Letter to the Editor

Pathophysiological determinants of arterial carbon dioxide tension ($PaCO_2$) in spontaneously breathing and mechanically ventilated patients

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Changes in $PaCO_2$ in hospitalised patients are common and associated with an increased risk of morbidity and mortality. Although many clinicians are aware of the physiological mechanisms for $PaCO_2$ homeostasis, they often have difficulty understanding how different compensatory mechanisms interact, and why such interactions are not always successful in achieving normocapnia. Incorrect interpretation of $PaCO_2$ level—even when it is within the normal range—can have dangerous consequences in a spontaneously breathing patient (1). In this correspondence, we briefly describe how we can visually interpret the interactions of different pathophysiological mechanisms in determining $PaCO_2$ in a spontaneously breathing or mechanically ventilated patient.

In a spontaneously breathing patient, there are two determinants of $PaCO_2$. The respiratory drive from the brain is an active system (which can increase minute ventilation up to 10 L/min for every 3 mmHg $PaCO_2$ increment unless $PaCO_2$ is exceedingly high) (1); whilst the mathematical relationship between alveolar CO_2 tension (or $PaCO_2$ for simplicity), carbon dioxide production (VCO_2 ~200 mL/min for an average adult that can increase up to 10 folds with vigorous exercise) and minute alveolar ventilation represents a passive system (*Figure 1A*) (2). Minute alveolar ventilation is equal to the minute ventilation minus the wasted ventilation due to the physiological dead space which is the sum of anatomical and alveolar dead space. The interaction between the *active* and *passive* systems defines the $PaCO_2$.

An increase in respiratory drive due to hypoxia or metabolic acidosis will increase the 'slope' of the *active* respiratory drive system, resulting in an increase in minute ventilation which will reduce $PaCO_2$. As such, a $PaCO_2$ within the normal range is actually abnormal in the presence of significant metabolic acidosis, and would signify concomitant respiratory drive depression (1). Respiratory depression due to opioids and sedatives will shift the *active* respiratory drive system to the right (*Figure 1B*), resulting in a lower minute ventilation and a higher $PaCO_2$. An increase in VCO_2 will shift the *passive* system upward, resulting in a higher $PaCO_2$, until the *active* respiratory drive system shifts the slope upward to normalise the $PaCO_2$ (*Figure 1C*).

An increase in alveolar dead space—which can occur due to emphysema, reduced pulmonary blood flow without a corresponding reduction in ventilation or over-ventilating poorly perfused alveoli [i.e., ↑ overall ventilation to perfusion (V/Q) ratio], ↑ V/Q heterogeneity in acute respiratory distress syndrome (ARDS) and pneumonia (3), or attenuation of the normal hypoxic pulmonary vasoconstriction due to oxygen supplementation)—will shift the *passive* system to the right, resulting in a higher $PaCO_2$ (*Figure 1D*). Acute pulmonary embolism would theoretically increase alveolar dead space; an elevation of $PaCO_2$ is, however, often not observed. This is because any increase in $PaCO_2$ and reduction in arterial oxygen tension (PaO_2) will be sensed by the medullary and carotid

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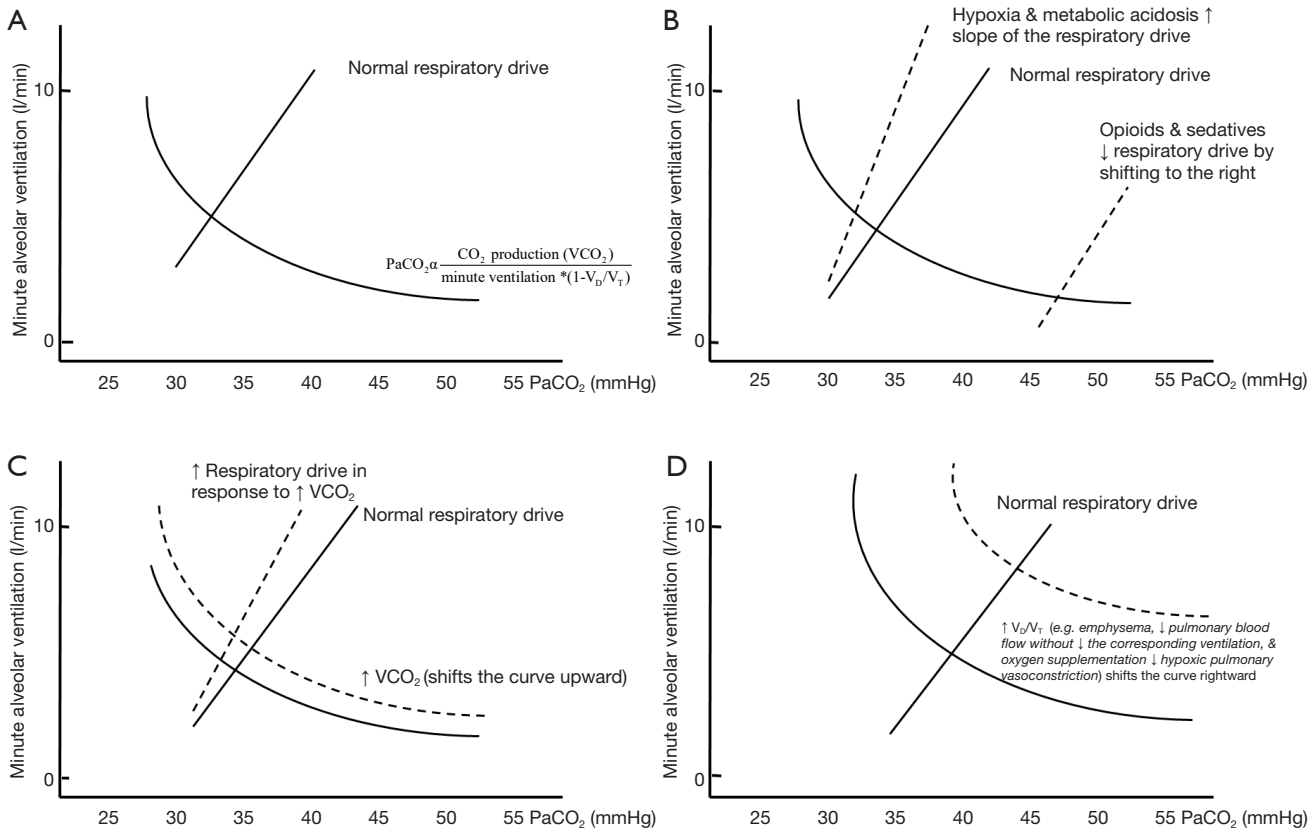

Figure 1 Pathophysiological determinants of arterial carbon dioxide tension ($PaCO_2$). (A) Shows that $PaCO_2$ is determined by interaction between the active respiratory drive system and one passive system that is affected by alveolar dead space, CO_2 production and minute ventilation. (B) Shows how changes in the active respiratory drives would affect $PaCO_2$. (C) Shows why an increase in CO_2 production may not affect the $PaCO_2$ due to the compensatory changes in respiratory drive. (D) Shows the importance of alveolar dead space in determining $PaCO_2$.V_D, alveolar dead space. V_T, tidal volume. Numerical data in the graphs are constructed by the authors for illustrative purposes and may not be necessarily translatable to real clinical conditions.

body chemoreceptors, respectively, which will increase the respiratory drive to increase minute ventilation, thereby lowering $PaCO_2$. In fact, 'overcompensation' resulting in respiratory alkalosis in acute pulmonary embolism due to reflex stimulation of irritant and juxta capillary sensors in the lung is common (4). As for a patient with emphysema, administrating *excessive* oxygen can increase the patient's alveolar dead space and aggravate any existing hypercapnia by abolishing the hypoxic pulmonary vasoconstriction. Due to an overinflated chest cavity and a flattened diaphragm, patients with emphysema will have a limited capacity to increase their minute ventilation to normalise their $PaCO_2$. Furthermore, oxyhaemoglobin has a relatively linear and also lower CO_2 binding capacity than deoxyhaemoglobin. Increasing PaO_2 with excessive supplemental oxygen can further aggravate hypercapnia through the Haldane effect (2).

Understanding the pathophysiological determinants of $PaCO_2$ also has utility for patients who are mechanically ventilated. Under such circumstances, the *active* respiratory drive system is replaced by the setting on the ventilator and the *passive* system affects the $PaCO_2$ level through its interactions with the ventilator. Increasing ventilating rate or tidal volume excessively in a patient with emphysema can induce dynamic hyperinflation which can increase hypercapnia by increasing alveolar dead space, in addition to creating a disadvantage in the respiratory mechanics disallowing any spontaneous breaths (2). In patients with ARDS, excessive positive-end-expiratory-pressure (PEEP) can over-distend alveoli that are already

well-ventilated, increasing alveolar dead space and hypercapnia (3). In judging whether a patient is ready for weaning off from a ventilator, a high $PaCO_2$ (>45 mmHg) despite a high minute ventilation (>10 l/min) suggests that there is a substantial elevation in alveolar dead space. In this situation, weaning is unlikely to be successful until an improvement in the underlying lung condition (e.g., ARDS and its associated increased V/Q heterogeneity) has occurred—which means more time on the ventilator is needed (1).

In summary, understanding how the pathophysiological determinants of $PaCO_2$ is useful in the appropriate interpretation of $PaCO_2$ and hence also the treatment of patients with type II respiratory failure.

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Footnote

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