | **Respiratory Lecture** | Medicine

Start Time/End Time: 10am to 11am Thursday 1 March 2012 Clancy Auditorium eMed
Link to Learning Activity - Respiratory System Development
([http://emed.med.unsw.edu.au/Map.nsf/0/6FF17DFEF645DABACA2573390006292A?](http://emed.med.unsw.edu.au/Map.nsf/0/6FF17DFEF645DABACA2573390006292A?OpenDocument&login)

OpenDocument&login)



Respiratory tract

The respiratory system does not carry out its physiological function (of gas exchange) until after birth, though the respiratory tract, diaphragm and lungs do begin to form early in embryonic development and continue through fetal development, only functionally maturing just before birth.

The respiratory tract is divided anatomically into 2 main parts:

1. **upper respiratory tract** - consisting of the nose, nasal cavity and the pharynx.
2. **lower respiratory tract** - consisting of the larynx, trachea, bronchi and the lungs.

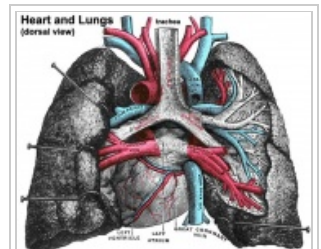
The respiratory "system" usually includes descriptions of not only the functional development of the lungs, but also related musculoskeletal (diaphragm) and vascular (pulmonary) development.

Aims

To understand the prenatal and postnatal developmental anatomy of human respiratory organs.

Key Concepts

1. Embryonic origin of respiratory components (tract, lungs, diaphragm, muscles)
2. Key stages in respiratory development.
3. Time course of respiratory development.
4. Respiration at birth.
5. Postnatal development of respiration.
6. Developmental abnormalities.



adult lungs

Textbooks

Schoenwolf, G.C., Bleyl, S.B., Brauer, P.R. and Francis-West, P.H. (2009). *Larsen's Human Embryology* (4th ed.). New York; Edinburgh: Churchill Livingstone.

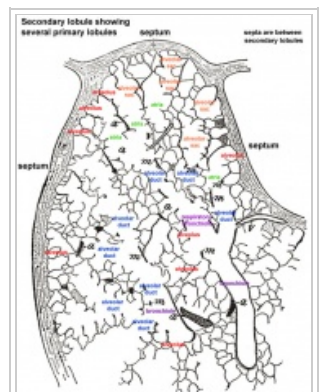


- Chapter 11 - Development of the Respiratory System and Body Cavities (<http://www.mdconsult.com/books/linkTo?type=bookPage&isbn=978-0-443-06811-9&eid=4-u1.0-B978-0-443-06811-9..10011-9>) (chapter links only work with a UNSW connection).

Moore, K.L. & Persaud, T.V.N. (2008). *The Developing Human: clinically oriented embryology* (8th ed.). Philadelphia: Saunders.



- Chapter 10 - The Respiratory System (<http://www.mdconsult.com/books/linkTo?type=bookPage&isbn=978-1-4160-3706-4&eid=4-u1.0-B978-1-4160-3706-4..50013-X>) (seem to no longer have UNSW connection?).

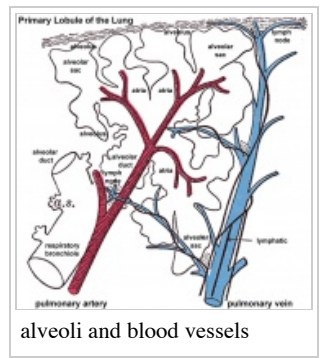


lung structure



Hill, M.A. (2011) *UNSW Embryology* (11th ed.). Sydney:UNSW.

- **Respiratory Links:** Introduction | Lecture - Respiratory Development | Stage 13 | Stage 22 | Upper Respiratory Tract | Diaphragm | Histology | Abnormalities | Category:Respiratory



Additional Textbooks

- Before We Are Born (5th ed.) Moore and Persaud Chapter 13 p255-287
- Essentials of Human Embryology Larson Chapter 9 p123-146
- Human Embryology Fitzgerald and Fitzgerald Chapter 19,20 p119-123
- Developmental Biology 8e Online Lung Branching Morphogenesis (<http://8e.devbio.com/article.php?ch=15&id=157>)
- Anatomy of the Human Body 1918 Henry Gray 1. The Respiratory Apparatus (<http://www.bartleby.com/107/235.html>)
- Blue Histology - Respiratory (<http://www.lab.anhb.uwa.edu.au/mb140/CorePages/Respiratory/respir.htm>)



Lectopia Lecture Audio

Science Respiratory Lecture 2011 (<http://lectopia.telt.unsw.edu.au/lectopia/lectopia.lasso?ut=153&id=110475>)

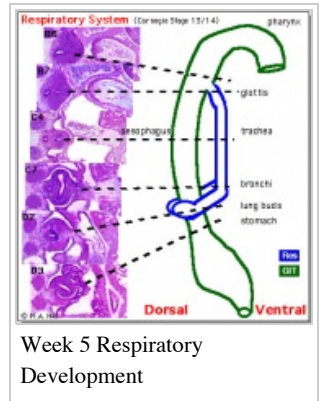
Developmental Overview

Lung Development

- week 4 - 5 embryonic
- week 5 - 17 pseudoglandular
- week 16 - 25 canalicular
- week 24 - 40 terminal sac
- late fetal - 8 years alveolar

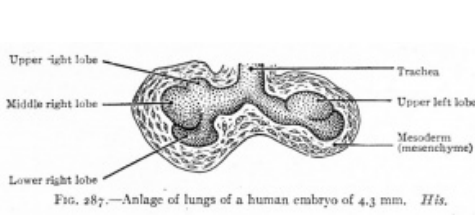
Germ Layers

- Endoderm and splanchnic mesoderm form majority of conducting and alveoli.
- Ectoderm will contribute the neural innervation.
- Mesoderm also contributes the supporting musculoskeletal components.

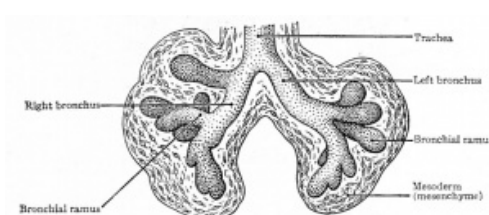


Week 5 Respiratory Development

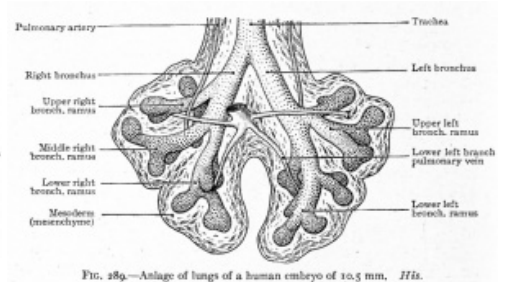
Events



Week 4-5 (Stage 12 to 13)



Week 5 (Stage 15 to 16)



Week 6 (Stage 16 to 17)

Week 4 - laryngotracheal groove forms on floor foregut.

Week 5 - left and right lung buds push into the pericardioperitoneal canals (primordia of pleural cavity)

Week 6 - descent of heart and lungs into thorax. Pleuroperitoneal foramen closes.

Week 7 - enlargement of liver stops descent of heart and lungs.

Month 3-6 - lungs appear glandular, end month 6 alveolar cells type 2 appear and begin to secrete surfactant.

Month 7 - respiratory bronchioles proliferate and end in alveolar ducts and sacs.

Lung Development Stages

The sequence is most important rather than the actual timing, which is variable in the existing literature.

- week 4 - 5 embryonic

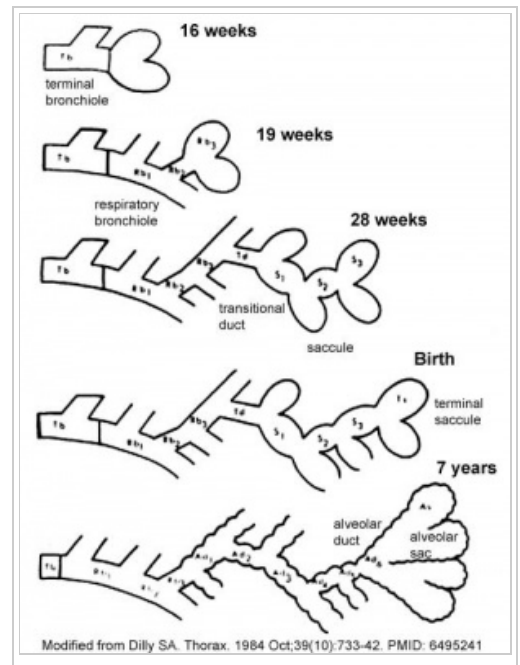
- week 5 - 17 pseudoglandular
- week 16 - 25 canalicular
- week 24 - 40 terminal sac
- late fetal - 8 years alveolar

Embryonic

- **week 4 - 5**
- Endoderm - tubular ventral growth from foregut pharynx.
- Mesoderm - mesenchyme of lung buds.
- Intraembryonic coelom - pleural cavities elongated spaces connecting pericardial and peritoneal spaces.

Pseudoglandular stage

- **week 5 - 17**
- tubular branching of the human lung airways continues
- by 2 months all segmental bronchi are present.
- lungs have appearance of a glandlike structure.
- stage is critical for the formation of all conducting airways.
 - lined with **tall columnar epithelium**
 - more distal structures are lined with **cuboidal epithelium**.

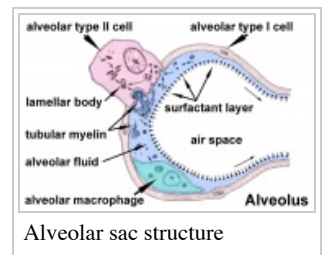


Canalicular stage

- **week 16 - 24**
- Lung morphology changes dramatically
- differentiation of the pulmonary epithelium results in the formation of the future air-blood tissue barrier.
- **Surfactant** synthesis and the canalization of the lung parenchyma by capillaries begin.
- future gas exchange regions can be distinguished from the future conducting airways of the lungs.

Saccular stage

- **week 24 to near term.**
- most peripheral airways form widened "airspaces", termed **sacculles**.
- sacculles widen and lengthen the airspace (by the addition of new generations).
- future gas exchange region expands significantly.
- Fibroblastic cells also undergo differentiation, they produce extracellular matrix, collagen, and elastin.
 - May have a role in epithelial differentiation and control of **surfactant secretion**.
- Alveolar Cells Type II (Type II pneumocytes)
 - begin to secrete **surfactant**, levels of secretion gradually increase to term.
 - allows alveoli to remain inflated
- Vascular tree - also grows in length and diameter during this time.



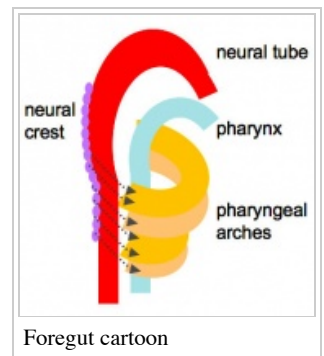
Links: Principal stages of lung development in humans (<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2920089/figure/f2-ehp.0901856/>)

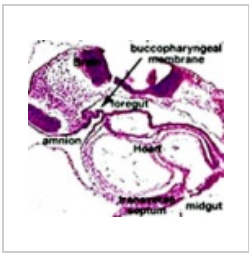
Foregut development

From the oral cavity the next portion of the foregut is initially a single gastrointestinal (oesophagus) and respiratory (trachea) common tube, the pharynx which lies behind the heart. Note that the respiratory tract will form from a ventral bud arising at this level.

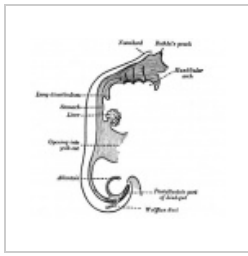
- Oral cavity
- Pharynx (esophagus, trachea)
- Respiratory tract
- Stomach

Upper respiratory tract

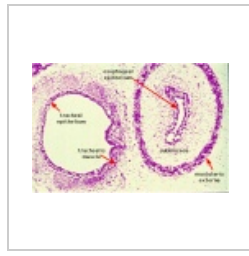




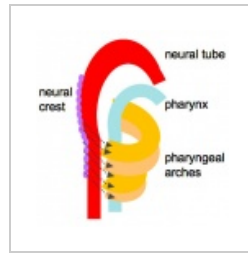
stage 11 foregut



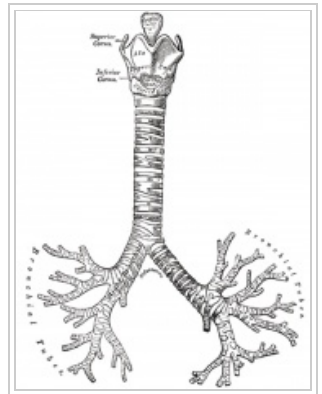
week 4 early respiratory endodermal bud



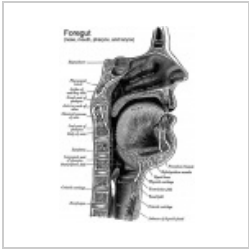
Stage 22 trachea



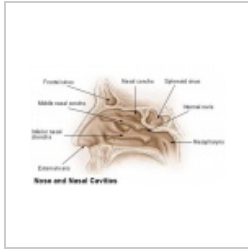
Head arches cartoon



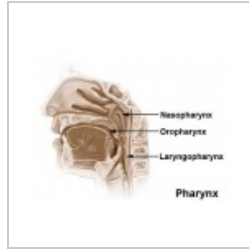
Adult upper respiratory tract conducting system



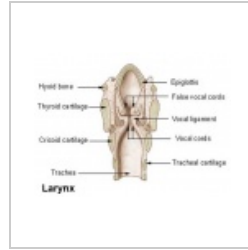
Pharynx



Nasal cavities



Pharynx

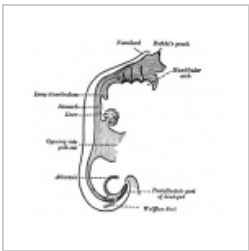


Larynx

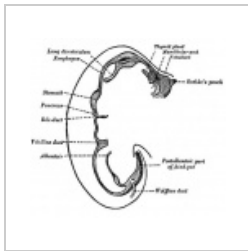
- part of foregut development
- anatomically the nose, nasal cavity and the pharynx
- the pharynx forms a major arched cavity within the pharyngeal arches

MH - pharyngeal arches will be described in head development lecture

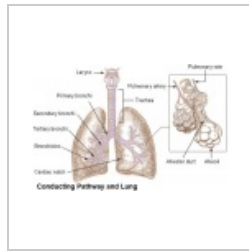
Lower respiratory tract



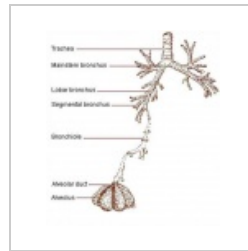
week 4 early respiratory endodermal bud



week 4 later ventral endoderm growth



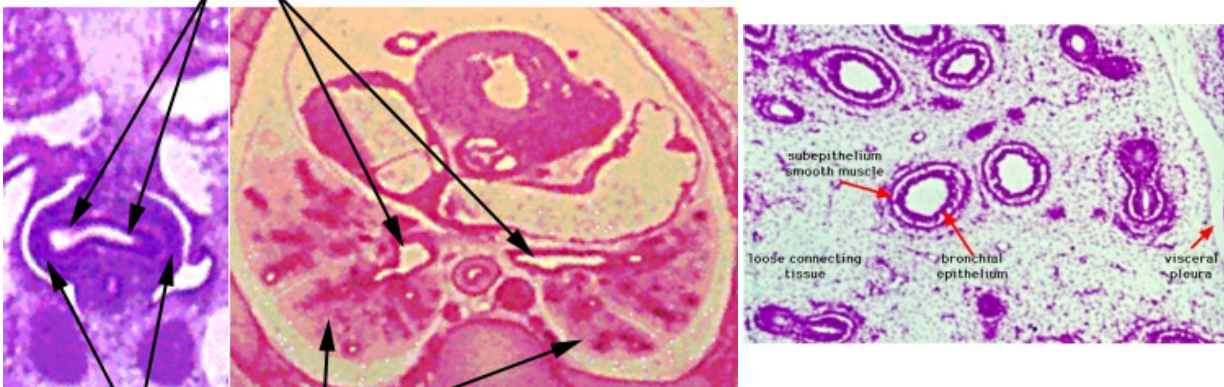
lower respiratory tract



conducting system bronchi to lungs

stage 14 **stage 22**

bronchi



developing lungs

- lung buds (endoderm epithelial tubes) grow/push into mesenchyme covered with pleural cells (lung border)

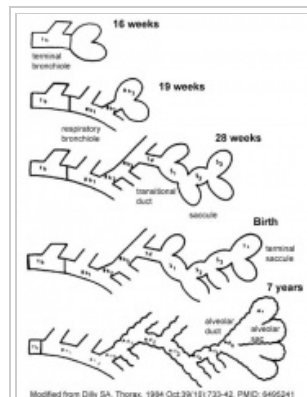
- generates a tree-like network by repeated:

1. elongation
2. terminal bifurcation
3. lateral budding

- The lungs go through an embryonic and 4 distinct histological phases of development

Growth initially of branched "conducting" system of bronchial tree, followed by later development of the "functional units" of the alveoli.

- **embryonic** - week 4 - 5 (stage 14 above)
- **pseudoglandular** - week 5 - 17 (stage 22 above)
- **canalicular** - week 16 - 25
- **terminal sac** - week 24 - 40
- **alveolar** - late fetal - 8 years (Latin, *alveus* = cavity or hollow)



Lung alveoli development cartoon

Fetal lung volume

Each human lung volume as determined by ultrasound and matched to gestational age ^[1]

Weeks (gestational)	Volume (ml)
12 to 13	0.05
19 to 22	0.5
29 to 32	1.9

Pleural Cavity

- anatomical body cavity in which the lungs develop and lie.
- pleural cavity forms in the **lateral plate mesoderm** as part of the early single **intraembryonic coelom**.
- This cavity is initially continuous with pericardial and peritoneal cavities and form initially as two narrow canals.
 - later becomes separated by folding (pleuropericardial fold, pleuroperitoneal membrane) and the later formation of the diaphragm.
- **pleuropericardial fold** - (pleuropericardial membrane) An early embryonic fold which restricts the communication between pleural cavity and pericardiac cavity, contains both the cardinal vein and phrenic nerve.
- **pleuroperitoneal membrane** - An early embryonic membrane that forms inferiorly at the septum transversum to separate peritoneal cavity from pleural cavity.

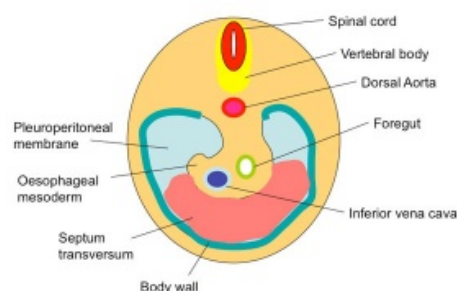
Pleura

- **serous membrane** covers the surface of the lung and the spaces between the lobes.
- arranged as a closed invaginated sac.
- two layers (**pulmonary, parietal**) continuous with each other, the potential space between them is the **pleural cavity**.

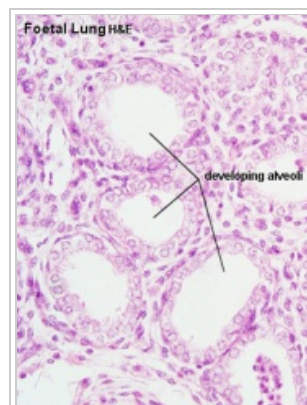
Diaphragm

- Not respiratory tract but musculoskeletal development, there are **5 embryonic elements** that contribute to the diaphragm.

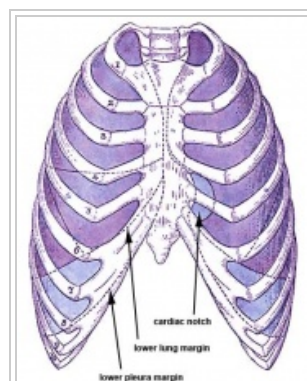
Developing Diaphragm



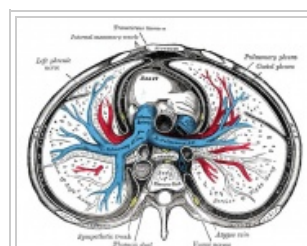
1. septum transversum- central tendon
2. 3rd to 5th somite- musculature of diaphragm
3. ventral pleural sac- connective tissue
4. mesentery of oesophagus- connective tissue around oesophagus and IVC
5. pleuroperitoneal membranes- connective tissue around central tendon



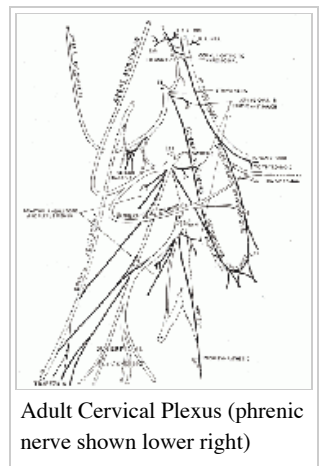
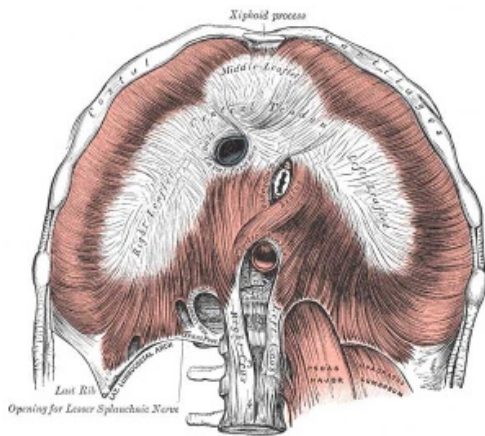
Fetal lung histology



pleura



pleura



- Innervation of the human diaphragm is by the **phrenic nerves**
 - arising from the same segmental levels from which the diaphragm skeletal muscles arise, segmental levels C3 to C5.
- The paired phrenic nerves are **mixed nerves**
 - motor neurons for the diaphragm
 - sensory nerves for other abdominal structures (mediastinum, pleura, liver, gall bladder).

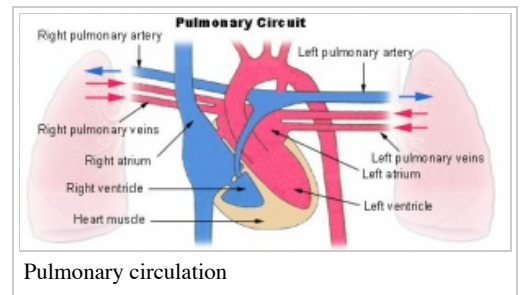
Pulmonary Circulation

- the pulmonary system not "functional" until after birth
- pulmonary arteries - 6th aortic arch arteries
- pulmonary veins - are incorporated into the left atrium wall
- bronchial arteries - branches from dorsal aorta

Fetal

Fetal Respiratory Movements

- Fetal respiratory movements (FRM) or Fetal breathing movements (FBM) are regular muscular contractions occurring in the third trimester.
- preparing the respiratory muscular system for neonatal function.
- may also have a role in late lung development.



Pulmonary circulation

The First Breath

- The respiratory system does not carry out its physiological function (gas exchange) prenatally and remain entirely fluid-filled until birth.
- At birth, fluid in the upper respiratory tract is expired and fluid in the lung aveoli is rapidly absorbed this event has also been called "dewatering of the lung".
 - The lung epithelia has to now rapidly change from its prenatal secretory function to that of fluid absorption.

The exchange of lung fluid for air leads to:

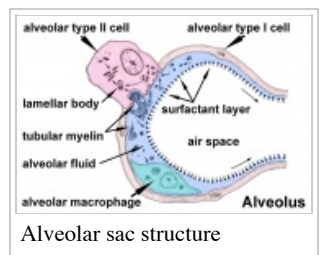
- fall in pulmonary vascular resistance
- increase in pulmonary blood flow
- thinning of pulmonary arteries (stretching as lungs increase in size)
- blood fills the alveolar capillaries

In the heart - pressure in the right side of the heart decreases and pressure in the left side of the heart increases (more blood returning from pulmonary).

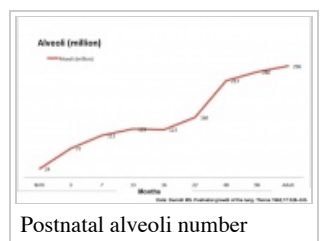
Postnatal

Alveoli

- At birth about 15% of adult alveoli number have formed
 - 20 - 50 million to in the adult about 300 million.
- remaining subdivisions develop in the first few postnatal years
- Alveoli Number



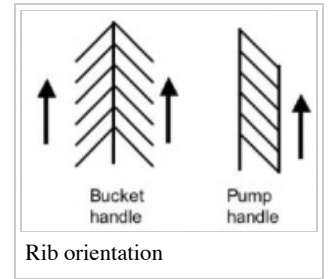
Alveolar sac structure



Postnatal alveoli number

Respiratory Rate

- neonatal rate is higher (30-60 breaths/minute) than adult (12-20 breaths/minute).
 - tachypnea - (Greek, rapid breathing) an increased respiratory rate of greater than 60 breaths/minute in a quiet resting baby



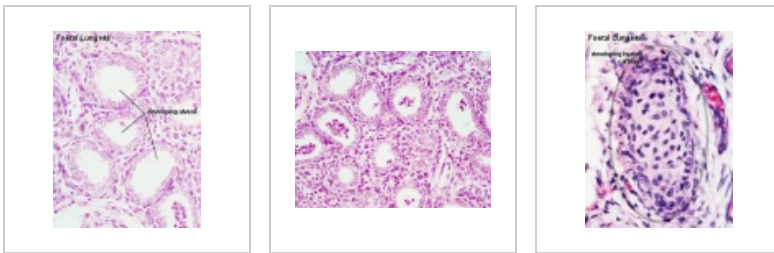
Age	Rate (breaths/minute)
Infant (birth - 1 year)	30 - 60
Toddler (1 - 3 years)	24 - 40
Preschool (3 - 6 years)	22 - 34
School age (6 - 12 years)	18 - 30
Adolescent (12 - 18 years)	12 - 16

Rib Orientation

- Infant rib - is virtually horizontal, allowing diaphragmatic breathing only.
- Adult rib - is oblique (both anterior and lateral views), allows for pump-handle and bucket handle types of inspiration.

Histology

Fetal Histology



late canalicular

unlabeled late canalicular

Hyaline cartilage

Fetal Respiratory: late canalicular | unlabeled late canalicular | Hyaline cartilage | Respiratory Histology

Adult Histology

(I will not be going through these images in the lecture)



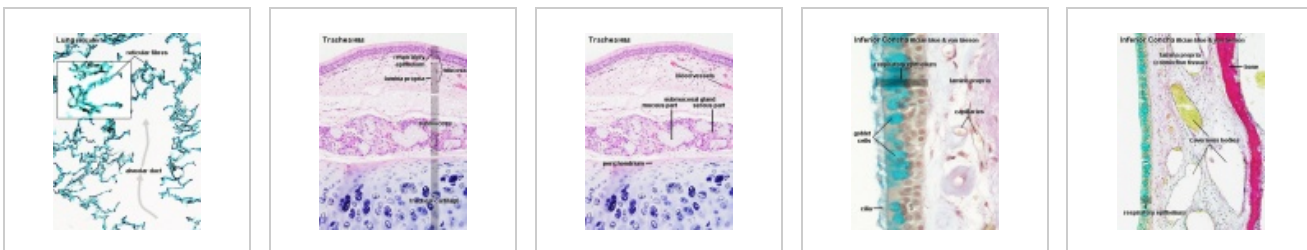
Bronchiole

labeled lung

Alveolar Duct

Alveoli

Alveoli Elastin



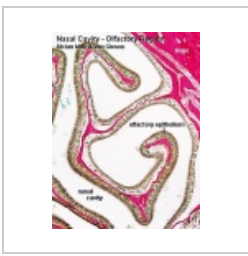
Lung Elastin

Trachea 1

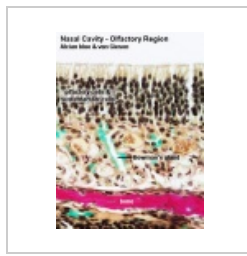
Trachea 2

Respiratory Epithelium

Respiratory Epithelium



Olfactory Epithelium



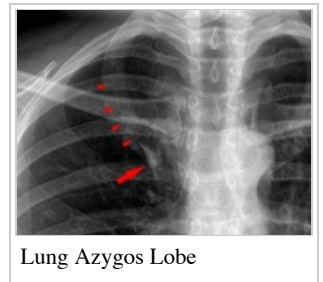
Olfactory Epithelium

Respiratory Histology: Bronchiole | Alveolar Duct | Alveoli | Alveoli Elastin | Trachea 1 | Trachea 2 | labeled lung | unlabeled lung | Respiratory Bronchiole | Lung Reticular Fibres | Nasal Inferior Concha | Nasal Respiratory Epithelium | Olfactory Region overview | Olfactory Region Epithelium

Respiratory Tract Abnormalities

Respiratory System - Abnormalities

- **Meconium Aspiration Syndrome** - (MAS) Meconium is the gastrointestinal contents that accumulate in the intestines during the fetal period. Fetal stress in the third trimester, prior to/at/ or during parturition can lead to premature meconium discharge into the amniotic fluid and subsequent ingestion by the fetus and damage to respiratory function. Damage to placental vessels meconium myonecrosis may also occur.
- **Newborn Respiratory Distress Syndrome** - Hyaline Membrane Disease (membrane-like substance from damaged pulmonary cells), absence of surfactant, if prolonged can be irreversible, intrauterine asphyxia, prematurity and maternal diabetes medline plus (<http://www.nlm.nih.gov/MEDLINEPLUS/ency/article/001563.htm>) | eMedicine (<http://www.medscape.com/article/976034-overview>)
- **Tracheoesophageal Fistula** - Tracheo-Oesophageal Fistula, Oesophageal Atresia - Oesophageal Atresia with or without tracheo-oesophageal fistula **Fistula** - an abnormal communication between 2 structures (organs, vessels, cavities) that do not normally connect.
- **Lobar Emphysema** (Overinflated Lung) - There is an overinflated left upper lobe There is a collapsed lower lobe The left lung is herniating across the mediastinum
- **Congenital Diaphragmatic Hernia** - (1 in 3,000 live births) Failure of the pleuroperitoneal foramen (foramen of Bochdalek) to close (left side), allows viscera into thorax -Intestine, stomach or spleen can enter the pleural cavity, compressing the lung. rare (Morgagni hernia) -an opening in the front of the diaphragm. GeneReviews (<http://www.ncbi.nlm.nih.gov/books/NBK1359>)
- **Azygos Lobe** - Common condition (0.5% of population). The right lung upper lobe expands either side of the posterior cardinal. There is also some course variability of the phrenic nerve in the presence of an azygos lobe.
- **Congenital Laryngeal Webs** - Laryngeal abnormality due to embryonic (week 10) incomplete recanalization of the laryngotracheal tube during the fetal period. Rare abnormality occurring mainly at the level of the vocal folds (glottis).
- **Bronchopulmonary Dysplasia** - A chronic lung disease which can occur following premature birth and related lung injury. Most infants who develop BPD are born more than 10 weeks before their due dates, weigh less than 1,000 grams (about 2 pounds) at birth, and have breathing problems.
- **Asthma** - Flow limitation during tidal expiration in early life significantly associated with the development of physician-diagnosed asthma by the age of 2 years. Infants with abnormal lung function soon after birth may have a genetic predisposition to asthma or other airway abnormalities that predict the risk of subsequent lower respiratory tract illness. PMID 8176553
- **Cystic Fibrosis** - Inherited disease of the mucus and sweat glands, causes mucus to be thick and sticky. Clogging the lungs, causing breathing problems and encouraging bacterial growth. (Covered elsewhere in the course)
- **Environmental Factors** see recent review below.



Lung Azygos Lobe

Mark D Miller, Melanie A Marty **Impact of environmental chemicals on lung development.** Environ. Health Perspect.: 2010, 118(8);1155-64 PMID:20444669

"Out of your element" respiratory terms

Glossary Links

A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z | Numbers | Symbols

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Categories: Respiratory | Endoderm

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