Congenital lung malformations in infants

A variety of congenital lung malformations arise from aberrations in different stages of lung development occurring in around 1 in 10-20,000 pregnancies. Occasionally these present in the neonatal period with symptoms, in which case treatment is invariably surgical resection. However, with universal screening for fetal anomalies, by ultrasound at 20 weeks' gestation, an increasing number of lung abnormalities are identified antenatally and the majority cause no symptoms. The management of these babies is controversial. This article discusses the diagnosis and management of the different types of congenital lung malformation.

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Keywords

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Key points

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1. Congenital lung malformations comprise a spectrum of disorders that includes cystic adenomatoid malformation, pulmonary sequestration, bronchogenic cyst and lobar emphysema.
2. Congenital lung malformations are frequently identified on antenatal ultrasound scan.
3. The management of infants with congenital lung malformations is controversial.

Lung embryology

The earliest signs of lung development occur around four weeks after conception with the appearance of a bud (the tracheal diverticulum) from the primitive foregut. Lung development can be described in four stages, embryonic, glandular, canalicular and sacular (**TABLE 1**).

Towards term more subtle changes in the structure of the terminal airspaces, including elastin deposition and septation, which result in the formation of alveoli, greatly increase the surface area available for gas exchange. This process continues after birth until around eight years of age[1].

Although the aetiology of congenital lung malformations is unknown these abnormalities probably arise from prenatal airway obstruction during the embryonic and glandular stages of lung development. It seems likely that the nature of the malformation is determined by the gestational age at which obstruction occurs.

Classification of congenital lung malformations

The pathological classification of congenital lung malformations is relatively straightforward (**TABLE 2**). In practice many lesions contain features of both cystic adenomatoid malformation (CAM) and sequestration and these are termed hybrid lesions.

- Cystic adenomatoid malformation (CAM)
- Pulmonary sequestration
- Bronchogenic cyst
- Lobar emphysema

TABLE 2 Pathological classification of congenital lung malformations.

Congenital cystic adenomatoid malformation

Congenital CAM (also called congenital pulmonary adenomatoid malformation, CPAM) is characterised by dense multicystic areas of abnormal lung tissue. The incidence is around 1 in 10-30,000 live births, with males and females affected equally[2].

The majority (95%) of CAMs involve one lobe of lung, most often a lower lobe. CAMs can be classified using a system described by Stocker (**TABLE 3**) although

	Weeks post-conception	Key features
Embryonic stage	4-6	The tracheal diverticulum elongates and bifurcates to form left and right lung buds
Glandular stage	6-16	Progressive branching of the lung buds occurs to form most of the bronchial tree
Canalicular stage	16-28	Further branching of the bronchial tree occurs but the major feature is vascularisation of the terminal airways. Type II pneumocytes start to appear around 24 weeks and respiration becomes possible
Saccular stage	26-term	Terminal respiratory airspaces called saccules develop rapidly and the type II pneumocytes secrete increasing amounts of surfactant

TABLE 1 Stages of lung development.

	Key features
Type 0	Very rare. Involves all lobes. Stillborn
Type I	Commonest type of congenital CAM. Often identified antenatally. Large cysts. May be asymptomatic
Type II	Microcystic. Uncommon. May be associated with other malformations
Type III	Uncommon. Solid lesions
Type IV	Uncommon. Large solitary cysts. May present with pneumothorax

TABLE 3 Stocker's classification of cystic adenomatoid malformations[3,4].

this is of minimal value in clinical practice because it fails to recognise the fact that hybrid lesions, which contain features of both CAM and pulmonary sequestration, are common[3-4].

Prior to the advent of antenatal ultrasound (US), infants with CAMs presented in the neonatal period with respiratory distress. A small number of stillbirths were attributable to CAMs. Clinical presentation in later childhood was mainly with pulmonary infection or, rarely, pneumo-thorax. Occasionally CAMs were detected coincidentally on a chest X-ray taken for other reasons.

Routine use of fetal US has meant that virtually all cystic lung malformations are now identified around 20 weeks' gestation during the anomaly scan (**FIGURE 1**). Usually these are isolated anomalies. The main differential diagnosis is a diaphragmatic hernia. In this condition the cystic abnormality seen in the fetal thorax represents herniated bowel and not cystic lung.

Usually the prognosis for a fetus with a CAM is good. However, the behaviour of fetal lung lesions is highly variable between 20-26 weeks' gestation and regular scanning during this period is wise. Rapid enlargement of up to 40% of cystic lung malformations may occur during this period and this can lead to mediastinal shift. Rarely this progresses to cause obstruction of the vena cavae and fetal hydrops (**FIGURE 2**). The majority of CAMs regress from around 28 weeks' gestation due to apoptosis, lack of adequate blood supply or relatively slow growth compared to the surrounding lung[5]. Some lesions will disappear completely on antenatal scanning, although these are invariably still visible on postnatal computerised tomography (CT) scanning. Regression of even giant CAMs with resolution of fetal hydrops has been reported[6].

Macrocystic lesions	Comprise multiple large cysts (>5mm diameter) on fetal sonography with thin intervening echogenic areas.
Microcystic lesions	Homogeneous echogenic appearance on fetal sonography, with no visible cystic spaces or cysts <5mm diameter

TABLE 4 Classification of fetal CAMs based on sonographic appearance.

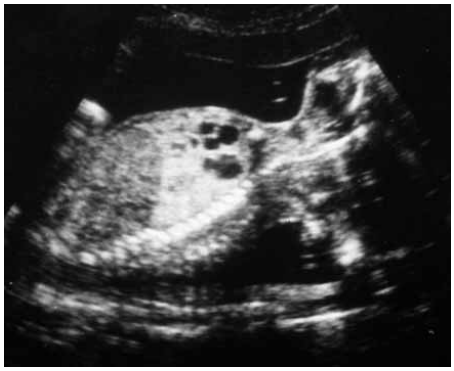

FIGURE 1 Antenatal ultrasound showing fetus with congenital CAM.

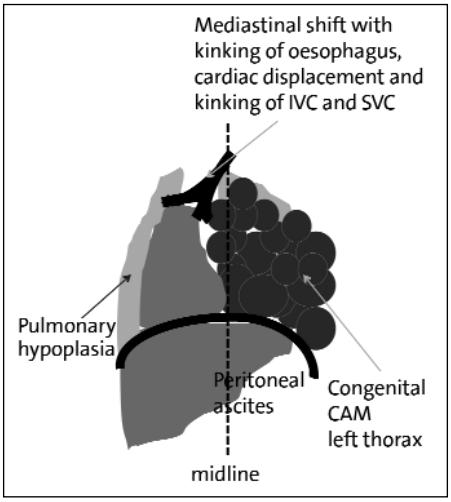

FIGURE 2 A large left congenital CAM produces fetal hydrops due to mediastinal shift. IVC – inferior vena cava, SVC – superior vena cava.

In-utero therapy has been attempted where the risk of fetal demise is high but determining which cases to treat is difficult. Hydrops may already be present at the time of diagnosis and these cases have generally been considered too late for fetal intervention. Percutaneous trans-uterine cyst aspiration carries least risk but is frequently unsuccessful. Open fetal surgery and thoracoamniotic shunt placements have both been described for treating large CAMs with mediastinal shift, the latter being suitable only for macrocystic lesions, with reports of up to 60% survival following fetal surgery[2,7-8]. The variable course of even large CAMs can make offering high risk fetal surgery difficult to justify.

The correlation between histology after resection and imaging, particularly prenatal imaging, is poor. Adzick et al proposed an alternative system based on gross anatomy and sonographic appearances (**TABLE 4**). Although this system correlates poorly with histology at subsequent surgical resection it has the benefits of simplicity and predictive value. Microcystic lesions tend to progress more rapidly antenatally and typically this group includes the fetuses with a worse prognosis[9].

A minority (13-43%) of babies with antenatally diagnosed CAMs will develop respiratory distress in the early neonatal period[10-11]. A chest X-ray will confirm the diagnosis. Macrocystic CAMs will appear as multiple air-filled cysts whereas microcystic lesions appear as persisting opacities after resolution of fetal lung fluid. Congenital diaphragmatic hernia is the main differential diagnosis although a normal intestinal gas pattern below the diaphragm will exclude this (**FIGURE 3**). Further confirmation can be gained from the position of a nasogastric tube or limited upper GI contrast study, which can be performed on the intensive care unit. There is consensus that symptomatic babies who can be stabilised should be treated by surgery to resect the CAM (**FIGURE 4**). Complete resection is almost always possible by lobectomy which then allows expansion of the normal lung and resolution of respiratory symptoms. A minority of babies who survive will have hypoplastic lungs and persistent respiratory problems.

Management of the asymptomatic infant with an antenatally-diagnosed CAM remains controversial. Whether an asymptomatic malformation should be resected to facilitate normal lung growth is not clear. CAMs may carry a risk of recurrent infection but the incidence is not clear. There are case reports of tumours (pleuropulmonary blastoma, rhabdomyosarcoma, bronchoalveolar carcinoma) arising in lung tissue where there is an underlying CAM but the risk is

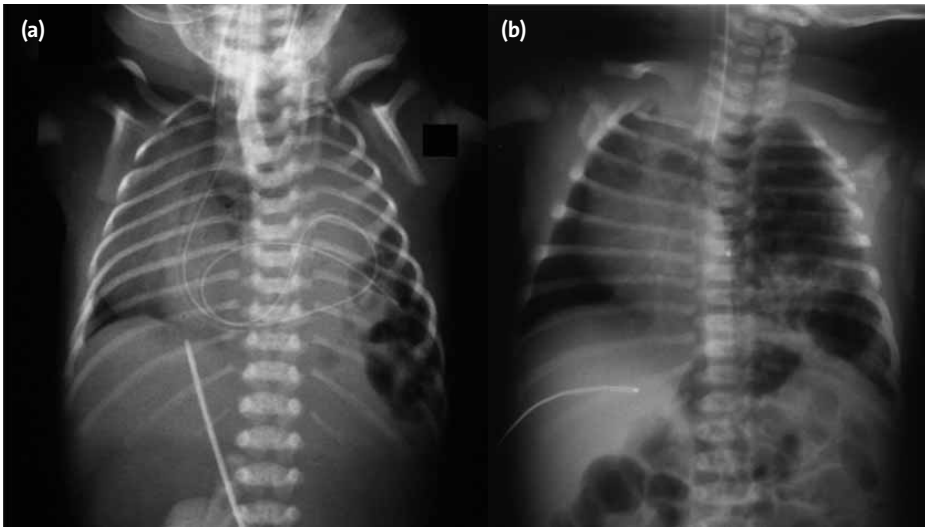

FIGURE 3 Chest X-rays of a left congenital diaphragmatic hernia (a) and a left lower lobe congenital cystic adenomatoid malformation (b). Mediastinal shift to the right and left lung changes are seen in both cases. In the congenital diaphragmatic hernia the nasogastric tube is seen within the stomach in the chest and there is no bowel gas below the diaphragm. In the CAM the left diaphragm appears intact and there is a normal bowel gas pattern in the abdomen.

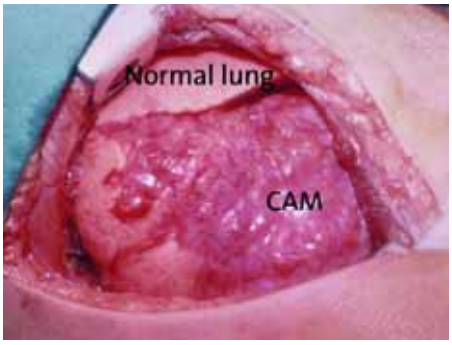

FIGURE 4 Cystic adenomatoid malformation at thoracotomy.

even less clear. Moreover, there are reports of malignancy arising elsewhere in the lung following complete removal of a CAM which implies that resection has no protective value. Many surgeons quote these risks to advocate resection of CAMs in early life and case series justifying this course of action predominate in the literature[11-14]. However, these surgeons disagree on the age by which resection should be performed to prevent these complications and they fall strangely silent on whether all antenatally diagnosed lesions should be resected, implying that small lesions are somehow exempt from the risk of serious complications.

Infants born with an antenatally diagnosed CAM should have a chest X-ray performed within the first few days of life. In the majority of cases the chest X-ray will appear normal although invariably the abnormality will be evident on CT[8,15-17]. One difficulty in adopting an expectant approach to the management of asymptomatic CAMs is how best to follow these patients. Repeated CT scanning is inadvisable because the radiation exposure is associated with a significant long-term risk of malignancy[18]. At present MR imaging is too slow for small children to tolerate without general anaesthesia. Intermittent clinical review of symptoms coupled with periodic chest X-rays and CT reserved for cases where there is clinical change is probably the best approach if observant management is adopted.

Pulmonary sequestrations

Pulmonary sequestrations are areas of lung tissue that have an anomalous blood supply arising from the systemic circulation. The venous drainage of a sequestration is variable but usually to the pulmonary circulation. There are two types of pulmonary sequestration: intra-lobar (ILS), surrounded by lung tissue, and extra-lobar (ELS) invested with their own layer of visceral pleura (**FIGURE 5**).

Sequestration accounts for around 10% of all congenital pulmonary malformations. Extra-lobar sequestrations are more frequently associated with other congenital malformations including cardiac disease and diaphragmatic hernia[7,13,19].

Sequestrations typically appear on US as well defined homogeneous echodense masses, most commonly in the left lower chest (**FIGURE 6**). Documenting a systemic blood supply by colour flow Doppler US is confirmatory (**FIGURE 7**)[20]. In equivocal cases fetal MR may be helpful in identifying a feeding vessel and distinguishing a sequestration from a CAM although

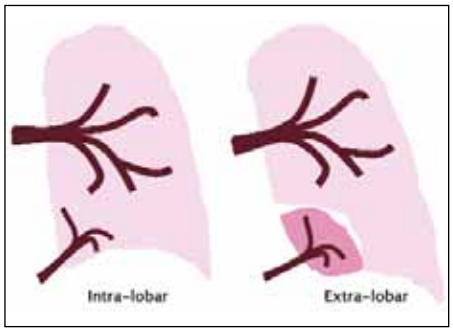

FIGURE 5 Intra-lobar and extra-lobar pulmonary sequestrations.

hybrid lesions are common[21]. Subdiaphragmatic sequestrations may be confused with neuroblastoma arising in the adrenal gland. Antenatal complications of sequestrations are rare although hydrops caused either by high output cardiac failure from left to right shunting of blood through the sequestration, or mechanical compression of the inferior vena cava (IVC), have been reported[22]. Resolution of antenatally-diagnosed sequestrations has been reported, possibly by torsion or simply 'outgrowing' their blood supply[8]. Hydramnios, secondary to compression of the oesophagus or stomach, has also been reported.

In the past, children with sequestrations presented in the newborn period with cardiac failure due to shunting through the anomalous circulation or in later childhood with haemoptysis or recurrent pulmonary infection. The majority of pulmonary sequestrations are now identified on antenatal US.

Surgical resection is necessary for symptomatic patients. Accurate preoperative assessment of the arterial supply and venous drainage of sequestrations is important (**FIGURE 7**). In 20% of cases the systemic feeding vessel may be subdiaphragmatic in origin and up to 15% have been reported to have more than one feeding vessel[23]. Inadvertent injury to these vessels during resection may result in torrential haemorrhage.

The management of asymptomatic children with pulmonary sequestrations is controversial. The relative frequency with which hybrid CAM-sequestration lesions occur means that the same arguments raised in favour of prophylactic resection of CAMs are used to justify resection of sequestrations[24].

Bronchogenic cysts

Bronchogenic cysts can be regarded as duplication cysts arising from the airway.

They are thought to arise when a group of cells becomes isolated from the normal lung during the glandular stage of development[25]. Bronchogenic cysts are typically found alongside the large airways or within the lung parenchyma, although they may arise anywhere in the mediastinum or the neck. Central lung cysts are typically solitary and usually asymptomatic until complicated by infection. Radiological imaging demonstrates a solitary solid mass (**FIGURE 8a**). Bronchogenic cysts invariably cause symptoms and require surgical resection (**FIGURE 8b**). Resection of peripheral lesions may require lobectomy.

Congenital lobar emphysema

Congenital lobar emphysema (CLE) is the postnatal over-distension of one or more lobes of the lung. The condition may arise from a segmental deficiency of cartilage in the bronchial tree resulting in bronchomalacia and distal air trapping. The left upper lobe is most commonly affected (47%) with the majority of other cases affecting the right upper or middle lobes; lower lobe involvement is rare (5%)[26].

Lobar emphysema may present in the newborn period with respiratory distress but more often presents in infancy with persistent tachypnoea or following an intercurrent respiratory viral infection. A chest X-ray is usually diagnostic (**FIGURE 9a**). The differential diagnosis in a neonate with respiratory distress is a tension pneumothorax. This is important to recognise because insertion of a chest drain into the emphysematous lobe may create a catastrophic air leak.

Treatment depends on symptoms. Infants with minimal symptoms can be managed expectantly because the condition tends to improve as the child grows[27]. Lobectomy is curative for symptomatic infants and it will allow the adjacent normal lung to re-expand (**FIGURE 9b**).

Conclusions

Congenital lung malformations in infants are a spectrum of disorders that arise from aberrations of lung development. Congenital CAM and congenital lobar emphysema may present in the neonatal period with respiratory distress, or pulmonary sequestrations with cardiac failure and require urgent surgical resection. Congenital lung malformations may become symptomatic in infancy or later childhood necessitating surgical management. The vast majority of patients

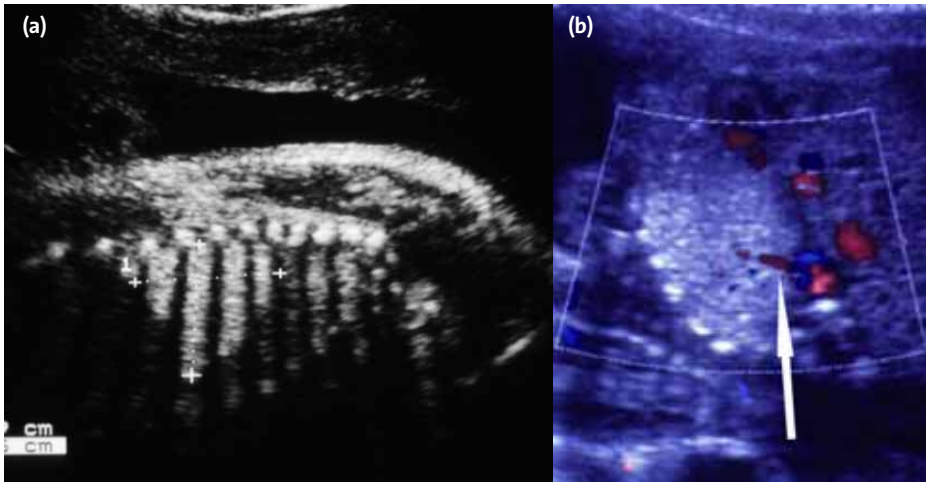

FIGURE 6 Fetal ultrasound showing a pulmonary sequestration (a). Doppler images clearly demonstrate the feeding vessel (arrow) (b).

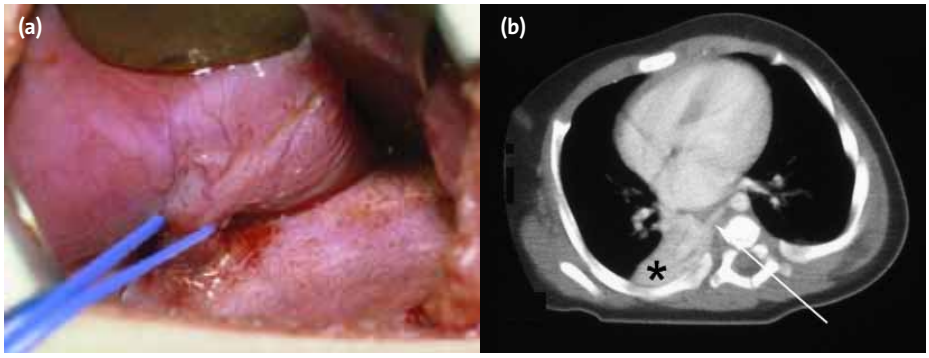

FIGURE 7 (a) Appearance of an extra-lobar sequestration at thoracotomy. The blue sling surrounds a large feeding vessel from the thoracic aorta. (b) Preoperative CT scan demonstrating the systemic arterial supply (arrow) to a sequestration (*).

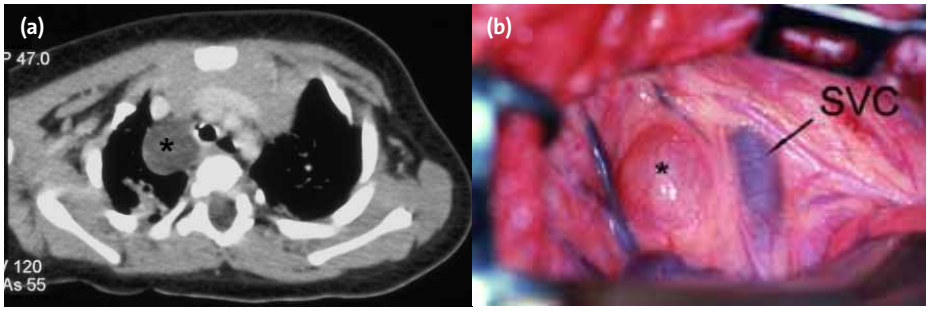

FIGURE 8 Bronchogenic cyst adjacent to the trachea on CT scan (*) (a) and in another case, a bronchogenic cyst (*) adjacent to the superior vena cava (SVC) at thoracotomy (b).

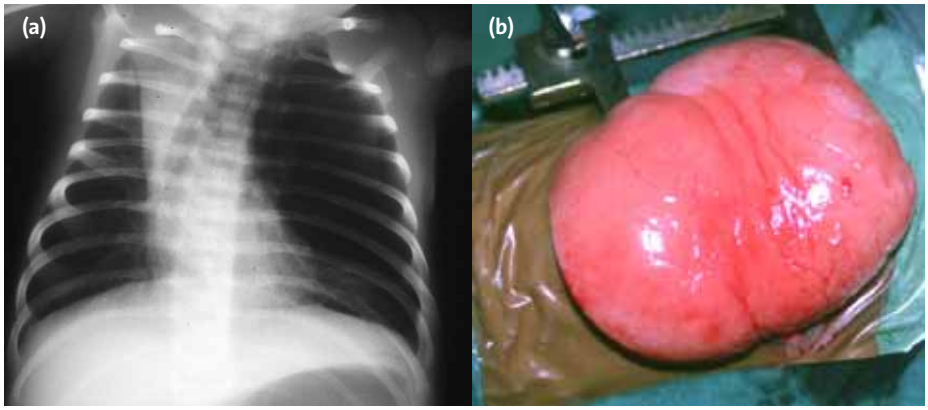

FIGURE 9 Congenital lobar emphysema. (a) Chest X-ray showing mediastinal shift and compression of the normal lung. (b) At thoracotomy the emphysematous lobe of lung is seen herniating out of the wound.

with congenital CAMs are now antenatally diagnosed but are entirely asymptomatic after delivery. The management of these congenital CAMs remains controversial.

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