Chapter 2
Development and anatomy of the fetal lungs and thoracic wall

In this chapter emphasis will be placed on the normal development and anatomy of the fetal lungs and thoracic wall using conventional two-dimensional real-time ultrasound. Colour coded Doppler has been studied extensively in the context of normal cardiac anatomy. This will not be discussed in this thesis. Lately, the introduction of more refined colour coded Doppler imaging systems has opened the possibility of investigating the arterial and venous pulmonary circulation[21].

2.1.1 Developmental aspects of the lungs

In the human, development of the fetal lung can be divided into five sequential phases with a gradual transition between each subsequent stage[18,27,32]. It is important to realise that this division is somewhat artificial as the process of development is a continuum and not a series of steps. Therefore, it is important to remember that the boundaries between these phases are not sharp, but that within each lung (and also when fetuses of the same age are compared) development may lead or lag behind the "normal".

The following stages can be recognized:

I. the embryonic period (conception - 5th week of gestation): the lung bud develops as a ventral diverticulum from the primitive foregut and is lined with endodermally derived epithelium;

II. the pseudoglandular period (5th - 17th week gestation): surrounding mesenchyme induces growth and development of the bronchial tree, which results in a series of dichotomous branchings of the initial bud (trachea) up to the level of the terminal bronchioles. The mesenchyme surrounding the lung bud diverticulum differentiates to form the early rudiments of cartilage, connective tissue, muscle, blood vessels, and lymphatics. Recently, it has become clear that these first two periods are histologically similar and should therefore be referred to as the pseudoglandular period[17];

III. the canalicular phase (13th - 24th week gestation): differentiation of airways with enlargement of the lumina and gradual thinning of the cuboidal epithelial lining, ingrowth and proliferation of a capillary network and further forming of cartilage, muscle and lymphatics. An overlap between this phase and the pseudoglandular period occurs because the cranial segments of the lungs mature faster than the caudal ones.

IV. the terminal sac or saccular phase (24th - 30th week gestation) is characterized by further differentiation of the respiratory portion of the lung with the transformation of some terminal bronchioles into respiratory bronchioles. An increase in respiratory exchange surface area occurs because thin-walled terminal sacs (primitive alveoli) develop at the end of the respiratory bronchioles;

V. the alveolar phase (30th week - term): further differentiation of epithelium into type I and II pneumocytes, appearance of surfactant, thinning of blood-gas barrier (alveoli), progressive branching of the respiratory airways. At the time of birth, the pattern of respiratory airway branching is complete, just as the pattern of conducting airway branching is completed by the end of the pseudoglandular phase.

Postnatal lung development is characterized by continuing lung growth with continued formation of alveoli until 8 years of age. Most rapid alveolar multiplications occurs during the first three years of childhood[9,37]. The increase in size of the lungs after birth thus results mainly from an increase in number of alveoli rather than from an increase in the size of the alveoli.

It is important to distinguish two processes in fetal lung development which are related though appear to be separately controlled, i.e., lung growth and lung maturation. Lung growth seems to be influenced primarily by physical factors (intrathoracic space, lung liquid volume and pressure, breathing movements, and amniotic fluid volume). Lung maturation has two components, structural and biochemical (surfactant). Structural maturation is regulated by physical factors, whereas biochemical maturation appears to be hormonally regulated by endocrine organs (pituitary, adrenal, thyroid)[11].

2.1.2 Normal sonographic appearance and anatomy of the fetal lungs

The fetal lungs are routinely visualized on ultrasound by the mid second trimester as two more or less echogenic paracardiac structures that fill the space between the heart and the rib cage. Optimal visualization may, however, be hampered by interference or overprojection of the fetal thoracic cage.

Normally, the cardiac position and axis both remain constant throughout the second and third trimester. Since intrathoracic lesions often displace the heart or mediastinum, determination of the cardiac position and axis provides useful information on the evaluation of the normal and abnormal fetal thorax[6]. The four-chamber view of the heart best evaluates the cardiac position and axis. Therefore, deviation of the fetal heart from the expected normal position warrants a search for either an abnormal intrathoracic mass or fluid collection, or a cardiac anomaly.

2.1.3 Lung biometry

Fetal lung biometry can be hampered by the bell-shaped form of the thorax which can make uniform and reproducible measurements difficult to obtain. However, transverse examination of the thorax, preferably at the level of the four-chamber view of the heart seems to provide sufficient reproducibility[29]. Others have included longitudinal thoracic measurements to improve accuracy[5], or compared thoracic and abdominal circumference[7,19]. More recently, reports have been published on fetal thoracic and pulmonary dimensions in the evaluation of thoracic and pulmonary growth[35], and on the measurement of fetal lung area as an indicator of lung weight in the evaluation of fetal lung growth[24].

The importance of the measurement of fetal chest circumference in the antenatal prediction of pulmonary hypoplasia has been addressed by several authors[19,29,30]. However, although useful, both a low fetal thoracic circumference and a low thoracic circumference to abdominal circumference ratio unfortunately are late indicators of pulmonary hypoplasia.

Newer techniques, including three-dimensional ultrasonography and magnetic resonance imaging, enable volume measurements of the fetal lung[2,8,14,23]. Until now, only data regarding uneventful pregnancies have been published[2,8,14,23].

2.1.4 Lung echogenicity

The fetal lungs create homogeneous mid-range echoes which vary along gestation. Their uniform echogenicity increases in comparison to that of fetal liver with increasing gestational age[33,36]. Subtle differences in echogenicity, however, have not been proven to be useful in the prenatal prediction of fetal pulmonary maturity[4,12,13]. More recently, magnetic resonance imaging has been proposed as a method of noninvasively assessing fetal lung maturity[38].

An increased echogenicity of fetal lung tissue has been described in several pathological conditions, i.e., microcystic congenital cystic adenomatoid malformation (CCAM), bronchopulmonary sequestration, diaphragmatic hernia, mediastinal teratoma[28], and in cases of tracheobronchial tree obstruction[10]. Also, several complete in-utero disappearances of hyperechogenic lung lesions have been reported[20,34], although this does not always signify an improvement in prognosis, especially when there is an association with fetal hydrops, polyhydramnios, mediastinal shift, and cystic lesions[25,34]. Most recently, cases of resolution of fetal lung hyperechogenicity, in the absence of CCAM or bronchopulmonary sequestration and resulting in the birth of normal infants have been described, postulated to be due to resolution of retention of a mucous plug in the tracheobronchial tree[1,26]. This mechanism was recently scrutinized[34], predominantly because of the observed reduction in size with diminishing and then resolving echogenicity, the absence of plugs in pathological reports of fetuses terminated because of these lesions and because of the non-viscous composition of lung fluid. The same authors stress that fetal lung biopsy is of limited value in the prenatal evaluation of hyperechogenic lung lesions[34].

2.1.5 Colour coded Doppler imaging of the normal pulmonary circulation

Early development of the pulmonary circulation starts within the pseudoglandular period, while further development occurs in the canalicular phase.

Pulmonary artery flow velocity waveforms have been recorded in normal first trimester pregnancies[39], as well as in normal second trimester fetuses[3]. Groenenberg et al.(1989) reported data on pulmonary artery waveforms in normal and growth-retarded third trimester fetuses[15].

Doppler ultrasound using colour Doppler or power angiographic techniques allows recording of venous and arterial lung flow velocity waveforms as far as the periphery of the lungs[21] (an example is shown on page 73). The pulmonary venous flow velocity waveform consists of a systolic and early diastolic forward flow component and a late diastolic forward component coincident with atrial contraction, equal to that established postnatally in humans. It was suggested that pulmonary venous flow is determined by suction from the pulmonary veins into the left atrium and left ventricle[21]. Abnormal arterial flow velocity waveforms have been established in a case of proven lung hypoplasia[22].

2.2 Fetal thoracic wall

The thoracic wall is developed from paramedian mesodermal structures. Paired mesenchymal bars form laterally to the midline at 6 weeks' gestation, migrate to the midline and undergo progressive chondrification and fusion by about 9 weeks'gestation[16]. Towards the end of the embryonic period, a well-formed cartilagenous thoracic cage is present, and the ribs assume a horizontal position rather than the sloping orientation seen in adult life. Early in the fetal period, from the 9th week onwards, a primary ossific center appears near the future angle of each rib, and enchondral ossification occurs mostly during the first trimester. The ventral ends of the cartilagenous ribs remain as the costal cartilages[31].

The fetal ribs are usually easy to identify on ultrasound examination and should represent smooth, curving lines of echoes when viewed in their length and a row of echogenic dots when viewed in transverse cross section. The rib cage should gradually enlarge toward the fetal abdomen in a bell shape. The skin line of the chest and abdomen should be continuous and should have no abrupt angles or disruptions. The biometry of the fetal thoracic cage has been addressed in the paragraph on lung biometry (paragraph 2.1.3).

2.3 References

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