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Rational monitoring of respiratory function during mechanical ventilation of infants and children

D. C. Shannon

Children's Service, Pulmonary Unit, Massachusetts General Hospital, Boston, Massachusetts, USA

Abstract. Oxygen and carbon dioxide homeostasis (effective pulmonary gas exchange) requires that lung exchange matches tissue exchange. The movement of gas in and out of the lung is determined by the mechanical properties of the system especially resistance and compliance and the work needed to provide this movement is supplied either by the patient's muscles or by the mechanical ventilator. If the latter is required, its optimal use demands that the user understands the relationship between the mechanical device and the mechanical properties of the patient's respiratory system so that optimal gas exchange can be provided. The following discussion provides the minimum physiological information needed for successful use of a mechanical ventilator and suggests that this requires measurement of at least four parameters: alveolar partial pressure of CO_2 (PA_{CO_2}), arterial oxygen saturation (Sa_{O_2}), the mechanical RC time constant (RC) and functional residual capacity (FRC).

Key words: Monitoring – Mechanical ventilation – Lung mechanics in infants

Gas exchange, alveolar ventilation and pulmonary blood flow

Ventilator management of children in most intensive care units is based solely on measurements of arterial blood gases along with corresponding measurements of inspired O_2 concentration. In more sophisticated units, other measurements are obtained including vital capacity, functional residual capacity, compliance, air flow resistance and maximal pressures generated during inspiration or expiration. Under certain conditions, one or more of these measurements of volume and mechanical characteristics might provide useful, even necessary information. Given that a ventilator and the respiratory system are both mechanical pumps, I have asked, for purposes of this presentation, what is the minimum information that the clinician requires in order to match the performance of the two pumps in order to maximize pulmonary gas exchange.

I conclude that the mechanical properties of the respiratory system must be matched by the mechanical ventilator in order to optimize exchange of oxygen and carbon dioxide. In simplest form, the respiratory system is considered to be analogous to an electrical circuit in which a capacitor (the lung) is filled by a driving pressure (diaphragm or mechanical ventilator) across resistors (airways). The capacitor then empties through the same resistors under the influence of stored energy, the elastic recoil of the system. Optimum monitoring of a patient during mechanical ventilation requires knowledge of the mechanical terms analogous to those of an electrical circuit; i.e. capacitance = compliance and resistance = air flow resistance. Lack of such knowledge can result in life threatening complications because of a mismatch between these mechanical properties of the respiratory system and those of the ventilator.

Under ideal conditions, oxygen and carbon dioxide exchange in the lung as a function of time matches oxygen utilization and carbon dioxide production in tissues delayed only by the circulation time from tissues to lung.

$$\dot{V}_{O_2 lung}\,(t) = \dot{V}_{O_2 tissue}\,(t)$$

$$\dot{V}_{CO_2 lung}\,(t) = \dot{V}_{CO_2 tissue}\,(t)\ .$$

Exchange in the lung depends on alveolar ventilation ($\dot{V}_A$), the amount of gas per unit time entering and exiting the alveoli, matching with pulmonary perfusion ($\dot{Q}_c$) where blood flow entering the pulmonary capillaries reflects tissue gas exchange.

$$\dot{V}_A\,(t) = \dot{Q}_c\,(t)$$

This equality is not surprising. Inspired air is about 20% oxygen by volume and blood at full saturation carries 20 ml O_2/dl by volume.

The alveolar gas equations are equations of state which define the alveolar partial pressures (or fractions) as a function of the alveolar ventilation rate at the prevailing rates of O_2 and CO_2 exchange in the lung.

$$PA_{O_2} = P_{IO_2} - \dot{V}_{O_2 lung}/\dot{V}_A \ (P_B - 47)$$
$$PA_{CO_2} = \dot{V}_{CO_2 lung}/\dot{V}_A \ (P_B - 47) \ .$$

Thus, we see that oxygen uptake $\dot{V}_{O_2 lung}$ and carbon dioxide elimination $\dot{V}_{CO_2 lung}$ both depend on alveolar ventilation $\dot{V}_A$. Note that the CO_2 case is simpler because PI_{CO_2} is usually zero. Otherwise these two equations are analogous.

Combining these two equations, we find that PO_2 of an alveolus is determined by the inspired pressure (P_{IO_2}), the level of alveolar ventilation (i.e. PA_{CO_2}) and the metabolic exchange ratio, $\dot{V}_{CO_2}/\dot{V}_{O_2}$, expressed as R.

$$PA_{O_2} = PI_{O_2} - PA_{CO_2}/R \ .$$

Since O_2 uptake depends on blood flow and CO_2 elimination depends on ventilation we see that R in an alveolus depends on both $\dot{V}_A$ and $\dot{Q}_c$, the volume of blood flowing through the pulmonary capillaries per unit time. This implies that PA_{O_2} also depends on these two parameters. In fact, the $\dot{V}_A/\dot{Q}_c$ ratio uniquely defines the PA_{O_2} for a given alveolus and arterial PO_2 is determined by the $\dot{V}_A/\dot{Q}_c$ ratios across the lung weighted by the respective fractions of lung so affected (Fig. 1).

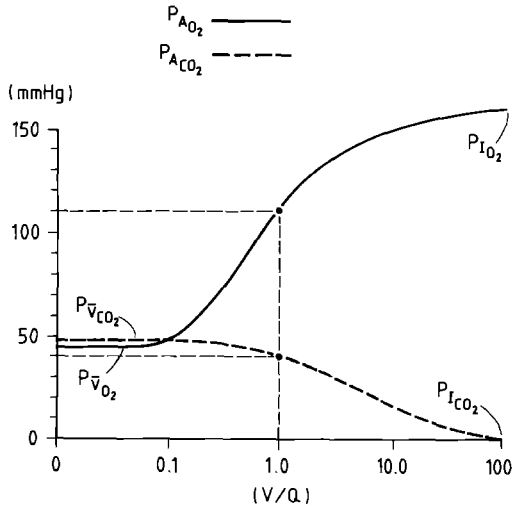

Fig. 1. The P_AO_2/P_ACO_2 diagram. The alveolar partial pressures of oxygen (solid line) and carbon dioxide (dashed line) are plotted as a function of the $\dot{V}/\dot{Q}$ ratios of single alveoli ranging from 0.01 to 100. These pressures are limited at the one extreme by the mixed venous partial pressures in alveoli with negligible ventilation and at the other extreme by inspired gas composition in alveoli with no blood flow

Ventilation, resistance and compliance

By definition, alveolar ventilation $\dot{V}_A$ is total ventilation minus dead space ventilation. It may be represented in terms of tidal and dead space volume and breathing frequency

$$\dot{V}_A = f(V_T - V_D) \ .$$

If one assumes that the mechanical properties of the respiratory system may be modeled by a resistance in series with a compliance, then tidal volume, is related to compliance (C) where

$$C = \Delta V/\Delta P \text{ (units of } L/cmH_2O)$$

and ventilation f(VT) is related to resistance (R) where

$$R = \Delta P/\dot{V} \text{ (units of } cmH_2O/L_{sec})$$

is a dependence that is analogous to Ohm's Law (Resistance = Voltage/Current).

If compliance (C) falls at constant pressure difference, equilibrium volume must fall; alternatively, VT can be maintained by a proportional increase in pressure difference and thus, work performed either by the patient or the mechanical ventilator. Likewise, if resistance (R) increases at a given pressure difference across the system, air flow rate falls. It follows then that since air flow rates and volumes depend on the mechanical properties of the respiratory system, R and C, so do $\dot{V}_{O_2 lung}$ and $\dot{V}_{CO_2 lung}$. Thus, pulmonary gas exchange depends on alveolar air flow rates on inspiration and expiration which, in turn, depend on R and C. Air flow rates in excess of those predicted by knowledge of resistance and compliance can only be achieved by increased muscular effort in the patient who is ventilating spontaneously. In the case of a mechanically ventilated patient who is receiving muscle relaxants, air flow rates on inspiration depend on the driving pressure difference generated by the mechanical device and those on expiration depend entirely on the driving pressure generated by lung elastic recoil. During both inspiration and expiration, the time course volume change is determined by the resistance and compliance. In order to provide optimal pulmonary gas exchange it is necessary to match the mechanical device to the mechanical properties of the respiratory system. This requires that we know the RC time constant.

The RC time constant

In order to estimate the time course of air flow within a breath we borrow the concept of a time constant

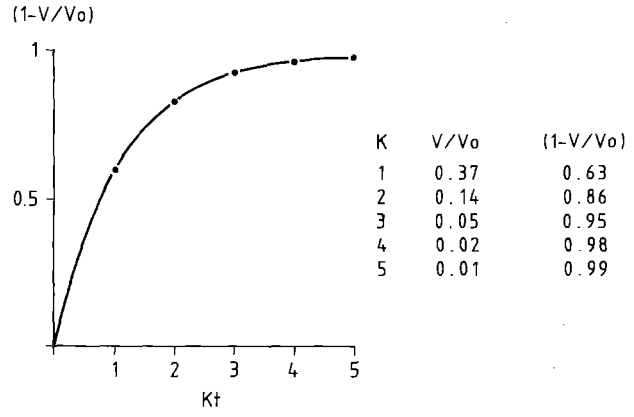

Fig. 2. The fraction of volume eliminated (1-V/VO) from the respiratory system (modeled as a capacitance) is plotted as a function of the mechanical RC time constant. Note that 98% of volume is eliminated in 4 time constants; this is generally called the equilibrium time constant

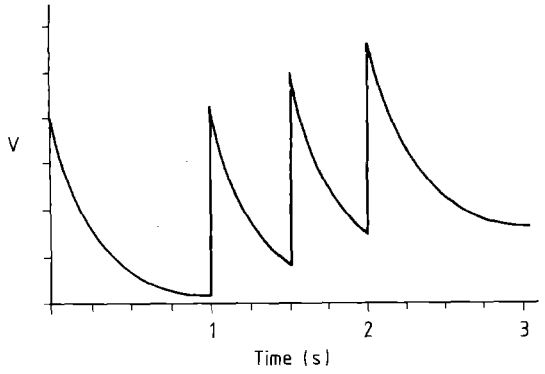

Fig. 3. Effect of increased frequency on equilibrium volume at fixed RC time constant. Volume (V) above equilibrium volume is plotted in a model respiratory system. The RC time constant is fixed at 0.25 s and instantaneous inspiration is assumed. For the second and third breaths, expiratory duration is half that for breaths one and four. Because only two time constants were permitted for breaths 2 and 3, equilibrium volume is not achieved. This is the equivalent of an increase in FRC

from electrical circuit theory and apply it to the respiratory system. If we add a volume (V) to a compliant system of volume, V_0, at time t = 0, the volume remaining in the compliance V/V_0 at some time t is a function of both the compliance and resistance K. Note that the relationship between fractional change in volume and K, the time constant is exponential.

$$V/V_0 = E^{-Kt}$$

$$K = 1/RC \ .$$

By convention the equilibrium time constant = 4 RC. In the respiratory system, this implies that equilibrium lung volume on inspiration and expiration is reached at 4 RC; in other words, breath size (VT) and, lung volume at expiration (FRC) are both determined by 4 RC.

Suppose that one time constant in a model respiratory system is 0.25 s and suppose that inspiration of a tidal volume is instantaneous; we may now invert Figure 2 to examine the general relationship between breathing frequency, equilibrium volume and the RC time constant (Fig. 3). Since 4 RC is defined as the equilibrium time constant, lung volume will return passively to equilibrium volume (FRC) following a tidal inflation at 4 (0.25 s) or 1 s. Therefore, maximum frequency, above which FRC will increase, is one breath per second. If breathing frequency doubles FRC increases as shown in the Figure. At first sight, it appears that, following an increase in the time constant, equilibrium volume will increase stepwise and the system will eventually explode. This is obviously not what we observe. The volume expired per time constant is the fraction of a larger volume above the initial equilibrium; thus in a few breaths, inspired and expired volume will be equal and a new equilibrium will be established. In addition, further inflation of the respiratory system stores more energy in elastic elements so that recoil pressure increases. In the figure a further increase is prevented by return to a frequency of one breath per sec. If a return to the initial equilibrium volume is desirable, there are three available strategies: (1) reduce frequency, (2) change R or C or (3) apply a larger pressure difference across the system. In the physiological system, compliant airways increase their radii with volume and air flow resistance decreases. In addition, the lungs and chest wall become less compliant especially at high lung volume and compliance decreases i.e. elastic recoil pressure increases. The net effect is to decrease RC at increasing volume and help to limit the expected rise in FRC. Expiratory muscles can be recruited to shorten expiratory time unless the patient has already reached the maximum flow limit. During use of muscle relaxants this latter mechanism is not available and mechanical ventilators are not designed to assist expiration. Since use of muscle relaxants eliminates this strategy that is designed to maintain FRC within physiologic limits it is even more important to know the RC product in such patients.

In order to examine the effects of the RC product on desirable tidal volume and frequency during mechanical ventilation consider the following. We will first assume that inflation of the lung occurs instantaneously and determine the time required for deflation. Note at the outset that if we wish to permit the lung to return to the same equilibrium volume breath after breath, maximum frequency (breaths per minute) must not exceed 60/4RC. Consider three cases, a baby with a healthy respiratory system being ventilated during anesthesia (normal R and C), a baby with hyaline membrane disease (HMD) (low C) and one with bronchopulmonary dysplasia (BPD) (high R and low C)

(Table 1). Given the assumption of instantaneous inflation, what is maximum frequency, f_{max}? In each case, mechanical ventilation at a frequency less than f_{max} permits the system to come to equilibrium (so called passive functional residual capacity). In the first case, this might be acceptable but remember that FRC is then determined by the balance between C_{lung} and $C_{chestwall}$. In the second case, this balance is biased toward an airless lung and we can conclude that f should exceed f_{max} in order to move FRC toward normal especially if chest wall compliance is low. In the BPD case, we have the opposite problem; the lung will reach equilibrium volume only after 16 s and will increase in volume at frequencies higher than 60/14 or about 4 per min. The assumption of instantaneous inspiration biases these estimates of f_{max} to be higher than they are in reality. However, this means that f_{max} in HMD is 120/min and in BPD may be less than 3/min. On the other hand, recall from the discussion above that airways dilate at increasing lung volume thereby reducing R and elastic recoil increases.

In a recent study by Richardson and co-workers, this theoretical relationship between the RC time constant and f_{max} was tested experimentally by comparing healthy to saline lung lavaged rabbits (low C). Mechanical ventilation was provided at an inspired-expired ratio of 1:2. In healthy animals the predicted maximum frequency was 38/min and the measured value above which FRC increased was 50/min. In saline lavaged animals, predicted maximum was 71/min, measured maximum was 85/min. If the equilibrium time constant was defined as 3 RC instead of 4 RC, i.e. 95% instead of 98%, theory and experiment agreed within a few percent. Therefore, within the accuracy of measuring a change in FRC, experimental results agreed with theory.

Practical application

We can conclude that rational application of mechanical ventilation requires that the following should be monitored.

1. $PaCO_2$ as a reflection of $\dot{V}_{CO_2}$ and $\dot{V}_A$ as defined in the alveolar gas equation.
2. Pa_{O_2} or Sa_{O_2} as a reflection of average $\dot{V}_A/\dot{Q}_c$.
3. R, C or RC.
4. FRC.

Table 1. Estimates of f_{max} for three representative babies, with healthy lungs, hyalin membrane disease and bronchopulmonary dysplasia respectively

	Healthy	HMD	BPD
R (cmH_2O/Ls^{-1})	40	40	200
C (L/cmH_2O)	0.010	0.002	0.02
RC (s)	0.4	0.08	4
4 RC (s)	1.6	0.32	16
60/4 RC (f_{max})	37.5	187.5	3.75

Except in the case of large dead space ventilation, $PA_{CO_2} = Pa_{CO_2}$ and it should be possible to evaluate the ratio of CO_2 elimination to alveolar ventilation from continuous sampling of expired P_{CO_2}, the final plateau of the recorded expiratory wave form being PA_{CO_2}. However, the effective time constant of the measurement (electronics plus mixing in sampling catheter) is about 0.20 s. From our discussion above, equilibrium then requires about 0.8 s and because expiratory time is likely to be about 50% of each cycle, we will underestimate the true PA_{CO_2} at frequencies higher than about 60/1.6 s or 38/min.

Sa_{O_2} is best measured by transcutaneous pulse oximetry which accurately reflects the value in blood except when the transducer is moving, blood flow is low or the diode indicates $Sa_{O_2} < 0.50$. R and C can be directly measured and the product calculated; with current methods this requires an oesophageal catheter to measure pressure and a sensitive gas flow meter. The product, RC, can also be estimated from the slope of the volume/time wave form collected during a passive expiration.

FRC can be estimated using one of several inert gas-dilution methods. The simplest assumes a one compartment model and estimates volume from the regression over 6 breaths of N_2 concentration during a step increase in inspired O_2 concentration.

In conclusion, rational monitoring of mechanical ventilation in infants and children requires knowledge of the mechanical characteristics of both the patient and the machine. Measurements should include

PA_{CO_2}
SaO_2
RC
FRC.

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Dr. D.C. Shannon
Pediatric Pulmonary Unit
Massachusetts General Hospital
Fruit Street
Boston, MA 02114
USA