RESPIRATORY ILLNESS IN CHILDREN

THIRD EDITION

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PREFACE

The first edition of *Respiratory Illness in Children* was published in 1975 with Dr Howard Williams as the senior author. The aim of the book was to present a comprehensive account of illnesses affecting the respiratory tract of children based on the authors' practice, experience and research. It emphasized in particular epidemiology, physiology and psychosocial factors in disease.

Since 1975, Howard Williams has retired from active clinical practice in paediatric thoracic medicine and the authors of this edition wish to record their great debt to him for his pioneering work in the field. Two of us (P.D.P. and L.I.L.) directly benefited over many years from his wisdom, perspective and outstanding clinical skills.

Our understanding of many chest diseases in children has changed considerably in the 8 years since the second edition was published. This has led to substantial rewriting of much of the book. The chapters on epidemiology of respiratory infection, asthma and cystic fibrosis have been almost completely updated with new information, and the less common lung diseases have been combined into one chapter entitled 'Miscellaneous Lung Diseases'. A new chapter has been added on tumours of the chest wall, mediastinum and lungs.

Without the assistance of our colleagues in the Department of Thoracic Medicine, Royal Children's Hospital and Department of Respiratory Medicine, Princess Margaret Hospital for Children, this book could not have been written. We wish to thank our secretaries, Mrs J. Saravanamuttu and Ms B. Crossland for their unfailing assistance.

CONTENTS

1 / LUNG GROWTH AND DEVELOPMENT

An understanding of pulmonary function in health and disease as well as an explanation for many of the developmental anomalies is enhanced by a knowledge of the pre- and postnatal growth and development of the lung. Growth and development of the lung starts soon after conception and continues until somatic growth ceases (Fig. 1.1). The division into pre- and postnatal phases is arbitrary but nevertheless does allow one to consider the important differences in extent of development and in functional demands between intrauterine and extrauterine existence.

PRENATAL

Four stages of human fetal lung development are recognized:

1 Embryonic stage.
2 Pseudoglandular stage.
3 Canalicular stage.
4 Terminal sac stage.

During the embryonic period the lung primordium is formed, while the pattern of bronchial branching occurs in the pseudoglandular stage. In the canalicular stage the branches elongate and the lining epithelium becomes flattened, while during the terminal sac stage thin-walled air passages are formed. The peripheral structures, the alveoli, do not develop to any extent until after birth, when considerable remodelling and growth of the acinus takes place.

EMBRYONIC STAGE
(First 5 weeks after ovulation)

The lung develops as a ventral diverticulum from the primitive foregut during the fourth week of gestation. In the human, the laryngotracheal groove appears in the endodermal foregut when the embryo is 26 days old and evaginates to form the lung bud, which branches at 26–28 days. The lining of the whole respiratory system, including the airways and alveoli, arises from this endodermal bud.

PSEUDOGLANDULAR STAGE
(5–16 weeks gestation)

The major airways develop during this period through dichotomous branching of the lung bud diverticulum. The mesenchyme condenses around the branching lung bud and will differentiate into the future cartilage, muscle, connective tissue, pulmonary blood vessels and lymphatics. Budding and branching of the lung bud occurs only in the presence of the surrounding mesenchyme, indicating an interaction between the two. The development of an epithelial organ such as the lung depends on interactions between the epithelial primordium and its underlying mesoderm. When these tissues are cultured separately *in vitro* neither component assumes its characteristic morphology. The isolated epithelium of a lung bud separated from its mesoderm continues to grow but bronchial branches fail to form; likewise in the absence of the epithelium the mesoderm does not develop its own structural organization.

The branching of the lung bud epithelium continues until the 16th week of gestation and results in a tree of narrow tubules with thick epithelial walls, separated from each other by poorly differentiated mesenchyme. This structure causes the stage of development to be called the pseudoglandular stage. At 16 weeks of gestation all the branches of the conducting portion of the tracheobronchial tree, from the trachea up to and including the terminal bronchioles, are established. These branches may increase in size with further lung

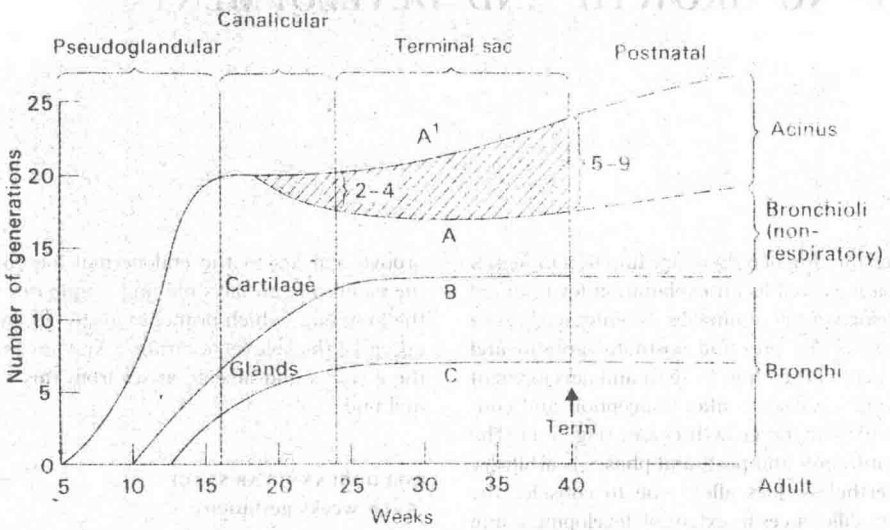

Fig. 1.1 Intrauterine and postnatal development of the bronchial tree. The number of bronchial generations is represented by line A, respiratory bronchioles and terminal sacs by the shaded area A–A_1. B represents the extension of cartilage along the bronchial tree, and C the extension of mucous glands. (After Bucher and Reid 1961 [1].)

growth, but after the 16th week of gestation no new branches are formed.

CANALICULAR STAGE
(16–24 weeks gestation)

This stage is characterized by the proliferation of the mesenchyme and the development of a rich blood supply within it. The lumina of the epithelial tubes widen and flattening of the lining epithelium occurs, giving the lung the appearance of a group of canals. The proliferation of the vascular supply, together with the relative decrease in the mesenchyme, brings the capillaries closer to the airway epithelium. Capillaries protrude into the epithelium and at this stage occasional areas of blood–airway interaction may be seen. Progressive thinning of the epithelium and protrusion of the capillaries gives rise to more areas of close approximation of the capillary lumen to the airway surface. At the end of the canalicular period respiration is possible.

TERMINAL SAC STAGE
(6–9 months gestation)

During this stage further differentiation of the respiratory portion of the lung occurs, with transformation of some terminal bronchioles into respiratory bronchioles and the appearance distally of terminal clusters of airways called saccules (Fig. 1.2). They are not true alveoli because they are larger and lack the smooth outline, but can function for gas exchange since the thickness of the blood–gas barrier is similar to that of adult alveoli.

Throughout gestation the epithelial thickness decreases and does so to a greater extent distally, so that at birth the proximal airways are lined by pseudostratified columnar epithelium, the intermediate ones are lined by cuboidal epithelium and the more distal airways by a flattened epithelium. At birth the epithelial lining of the saccule is thin and continuous with the type I and type II epithelial cells which first become discernible during the sixth month of gestation.

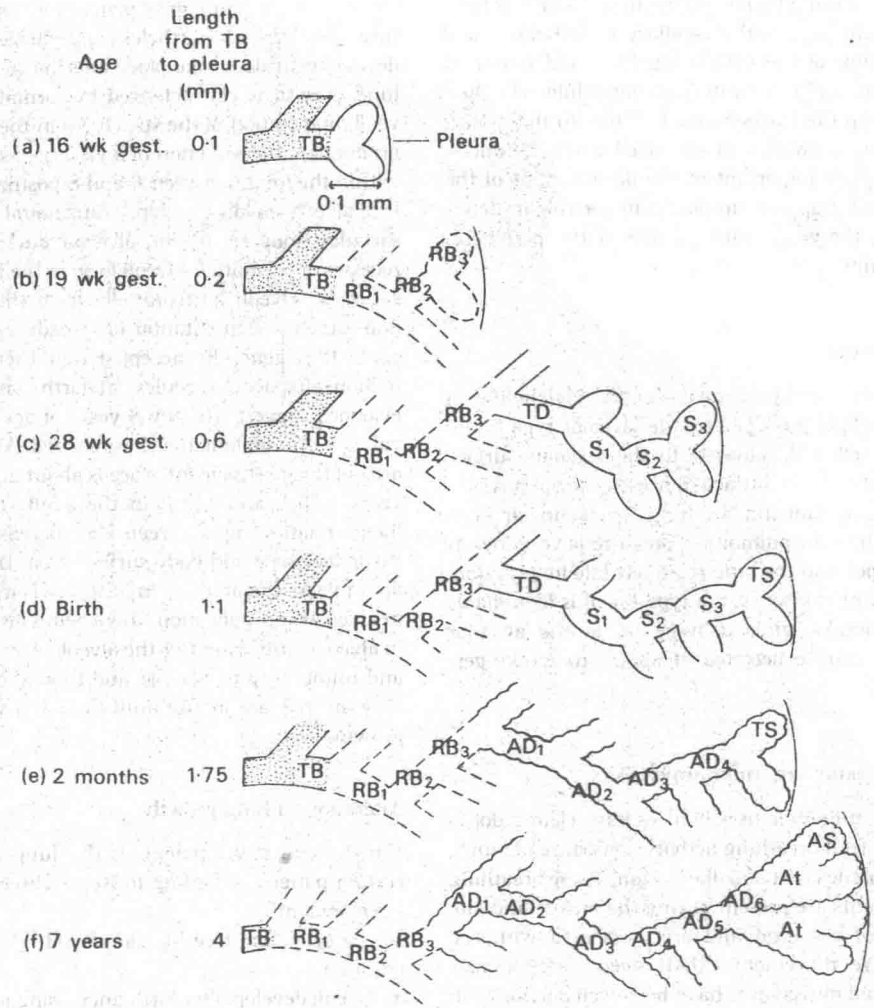

Fig. 1.2 Diagrammatic representation of the acinus at six stages of development. At all ages airway generations are drawn the same length, so that increase in length represents an increase in generations. A given generation may be traced down the same vertical line, permitting remodelling in its structure to be followed. Actual increase in size is shown by the length from terminal bronchiolus (TB) to pleura. RB = respiratory bronchiolus, TD = transitional duct. S = saccule, TS = terminal saccule. AD = alveolar duct, At = atrium, AS = alveolar sac. (From Reid 1979 [2].)

Prenatal lung function

1 Fetal lung liquid.
2 Surfactant.
3 Intrauterine breathing movements.

FETAL LUNG LIQUID (FLL)

The lungs of the fetus are filled with fluid. The volume is similar to that of the functional residual capacity of a newborn infant; about 30 ml/kg body

weight. The fluid is formed by the transfer of solutes and water across the capillary endothelium and epithelium of the developing lung and is not as earlier thought, aspirated amniotic fluid. The fluid moves up the tracheobronchial tree to the mouth where it is swallowed or added to the amniotic fluid. FLL is important in the development of the lung and it appears to play a major role in determining the shape and volume of the peripheral lung units.

SURFACTANT

Surfactant is dipalmitoyl phosphatidylcholine, a phospholipid produced by the alveolar type II epithelial cell and delivered to the alveolar surface where it forms a surface film with special physical properties, allowing the lungs to retain air even when the transpulmonary pressure is very low. It first appears in the lung relatively late in gestation. Surfactant storage in the type II cell is identifiable at 24 weeks while delivery on to the alveolar surface can be detected at about 30 weeks gestation.

INTRAUTERINE BREATHING MOVEMENTS

Studies in lamb fetuses *in utero* have clearly documented fetal breathing activity consisting of movements of the chest and diaphragm. These breathing movements are present during the middle and late period of gestation and are associated with the rapid eye movement (REM) sleep state. Similar chest wall movements have been well documented in human fetuses using ultrasonic techniques. The reasons for these movements are not clear. There is speculation that the fetus is 'practising for extrauterine life'. It is also possible that the movements play some role in the flow of the FLL.

POSTNATAL GROWTH

The airways are fully mature in their structure and branching pattern at birth and there are no major changes in the number of generations or in structure after birth. Nevertheless, a great deal of lung development does take place after birth. Postnatal lung growth is characterized by formation of alveoli, maturation of the structures in the lung and production and secretion of a variety of substances within the lung. Between 6 and 8 postnatal weeks true alveoli rapidly develop. Transitional ducts and saccules elongate to form alveolar ducts. Shallow recesses or premature alveoli form in the wall of the saccules. Alveoli form initially from the saccules and later by segmentation of already existing alveoli. It is generally accepted that there are 20 million airspaces (saccules) at birth, and present evidence suggests that by 8 years of age the adult value of 300 million alveoli is reached. At birth the area of the air–tissue interface is about 2.8 m^2, at 8 years 32 m^2, and 75 m^2 in the adult. There is a linear relationship between the increase in air–tissue interface and body surface area. During the first 3 years the increase in lung size is mainly due to alveolar multiplication, there being little change in alveolar size. After this the alveoli increase in size and number up to 8 years and thereafter there is only an increase in size until the chest wall stops growing.

Alteration in lung growth

Growth and development of the lung follows a certain pattern according to Reid's three 'Laws of Development':

1 The bronchial tree has developed by 16 weeks gestation.

2 Alveoli develop after birth, increasing in number until 8 years of age and then increasing in size until completion of growth of the chest wall in young adulthood.

3 The growth of blood vessels supplying the conducting airways (preacinar) parallels the development of the airways, while development of the intraacinar vessels parallels alveolar development. Muscularization of the intraacinar arteries lags behind the appearance of new arteries.

Different effects on lung growth can occur depending on the timing of an insult or injury, e.g. congenital diaphragmatic hernia. If the hernia develops before 16 weeks the number of bronchial

divisions is reduced. However, since the hernia is also present during the later stages of lung growth airway size is also diminished and the number of saccules, alveoli, preacinar and intraacinar blood vessels are decreased. The lungs of infants with renal agenesis are hypoplastic both in airway and alveolar development. A similar picture is seen in other situations where oligohydramnios has been present, indicating that the presence of a critical amount of amniotic fluid is necessary for normal lung growth and maturation. Acquired disease in childhood will mainly affect alveolar number and size and associated blood vessels. Although the airways may be obliterated or dilated their complement is already complete.

DEVELOPMENT OF THE PULMONARY CIRCULATION

The adult lung has a double arterial supply and a double venous drainage. The pulmonary arteries carry most of the pulmonary blood flow, while the bronchial arteries carry oxygenated blood and supply the conducting airways and pulmonary blood vessels. The two circulations communicate by capillary anastomoses proximal to the terminal bronchiole. Blood from the pulmonary arterial system, together with most of the blood from the bronchial arterial system, drains to the pulmonary veins and into the left atrium. The remaining bronchial arterial blood flow drains into the bronchial veins and the azygos or systemic intercostal veins and thus into the right atrium.

Prenatal growth and development of the pulmonary blood vessels is closely linked to that of the bronchial tree. Six pairs of aortic arches, connecting a ventral aortic sac to the right and left dorsal aortas appear in turn during the fifth week of gestation. The main pulmonary artery and its two main branches, develop from the left-sided sixth arch. At about 37 days gestation the aortic sac is divided so that only blood from the right ventricle flows to the sixth arch and the lungs. At the earliest stage of lung bud formation, the microcirculation drains into a systemic venous plexus which is common to the lung and foregut but at 4–5 weeks an outgrowth from the atrial region connects with and separates the pulmonary venous system.

During the pseudoglandular and canalicular periods the pulmonary arteries develop alongside the airways with branching at each airway division (preacinar arteries). By 16 weeks gestation all preacinar arteries are present. In addition each of the so-called conventional branches gives off 2–4 'supernumerary' arteries which penetrate and supply the adjacent lung without being distributed according to the pattern of airway subdivision.

In the later weeks of gestation (after 16 weeks), airways develop beyond the terminal bronchioles, first respiratory bronchioles and then saccules. Arteries develop alongside them and are called intraacinar arteries. During childhood as new alveolar ducts and alveoli appear and enlarge, additional arteries form. Few new conventional vessels appear but supernumeraries increase considerably and are more numerous at acinar levels. They supply the alveoli directly.

During fetal life the large intrapulmonary arteries have the same structure as the main pulmonary artery, a lamina media of elastic and muscle fibres with adventitia and intima. They are termed elastic arteries because there are at least seven elastic laminae. The muscle cells lie between the elastic laminae. Progressing peripherally the elastic laminae decrease in number to between four and seven, and are termed transitional. More peripherally still the elastic laminae are replaced by a muscular structure. Along the pathway the wholly muscular wall becomes thinner and eventually the muscle becomes incomplete and is present only as a spiral (partially muscular). Further to the periphery, the muscle disappears.

In the fetus the arteries are more muscular than in the adult. The wall thickness of a given sized artery in the fetus is double that in the adult. At birth the blood flow to the lung increases as pulmonary vascular resistance falls. The drop in pulmonary artery pressure after birth is associated with a decrease in wall thickness of the pulmonary arteries. Because of the rapid initial drop in resistance there must be dilatation of at least some part of the vascular bed. Studies have shown that by 3 days of age the small vessels had decreased to adult

thickness, by 4 months most vessels had done so and by 10 months all were of adult thickness [2].

CHANGES IN PULMONARY CIRCULATION AT BIRTH

The distribution of blood flow in the fetal circulation is determined in large part by the very high pulmonary vascular resistance and the presence of communications between the systemic and pulmonary circulations.

During fetal life only about 12% of the combined cardiac output goes to the lungs. Because of the very high resistance, the fetal pulmonary circulation is a high pressure low flow system. At birth two important events take place: (a) removal of the low-resistance placental circulation; and (b) reduction in the pulmonary vascular resistance. This leads to the closure of the foramen ovale and ductus arteriosus and to the separation of the pulmonary and systemic circulations. The major factor causing pulmonary vasodilation and decreased resistance is ventilation of the lungs. Both the physical expansion of the lungs and the increase in alveolar P_O, contribute to the vasodilation. The pulmonary arterial systolic pressure decreases from 70–75 mmHg to 30 mmHg within the first 24 hours. Thereafter the pressure slowly decreases to reach adult values (9 mmHg) several weeks to months later.

Alterations in the normal postnatal growth and remodelling of the pulmonary circulation occur in response to hypoxia, persistent pulmonary hypertension of the newborn infant or an augmented pulmonary blood flow resulting from a congenital heart lesion. These conditions delay or prevent the normal decrease in pulmonary vascular resistance occurring after birth. The ensuing pulmonary hypertension is characterized morphologically by retention of the fetal structures of the pulmonary vasculature with retardation or absence of the normal postnatal thinning of pulmonary arterial smooth muscle. In addition smooth muscle extends further into smaller arteries than normal.

ONSET OF RESPIRATION

Extrauterine respiration appears to be initiated by the interaction of a variety of triggering mechanisms. Birth 'asphyxia' (hypoxia and hypercapnia) is probably the strongest stimulus for the onset of breathing. Other factors such as temperature change, pain and tactile stimuli probably facilitate or interact to successfully establish respiration.

During a vaginal delivery the thoracic cage is compressed to pressures of 60–100 cm H_2O as it passes through the birth canal. The subsequent recoil of the chest wall is thought to produce a small passive inspiration of air. A significant effort is needed to start breathing and negative pressures of 40–70 cm H_2O have been recorded during the first breaths. Following inspiration the infant often makes an expiratory effort against a closed glottis thus raising the intrathoracic pressure to as much as 60 cm H_2O. This positive pressure could aid in forcing liquid from the air spaces into the pulmonary interstitium and the vascular lymph channels. The volume of the first inspiration varies from 2–16 ml and of this about 20–40% remains after expiration, the first stage in forming the functional residual capacity (FRC). It probably takes a few hours for the FRC to be established.

The elastic recoil of the thorax opposing either expansion or compression in newborn infants is extremely low, due to the very soft bony structure of the rib cage. Because of the small force opposing pulmonary elastic recoil, the stabilizing effect of surfactant is particularly important in the retention of a portion of the inspired air in order to establish the FRC.

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2 / NEONATAL RESPIRATORY DISORDERS

Neonatal respiratory disorders comprise a wide variety of different conditions. It is not the intention in this chapter to discuss all of these as there are many excellent reviews available [1–5]. Rather, a clinical approach to the newborn with respiratory distress will be presented, followed by a discussion of some of the more common conditions and of the chronic respiratory disorders seen in early infancy that have their onset in the neonatal period.

NEONATAL RESPIRATORY DISORDERS—A CLINICAL APPROACH

Respiratory distress in the newborn infant is a clinical diagnosis made when the following major clinical signs are present.

1 Tachypnoea (greater than 60 breaths per minute).
2 Expiratory grunting.
3 Cyanosis (in room air).
4 Retraction of the chest wall.

Each sign on its own is not diagnostic of respiratory distress and may occur transiently in normal infants. However, when respiratory distress is in evidence, two or more of the signs are usually present and the diagnosis is not difficult. The clinical diagnosis of respiratory distress is not sufficient and further assessment is mandatory in order to define the cause of the distress so that appropriate therapy may be instituted.

The newborn infant has a limited ability to respond to a variety of stimuli, thus not all respiratory distress is due to pulmonary disease nor does every cyanotic rapidly breathing infant have hyaline membrane disease. A simple working classification of causes of respiratory distress is shown in Table 2.1. All the possible causes of respiratory distress are not listed but the approach to the differential diagnosis should be evident. There are obviously factors that would tend to point in one direction or another and these need to be considered when assessing the infant. For example, hyaline membrane disease would be the most likely diagnosis in a small preterm infant. The presence of meconium staining in a post-term baby would

Table 2.1 Clinical diagnosis of respiratory distress (tachypnoea, grunting, cyanosis, retractions).

Respiratory		Non-respiratory		
Pulmonary	Extrapulmonary	Cardiovascular	Central nervous system	Metabolic
Hyaline membrane disease	Choanal atresia	Congenital heart disease	Haemorrhage	Hypoglycaemia
Aspiration syndromes	Glottic disorders	Persistent fetal circulation	Infection	Hypothermia
Neonatal pneumonia	Diaphragmatic hernia	Blood loss		Acidosis
Pneumothorax	Eventration of the diaphragm	Twin–twin transfusion		
Transient tachypnoea of the newborn	Tracheo-oesophageal fistula			
Pulmonary haemorrhage	Phrenic nerve palsy			
Congenital lung disorders: Lobar emphysema, Aplasia, hypoplasia				

make the diagnosis of aspiration more likely. Prolonged rupture of the fetal membranes would raise the possibility of pneumonia. Certain basic investigations are essential in evaluating these infants and the most important by far is a chest radiograph. The radiological appearance of many of the conditions listed in Table 2.1 are diagnostic. Other investigations would include blood chemistry, blood gases and blood cultures as well as electrocardiograph, echocardiograph and lumbar puncture in some infants. By using the simple approach, an aetiologiocal diagnosis is possible in the vast majority of infants presenting with respiratory distress. The specific diagnosis in some instances of congenital heart disease may require more detailed investigations such as cardiac catheterization.

Hyaline membrane disease (HMD)

Hyaline membrane disease is the most common cause of respiratory distress in the newborn infant. It occurs in about 0.5–1% of all deliveries and in about 10% of all preterm infants with a male : female ratio of 1.7 : 1.0. It is seen almost exclusively in preterm infants born before 37 weeks gestation and the more preterm the infant the greater the likelihood of developing HMD. It occurs more frequently in infants of diabetic mothers, the second of twins and is said to be more frequent following Caesarian section. However, it is likely that the degree of maturity of the infant and the indication for the Caesarian section are more important predisposing factors than the Caesarian section itself. Conditions that result in birth asphyxia, such as antepartum haemorrhage (if associated with preterm delivery), are probably also important in the pathogenesis of HMD. Some maternal conditions are thought to have a sparing effect, viz. conditions resulting in intrauterine growth retardation, maternal steroid therapy and at times prolonged labour following rupture of the membranes.

PATHOLOGY

Macroscopically the lungs are dark, liver-like in appearance and sink in water or formalin. Microscopically much of the lung appears solid due to the apposition of most of the alveoli walls. Scattered throughout are dilated air spaces, respiratory bronchioles, alveolar ducts and a few alveoli whose walls are lined with pink-staining 'hyaline' material. The capillaries are congested and there may be pulmonary oedema and lymphatic distension.

PATHOGENESIS

There seems little doubt that HMD is related to a relative deficiency of surfactant (see p. 4). Surfactant must not only be present at birth but must be capable of being regenerated at a rate equal to its disappearance. This implies that the alveolar type II cell must be functionally intact and viable. Tissue storage of surfactant is detectable at about 24 weeks gestation and delivery on to the alveolar surface occurs at about 30 weeks, but it is only at 35–36 weeks that adequate amounts are being produced. However, the timing is variable and adequate production may occur as early as 30 weeks or as late as 38 weeks. For an equivalent period of gestation, female infants have higher indices of pulmonary maturity than do male infants. This could account for the higher incidence of hyaline membrane disease in male infants [6]. Male infants also have a higher mortality.

A simplification of the basic pathogenesis of HMD is summarized in Fig. 2.1. Inadequate surfactant leads to progressive expiratory atelectasis. The lung compliance falls and the work of breathing increases. The resultant hypoxaemia and alveolar hypoventilation result in acidosis. The ensuing reduction in pulmonary blood flow and inhibition of the enzyme systems further impair surfactant synthesis and a vicious cycle results.

CLINICAL PICTURE

Some infants may appear normal at birth but many show evidence of intrapartum asphyxia with depressed Apgar scores and may require active resuscitation. Within minutes, even in those who appeared normal at birth, signs of abnormal respiration become evident. Initially it may just be tachypnoea but soon expiratory grunting and intercostal recession become evident and cyanosis may develop. If an infant has breathed

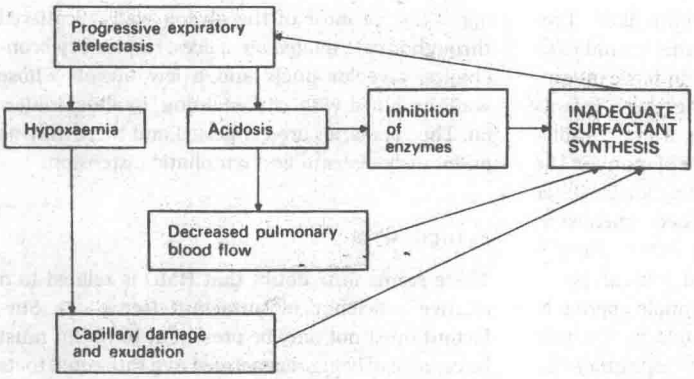

Fig. 2.1 The pathogenesis of hyaline membrane disease.

normally in all respects for the first few hours of life and then develops respiratory distress, it is most unlikely that the cause is HMD.

RADIOLOGICAL APPEARANCE

The radiological appearance is fairly characteristic (Fig. 2.2). There is a diffuse, fine reticulogranular pattern involving both lung fields with air bronchograms extending beyond the cardiac border out into the periphery of the lung (ground glass appearance). In infants with severe disease there may be a dense uniform granularity or even a 'white out' with the air bronchogram being the only visible lung markings.

NATURAL HISTORY

The natural history of the disease in the absence of assisted ventilation is characterized by progressive deterioration in the first 24–48 hours, the highest mortality being in the first 72 hours. Approximately 50% of all deaths occur within 24 hours, 70% within 48 hours and 90% within 72 hours [7]. If babies survive longer than 72 hours then recovery is the rule. In the majority there are no

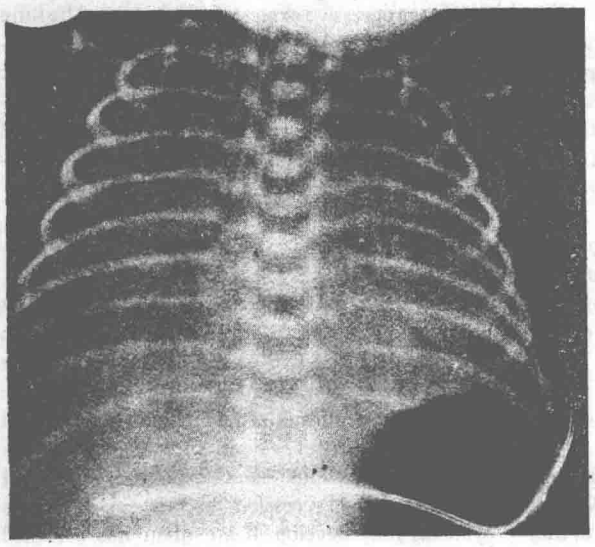

Fig. 2.2 Chest radiograph of an infant with hyaline membrane disease. Note the diffuse fine reticulogranular pattern and the air bronchogram.

long term sequelae. Some, particularly if they require ventilation with high pressures and a high concentration of oxygen, may develop bronchopulmonary dysplasia which is discussed on p. 18.

TREATMENT

Successful management of hyaline membrane disease encompasses many facets. It is not the intention to discuss these in detail but rather to outline the principles of treatment. Treatment is essentially supportive to allow time for spontaneous recovery of adequate surfactant production to occur and prevent and treat complications should they arise. The principles of supportive care are as follows:

1 *Oxygenation.* Attempts at maintaining adequate oxygenation will range from a simple increase in the environmental oxygen, through continuous positive airway pressure (CPAP), to intermittent positive pressure ventilation (IPPV). The deleterious effects of too much oxygen and the potential harmful effects of endotracheal intubation and IPPV need to be carefully balanced against the dangers of hypoxia.

2 *Electrolyte and acid–base status.* Maintenance of adequate but not excessive fluid intake, appropriate caloric needs and electrolyte balance as well as maintenance of acid–base status are required.

3 *Temperature control.* Maintenance of a thermal-neutral environment. i.e. a thermal environment in which oxygen consumption is at a minimum.

Initial attempts to introduce surfactant (dipalmitoyl lecithin, DPL) into the lungs of patients failed to produce convincing benefits. However, there was a resurgence of interest following the report of Fujiwara *et al.* [8] who demonstrated a marked improvement in oxygenation in ten ventilated babies with HMD after direct instillation of a solution of natural surfactant into the trachea. However, nine of the ten infants developed a patent ductus arteriosus. An artificial surfactant was introduced by Morley *et al.* [9] and there have now been several studies using both preparations, either as prevention or treatment of HMD [10–14]. Present evidence would suggest that surfactant replacement therapy may be effective in lessening the severity of HMD in the short term, but not in curing the disease.

PREVENTION

If one was able to prevent all preterm delivery then the problem of HMD would virtually cease to exist. However, this not being possible, other methods of accelerating lung maturation have been sought. Corticosteroids in particular have been administered to accelerate lung maturation particularly with respect to surfactant production.

In 1972 Liggins and Howie [15] first suggested that antenatal corticosteroid administration might reduce the incidence of HMD. Since that time there have been numerous studies with varying results. The general consensus is that antenatally administered corticosteroids do have a beneficial effect but only in a specific group of relatively mature babies. In a large collaborative study [16] the only significant difference found was in babies of 30–34 weeks gestation when dexamethasone had been administered antenatally for more than 24 hours and less than 7 days. The incidence and severity of HMD was no different in twins, triplets or in babies of less than 30 weeks gestation or greater than 34 weeks gestation.

The effects of steroids on other organ systems and any potential harmful effects have as yet not been clearly delineated and the question as to whether a large number of mothers and babies should be submitted to corticosteroid therapy for the benefit of relatively few remains open.

Meconium aspiration

The passage of meconium either *in utero* or intrapartum presents an opportunity for its aspiration into the tracheobronchial tree. Meconium staining of the amniotic fluid occurs in about 10% of all pregnancies. Infants born with meconium-stained amniotic fluid have frequently suffered intrapartum asphyxia. The asphyxia which is often associated with the passage of meconium also leads to gasp-like respiratory efforts thus aiding in the aspiration of meconium into the tracheobronchial tree.

The infant presents a fairly typical picture [17]. He is usually at term or post-term with features of intrauterine growth retardation. He is often depressed at birth and requires active resuscitation. Meconium staining of the skin is usually present.

Signs of respiratory distress appear and the chest is typically hyperinflated and barrel shaped. The chest radiograph reveals coarse mottled densities distributed throughout both lung fields mixed with areas of increased radiolucency (Fig. 2.3). The chest is hyperexpanded with an increase in the AP diameter and flattening of the diaphragm. The aspiration pattern is seldom confused with any other cause of respiratory distress except for the occasional neonatal pneumonia. Pneumomediastinum and pneumothorax are frequent complications and significant hypoglycaemia is often present.

MANAGEMENT

Many of these infants require active resuscitation at birth and before any positive pressure ventilation is applied, meconium in the mouth, larynx and trachea should be sucked out. Tracheal and bronchial lavage is of no value and is potentially dangerous. There is no specific therapy and supportive care as outlined previously for hyaline membrane disease is required. Steroids have been advocated by some authors in order to prevent and treat chemical pneumonitis but sufficient control studies are not available to indicate their value. Many authors would support the use of antibiotics for two main reasons:

1 The differential diagnosis between bacterial pneumonia and meconium aspiration may be difficult.

2 Experimental evidence in rats suggest that the presence of meconium in the airways predisposes to *Escherichia coli* infection.

A recent publication has drawn attention to possible long term consequences of neonatal meconium aspiration [18]. The authors reported that in 18 children aged 6–11 years of age they found a much higher prevalence of asthmatic symptoms and abnormal bronchial reactivity than in the general childhood population.

Neonatal pneumonia

Pulmonary infection may be acquired *in utero*, during delivery or in the neonatal period. There are three main routes of infection. These are:

1 Blood borne, transplacental.

2 Vertical, i.e. via the maternal genital tract.

3 Horizontal, i.e. nursery, acquired from the environment, equipment and personnel.

Intrauterine pneumonia may occur in the prepartum period usually as a result of haemato-

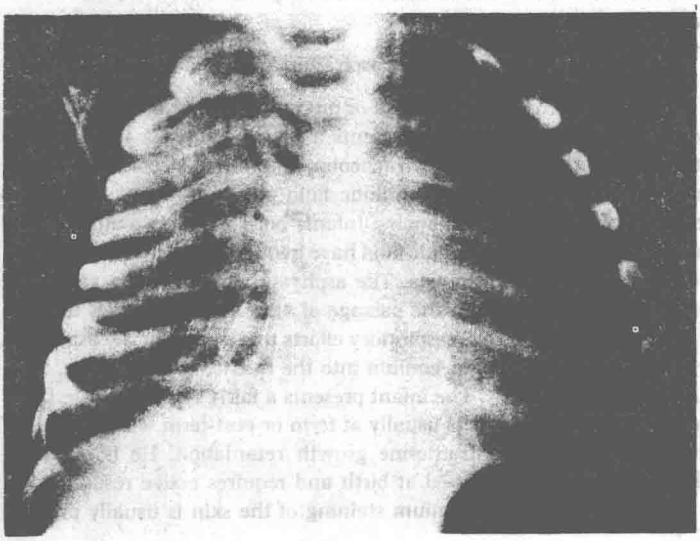

Fig. 2.3 Chest radiograph of an infant with meconium aspiration. Note the coarse irregular densities particularly on the right side.