9 Basic Principles of Mechanical Ventilation

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I. The ventilatory needs of a patient depend largely upon the mechanical properties of the respiratory system and the type of abnormality in gas exchange.
II. Pulmonary Mechanics
   A. The mechanical properties of the lungs determine the interaction between the ventilator and the infant.
   B. A pressure gradient between the airway opening and alveoli drives the flow of gases during inspiration and expiration.
   C. The pressure gradient necessary for adequate ventilation is largely determined by the compliance and resistance (see below).
III. Compliance
   A. Compliance describes the elasticity or distensibility of the lungs or respiratory system (in neonates the chest wall is very distensible and in general does not contribute substantially to compliance).
   B. It is calculated as follows:

$$\text{Compliance} = \frac{\Delta\,\text{Volume}\,(\text{mL})}{\Delta\,\text{Pressure}\ (\text{cm}\,\text{H}_2\text{O})}$$

   C. Compliance in infants with normal lungs ranges from 3 to 5 mL/cm H_2O/kg.
   D. Compliance in infants with respiratory distress syndrome (RDS) is lower and often ranges from 0.1 to 1 mL/cm H_2O/kg (Fig. 9.1).
IV. Resistance
   A. Resistance describes the ability of the gas conducting parts of the lungs or respiratory system (including the chest wall) to impede airflow.

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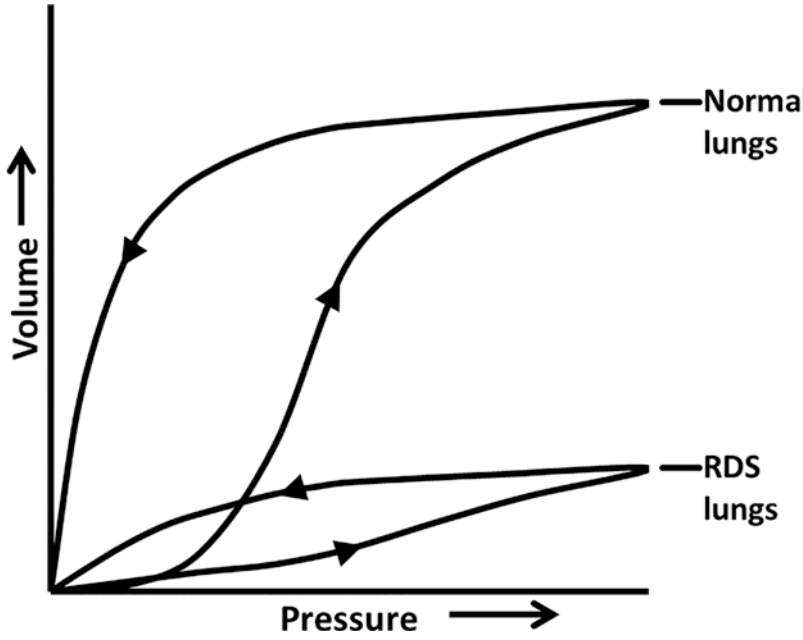

Fig. 9.1 Representation of pressure-volume relationship of the lungs for an infant with normal lung compliance and an infant with respiratory distress syndrome (RDS). The decreased lung compliance manifests as a decreased volume change for a given change in pressure

B. Pressure is needed to force gas through airways (airways resistance includes the nose, nasopharynx, larynx, trachea, and bronchi and accounts for approximately 55% of the total) and to exceed the viscous resistance of the lung tissue (tissue resistance from tissue moving against tissue accounting for 20% of the total) and chest wall (higher in neonates accounting for approximately 25% of the total).
C. It is calculated as follows:

$$\text{Resistance} = \frac{\Delta\,\text{Pressure}\left(\text{cm}\,\text{H}_2\text{O}\right)}{\Delta\,\text{Flow}\ \left(\text{L}/\text{sec}\right)}$$

D. Resistance in infants with normal lungs ranges from 25 to 50 cm H_2O/L/sec. Resistance is not markedly altered in infants with RDS or other acute pulmonary disorders but can be increased in infants with BPD.
E. Resistance can also be increased to 100 cm H_2O/L/sec or more by small endotracheal tubes. It is good practice to use appropriately sized endotracheal tubes and to cut tubes as short as practicable after insertion.

$$\text{Poiseuille's Law}: \text{Resistance} \propto L\eta / r^4$$
$$\left(L = \text{length}, \eta = \text{viscosity, and}\, r = \text{radius}\right)$$

V. Time Constant
A. The time constant is a measure of the time (expressed in seconds) necessary for the alveolar pressure (or volume, or flow) to reach 63% of its steady-state value in response to a stepwise changes in airway pressure (Fig. 9.2).

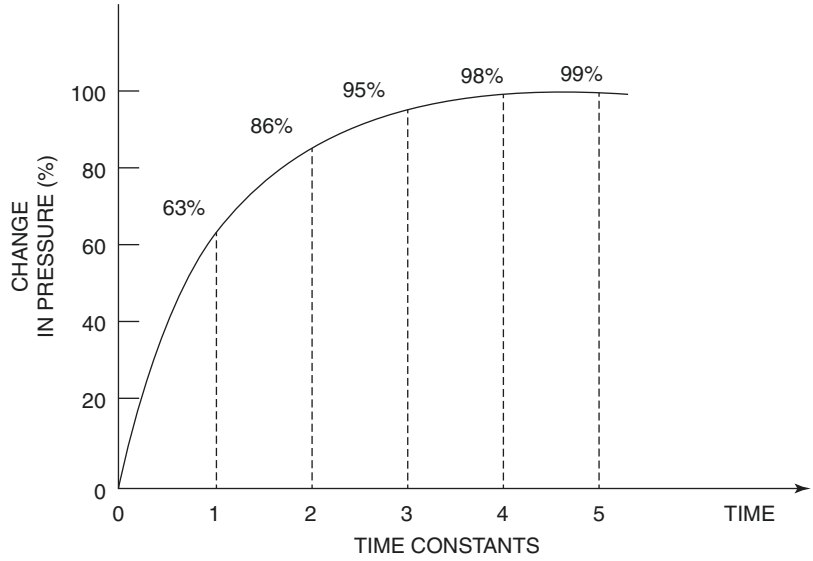

Fig. 9.2 Percentage change in pressure in relation to the time (in time constants) allowed for equilibration. As a longer time is allowed for equilibration, a higher percentage change in pressure will occur. The same rules govern the equilibrium for step changes in volume. Changes in pressure during inspiration and expiration are illustrated. (Modified from Carlo WA, Chatburn RL. Assisted ventilation of the newborn. In Carlo WA, Chatburn RL, editors. Neonatal respiratory care. 2nd ed. Chicago: Year Book Medical Publishers; 1988, p.323, with permission)

B. It is calculated as follows:

$$\text{Time constant} = \text{Compliance} \times \text{Resistance}$$

For example, if an infant has lung compliance of 2 mL/cm H_2O (0.002 L/cm H_2O) and a resistance of 40 cm H_2O/L/sec, the time constant is calculated as follows:

$$\text{Time constant} = 0.002\,\text{L/cm}\,H_2O \times 40\,\text{cm}\,H_2O/\text{L/sec}$$

$$\text{Time constant} = 0.080\,\text{sec}$$

(Note that in the calculation of the time constant, compliance is not normalized to body weight.)

C. A duration of inspiration or expiration equivalent to 3–5 time constants is required for a relatively complete inspiration or expiration, respectively. Once pressure is equilibrated, there will be no more airflow or volume change. Little further equilibration occurs beyond 3–5 time constants (Fig. 9.2). Thus, in the infant described above, inspiratory and expiratory duration should be around 240–400 msec each (or 0.24–0.4 sec).

D. The time constant will be shorter if compliance is decreased (e.g., in patients with RDS) or if resistance is decreased. The time constant will be longer if compliance is high (e.g., big infants with normal lungs) or if resistance is high (e.g., infants with BPD or airway obstruction).

E. Patients with a short time constant ventilate well with short inspiratory and expiratory times and higher ventilatory frequency, whereas patients with a long time constant require longer inspiratory and expiratory times and lower rates.

F. If inspiratory time is too short (i.e., a duration shorter than approximately 3–5 time constants), there will be a decrease in tidal volume delivery (Fig. 9.3).

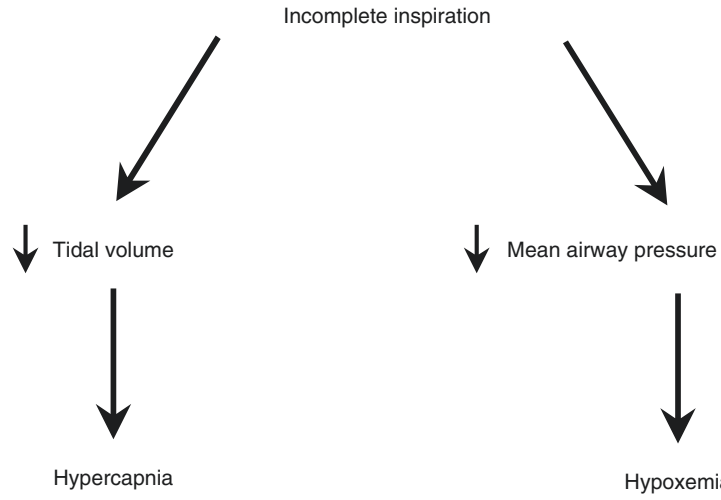

Fig. 9.3 Effect of incomplete inspiration on gas exchange. (From Carlo WA, Greenough A, Chatburn RL. Advances in mechanical ventilation. In Boynton BR, Carlo WA, Jobe AH, editors. New therapies for neonatal respiratory failure: a physiologic approach. Cambridge: Cambridge University Press; 1994. p. 137, with permission)

G. If expiratory time is too short (i.e., a duration shorter than approximately 3–5 time constants), there will be gas trapping and inadvertent positive end expiratory pressure (auto PEEP) (Fig. 9.4). The presence of auto PEEP decreases the driving pressure between airway opening and the alveoli, thus decreasing the tidal volume and potentially shifting the pressure-volume curve away from the PEEP of best compliance.

H. While the respiratory system is often modeled as being composed of a single constant compliance and resistance, it is known that lung mechanics vary with changes in the lung volume, differ from breath to breath, and even change somewhat between inspiration and expiration as resistance is higher during exhalation. In addition, in heterogeneous lung disease such as BPD, different areas of the lungs can have varying mechanical characteristics.

VI. Equation of Motion

A. The pressure necessary to drive the respiratory system is the sum of the elastic, resistive, and inertial components and can be calculated as follows:

$$P = \frac{1}{C}V + R\dot{V} + I\ddot{V}$$

Where
P is pressure
C is compliance
V is volume
R is resistance
$\dot{V}$ is flow
$\ddot{V}$ is the rate of change in flow
I is inertance

B. Inertance is a measure of the tendency of the respiratory system to resist changes in flow. In healthy adults and children, inertance is a minor component of the forces in the respiratory

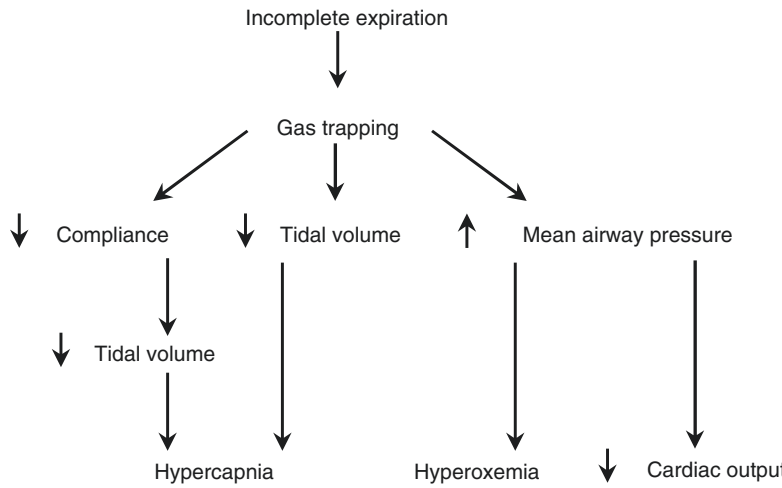

Fig. 9.4 Effect of incomplete expiration on gas exchange. (From Carlo WA, Greenough A, Chatburn RL. Advances in mechanical ventilation. In Boynton BR, Carlo WA, Jobe AH, editors. New therapies for neonatal respiration failure: a physiologic approach. Cambridge: Cambridge University Press; 1994. p. 137, with permission

system. As the inertial component is small at physiologic flows, the last component (IV) can generally be neglected. However, it should be noted that inertance increases as ventilatory rates increase, as is more commonly seen in newborn infants.

C. The equation of motion above can be used to derive estimates of compliance and resistance. For example, between points of V = 0 (points of no flow), the pressure gradient results from compliance only (some ventilators can calculate static compliance between inspiratory and expiratory pauses). Between points of equal volume (e.g., inspiration vs expiration), the pressure gradient results from resistance only. Alternatively, dynamic compliance can be calculated by fitting the equation of motion to multiple measurements of pressure, volume, and flow (e.g., collected every 20 msec during inspiration or expiration).

D. Reactance is a measure of the energy conservation in the respiratory system and includes the elasticity of the lung tissue (that determines lung compliance) and inertia in the airway tree and lung tissues to the forces of acceleration and deceleration of the air column.

VII. Gas Exchange

A. Hypercapnia and/or hypoxemia occur during respiratory failure.

B. Although impairment in CO_2 elimination and oxygen uptake and delivery may coexist, some conditions may affect gas exchange differentially.

VIII. Gas Exchange During Transition to Extrauterine Life

A. Hemodynamic changes during transition to extrauterine life.

1. Systemic vascular resistance increases.
   - Low resistance placental circulation removed.
2. Pulmonary vascular resistance decreases.
   - Lung inflation causes reflex pulmonary vasodilation.
3. Pulmonary blood flow increases.
   - Patent foramen ovale functionally closes as left atrial pressure increases decreasing right to left shunting.
   - Oxygen exposure and nitric oxide production further dilate pulmonary blood vessels.
   - Higher oxygen levels assist PDA closure decreasing right to left shunting.

B. Blood gas values in the perinatal period.

	At birth	10 min of age
PaO_2 (torr)	15–20	46–57
$PaCO_2$ (torr)	49–76	40–47
pH	7.10–7.24 (normalizes by 3–5 hours after birth)	

IX. Determinants of Pulmonary Gas Exchange
- A. Composition and volume of alveolar gas.
- B. Composition and volume of mixed venous blood.
- C. Ratio of ventilation to perfusion in the lungs.
- D. Mechanisms of gas exchange.

X. Composition of Inspired and Alveolar Gases

A. Partial pressure of oxygen in dry air.

Partial pressure of O_2 = fractional content x total gas pressure

If barometric pressure = 760 mmHg, then

$$PO_2 = 0.21(760\,\text{mmHg})$$
$$PO_2 = 160\,\text{mmHg}$$

B. Partial pressure of oxygen in humidified air is affected by humidification as water vapor also exerts a partial pressure.

Partial pressure O_2 = fractional content x (total gas pressure - water vapor pressure)

$$PiO_2 = 0.21(760 - 47\,\text{mmHg})$$
$$PiO_2 = 149\,\text{mmHg}$$

C. Alveolar air equation. Partial pressure of oxygen in humidified alveolar gas is further affected by the presence of carbon dioxide continuously diffusing from capillary blood.

$$\text{Partial pressure of alveolar } O_2 = PiO_2 - PaCO_2\left(FiO_2 + \left[1 - FiO_2\right]/R\right)$$

where P_ACO_2 is alveolar PCO_2 and *R* is the respiratory quotient. R represents the ratio of CO_2 elimination to O_2 uptake and has a typical value of 0.8. Because CO_2 diffuses very well through the alveoli, $PACO_2 \approx PaCO_2$. If barometric pressure = 760 mmHg and water vapor pressure is 47 mmHg, if FiO_2 = 100, then PiO_2 = 713.

If FiO_2 is 1.00, (FiO_2 + [1–FiO_2]/R) = 1.0, then P_AO_2 = 713–40 = 673 mmHg

If FiO_2 is 0.21, then P_AO_2 = 0.21 × (760–47) – 40 × (0.21 + [1–0.21]/0.8) = 102 mmHg.

D. Practical examples of alveolar air equation:

1. Changing FiO_2: If the FiO_2 requirement changes, the CO_2 may also have changed.

For example, if the FiO_2 increases from 0.30 to 0.40 in an infant whose pCO_2 was 45 mmHg and assuming that the A-a DO_2 has not changed and the infant is at sea level, how high may the pCO_2 have increased to? The alveolar gas equation is used to determine the new P_ACO_2 (and pCO_2) as follows:

$$0.40 \times (713) - PaCO_2 / 0.8 = 0.30 \times (713) - 45 / 0.8$$
$$PaCO_2 = 0.8(285 - (214 - 56)) = 102\,\text{mm Hg}$$

Therefore, it is common practice to follow the CO_2 if there is an increasing FiO_2 requirement due to the potential of hypercapnia.

2. Changing altitude: If an infant moves from one altitude to a different altitude, the FiO_2 requirement may change as the barometric pressure changes.

   For example, what FiO_2 may be needed in a cabin (c) pressurized to 570 mmHg during air transport of an infant on FiO_2 = 0.3 at sea-level (s)? First, simplify the equation by solving as follows:

$$\begin{aligned}(Pc - PH2O)\,xFiO2c &= (Ps - PH2O)\,xFiO2s\\ FiO2c &= (760 - 47)\,x0.30 / 570 - 47\\ &= 214 / 523 = 0.41\end{aligned}$$

Therefore, infants may require additional supplemental oxygen to maintain partial pressure of oxygen during air transport in a pressurized cabin or when moving to a higher altitude.

XI. Composition of Mixed Venous Blood

A. Mixed venous PO_2 (PvO_2) depends on arterial O_2 content, cardiac output, and metabolic rate.

B. Oxygen content of blood per 100 mL is the sum of blood dissolved in the plasma (minor component) and oxygen bound to hemoglobin (major component).

   Dissolved O_2 = 0.003 mL O_2 per mmHg of PaO_2

   Hemoglobin bound O_2 = O_2 Sat × 1.34/gm hemoglobin × hemoglobin concentration

   For example, 1 kg infant (blood volume ≈ 100 mL) with PaO_2 = 100 mmHg (O_2 sat = 100%, or 1.0), and hemoglobin =17 mg/dL

$$\begin{aligned}&O_2\text{content} = \text{hemoglobin bound}\,O_2 + \text{dissolved}\,O_2\\ &O_2\text{content} = 1.00 \times 1.34 \times 17 + 0.003 \times 100\\ &O_2\text{content} = 22.78 + 0.3\,\text{mL}\,O_2\\ &O_2\text{content} = 23.08\,\text{mL}\,O_2\end{aligned}$$

C. CO_2 content of blood.

   CO_2 is carried in three forms: (1) as carbonic acid dissolved in plasma (main component) and red cells; (2) as bicarbonate; and (3) bound to hemoglobin as carbamine compounds.

XII. Hypoxemia

The pathophysiologic mechanisms responsible for hypoxemia are in order of relative importance in newborns: ventilation-perfusion mismatch, shunt, hypoventilation, and diffusion limitation (Figs. 9.5, 9.6, and 9.7):

A. Ventilation-perfusion ($\dot{V}/Q$) mismatch

   $\dot{V}/Q$ mismatch is an important cause of hypoxemia in newborns. Supplemental oxygen can largely overcome the hypoxemia resulting from $\dot{V}/Q$ mismatch by displacing nitrogen from the alveoli.

B. Shunt

   Shunt is a common cause of hypoxemia in newborns. A shunt may be physiologic, extrapulmonary (e.g., PPHN, congenital cyanotic heart disease), or intrapulmonary (e.g., atelectasis). It can be thought of as a $\dot{V}/Q = 0$ and supplemental O_2 cannot reverse the hypoxemia caused by a large shunt (>30%).

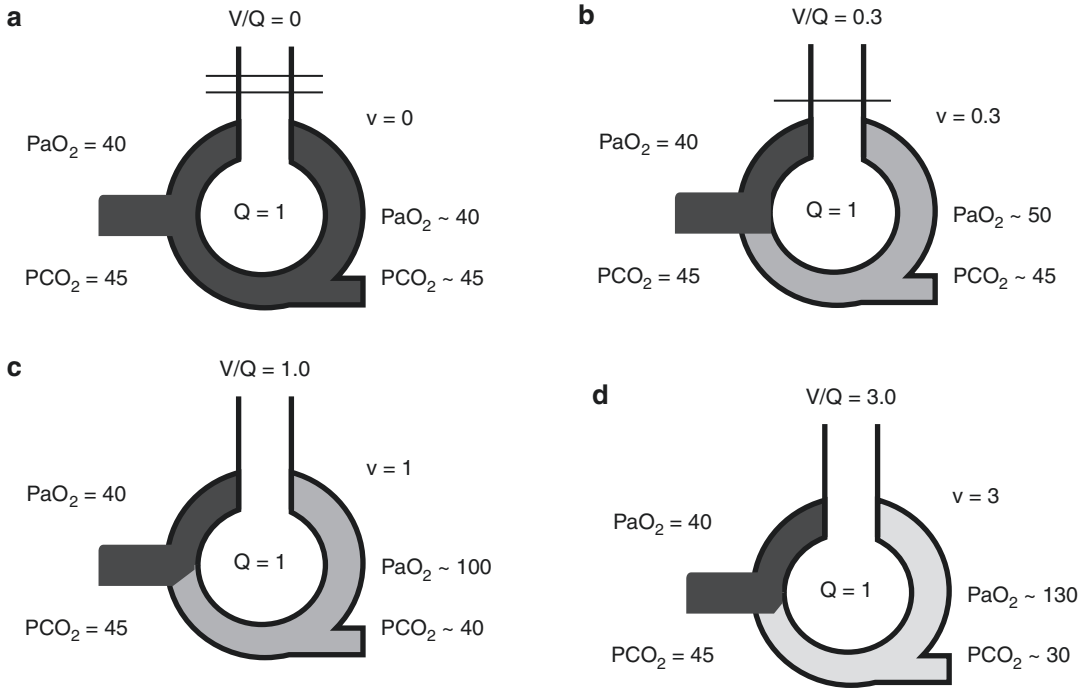

Fig. 9.5 Effects of various ventilation/perfusion ratios on blood gas tensions. (**a**) Direct venoarterial shunting ($V_A/Q = 0$). (**b**) Alveolus with a low V_A/Q ratio. (**c**) Normal alveolus. (**d**) Underperfused alveolus with high V_A/Q ratio

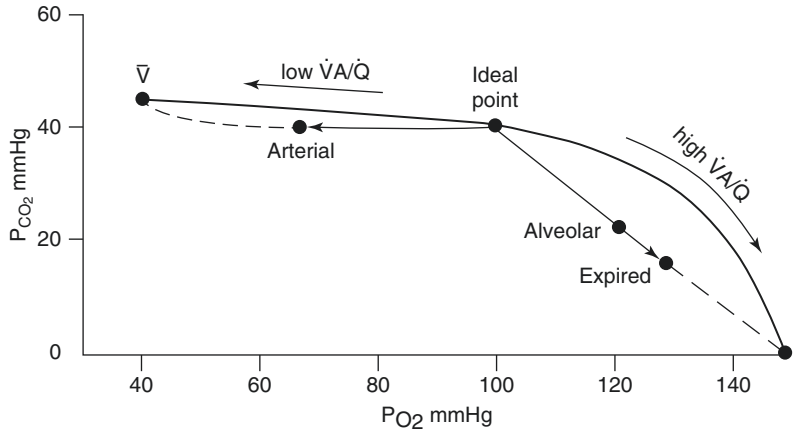

Fig. 9.6 O_2-CO_2 diagram showing the arterial, ideal, alveolar, and expired points. The curved line indicates the PO_2 and PCO_2 of all lung units having different ventilation/perfusion ratios. (From West JB. Gas exchange. In West JB, editor. Pulmonary pathophysiology: the essentials. Baltimore: Williams & Wilkins; 1977. p. 27, with permission)

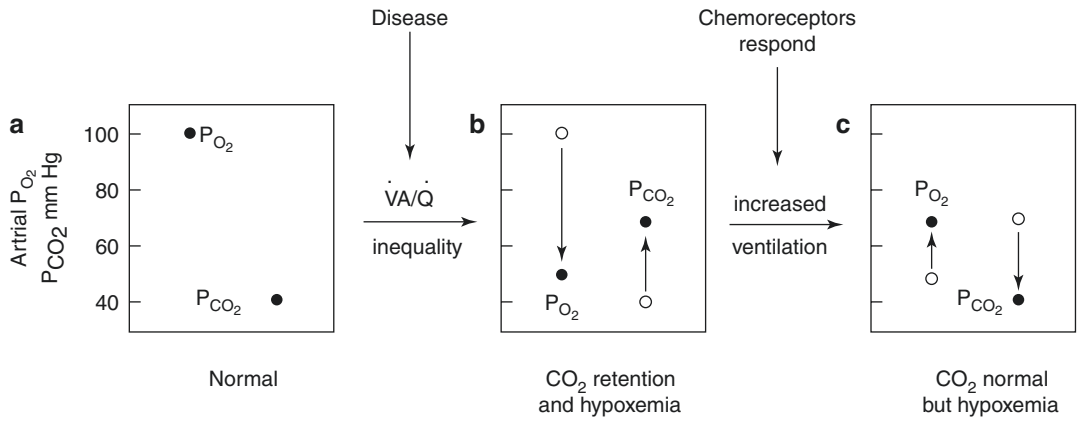

Fig. 9.7 PO_2 and PCO_2 in different stages of ventilation/perfusion inequality. Initially, there must be both a fall in oxygen and a rise in carbon dioxide tensions. However, when the ventilation to the alveoli is increased, the PCO_2 returns to normal, but the PO_2 remains abnormally low. (From West JB. Gas exchange. In West JB, editor. Pulmonary pathophysiology: the essentials. Baltimore: Williams & Wilkins; 1977. p. 30, with permission)

C. Hypoventilation

Hypoventilation results from a decrease in minute alveolar ventilation such that the metabolic consumption of oxygen exceeds the supply. Thus, alveolar PO_2 falls and PaO_2 decreases. It can be thought of as low $\dot{V}/Q$ and supplemental O_2 can overcome the hypoxemia easily (see alveolar air equation). Causes of hypoventilation include depression of respiratory drive, weakness of the respiratory muscles, restrictive lung disease, and airway obstruction.

D. Diffusion limitation

Diffusion limitation is an uncommon cause of hypoxemia in neonates, even in the presence of lung disease. Diffusion limitation occurs when mixed venous blood does not equilibrate with alveolar gas. Supplemental O_2 can overcome hypoxemia secondary to diffusion limitation.

XIII. Oxygenation During Assisted Ventilation.

A. Oxygenation may be increased by increasing the concentration gradient (FiO_2), by optimizing lung volume (surface area), which in turn depends on mean airway pressure (Fig. 9.8), or by maximizing blood flow to ventilated areas of the lungs (decreasing shunts).

B. Mean airway pressure is the average pressure to which lungs are exposed during the respiratory cycle. Graphically, it is equivalent to the area between the airway pressure vs time curve, for one cycle, divided by the cycle time (i.e., inspiratory time plus expiratory time).

C. During pressure targeted modes, increasing any of the following will increase mean airway pressure: inspiratory flow (i.e., if it is adjustable and it indirectly decreases the pressure rise time), peak inspiratory pressure (PIP), the inspiratory to expiratory (I:E) ratio, or PEEP. Decreasing the pressure rise time (when the control is available) also has a small effect of increasing mean airway pressure. Faster ventilator rates may also have an effect on mean airway pressure, as there are more "areas under the curve" in the same time interval.

D. Mean airway pressure maybe calculated as follows:

$$\textit{Mean airway pressure} = K\left(PIP - PEEP\right)\left[TI/\left(TI + TE\right)\right] + PEEP$$

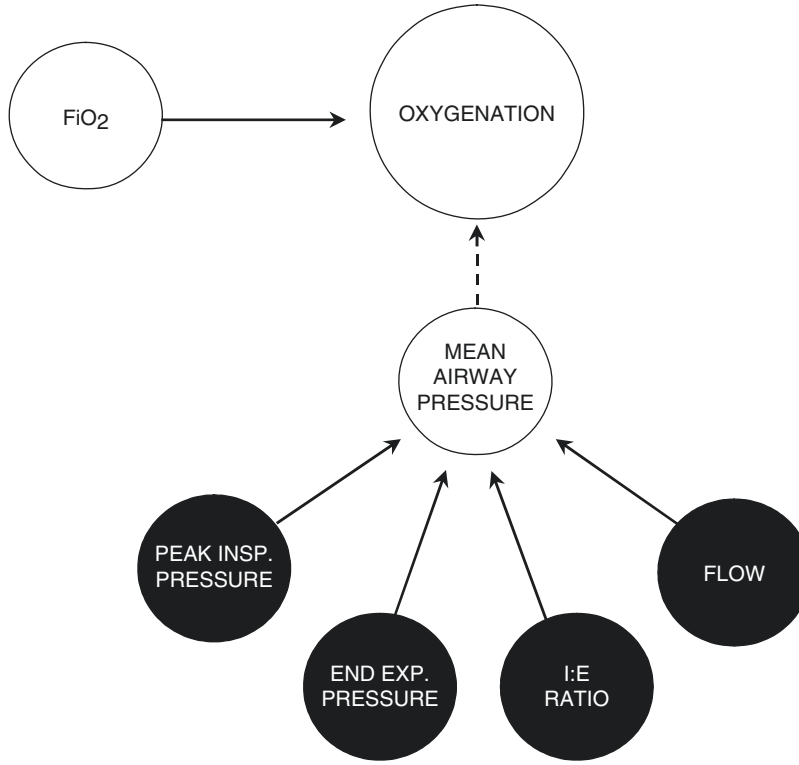

Fig. 9.8 Determinants of oxygenation during pressure-limited, time-cycled ventilation. Shaded circles represent ventilator-controlled variables. Solid lines represent the simple mathematical relationships that determine mean airway pressure and oxygenation, whereas dashed lines represent relationships that cannot be quantified. (From Carlo WA, Greenough A, Chatburn RL. Advances in mechanical ventilation. In Boynton BR, Carlo WA, Jobe AH, editors. New therapies for neonatal respiration failure: a physiologic approach. Cambridge: Cambridge University Press; 1994. p. 134, with permission)

where K is a constant that depends on the rate of rise of the early inspiratory part of the airway pressure curve (K ranges from approximately 0.8 to 0.9 during pressure targeted modes of ventilation); T_I is inspiratory time; and T_E is expiratory time.

For the same change in mean airway pressure, increases in PIP and PEEP increase oxygenation more.

E. The relationship of mean airway pressure to oxygenation is not linear. A very high mean airway pressure transmitted to the intrathoracic structures may increase pulmonary vascular resistance and increase right to left shunting across a patent ductus arteriosus or patent foramen ovale causing decreased pulmonary blood flow and decreased oxygen transport despite an adequate PaO_2.

XIV. Hypercapnia

The pathophysiologic mechanisms responsible for hypercapnia are $\dot{V}/Q$ mismatch, shunt, hypoventilation, and increased physiologic dead space. The physiologic dead space results in part from areas of inefficient gas exchange because of low perfusion (wasted ventilation). Physiologic dead space includes ventilation to conducting airways and alveolar spaces not perfused (i.e., anatomical dead space).

XV. CO_2 Elimination During Assisted Ventilation

A. CO_2 diffuses easily into the alveoli and its elimination depends largely on the total amount of gas that comes in contact with the alveoli (alveolar ventilation). Minute alveolar ventilation is calculated from the product of the frequency (number of breaths per minute) and the alveolar tidal volume (tidal volume minus dead space).

$$\text{Minute alveolar ventilation} = \text{frequency} \times \begin{pmatrix} \text{tidal volume} \\ \text{minus dead space} \end{pmatrix}$$

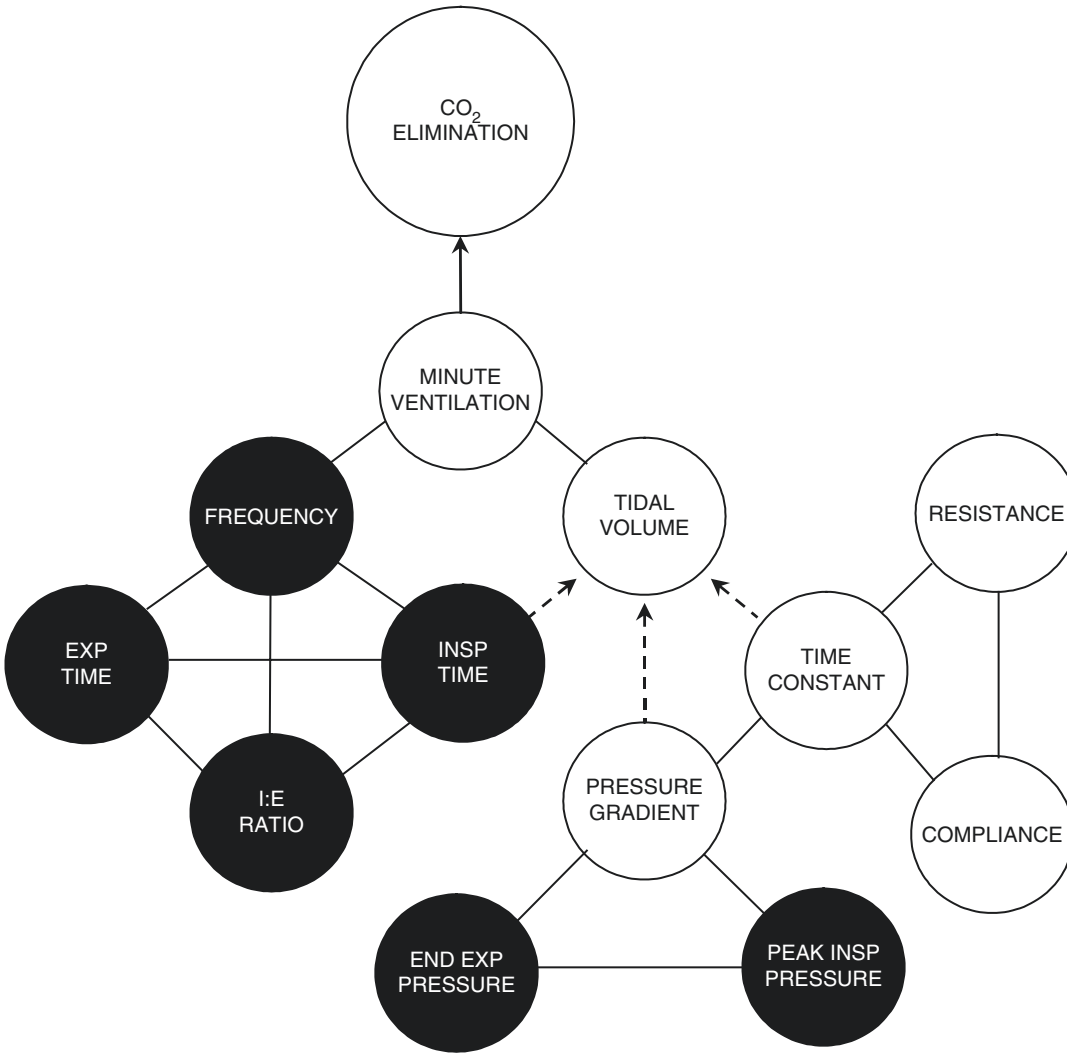

Fig. 9.9 Relationships among ventilator-controlled variables (shaded circles) and pulmonary mechanics (unshaded circles) that determine minute ventilation during time-cycled, pressure-limited ventilation. Relationships between circles joined by solid lines are mathematically derived. The dashed lines represent relationships which cannot be precisely calculated without considering other variables such as pulmonary mechanics. Alveolar ventilation can be calculated from the product of tidal volume and frequency when dead space is subtracted from the former. (From Carlo WA, Greenough A, Chatburn RL. Advances in mechanical ventilation. In Boynton BR, Carlo WA, Jobe AH, editors. New therapies for neonatal respiration failure: a physiologic approach. Cambridge: Cambridge University Press; 1994. p.133, with permission)

Anatomical dead space is relatively constant. Therefore, changes in tidal volume and frequency increase alveolar ventilation.

B. During volume targeted ventilation (i.e., preset tidal volume and inspiratory flow), the desired tidal volume is preset. During pressure targeted ventilation, the tidal volume depends on the pressure gradient between the airway opening and the alveoli; this is peak inspiratory pressure (PIP) minus the positive end expiratory pressure (PEEP) or amplitude (ΔP).
C. Depending upon the time constant of the respiratory system (and the expiratory path of the patient circuit of the ventilator), an inspiratory time (T_I) that is too short may reduce the tidal volume, and an expiratory time (T_E) that is too short may cause gas trapping and inadvertent PEEP, thereby reducing tidal volume (see above).
D. Figure 9.9 illustrates the relationships among ventilator controls, pulmonary mechanics, and minute ventilation. Ventilator controls are shown in shaded circles.
E. Adequate PEEP prevents alveolar collapse and maintains lung volumes at end expiration. Mechanical ventilation without PEEP causes surfactant inactivation, decreased lung compliance, and atelectotrauma from recurrent shear forces from the reopening of collapsed terminal airways. However, use of excessive PEEP may decrease lung compliance and decrease tidal volume for a given ΔP without substantially improving oxygenation.

XVI. Blood Gas Analysis

A careful interpretation is essential for appropriate respiratory care (Table 9.1, Figs. 9.10 and 9.11, Chap. 20).

A. Respiratory acidosis (low pH, high $PaCO_2$, normal HCO_3).
   1. From $\dot{V}/Q$ mismatch, shunt, and/or hypoventilation.
   2. Secondary renal compensation begins within 6–12 hours.
      (a) Reduction in bicarbonate excretion.
      (b) Increased hydrogen ion excretion.

      Activation of alternative buffer systems may begin immediately (e.g., hemoglobin, albumin, globulin, and phosphate)
B. Respiratory alkalosis (high pH, low $PaCO_2$, normal HCO_3^-).
   1. From hyperventilation.

Table 9.1 Blood gas classifications [a]

Classification	pH	$PaCO_2$	HCO_3^-	BE
Respiratory disorder				
Uncompensated acidosis	↓	↑	N	N
Partly compensated acidosis	↓	↑	↑	↑
Compensated acidosis	N	↑	↑	↑
Uncompensated alkalosis	↑	↓	N	N
Partly compensated alkalosis	↑	↓	↓	↓
Compensated alkalosis	N	↓	↓	↓
Metabolic disorder				
Uncompensated acidosis	↓	N	↓	↓
Partly compensated acidosis	↓	↓	↓	↓
Uncompensated alkalosis	↑	N	↑	↑
Partly compensated alkalosis	↑	↑	↑	↑
Compensated alkalosis	N	↑	↑	↑

From Carlo WA, Chatburn RL. Assessment of neonatal gas exchange. In Carlo WA, Chatburn RL, editors. Neonatal respiratory care. 2nd ed. Chicago: Year Book Medical Publishers; 1988, p. 51, with permission

[a] *Arrows* elevated or depressed values, *N*, normal; *BE* base excess

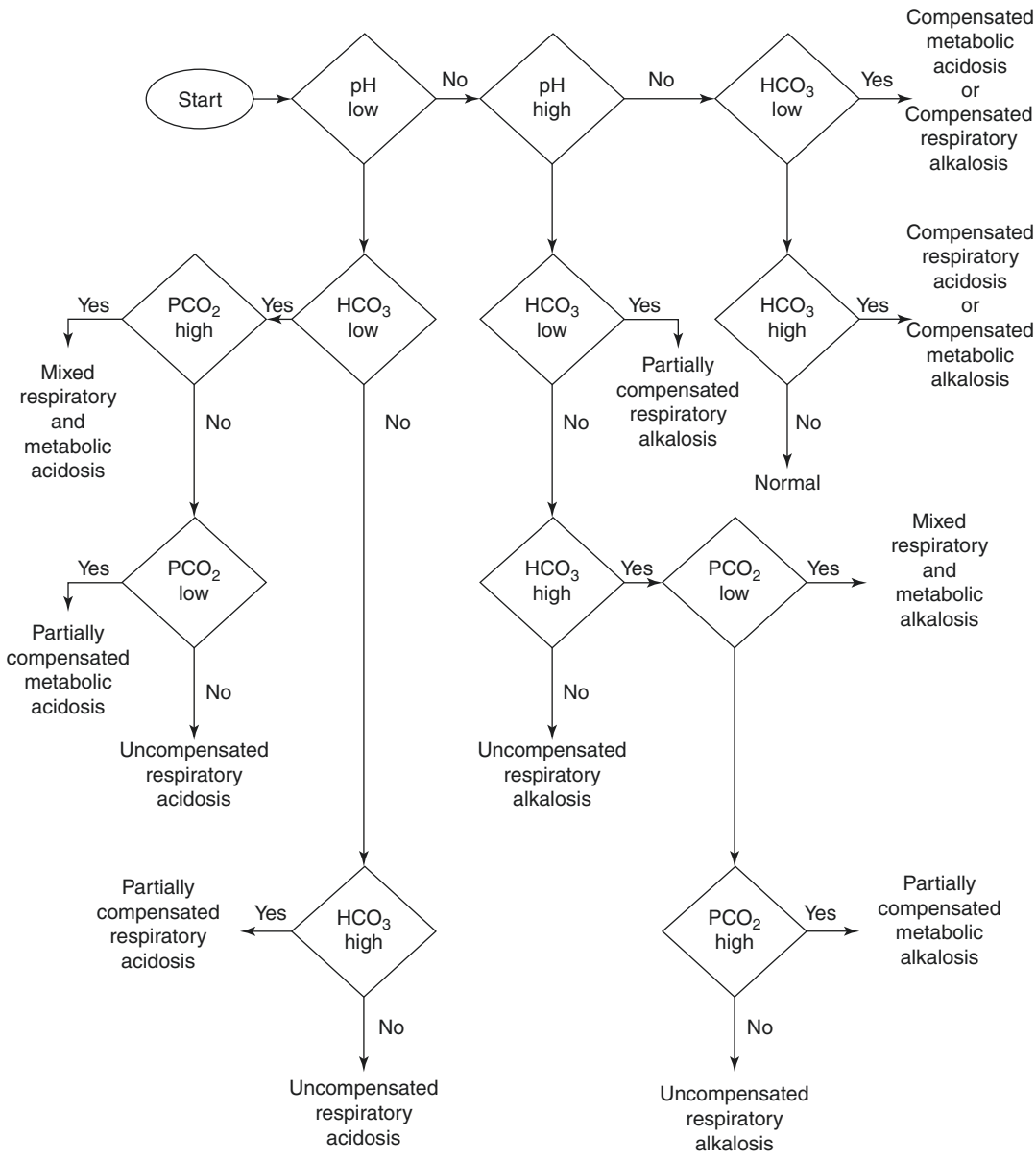

Fig. 9.10 A flow chart illustrating the algorithm through which a set of arterial blood gas values may be interpreted (From Chatburn RL, Carlo WA. Assessment of neonatal gas exchange. In Carlo WA, Chatburn RL, editors. Neonatal respiratory care. 2nd ed. Chicago: Year Book Medical Publishers; 1998. p 56, with permission)

2. Secondary renal compensation begins within 6–12 hours.

   (a) Increased bicarbonate excretion.
   (b) Retention of chloride.
   (c) Reduced excretion of acid salts and ammonia.

C. Metabolic acidosis (low pH, normal $PaCO_2$, low HCO_3^-).

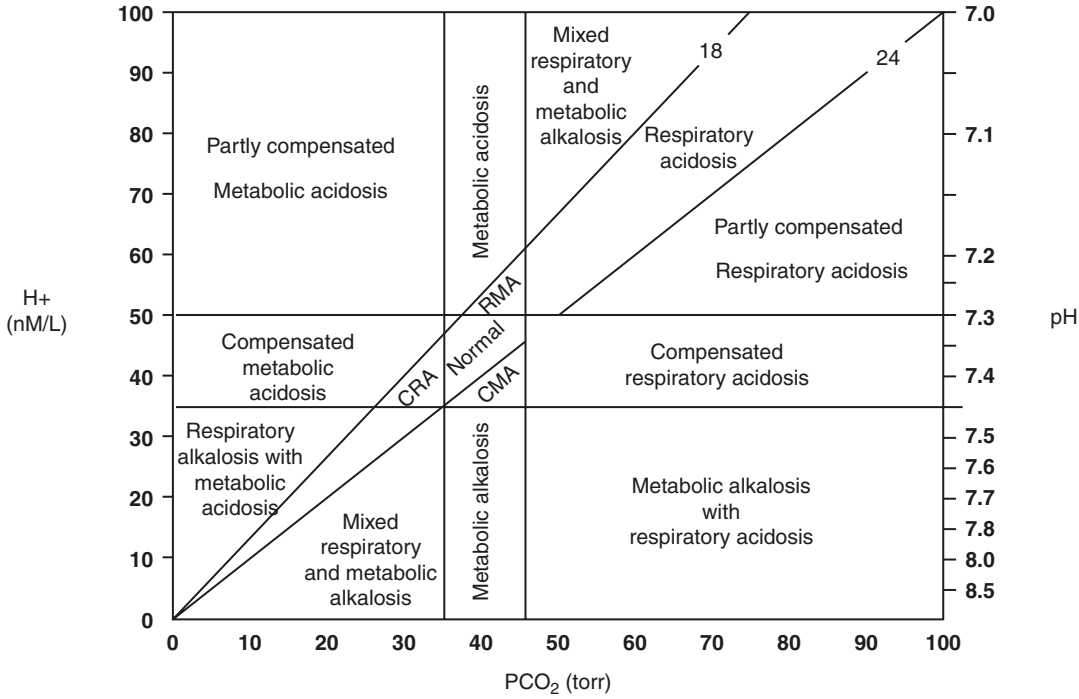

Fig. 9.11 A neonatal acid-base map. CRA compensated respiratory acidosis, CMA compensated metabolic acidosis, RMA mixed respiratory and metabolic acidosis. (From Chatburn RL, Carlo WA. Assessment of neonatal gas exchange. In Carlo WA, Chatburn RL, editors. Neonatal respiratory care. 2nd ed. Chicago: Year Book Medical Publishers; 1998. p 58, with permission)

1. From increased acid production (e.g., sepsis, inborn errors of metabolism) or intake (e.g., acidified human milk fortifiers), or excessive bicarbonate elimination (e.g., renal tubular acidosis, diarrhea).
2. Secondary pulmonary compensation may begin almost immediately – hyperventilation with decreased $PaCO_2$.
3. Activation of alternative buffer systems may begin immediately (e.g., hemoglobin, albumin, globulin, and phosphate).

D. Metabolic alkalosis (high pH, normal $PaCO_2$, high HCO_3^-)
1. From excessive $NaHCO_3$ or acetate administration, diuretic therapy, and loss of gastric secretions (e.g., gastric suctioning, emesis).
2. Secondary pulmonary compensation may begin almost immediately – hypoventilation with increased $PaCO_2$.

Suggested Reading

Carlo WA, Chatburn RL. Assisted ventilation of the newborn. In: Carlo WA, Chatburn RL, editors. Neonatal respiratory care. 2nd ed. Chicago: Year Book Medical Publishers; 1988. p. 320–46.

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