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Review

Sequential gas delivery provides precise control of alveolar gas exchange

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ABSTRACT

Of the factors determining blood gases, only alveolar ventilation ($\dot{V}A$) is amenable to manipulation. However, current physiology text books neither describe how breath-by-breath $\dot{V}A$ can be measured, nor how it can be precisely controlled in spontaneously breathing subjects. And such control must be effected independent of minute ventilation ($\dot{V}E$) and the pattern of breathing. Control of $\dot{V}A$ requires the deliberate partition of inhaled gas between the alveoli and the anatomical deadspace. This distribution is accomplished by sequential gas delivery (SGD): each breath consists of a chosen volume of 'fresh' gas followed by previously exhaled gas. Control of $\dot{V}A$ through SGD is a simple, inexpensive, yet powerful tool with many applications. Here we describe how to implement SGD, how it precisely controls $\dot{V}A$, and consequently how it controls arterial blood gases.

1. Introduction

This article was inspired by an essay written by the great Dr. E.J. Moran Campbell, "Multum in parvo: explorations with a small bag of carbon dioxide" in the Canadian Respiratory Journal (Campbell, 2001). Although rebreathing from a rubber bag is essentially the equivalent of breath holding, giving an effective $\dot{V}A$ of zero, its application led to important advances in respiratory physiology. In this article we describe an extension of this approach by adding a simple manifold consisting of three one-way valves; this expansion enables implementation of *any* $\dot{V}A$ and therefore precise control of arterial blood gases. As Moran Campbell did in his essay, we here describe our explorations with sequential gas delivery (SGD).

Historically, $\dot{V}A$ has been difficult to measure breath by breath, and impossible to impose due to an inability to influence the distribution of inhaled gas between the alveoli and the anatomical dead space. Indeed Farhi and Rahn (1960) went as far as stating that: "Alveolar ventilation is a calculated value; in physiological experiments there is *no method which will produce an exactly predetermined change in alveolar ventilation* (emphasis added); therefore the final $PACO_2$ cannot he predicted." However, SGD not only overcomes the latter restriction, thereby enabling precise regulation of $\dot{V}A$, but does so independent of either minute ventilation ($\dot{V}E$) or the pattern of breathing. Indeed SGD can be used to both simultaneously and independently control $\dot{V}A$ for CO_2, O_2 and any number of other gases, as the many publications listing this approach in their Methods section attest. For example, SGD has been used to (a) enable hyperpnea (not hyperventilation) to accelerate clearance of carbon monoxide (CO) (Fisher et al., 2011), as well as of volatile hydrocarbons like anaesthetics (Katznelson et al., 2011a), from the blood, but without clearing CO_2; (b) precisely target end-tidal PCO_2 and PO_2 for measuring cerebrovascular reactivity (Blockley et al., 2011); and (c), for the first time, independently measure all the terms required to calculate cardiac output ($\dot{Q}$) non-invasively using the differential Fick equation (Klein et al., 2015).

2. Controlling alveolar ventilation

2.1. Complete rebreathing: A = 0

Rebreathing from a bag produces the same effect on respiratory gases as holding one's breath (Fig. 1A). There is a rapid equilibration of PCO_2 and PO_2 between alveolar gas and blood at the start of the rebreathing (Read, 1967). Subsequently, the interchange of

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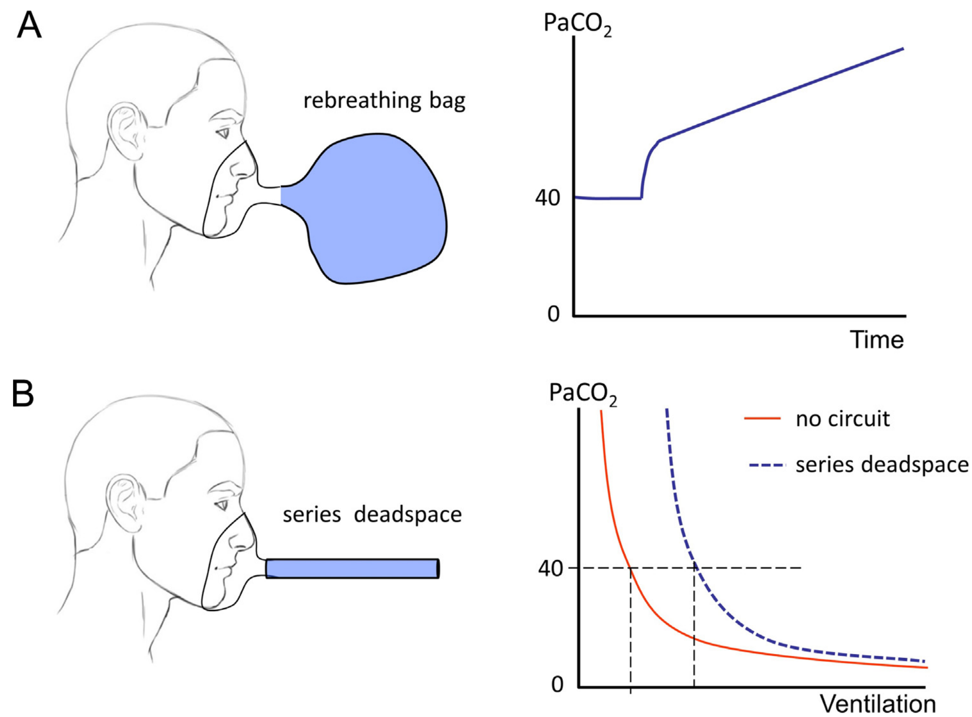

Fig. 1. (A) Rebreathing bag. $PaCO_2$ is independent of ventilation but not isocapnic. (B) Series dead space. Despite the presence of a series dead space, $PaCO_2$ remains a function of ventilation.

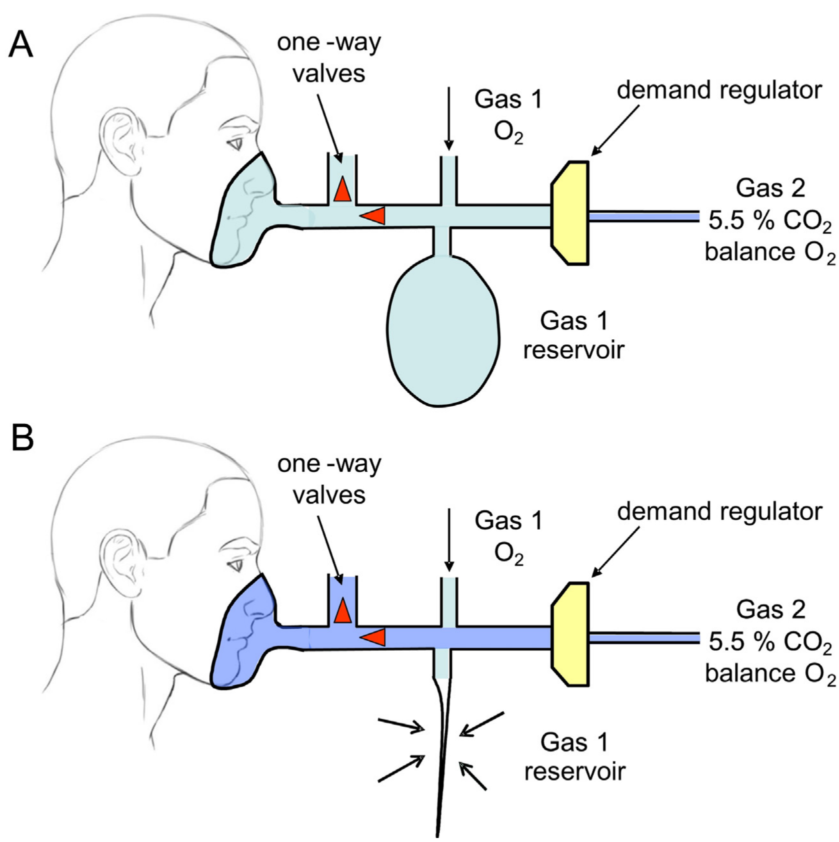

Fig. 2. Sequential gas delivery (SGD) via a non-rebreathing method. The SGD circuit consists of a non-rebreathing configuration of one-way valves, a source of fresh gas (Gas 1), a gas reservoir which fills with Gas 1 on exhalation (A) and collapses on inhalation (B), a negative pressure relief valve, in this case in the form of a demand regulator, and a source of Gas 2 which is *neutral* (see text for definition) with respect to CO_2.