Lung Imaging

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Nuclear medicine provides physiological and sensitive methods for assessing regional lung perfusion and ventilation. In adults, the most established indication for these studies has been suspected pulmonary embolism. In children, both perfusion and ventilation imaging have been used for a broader range of indications. In children with congenital heart disease, perfusion scintigraphy is used to assess differential (left vs. right) and regional lung perfusion. Perfusion scintigraphy also is useful for demonstrating shunts between the right (pulmonary) and left (systemic) circulation. In children with parenchymal and airway diseases, static or dynamic ventilation scintigraphy can be used to assess lung ventilation and differential lung volumes. Ventilation/perfusion (V/Q) uses both ventilation (V) and perfusion (Q) scans for the evaluation of pulmonary embolism or to demonstrate ventilation/perfusion mismatches in developmental or acquired lung diseases.

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Methods

Little or no patient preparation is needed before performing lung scintigraphy. It may be helpful to confirm at the time of scheduling the study that a patient's respiratory status will not preclude cooperation with the study. Some guidelines suggest treating a patient to optimize control of chronic lung disease before performing a nonurgent lung scan. Although this preparation might decrease the likelihood that regional airway obstruction will interfere with study interpretation, it is not a part of routine clinical practice.

Assessment of Pulmonary Blood Flow

Regional pulmonary blood flow typically is determined with ^{99m}Tc-labeled macroaggregated albumin (MAA). After administration into the peripheral venous circulation, MAA particles

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circulate through the right heart and into the pulmonary circulation where they are trapped within the capillaries of the lungs. The distribution of ^{99m}Tc-MAA within the lungs reflects regional and differential pulmonary blood flow. An alternative, and now rarely used, method to demonstrate pulmonary blood flow is the intravenous administration of ^{133}Xe dissolved in saline [1].

Macroaggregated albumin (MAA) particles are created by the acid aggregation of human albumin to produce aggregated particles with diameters between 10 and 100 μm, with most between 10 and 40 μm [2]. This is greater than the diameter of pulmonary capillaries, so that MAA particles in the pulmonary circulation will be trapped at the transition from arteriole to alveolar-capillary. Macroaggregated albumin particles are labeled with ^{99m}Tc for lung perfusion scintigraphy. In an adult, the typical dose of 500,000 particles of ^{99m}Tc-labeled MAA temporarily will occlude approximately 1 in 1,000 pulmonary arterioles and have essentially no effect on normal adult lung function. The MAA particles have a biological half-life of only a few hours as they are degraded to smaller particles and polypeptides, which reenter the circulation and are cleared by the liver.

A smaller number of MAA particles are recommended for infants and young children, as their pulmonary vasculature is immature [3]. The number of pulmonary capillary beds increases during the first years of life, but reaches only one-half of the adult number by 3 years of age [4]. This suggests that the number of administered particles should not exceed 50,000 in a newborn or 165,000 in a 1-year-old child [5]. The smallest number of particles necessary should be used for all perfusion lung scans, and the number of MAA particles necessary for an adequate study will depend on the indication for lung scintigraphy and patient characteristics. When the indication for the lung scan is to assess differential or regional pulmonary perfusion (and not pulmonary embolus), nearly all pediatric lung scans can be performed with only 10,000 MAA particles. A similar number of MAA particles should be used in patients of all ages with pulmonary hypertension or with a known (or suspected) right-to-left cardiac shunt. There have been unpublished anecdotal reports of transient cerebral ischemia following administration of an adult dose of MAA particles to a pediatric patient with a pulmonary-to-systemic shunt. When higher quality lung images are needed for the evaluation of possible pulmonary embolism, a greater number of MAA particles may be required to ensure uniform particle distribution within the microcirculation of the lungs.

Image quality also will depend on the administered dose of ^{99m}Tc. The typical radiopharmaceutical preparation of MAA particles provides approximately 1 mCi per 100,000 particles (so the typical dose is 0.1 mCi or 10,000 particles). Administration of a limited number of MAA particles with this specific activity rarely provides sufficient counts for routine gamma camera imaging. Therefore, for pediatric lung scintigraphy, special preparation of ^{99m}Tc-labeled MAA particles may be needed to provide MAA particles with a higher specific activity.

Typically, ^{99m}Tc-MAA is administered by intravenous injection while the patient is supine, so that differential regional blood flow between the apex and base of the lungs is reduced. Extreme care must be taken to avoid drawing blood into the injection syringe, as this will result in formation of clots containing blood and MAA particles. If injected into the circulation, these clots will heterogeneously distribute within the pulmonary circulation. This will limit the diagnostic utility of the imaging study and could be dangerous to the patient.

Image acquisition depends on the clinical indication for lung perfusion scintigraphy. As MAA particles are trapped within the lung with a distribution reflecting pulmonary perfusion, there is no reason to perform dynamic lung imaging. Planar images are acquired with a high-resolution collimator with each view collected for 300,000–500,000 counts. Differential lung perfusion usually can be assessed with images acquired in the anterior and posterior projections. Region-of-interest analysis is used to quantitatively assess differential or regional lung perfusion. For evaluation of pulmonary embolism, planar images are acquired in multiple projections, typically anterior, posterior, and four oblique projections. Some institutions also will acquire images in the two lateral projections. Recent studies have suggested a role for lung SPECT or SPECT/CT in

the assessment of functional lung volume or evaluation for pulmonary embolism [6].

Lung Ventilation Scintigraphy

The airspaces of the lungs can be assessed by imaging the lungs after the patient inhales either radiolabeled aerosols or radioactive gases. Inhaled aerosolized nanoparticles are distributed and trapped in the pulmonary airspace in proportion to regional ventilation. Once the radiolabeled nanoparticles are trapped in the lungs, static images of the lungs can be acquired in multiple projections. The most commonly used radioactive gas for lung ventilation scintigraphy is ^{133}Xe, although other inert gases, such as ^{81m}Kr, also have been used. As inhaled gases are not trapped within the lungs, dynamic imaging of lung ventilation can be performed. With rebreathing, inhaled gases can redistribute throughout the pulmonary airspace, which permits imaging and volume assessment of the entire aerated lung volume.

^{133}Xe for Inhalation

Xenon-133 (physical half-life 5.2 days) is an inert gas at room temperature and normal pressure. Xenon-133 decays with a principal gamma emission of 87 kEv (37 % abundance). There are many commercially available systems for administration of inhaled ^{133}Xe gas for lung scintigraphy. Many require some degree of patient cooperation, but ^{133}Xe gas can be administered successfully to children with limited cooperation. Xenon-133 gas also can be administered through the endotracheal tube of intubated patients. During a rebreathing study, care must be taken to ensure that the patient is provided with adequate oxygen. One disadvantage to the use of ^{133}Xe gas for lung ventilation scintigraphy is the requirement to trap and exhaust the exhaled ^{133}Xe gas.

Dynamic ventilation studies can be performed with the patient supine over a camera equipped with a low-energy collimator [7]. Dynamic images typically are acquired in the posterior projection at a rate of one frame every five seconds. After inhalation of a single breath, the distribution of ^{133}Xe gas corresponds to regional ventilation within the lungs. After multiple breaths through a rebreathing inhalation system, the ^{133}Xe gas reaches equilibrium within the airways. ^{133}Xe distribution will reflect the distribution of aerated airspace volumes. After ^{133}Xe inhalation is stopped, continued dynamic imaging during the washout phase can be used to measure regional ventilation and to determine if there is regional air trapping within the lungs. Region-of-interest analysis is used for quantitative assessment of regional ventilation, lung volume, and air trapping.

Lung Ventilation with ^{99m}Tc-Labeled Aerosols

A variety of ^{99m}Tc-labeled aerosolized particles can be used for lung ventilation imaging. Aerosolized particles are administered through a face mask connected to an ultrasonic or jet nebulizer. In the USA, the most commonly used is aerosolized ^{99m}Tc-labeled diethylenetriamine pentaacetic acid (^{99m}Tc-DTPA). Less commonly used is aerosolized ^{99m}Tc-labeled sulfur colloid. Technetium-99m-labeled carbon nanoparticles (Technigas ®) have been used widely throughout the world [8], but this radiopharmaceutical is not approved for use in the USA. After aerosolized particles are inhaled and deposited within the small airways, planar images can be acquired in multiple projections. Because particles persist within the airways, dynamic ventilation imaging cannot be performed. Some studies have described the use of SPECT or SPECT/CT with ^{99m}Tc-labeled carbon nanoparticles to assess lung ventilation [6].

Once deposited in the alveolar space, ^{99m}Tc-DTPA is slowly absorbed through the alveolar-capillary membrane with a clearance half-time of approximately one hour in adults [9]. Technetium-99m-DTPA clearance is increased with exercise [10] and can be affected by conditions that alter alveolar membrane permeability, such as hyaline membrane disease [11]. Once absorbed into the circulation, ^{99m}Tc-DTPA is excreted by the kidneys, and a renogram pattern can be seen with delayed imaging. Inappropriate aerosolization technique can produce larger size nanoparticles which will deposit in the inhalation apparatus, oropharynx, and large airways. This results in inadequate aerosol delivery to the small airways and poor image quality. Normal mucociliary

action will clear tracer from the large airways to the oropharynx, where particles can then be swallowed and accumulate in the esophagus and stomach. These patterns of extrapulmonary tracer accumulation can interfere with study interpretation.

Clinical Applications

Lung scintigraphy can be used in the evaluation of a wide range of pulmonary, cardiac, and systemic diseases. For many indications, either a perfusion lung scan or a ventilation lung scan may be sufficient. For other indications, such as pulmonary embolism, congenital diaphragmatic hernia, and some complex congenital heart problems, a ventilation/perfusion ("V/Q") scan can be used to compare patterns of ventilation and perfusion.

Congenital Heart Disease

In most pediatric institutions, congenital heart disease is the most common indication for lung scintigraphy. A perfusion lung scan is a rapid and noninvasive method for quantitative assessment of differential (left vs. right) and regional pulmonary blood flow. As many of these patients will have a pulmonary-to-systemic (right-to-left) shunt, lung perfusion scans should be performed with the smallest possible number of MAA particles. In our experience, patients with congenital heart disease are evaluated successfully with perfusion lung scans using only 10,000 MAA particles. Although image quality can be limited and particle distribution within the lungs may appear slightly heterogeneous, this number of particles is sufficient to assess regional and differential pulmonary blood flow.

Many forms of congenital heart disease are associated with altered pulmonary perfusion (Fig. 6.1). Pulmonary artery atresia or stenosis of a main or branch pulmonary artery commonly is associated with tetralogy of Fallot. Differential lung perfusion can be used for initial evaluation and for postsurgical assessment of pulmonary blood flow after pulmonary arterioplasty or conduit placement [12]. Pulmonary vein stenosis or anomalous pulmonary venous return can affect differential lung perfusion, and a lung perfusion scan can be used to assess the severity of venous disease. In patients undergoing cardiac catheterization with balloon dilation or stenting of a pulmonary vessel or conduit, a lung perfusion scan can be performed after the procedure to assess for improved differential pulmonary perfusion and to confirm that instrumentation did not result in occlusion of the vessel. Differential lung perfusion can occur in patients with pulmonic valve stenosis. The jet of blood flow through the stenotic pulmonic valve can be preferentially directed to the left, so that the differential pulmonary blood flow will be greater in the left lung [13].

Anomalous pulmonary blood flow also can occur after corrective surgery performed for congenital heart disease. Alterations in the normal pattern of blood flow will depend on both the underlying cardiopulmonary anatomy and the surgical procedures [14]. For example, in patients with a classic Glenn shunt (end-to-end anastomosis), blood return from the superior vena cava is directed to the right lung, while the inferior vena cava blood return is to the left lung. In these patients, ^{99m}Tc-MAA intravenously administered in an upper extremity will travel only to the right lung, while tracer administered in a lower extremity vein will travel to the left lung. In patients treated with a bidirectional Glenn shunt (end-to-side anastomosis), venous return from the upper extremities is directed to both lungs, while venous return from the inferior vena cava is returned directly to the systemic circulation. In this situation, when ^{99m}Tc-MAA is administered in an upper extremity vein, it should accumulate in the pulmonary circulation of both lungs, while tracer administered intravenously in a lower extremity will bypass the pulmonary circulation and enter the systemic circulation. Thus, the pulmonary perfusion pattern depends on the pattern of cardiopulmonary circulation and the site of intravenous administration of ^{99m}Tc-MAA, and it is important to confirm the original and presumed

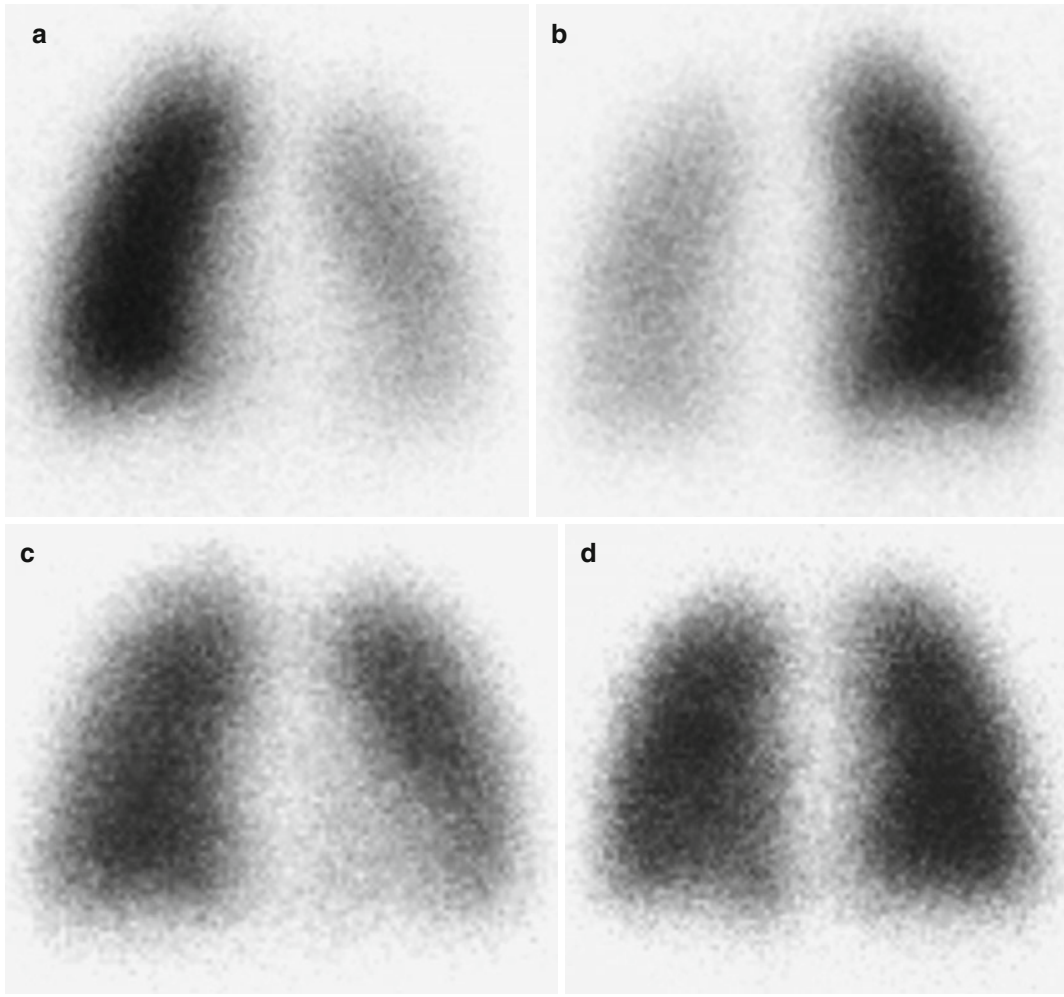

Fig. 6.1 Correction of persistent pulmonary artery stenosis in tetralogy of Fallot. In a 3-year-old girl with surgically corrected tetralogy of Fallot, a perfusion lung scan imaged in anterior (**a**) and posterior (**b**) projections shows asymmetric pulmonary perfusion (21 % left lung, 79 % right lung). Cardiac catheterization showed stenosis of the proximal left pulmonary artery, and a stent was placed at this location. A follow-up perfusion lung scan imaged in anterior (**c**) and posterior (**d**) projections demonstrates improved differential perfusion to the left lung (46 % left lung, 54 % right lung)

postoperative circulatory anatomy before performing a lung perfusion scan.

Pulmonary Shunting

A pulmonary-to-systemic (right-to-left) shunt will result in systemic penetration of intravenously administered ^{99m}Tc-MAA [15]. Tracer that has been shunted into the systemic circulation will be trapped within precapillary arterioles of organs other than the lungs. As MAA trapping will reflect relative blood flow, the largest amount of MAA accumulation is seen within the organs receiving the greatest fraction of cardiac output, such as brain and kidneys. Quantitative assessment of a right-to-left shunt may be somewhat limited by overlap between tissues with systemic circulation and the lungs, but the degree of right-to-left shunt can be evaluated qualitatively or assessed semiquantitatively using region-of-interest analysis (Fig. 6.2).

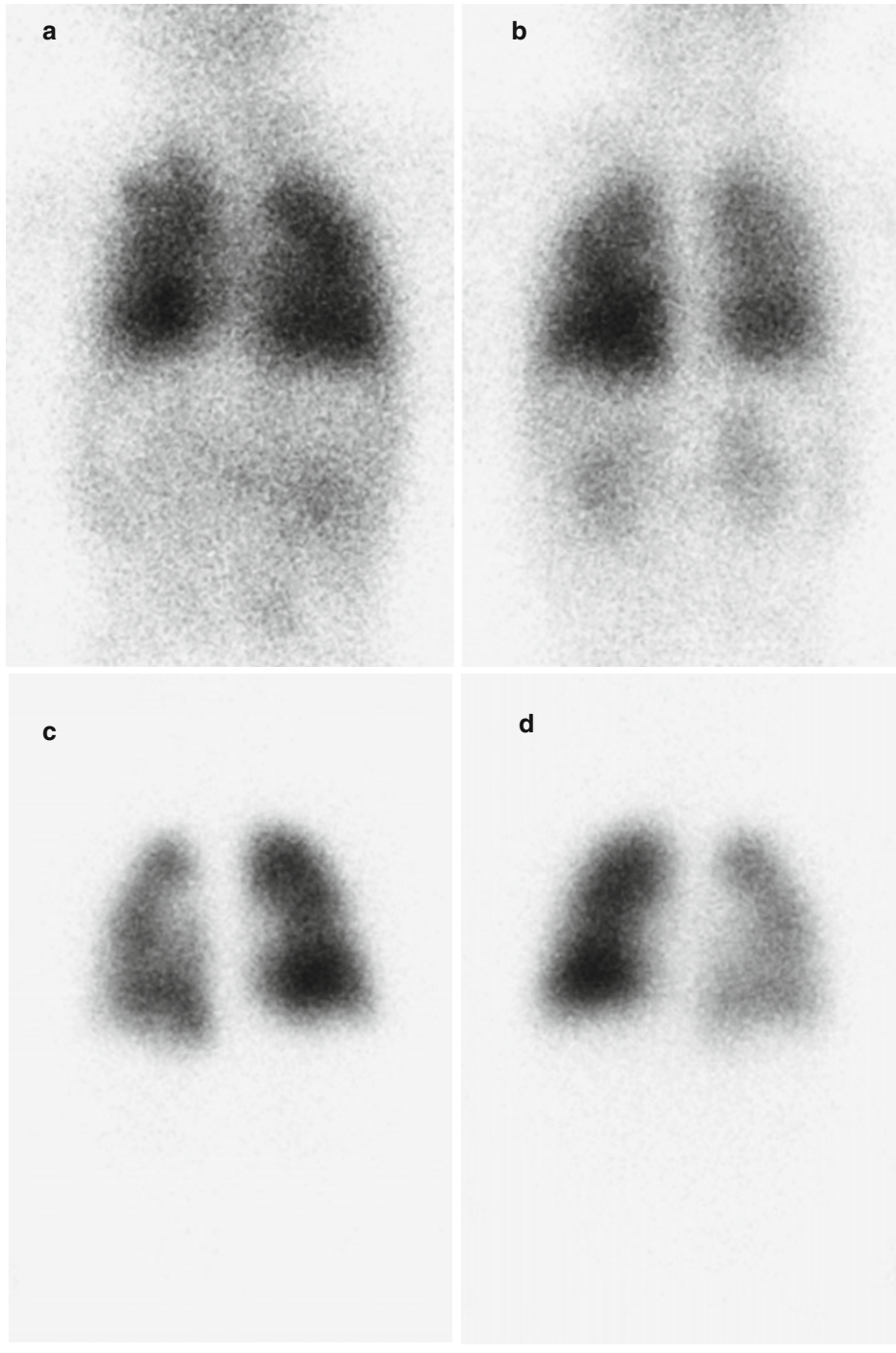

Fig. 6.2 Cardiac right-to-left shunt. In a 1-year-old girl with tetralogy of Fallot and pulmonary atresia corrected with a pulmonary artery conduit, a perfusion scan was performed with ^{99m}Tc-MAA. Anterior (**a**) and posterior (**b**) images show systemic penetration of tracer indicative of a severe intracardiac right-to-left shunt. After corrective surgery, a perfusion scan imaged in anterior (**c**) and posterior (**d**) projections shows resolution of the right-to-left shunt

Typically, right-to-left shunts are identified in patients with an atrial or ventricular septal defect. In these patients, the degree of shunting may correspond to the severity of pulmonary hypertension, with increased shunting into the systemic circulation as arterial pressures increase in the pulmonary circulation and right heart. Shunting also can occur in patients with more complex congenital heart disease that permits communication or mixing between the right and left heart circulations, such as a common ventricular outflow tract or patent ductus arteriosus.

Patients treated with a surgical cavopulmonary anastomosis, such as a Glenn shunt, also can develop intrapulmonary arteriovenous shunts, possibly reflecting dysregulated pulmonary vasodilation [14]. In a patient with a classic Glenn shunt, the degree of right-to-left shunt may be different for the superior and inferior vena cavae, so that it may be necessary to perform two lung perfusion studies and to calculate the shunt after ^{99m}Tc-MAA administration into either the upper or lower systemic venous circulation [16].

Intrapulmonary arteriovenous shunting also may develop in patients with chronic liver disease. These shunts produce systemic penetration of tracer on a perfusion lung scan [17]. Lung scan may be more sensitive than other techniques, such as contrast-enhanced echocardiography, for detecting physiologically significant intrapulmonary shunts in children with chronic liver disease [18].

Parenchymal and Bronchial Lung Disease

Ventilation lung scans can be used to evaluate parenchymal and bronchial lung disease. Ventilation scans can be helpful to assess differential and regional pulmonary function in patients with primary lung diseases, such as cystic fibrosis lung disease, bronchiectasis, and pulmonary fibrosis [19, 20]. Dynamic ventilation scans performed with ^{133}Xe can be used to identify functional airway obstruction or air trapping in patients with obstructive lung diseases, such as congenital lobar emphysema (Fig. 6.3) [21]. Ventilation/perfusion scans can be used to compare relative ventilation and perfusion or to identify a regional ventilation/perfusion mismatch that can result from obstruction of a segmental pulmonary artery. However, these studies must be interpreted with care. In patients with primary lung disease, airway obstruction will produce local hypoxia and lead to vasoconstriction and shunting of pulmonary blood flow away from the affected lung region. Therefore, airway obstruction may produce matched ventilation and perfusion defects [22].

Airway Obstruction

Lung scintigraphy can help in the functional evaluation of suspected upper airway obstruction. Airway obstruction can result from intrinsic obstruction of the lumen, such as by a foreign body or mucous plug, or by extrinsic compression of the tracheal or bronchial from an adjacent tumor or dilated vessel. A radionuclide ventilation scan can provide information about differential or regional ventilation that cannot be obtained with pulmonary function testing or other imaging. Combined ventilation and perfusion imaging has been used to evaluate children with a unilateral hyperlucent lung [23, 24]. Bronchiolitis obliterans (Swyer-James syndrome) demonstrates markedly diminished ventilation and perfusion. Airway obstruction will demonstrate absent ventilation, with a variable alteration in perfusion in response to local hypoventilation [25, 26]. In cases of partial airway obstruction, a dynamic ventilation scan performed with ^{133}Xe can be helpful in assessing the degree and extent of airway obstruction. Lung regions beyond a partial airway obstruction will demonstrate delayed tracer wash-in and delayed washout suggestive of air trapping.

Structural Abnormalities of the Chest

Ventilation/perfusion lung scans are used to assess lung function in patients with structural abnormalities of the chest, such as congenital diaphragmatic hernia, pectus excavatum, and spinal scoliosis.

Congenital diaphragmatic hernia classically presents with the triad of diaphragmatic defect,

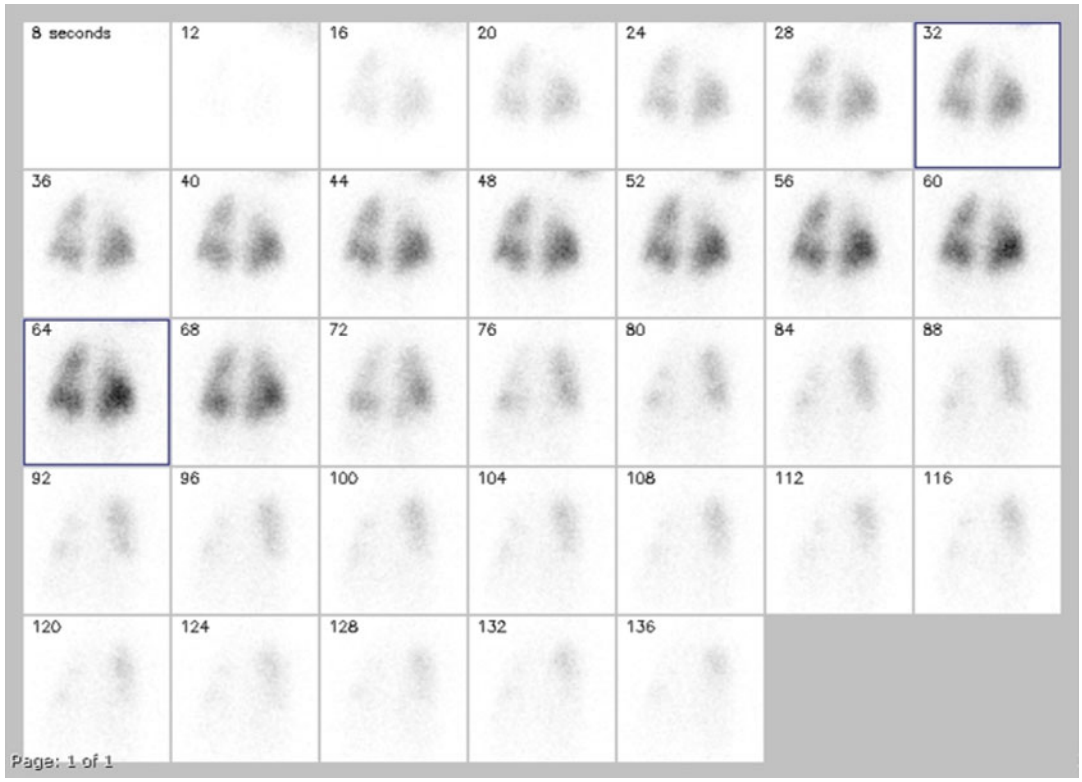

Fig. 6.3 Air trapping in congenital lobar emphysema. In a 10-month-old boy with congenital lobar emphysema of the upper right lung, a dynamic ventilation lung scan performed with ^{133}Xe gas shows both marked delay in ventilation and delayed washout consistent with air trapping in the upper right lung. Recurrent hypercapnia improved after surgical resection of the upper and middle lobes of the right lung

pulmonary hypoplasia, and pulmonary hypertension. Diagnosis now frequently is made prenatally. CDH most frequently occurs on the left (85 %), less frequently on the right (13 %), and rarely bilaterally (2 %) [27]. With surgical repair of the diaphragmatic hernia, the pulmonary sequelae become the long-term clinical effects of CDH [28]. After repair of the diaphragm, the affected lung expands to fill the affected lung cavity. Thus, the ventilation volume of the lung will increase, but the recovery of relative pulmonary perfusion is uncertain and may depend on patient age [29]. In most patients, there may be little postsurgical increase in lung perfusion. However, if the diaphragmatic hernia is corrected early in life, there may be further maturation of pulmonary circulation, so that lung perfusion will increase to nearly match lung volume [30]. In an individual patient, the degree of lung maturation is unpredictable, and ventilation/perfusion scans can be used to assess the degree of ventilation/perfusion mismatch [28] and to follow these patients after surgery (Fig. 6.4).

In patients with severe spinal scoliosis or pectus excavatum, differential compression of the pulmonary vessels and airways can produce regional or whole-lung ventilation/perfusion mismatches. For example, patients with pectus excavatum most typically have a mild reduction in ventilation and a greater reduction in perfusion in the left lung. The severity and progression of ventilation and perfusion abnormalities may help determine the need for surgery [31]. The effect of surgery, one goal of which is improvement of these ventilation and perfusion abnormalities, can be assessed with postoperative lung scintigraphy.

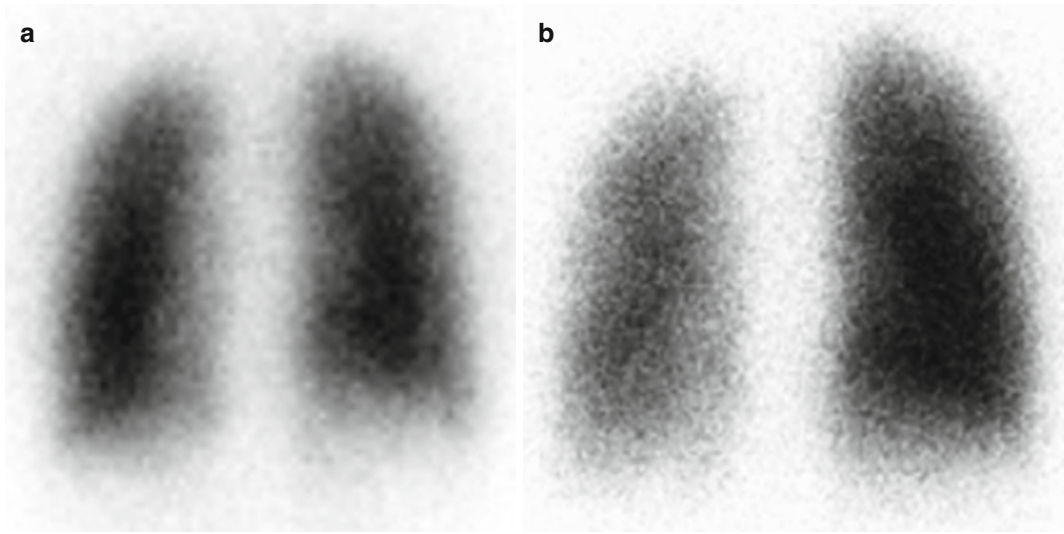

Fig. 6.4 Persistent lung hypoperfusion after repair of a congenital diaphragmatic hernia. A ventilation/perfusion scan was performed in an 8-year who had undergone repair of a left congenital diaphragmatic hernia as an infant. A lung ventilation scan shows ventilation of both lungs with no air trapping. At respiratory equilibrium, merged posterior images (**a**) show differential lung volumes of 49 % left lung and 51 % right lung. However, a lung perfusion scan imaged in the posterior projection (**b**) shows persistent hypoperfusion of the left lung with differential lung perfusion of 30 % left lung and 70 % right lung

Pulmonary Embolism

Pulmonary embolism occurs less frequently in children than adults, but over the past few decades, the reported incidence has increased. This increased frequency of diagnosis has been attributed to a heightened awareness and an increased likelihood of evaluation of pulmonary embolism [32]. However, it also likely represents a true increase in the occurrence of pulmonary embolism in children. This increased incidence has been attributed to increased long-term therapy and prolonged survival of children with predisposing diseases, such as cancer, and the increased use of indwelling venous catheters to provide the therapy for these diseases. The incidence of pediatric pulmonary embolism has a bimodal distribution, with incidence peaks in children less than 1 year of age and in teenagers [33, 34].

While up to one-third of adults with pulmonary embolism have no apparent risk factor, nearly all children have at least one identifiable risk factor [35]. More than one risk factor can be identified in over half of all children with pulmonary embolism [33, 35]. In children, most risk factors relate to an underlying medical condition or a medical intervention [33, 34]. In children, the most common risk factor for pulmonary embolism is an indwelling central venous catheter, which can serve as a nidus for a deep venous thrombosis [34, 36]. This may be related to venous obstruction, abrasion of the vessel wall caused by the catheter, or damage to the vessel wall by medications infused through the venous catheter. Venous thrombosis is more likely when an indwelling catheter becomes infected [37]. However, even in the apparent absence of these factors, venous thrombosis related to indwelling catheters can embolize to the lungs [38]. Deep venous thrombosis, and thus pulmonary embolism, is more common with central venous catheters in an upper extremity [39], and possibly more prevalent when the catheter has been placed in the left upper extremity [40].

The clinical risk factors for pulmonary embolism are different in different age groups. In infants, more than three-quarters of patients diagnosed with pulmonary embolism may have an indwelling venous catheter [34, 36]. Other less

common risk factors in this age group are congenital heart disease and recent surgery [35]. In older children, indwelling venous catheters remain a common cause of pulmonary embolism, but older patients are more likely to have other, possibly concurrent risk factors. These risk factors include immobility or recent surgery [35], malignancy [35], or an underlying clotting disorder [34]. Some clotting disorders represent a previously undiagnosed inherited thrombophilia, while others represent an acquired clotting disorder associated with a wide range of conditions, including malignancy, autoimmune disorders, and nephrotic syndrome. Birth control pills and pregnancy increase the risk of pulmonary embolism [41, 42].

The diagnosis of pulmonary embolism can be more difficult in children than adults. One autopsy study suggested that half of all children with pulmonary embolism did not have clinical findings to suggest the diagnosis [43]. Young children may be unable to express subtle symptoms. Children typically have a higher cardiopulmonary reserve and so may have milder symptoms than in an older patient [34]. Some investigators have suggested that, in most children, few symptoms will be apparent if less than 50 % of the pulmonary circulation is obstructed. However, the sensitivity to pulmonary arterial obstruction may depend on the presence of other cardiopulmonary disease and levels of circulating vasoactive molecules [42].

Pulmonary arterial obstruction creates a ventilation/perfusion mismatch and a right-to-left intrapulmonary shunt, which together result in systemic hypoxemia [44, 45]. If a significant portion of the pulmonary circulation is obstructed, then the right ventricle dilates in response to the increased afterload. Leftward shift of the interventricular septum can decrease left ventricle filling, which results in decreased cardiac output [32].

The identification of a patient with a pulmonary embolism begins with clinical assessment. Although the clinical prediction rules and D-dimer testing used in adults have not been validated in children [32], clinical risk assessment still has an important role in determining which patients should undergo further evaluation for pulmonary embolism. The diagnosis of pulmonary embolism is based on an identifiable perfusion defect within the pulmonary circulation. The traditional approach to the diagnosis of pulmonary embolism has been with a lung ventilation/perfusion (V/Q) scan. A perfusion scan may be sufficient to make the diagnosis in some patients. However, the addition of a ventilation lung scan increases the accuracy and confidence of the study.

A variety of protocols have been used for performing a V/Q scan. The ventilation study can precede or follow the perfusion scan. If the perfusion scan is performed first, then the subsequent ventilation scan must be performed with a higher radiopharmaceutical dose to overcome interference from the perfusion scan. The ventilation scan can be performed with either ^{133}Xe gas or inhaled aerosol. One advantage of assessing perfusion first is that a normal perfusion scan may eliminate the need for a subsequent ventilation study. If the ventilation scan is performed first with an inhaled aerosol, then the perfusion scan must be performed with a higher dose of ^{99m}Tc-MAA. If the ventilation scan is performed first with ^{133}Xe gas, the rapid washout of gas limits the number of views that can be acquired, but as there is little interference with the subsequent perfusion scan, the perfusion scan can be performed with a lower administered dose of ^{99m}Tc-MAA. A recent chest radiograph is essential to the correct interpretation of many V/Q scans. If a chest radiograph has not been performed as part the evaluation of the patient's presenting symptoms, then one should be obtained before performing the V/Q scan. As in adults, the diagnosis of pulmonary embolism in children is based on diagnostic criteria used for lung scintigraphy in PIOPED II (Prospective Evaluation of Pulmonary Embolism Diagnosis), but neither the original [46] nor modified [47] PIOPED II criteria have been fully validated in pediatric patients.

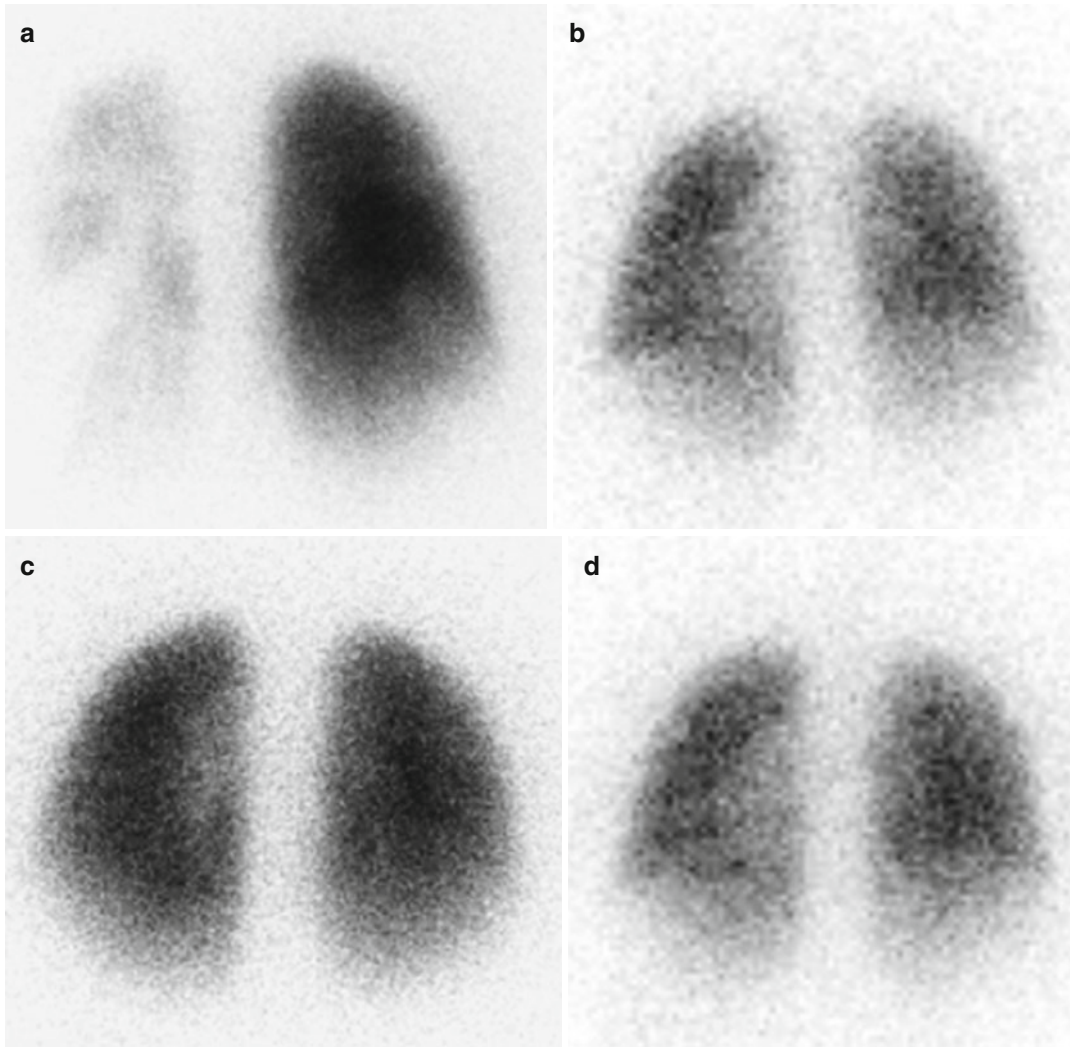

Fig. 6.5 Massive pulmonary embolism identified by ventilation/perfusion scan. A 13-year-old girl with Cushing's disease developed a postoperative deep venous thrombosis and shortness of breath. A perfusion study (**a**, posterior projection) performed with ^{99m}Tc-MAA shows markedly decreased perfusion to the left lung, while a ventilation study (**b**, posterior projection) performed with ^{133}Xe shows a normal ventilation pattern in both lungs. A follow-up study performed 6 weeks later shows resolution of the pulmonary embolism, with normal perfusion (**c**) and ventilation (**d**) in both lungs

Resolution of pulmonary embolism typically occurs spontaneously by fibrinolysis within a few days after the embolic event. However, normal pulmonary blood flow may not return for weeks. Restoration of pulmonary blood flow may be faster in younger patients [48]. Follow-up ventilation/perfusion imaging may be helpful to assess resolution of perfusion defects in patients with pulmonary embolism (Fig. 6.5). This can be particularly helpful in establishing a new baseline for patients at risk for recurrent pulmonary emboli. Ventilation/perfusion imaging also can be helpful in detecting chronic thromboembolic disease in patients with pulmonary hypertension [49].

Ventilation/perfusion scans have been replaced largely by computed tomographic (CT) angiography for evaluation of possible pulmonary embolism in both adults [50] and children [51–53], although there has been a recent resurgence in the use of lung scintigraphy. Ventilation/perfusion scans may be used in patients with contraindications to CT angiography, such as an allergy to iodinated contrast, renal insufficiency, or concerns about radiation dose [54]. In pregnant or lactating patients with suspected pulmonary embolism, the breast radiation dose is less with ventilation/perfusion scan than with CT angiography [54]. Recently, increased concern about radiation exposure, especially in children, has led to a reassessment of the role of ventilation/perfusion scans in the diagnosis of pulmonary embolus. Despite the higher radiation dose with CT angiography, the higher anatomic detail led to its widespread adoption for evaluating possible pulmonary embolism. However, with the adoption of CTA, there has been increased diagnosis of pulmonary embolism, without a clear benefit in patient mortality. This has led some investigators to question if detection of small, subsegmental emboli leads to overdiagnosis of pulmonary emboli [55, 56].

Magnetic resonance imaging techniques have been proposed as alternatives for the diagnosis of pulmonary embolism. The three most common techniques are magnetic resonance angiography (MRA), real-time MR, and MR perfusion. The sensitivity and specificity of each technique may be different, and overall, MR may be slightly less sensitive than CTA [57]. Magnetic resonance techniques have yet to be validated as a reliable method for excluding pulmonary embolism. Other current disadvantages include longer acquisition time, the need for greater patient cooperation with a prolonged breathhold, and less emergent access to MR scanners.

Notwithstanding concerns about the clinical significance of some small angiographic findings, another reason for the widespread adoption of CT angiography has been the perception of higher diagnostic certainty. However, children may have a low rate of indeterminate studies [58]. Use of single-photon emission computed tomography (SPECT) or SPECT/CT for acquiring both the ventilation and perfusion scans may increase diagnostic accuracy and, with fewer indeterminate studies, increase confidence in the interpretation of ventilation/perfusion scan [6, 59]. New diagnostic criteria, similar to PIOPED, may be needed for diagnosing pulmonary embolism by lung SPECT [60]. There has been little reported experience with using SPECT or SPECT/CT for the diagnosis of pulmonary embolism in children.

Other Causes of Pulmonary Perfusion Defects

Every pulmonary embolus does not represent a venous thromboembolism. Pulmonary embolism also can occur with tumor emboli, which may be associated with more extensive obstruction of pulmonary circulation and with systemic hypotension [61, 62]. Other causes of pulmonary emboli include foreign bodies, such as catheter fragments, and posttraumatic fat emboli [61]. Occlusion of a main or branch pulmonary artery or pulmonary vein can occur with extrinsic compression due to tumors at the hilum or in the lung parenchyma [63]. Intrinsic pulmonary artery diseases, including collagen vascular diseases and arteritis, can produce pulmonary artery occlusion [64, 65]. With pulmonary sequestration [66], the involved region of lung typically receives its blood supply from the systemic circulation and will not be visualized after intravenous administration of ^{99m}Tc-MAA. In most cases of pulmonary sequestration, there is no communication with the normal tracheobronchial tree resulting in a matching defect on a ventilation lung scan. Occasionally, a pulmonary sequestration will have an anomalous systemic blood supply with normal connection to the tracheobronchial tree (Fig. 6.6), which produces a ventilation/perfusion mismatch.

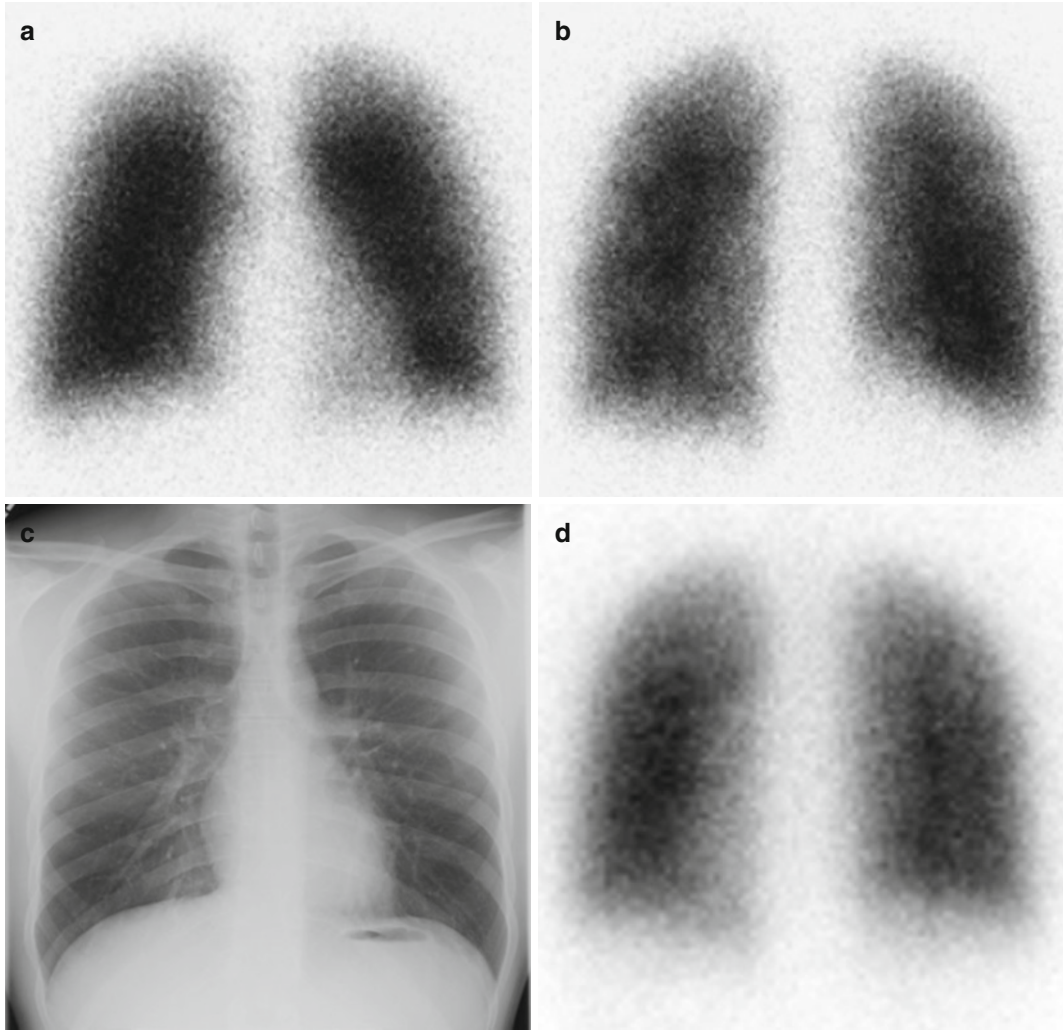

Fig. 6.6 Anomalous blood supply to a lower segment of the right lower lung. A 19-year-old male was found to have an aortopulmonary collateral supplying a segment of the lower lobe of the right lung. After surgical ligation, a ventilation/perfusion scan was performed. A perfusion lung scan in the anterior (**a**) and posterior (**b**) projections shows decreased perfusion at the posterior base of the right lung and confirms the absence of pulmonary perfusion to this region of lung. A postoperative chest radiograph (**c**) shows no abnormalities. A ventilation lung scan was performed with ^{133}Xe and, at respiratory equilibrium, merged posterior images (**d**) demonstrate normal ventilation at the site of the perfusion abnormality. These findings indicate pulmonary sequestration with anomalous systemic perfusion, but an intact tracheobronchial tree

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