A 30-week-gestation infant is born precipitously and has respiratory distress at 30 minutes of age. You suspect the respiratory distress syndrome of prematurity, and obtain a chest radiograph (Figure).

Figure: Chest radiograph of a newborn with respiratory distress syndrome. Note the ground-glass appearance to the lung-fields. Arrows point to air bronchograms (from AAP PREP Self-Assessment, Item 238A, courtesy of Brian Carter, MD)

You note air bronchograms (arrows) and a ground-glass appearance of the lung-fields on the radiograph.

Of the following, the basic gas law that BEST explains the ground-glass appearance is the law of:

- [ ] Boyle
- [X] Charles
- [ ] Dalton
- [ ] Laplace
- [ ] Poiseuille

You selected [X], the correct answer is [X].

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The basic gas laws are useful to understand respiratory physiology. Boyle’s law relates gas...
pressure and volume. Charles’s law relates volume and temperature. Dalton’s law relates the partial pressures in a gas mixture to the total pressure. Poiseuille’s law relates gas flow through a tube to the tube radius. Laplace’s law relates pressure to surface tension and radius of curvature. Of these, Laplace’s law applied to the small airways of the neonatal lung best explains the microatelectasis that produces the ground-glass appearance of the respiratory distress syndrome on chest radiography.

Laplace’s law states that the gas pressure in a circumscribed volume increases directly with the surface tension at the gas-fluid interface, and inversely with the radius of curvature. As a mammalian lung deflates, the small airways collapse before the alveoli. A small airway with a high surface tension pulling on its surface will close at a higher air pressure than a similar small airway with a low surface tension, as expected by the Laplace law.

Pulmonary surfactant serves to lower the surface tension of small airways and keep them patent at low air pressures. A lack of surfactant causes the small airways to collapse and prevents air from entering the more distal alveoli. Alveolar air is then resorbed and the alveoli collapse. Air is redirected to small airways that have either some surfactant or a larger radius of curvature. The collapse of a large number of small airways causes the diffuse microatelectasis of the respiratory distress syndrome and the ground-glass appearance on radiography.

The Laplace law was applied in the past to the individual alveolus, erroneously assuming independent alveoli of spherical shape and constant curvature. Alveoli are, instead, interdependent, with flat polygonal surfaces. Radial traction from neighboring alveoli and the lung matrix resists alveolar collapse. The two-bubble model of Laplace’s law applied to independent spherical alveoli is no longer presented in current texts.

Boyle’s law states that, given a constant temperature, the product of a gas’s pressure and its volume is constant. Charles’s law states that, given a constant pressure, the ratio of a gas’s volume to its temperature is constant. These relationships are often combined with the laws of Gay-Lussac and Avogadro to give the familiar ideal gas law:

\[ PV = nRT \]

where \( P \) is the pressure in pascals, \( V \) is the volume in cubic meters, \( n \) is the number of moles of gas, \( R \) is the ideal gas constant (8.315 J/mol/K), and \( T \) is the temperature in Kelvins. The ideal gas law allows calculations of gas exchange and ventilation, including the basic observation that delivering more gas to a lung (increasing \( n \)) will cause an increase in \( P \) or \( V \) or both.

Dalton’s law states that the total pressure of a mixture of gases is the sum of each gas’s partial pressure. This law is used in the alveolar gas equation when the partial pressure of water vapor at body temperature (47 mm Hg) is subtracted from the barometric pressure.

Poiseuille’s law relates laminar flow in a tube to several factors. It is often reduced to the concept that the flow varies directly with the fourth power of the radius. This is useful to keep in mind when considering a change to a larger endotracheal tube. A change in inner diameter, from 2.5 mm to 3.0 mm, under the theoretical conditions of an ideal Newtonian gas and laminar flow, allows a doubling of gas exchange for the same pressure. In the cardiovascular system, it is more efficient to regulate blood flow by varying the diameter of a blood vessel than by varying blood pressure. Vasodilation by 50% will increase the blood flow by a factor of 5. A decrease in vessel diameter by 30% will reduce blood flow to one-quarter of its previous rate.

References:


**American Board of Pediatrics Content Specification(s):**

Understand the basic gas laws and how they apply to the clinical setting

Understand the pathophysiology of RDS

Recognize the radiographic features of RDS
An infant was born at 27 weeks' gestation and is now 5 days old. She has a clinically significant patent ductus arteriosus. The infant's resident calls you to report that no urine has been detected since indomethacin treatment was started 12 hours ago. You review the reasons for oliguria and the pathophysiology involving the renin-angiotensin system in preterm infants with the resident.

Of the following, the peptide MOST active in the lung is:

1. angiotensin I
2. angiotensin II
3. angiotensin-converting enzyme
4. angiotensinogen
5. renin

You selected 4, the correct answer is 3.

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A primary function of the renin-angiotensin system is maintenance of blood pressure and fluid volumes (Figures 1 and 2).

Figure 1: Renin-angiotensin system
When stimulated by a drop in blood pressure, the renin-angiotensin system becomes fully active in about 20 minutes. This system also responds to small changes in blood volume, and effects changes in water and sodium retention to maintain homeostasis. The main elements of the system are peptides acting in various body tissues. The main site of action of angiotensin-converting enzyme is the lung.

Renin is a proteolytic glycoprotein made of 340 amino acid residues. It is made and stored in the juxtaglomerular apparatus of the kidney. The stimuli for its release are decreased perfusion pressure in the afferent arterioles, decreased sodium reabsorption through the macula densa,
beta-adrenergic stimulation by the sympathetic nervous system. Angiotensin II inhibits renin secretion. The half-life of renin in the circulation is 15 minutes.

Angiotensinogen, or renin substrate, is an a2-globulin made mainly in the liver. It is a glycoprotein with a molecular weight of 55 to 60 kD, containing 452 amino acid residues. It is split in the circulation by renin to form angiotensin I. Oral contraceptives with estrogen are thought to induce hypertension by increasing serum concentrations of angiotensinogen.

Angiotensin I is a decapeptide made from angiotensinogen in the circulation. It has only a mild vasoconstrictive effect. It serves mainly as a precursor for angiotensin II.

Angiotensin-converting enzyme is a glycoprotein with 1,277 amino acid residues and a molecular weight of 170 kD. It rapidly converts angiotensin I to the vasoconstrictor angiotensin II, and helps in the breakdown of the vasodilator bradykinin. It is made by endothelial cells of the vascular system, and is concentrated in the endothelial cells of the lungs.

Angiotensin II is an octapeptide made from angiotensin I by cleavage with angiotensin-converting enzyme. It is a strong vasoconstrictor, 40 times more potent than norepinephrine and 100 times more potent than angiotensin I. It acts within seconds after an acute dose, but is degraded within minutes. It acts on the arterioles to cause an increase in total peripheral resistance, and on the veins to augment venous return to the heart. It increases norepinephrine release from sympathetic nerves. In the kidneys, it stimulates the proximal tubule to reabsorb sodium. It causes the adrenal gland to make more aldosterone, which also increases salt and water retention.

The oliguria caused by indomethacin likely has two explanations. The first involves vasopressin. In the kidney of the premature neonate, prostaglandin E inhibits fluid retention caused by vasopressin and renin-angiotensin peptides. Indomethacin blocks the production of prostaglandin E, thereby allowing vasopressin and renin-angiotensin peptides to effect fluid retention and oliguria. Before the renin-angiotensin system can downregulate, the potent action of vasopressin combines with the normal action of the renin-angiotensin system to conserve water and cause oliguria.

A second explanation for the neonatal oliguria with indomethacin is based on the observation that indomethacin redistributes renal blood flow away from the mature nephrons of the inner cortex, toward the immature nephrons of the outer cortex. These nephrons have only a limited capacity to excrete sodium and water.

Oliguria associated with indomethacin use is not changed by the concurrent use of dopamine or furosemide, but may be reversed in experimental animal models with the use of a vasopressin inhibitor.

The short answer to the resident in the vignette is that indomethacin disturbs the balance in the kidneys between prostaglandins and the renin-angiotensin system, and between prostaglandins and vasopressin.

References:


American Board of Pediatrics Content Specification(s):
Understand the pathway and control of angiotensin peptide production
Know the actions of the components of the renin-angiotensin system