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2.1 Overview of Respiratory Physiology

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In analyzing a chest radiograph, it is important to have an understanding of some of the basic principles of respiratory physiology, and to appreciate how certain pathophysiological processes can cause distinct disease states, each with its own specific

clinical signs and symptoms [1, 2]. These can be divided into broad categories, which include obstructive lung disorders, restrictive lung disorders, disorders of gas diffusion, shunts, and ventilation-perfusion abnormalities. The following is a short overview of the physiologic considerations of these complex disorders. For more detail, the reader is advised to refer to the references below.

2.1.1 Obstructive Disorders

Obstructive disorders affect the conducting airways, and result from increased resistance to airflow within the airways and/or increased compliance of the airways. These disorders can be diffuse or localized. They can be caused by the presence of congenitally narrowed bronchi, scarred bronchi (such as in post-infectious bronchiolitis obliterans), intraluminal lesions, debris, or secretions (such as in acute bronchiolitis); dynamic airway wall changes leading to increased resistance to airflow as seen with bronchoconstriction, or increased compliance as is seen in emphysema; and extraluminal compression by a blood vessel or mass. Depending upon which segment of the conducting airways the obstruction is located in, the mechanism involved, and its severity, different phases of the respiratory cycle can be affected. Extrathoracic obstruction primarily causes problems in the inspiratory phase (though the stridor, expiratory phase can be affected as well), and intrathoracic obstruction will cause predominantly expiratory abnormalities (though here too, the Wheezing, inspiratory phase can be affected). The underlying mechanism of this variable behavior is that during inspiration, negative intrathoracic pressure is generated by the inspiratory muscles, drawing air and the walls of the extrathoracic airways

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inward while the intrathoracic airways expand. During expiration, positive pressure is generated within the chest, propelling air outward, causing the intrathoracic airways toward closure, and the extrathoracic airways to expand. When intrathoracic obstruction is significant enough to cause inhomogeneity of emptying in some or many parts of the lung, the chest radiograph shows hyperinflation and air trapping. Examples of common diffuse obstructive disorders include asthma, cystic fibrosis (CF), bronchiolitis obliterans, bronchiectasis, and bronchopulmonary dysplasia. A bronchial foreign body represents a localized obstructive defect. Spirometry, which measures airflow, can quantify the degree of obstruction and is the standard pulmonary function test.

2.1.2 Restrictive Lung Disorders

Restrictive lung disorders occur when the lungs are unable to inflate to normal volumes. They can occur with parenchymal abnormalities, such as interstitial lung disease (idiopathic or secondary to an underlying disorder, such as a surfactant protein deficiency). They can also be caused by a musculoskeletal or neuromuscular abnormality which prevents the chest wall from expanding to full capacity during a maximal inspiratory effort. Examples of this type of restrictive process include congenital myopathies and neuromuscular disorders (such as spinal muscular atrophy). Bony chest wall abnormalities (such as scoliosis and thoracic dysplasia) inhibit lung growth and expansion, as do intrathoracic processes (such as a diaphragmatic hernia, large pleural effusion, or tumor). The chest radiograph may show reduced lung volumes, albeit this may be difficult to pick up in the young child with a limited inspiratory effort. More obvious are distorted or bell-shaped chest walls, scoliosis, or an abnormally diffuse parenchymal process, depending upon the underlying disorder. Physiologic assessment of these disorders is made with lung and thoracic gas volumes measurement using plethysmography and helium dilution methods to quantify the degree of restriction, and measurement of maximal respiratory pressures to assess muscle weakness. With a few exceptions, these methods require patient cooperation and are therefore limited in the young child. While the regular chest radiograph has limited value for quantification

of restriction, algorithms exist to assess lung volumes using chest computed tomography (CT) scans.

2.1.3 Gas Diffusion Disorders

Gas diffusion disorders affect the absorption of oxygen into the bloodstream with resulting hypoxemia. This typically occurs due to a structural abnormality or thickening of the alveolar wall through which the gas exchange between the alveolus and the adjacent capillary occurs, resulting in hampered gas exchange. This can be seen in disease states such as interstitial lung diseases and pulmonary edema. Gas diffusion disorders may present symptomatically with dyspnea upon exertion or at rest, tachypnea, and/or hypoxemia. The chest radiograph often shows an abnormally diffuse parenchymal process. Measurement of the diffusion capacity of the lung with carbon monoxide (DLCO) is diagnostic.

2.1.4 Shunt

Shunt occurs when there is perfusion of a portion of lung without concomitant ventilation of the same area. This results in unoxygenated blood returning to the heart and being pumped into the arterial blood stream, leading to hypoxemia. The hypoxemia caused by shunts does not typically respond to the administration of oxygen. This is because the blood that is being shunted does not come in contact with the supplemental oxygen, while the blood flowing through the normally perfused portions of the lung is already well saturated. Shunts can be seen with arteriovenous malformations, pneumonias, and acute atelectasis. The chest radiograph is frequently reflective of the underlying pathology; however, small vascular malformation in the lungs can be elusive to the standard chest radiograph and need more advanced radiologic methods such as chest CT or MRI imaging.

2.1.5 Ventilation-Perfusion Abnormalities

Ventilation-perfusion abnormalities (also known as V/Q mismatch) occur when there is ventilation of a portion of lung without its concomitant perfusion. They can occur in congenital disorders such as absent

development of a pulmonary artery, or due to intravascular processes such as pulmonary emboli. The physiologic/clinical effect of these disorders is mild relative to shunt, in particular with the long-standing circumstances such as congenital vascular anomalies, often with absence or minor hypoxic effects. The common chest radiograph often is of limited diagnostic value. Thus, when a V/Q mismatch is suspected, a ventilation-perfusion scan may give the clue, and, in cases where a pulmonary embolus is suspected, a CT with IV contrast can be diagnostic.

2.2 Lung Development and Effects on Lung Physiology

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For the pediatric radiologist, lung mechanics and in particular those related to changes in lung volume are of crucial significance. One has to keep in mind that the radiograph of the noncooperative young child is never obtained at the optimal full inflation typical for the older person who inhales to full lung capacity (thus, total lung capacity or TLC) and breath-holds. The lung volumes reflected in the pediatric radiograph (assuming quiet breathing) span a volume range from functional residual capacity (FRC) (the volume at end expiration) to peak of tidal volume (the volume at end inspiration). Thus, by definition, the volume of the normal pediatric radiograph is *always* well below the lung volume of the cooperative patient, with all the implications that this has on the quality of the radiograph. Obviously, the lower the lung volume, the less reliable is the interpretation of pathology.

2.2.1 Stages of Lung Development

Early growth and development of the human lung is a continuous process that is highly variable between individuals and has traditionally been divided into five stages [3]. The first is the embryonic phase (26 days to 6 weeks of gestational age [wGA]), followed by the pseudoglandular (6–16 wGA) stage. At the end of this stage, the major elements of the bronchial tree complete their branching. The third is the canalicular stage (16–28 wGA). In its later phase of this stage, the

prealveolar elements may allow infant survival. The saccular stage (28–36 wGA) is the one in which most premature infants are born, and is followed by the alveolar (36 wGA–term) phase, which continues into childhood. The saccular period, 28–36 wGA, is a transitional phase before full maturation of alveoli occurs. The primitive alveoli that become gradually more effective as gas exchangers have alveolar walls that are more compact and thicker than the final thin walls of alveoli; they also have an immature capillary structure. However, this partially developed structure is capable of carrying out a limited function of gas exchange that fully matures in the alveolar phase. Mature alveoli are not uniformly present until 36 wGA at which time the epithelium and interstitium decrease in thickness, air space walls proliferate, and the capillary network matures to its final single capillary network. Alveolar proliferation represents the predominant element of lung growth after birth. The alveolar proliferation rate is maximal in the first 2 years of life, and subsequently decelerates; however, it is not well established until what age alveolar proliferation is maintained.

The structural changes associated with the transition to mature alveoli through the alveolar stage, and the following alveolar proliferation, account for the subsequent gains in lung volume. Physiologically, these maturational changes not only affect gas exchange, but together with the changes in the chest wall that will be discussed below, have profound effects on the mechanical properties of the respiratory system, and as such on the radiographic characteristics that are affected by these structural and mechanical considerations.

2.2.2 Changes in Lung Volume During the Last Trimester of Gestation

Calculations by Langston et al. [3] revealed that total lung volume undergoes rapid changes during the last trimester of gestation. At 30 wGA, the lung volume is only 34% of the ultimate lung volume at mature birth, and at 34 weeks only reaches 47% of the final volume at maturity. In contrast, the air space walls decrease in thickness such that at 30 and 34 weeks, they are 164% (28 μm) and 135% (23 μm), respectively, relative to the ultimate wall thickness at mature birth (17 μm). In parallel, dramatic increases in air space surface area occur. Surface area increases from 1.0–2.0 m^2 at 30–32 wGA, to 3.0–4.0 m^2 at term.

These volume changes likely have direct mechanical implications in reducing the vulnerability caused by a low and unstable FRC. Maturation of the alveolar network improves parenchymal elastance and therefore airway tethering.

2.2.3 Functional Residual Capacity Tends to be Low and Unstable in Infancy

Maintenance of a stable and adequate FRC is important to secure effective gas exchange. FRC is determined by the balance between the opposing forces of the chest wall and lung and is thus a direct function of their respective mechanical properties. In early life, a compliant chest wall offers little outward recoil to the respiratory system and thus the elastic characteristics of the respiratory system approximate those of the lung. The lung is also more compliant (i.e., has less elastance) in premature and newborn infants. The lung becomes less compliant (i.e., increases in elastance) as it undergoes alveolization and the interstitial network becomes more intricately woven. (*Note:* interstitium here represents the alveolar wall; a different concept from the same term utilized in radiology). Compliance of the chest wall is extremely high in premature infants and undergoes rapid stiffening in late intrauterine life [4], but this stiffening (or decline in compliance) continues over the first 2 years of life [5]. Therefore, in early life (and more so in premature infants), the lung–chest wall equilibrium results in a mechanically determined FRC that is low relative to older children and adults.

Thus, the baseline FRC in the young infant tends to drive itself to low volumes because of the mechanical characteristics discussed above. To circumvent this limitation, infants, unlike older children, actively elevate their FRC. At least three mechanisms are involved in the protection of a high end-expiratory volume: (a) initiation of inspiration at an end-expiratory volume above that determined by the mechanical properties of the chest wall and lung [6]. The other two mechanisms modulate the expiratory flow; (b) use of laryngeal braking during tidal expiration [7], and (c) persistence of inspiratory muscle activity into the expiratory phase [8].

The age at which transition to an *adult* pattern and cessation of these protective mechanisms has not been established for all of them, but based on one study [9] they persist at least into late in the first year and into the second year of life. It is likely that for

premature infant the transition may be delayed. Interference with these active protective mechanisms, such as apnea or sedation, immediately drives the system toward low lung volumes. Also to be kept in mind is that the infant's sleeping state, supine position, and REM sleep (predominant in infancy) all substantially reduce lung volumes [10].

2.2.4 Airway Tethering

An additional crucial mechanism that secures airway patency and thus adequate maintenance of FRC is airway tethering. Tethering is mediated through the elastic components in alveolar walls that surround bronchi. These elastic fibers are anchored to each other creating an extended mesh that exerts a circumferential pull on the intraparenchymal airways. This complex elastic network transmits tension from the pleural surface to individual bronchi; thus, tethering couples lung volume changes to airway caliber. The force oscillates with the inspiratory cycle, and increases during inspiration, increasing airway caliber. The cross-sectional area of the airway decreases with decline in lung volume and airways may close if the lung volume is driven to critically low ranges of FRC (as may occur through the processes described above). Tethering of airways was shown to be absent or less effective in young experimental animals [11] and most likely in infants in whom alveolization and the associated parenchymal elastic network are still in early stages of development. The effect of reduced tethering is decreased airway stability, increased tendency to closure, increased airway resistance, and, ultimately, a tendency to collapse alveolar units in the lung periphery.

2.2.5 Lessons for the Pediatric Radiologist

With the above observations, the radiologist needs to keep in mind that the predictable deficiencies in lung volume in infants, and in particular when interference occurs with the mechanisms that protect lung volume (e.g., sedation), have an immediate effect on the quality of imaging. Chest radiographs and in particular chest CT scans obtained at low lung volumes have artifactual infiltrates in the lung fields that result from closure of airways and atelectases. This occurs in particular in the periphery of the lung and in

dependent areas of the lung that are subjected to gravitational effects. To overcome these effects inflation of the lungs during the acquisition of the imaging is desirable. Most attractive for this purpose is the methodology developed by Long and Castile [12].

Some further physiological concepts related to pediatric respiratory physiology may be of use to the pediatric radiologist. Lung emptying in expiration is under normal circumstances a passive maneuver. Expiratory flow rate is determined by the interplay between a force that expels the air from the lung and the properties of the airways through which this exhaled air traverses. This flow rate is termed the expiratory time constant (τ) and is indeed a product of the compliance of the respiratory system (C) and the resistance of the airways (R) (thus, $\tau = C \times R$). To clarify, the force driving the air out upon relaxation at end inspiration is the elastance of the respiratory system (combined elastic properties of the lung and chest wall); this term is the reciprocal of the previously discussed compliance. In other words, compliant structures such as are the chest wall and the lung in the very young, as discussed above, offer little driving force in exhalation. Small airways, the patency of which is impaired because of relatively small lung volumes and insufficient tethering, offer relatively high resistance to flow. This may be complicated in conditions of uneven structures of airways and parenchyma, because of damage related to trauma to the lung, e.g., by mechanical ventilation, or infection, creating regions that offer uneven emptying profiles, or uneven expiratory time constants, bringing about inhomogeneity in lung emptying.

The need to protect lung volumes through the mechanisms described above results in a rapid breathing rate, short expiratory time, and absent expiratory pauses (rapid transition from expiration to inspiration). In such circumstances, when the breathing rate increases (for reasons such as hypoxia, fever, or infection) there may be insufficient time for full lung emptying, in particular when emptying inhomogeneity is present. This may result in air

trapping and a radiological interpretation of *hyperinflation*. While no systematic studies exist on the duration of this phenomenon, it is likely to resolve within the second year of life when the maturational processes bring about a shift to the *adult* pattern of breathing.

References

1. Bryan AC, Wohl ME. Respiratory mechanics in children. In: Macklem P, Mead J, editors. Handbook of physiology, Sect. 3, Vol. 111: Part 1: Mechanics of Breathing, Chap. 12. American Physiological Society, Bethesda; 1986.
2. West JB. Respiratory physiology: the essentials. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2008.
3. Langston C, Kida K, Reed M, et al. Human lung growth in late gestation and in the neonate. *Am Rev Respir Dis*. 1984;129(4):607–13.
4. Gerhardt T, Bancalari E. Chestwall compliance in full-term and premature infants. *Acta Paediatr Scand*. 1980;69(3):359–64.
5. Papastamelos C, Panitch HB, England SE, et al. Developmental changes in chest wall compliance in infancy and early childhood. *J Appl Physiol*. 1995;78(1):179–84.
6. Kosch PC, Davenport PW, Wozniak JA, et al. Reflex control of expiratory duration in newborn infants. *J Appl Physiol*. 1985;58(2):575–81.
7. Kosch PC, Hutchinson AA, Wozniak JA, et al. Posterior cricoarytenoid and diaphragm activities during tidal breathing in neonates. *J Appl Physiol*. 1988;64(5):1968–78.
8. Mortola JP, Milic-Emili J, Noworaj A, et al. Muscle pressure and flow during expiration in infants. *Am Rev Respir Dis*. 1984;129(1):49–53.
9. Colin AA, Wohl ME, Mead J, et al. Transition from dynamically maintained to relaxed end-expiratory volume in human infants. *J Appl Physiol*. 1989;67(5):2107–11.
10. Henderson-Smart DJ, Read DJ. Reduced lung volume during behavioral active sleep in the newborn. *J Appl Physiol*. 1979;46(6):1081–5.
11. Gomes RF, Shardonofsky F, Eidelman DH, et al. Respiratory mechanics and lung development in the rat from early age to adulthood. *J Appl Physiol*. 2001;90(5):1631–8.
12. Long FR, Castile RG. Technique and clinical applications of full-inflation and end-exhalation controlled-ventilation chest CT in infants and young children. *Pediatr Radiol*. 2001;31(6):413–22.



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