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Editorial II

Deadspace: invasive or not?

The recent paper by Tang and colleagues[1] brought a refreshing discipline to measurements of respiratory deadspace. With capnography being widely available and more sophisticated, respiratory deadspace is more relevant in anaesthesia and intensive care, and physiological deadspace may become an important clinical measurement. In a recent study of patients in the first day of onset of ARDS, increased physiological deadspace fraction was an independent and powerful predictor of mortality.[2] The relative risk of death increased by 45% if deadspace was increased by 5%. This increased risk was greater than for other predictive features, such as a score of illness severity or respiratory compliance. However, oxygenation was also significantly worse in the non-survivors (more of which will be explained later).

Deadspace can be calculated invasively or non-invasively: the difference may be subtle but very important, particularly in lung disease. Non-invasive information is obtained from the carbon dioxide single breath test (SBT-CO_2), in which expired carbon dioxide fraction is plotted against expired volume (Fig. 1). This plot yields three parts; a carbon dioxide-free first phase, which is gas from the large conducting airways; phase II represents the transition between gas from the airways and alveolar gas, and phase III represents alveolar gas. A point midway through phase II is taken as the position of the alveolar/fresh gas interface at the start of expiration. This point, usually determined by Fowler's classic 'equal area' method,[3] defines the volume of the airway proximal to the diffusive boundary, known as the anatomical deadspace, although for obvious reasons the term 'airway' deadspace is preferable. An alternative method was used by Tang and colleagues, which was to plot the cumulative volume of carbon dioxide exhaled against the exhaled volume.[4] This is the integral of the SBT-CO_2. Although it adds little extra information, it does show nicely the gradual onset of carbon dioxide output as airway deadspace gives way to alveolar gas (Fig. 2), and can also be used to define the anatomical or airway deadspace. In intubated adults, this volume is ~85 ml. Since its volume is determined by a diffusive boundary, it is reduced by breath-holding or by an end-inspiratory pause, which allows more time for alveolar gas to mix by diffusion with the static gas in the airways.

The shape of phases II and III is determined by the degree of gas mixing within the lung, and in disease it may be difficult to determine where one ends and the other begins. Obstructive airways disease reduces ventilation in some units more than others, causing an increased scatter of ventilation/perfusion (V/Q) ratios and thus of the range of alveolar P_{CO_2} values. The SBT-CO_2 reflects the changing composition of the alveolar expirate as an upward slope of phase III, for which there are two commonly accepted explanations. The first is asynchronous emptying, in which low P_{CO_2} (i.e., high V/Q) regions empty quickly, before less well ventilated, slower ones with lower V/Q ratios.[5] This is a 'between units' cause of mismatching, or regional inhomogeneity. Regional differences *within* a unit, where the more distal alveolar sacs are less well ventilated and thus have a lower V/Q than the more proximal ones, produce 'stratified inhomogeneity', which is time-dependent. As with the airway deadspace, this mixing defect can be reduced by breath-holding or an end-inspiratory pause.

A large alveolar deadspace can also be present despite an apparently normal phase III slope, as in pulmonary embolism and the right to left (R–L) intracardiac shunting of congenital cyanotic heart disease. In contrast, the intrapulmonary shunting of severe lung disease is usually associated with both a steep phase III slope and very large deadspace. In small airways obstructive disease, an increased slope is often

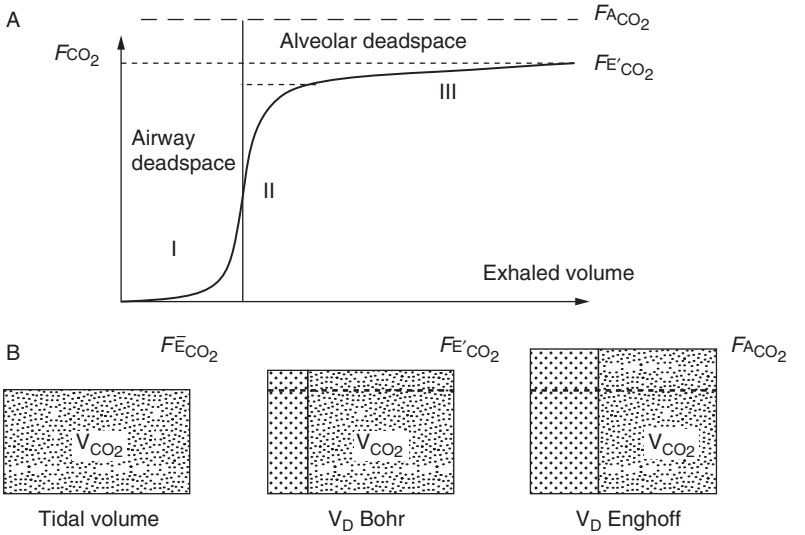

Fig 1 (A) The SBT-CO_2 showing the three phases of the plot, airway deadspace (phase I), the interchange between airway and alveolar gas (phase II), and the sloping alveolar plateau (phase III). (B) Block diagrams exist to illustrate the different equations for deadspace. The volume of carbon dioxide exhaled in a single breath (shaded box) can be considered to be exhaled in a given volume of gas containing end tidal carbon dioxide, or a smaller volume containing gas equilibrated with arterial blood. In each case, the calculated deadspace is different.

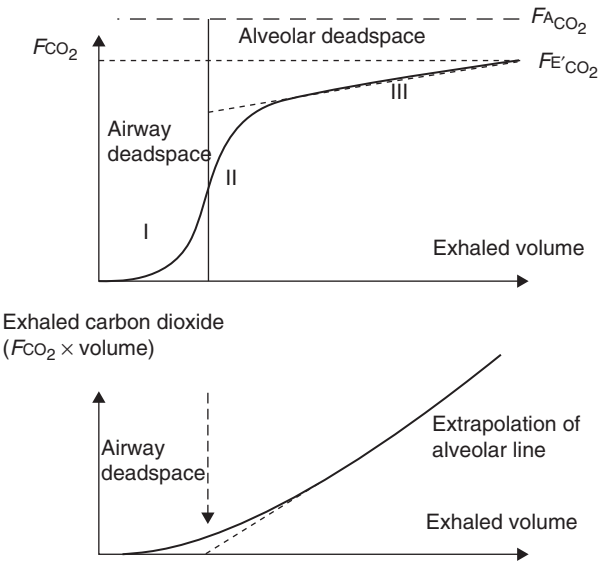

Fig 2 The use of the cumulative exhaled carbon dioxide *vs* volume plot to estimate airway deadspace.

combined with an indistinct transition from phase II to phase III which is easily recognized, even on the time plot. The slope of phase III is also caused by the continuing evolution of carbon dioxide from the mixed venous blood into a progressively emptying lung (and here the rate of expiration is crucial—the slower expiration of obstructive lung disease guarantees a steeper slope[6]).

SBT-CO_2 is the standard tool for understanding carbon dioxide elimination and the deadspace concept. The area under the curve gives the volume of carbon dioxide in the breath, from which we calculate not only minute carbon dioxide production, a metabolic indicator, but also mixed expired F_{CO_2}, which would be the carbon dioxide concentration in the breath if the exhaled carbon dioxide were uniformly distributed throughout the exhalation. By assuming that the last part of the expirate represents the composition of alveolar gas, we can estimate the Bohr deadspace (Fig. 1). However in disease, this is an inappropriate assumption. Arterial blood sampling allows us to infer the average composition of alveolar gas, by calculating the F_{CO_2} of a gas in equilibrium with arterial blood, and substituting this value into the deadspace equation (Fig. 1). This use of arterial P_{CO_2} ($P_{a_{CO_2}}$) as described by Enghoff,[7] leads to the now standard Bohr–Enghoff equation. Riley and his co-workers[8] described the rationale of using arterial blood as 'a physiological integrator of the carbon dioxide pressures existing in all parts of the lung'. On SBT-CO_2, a horizontal line representing the F_{CO_2} of a gas in equilibrium with the arterial blood illustrates the physiological deadspace. The alveolar deadspace ($V_{D_{alv}}$) is the area between phase III and the blood F_{CO_2} line. The alveolar and airway deadspaces together constitute the physiological deadspace $V_{D_{phys}}$.

Tang and colleagues used a computer simulation in which V/Q distribution, $V_{D_{alv}}$, and R–L intrapulmonary shunt, could be adjusted in a tidally breathing cardio-respiratory model. They calculated airway deadspace by Fowler's method, by Bohr's method (calculated from ideal alveolar gas rather than end tidal F_{CO_2} ($F_{E'_{CO_2}}$) as originally described), using the Bohr–Enghoff equation, and also using a graphical method based on the plot of cumulative expired carbon dioxide volume against expired volume, recently described by Koulouris and colleagues.[9] This latter 'non-invasive' method essentially combines the impairment of carbon dioxide elimination by airway and alveolar deadspaces. Tang and co-workers' simulation shows that when

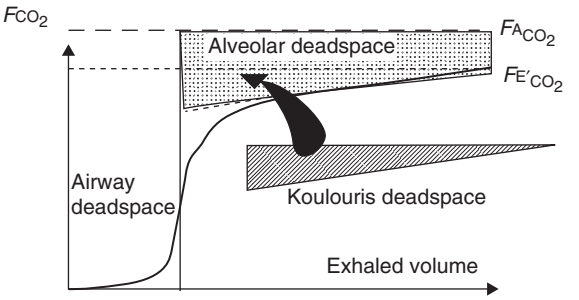

Fig 3 Using of the slope of the alveolar plateau to estimate the efficiency of carbon dioxide elimination, by the Koulouris[8] or Romero[10] methods.

$V_{D_{alv}}$ is increased by V/Q mismatch as might occur in obstructive airways disease, $V_{D_{phys}}$ is correctly measured by the Bohr–Enghoff equation and the original Bohr equation, but not by the Koulouris method.

It is not generally appreciated that R–L shunting, either intrapulmonary or intracardiac, can also affect the Bohr–Enghoff measure of deadspace. This is because the shunted mixed venous blood contains more carbon dioxide than pulmonary capillary blood, which loses some carbon dioxide as it equilibrates with the alveolar gas. Thus, shunted blood carries more carbon dioxide into the arterial blood, so that the P_{CO_2} is now greater than we would expect if the arterial blood were 'integrating' the blood from the lungs (Fig. 3). Thus, the assumption that the carbon dioxide in arterial blood is a measure of the alveolar F_{CO_2} becomes incorrect. This effect of shunt can be represented in SBT-CO_2, where it raises the F_{CO_2} line, giving rise to an 'apparent' alveolar deadspace.[10] A moment's experimentation with the classic shunt equation, rewritten for carbon dioxide, can demonstrate this phenomenon.

The apparent deadspace of R–L shunting is reflected by the calculated Bohr–Enghoff deadspace, but not by the Bohr or Koulouris deadspaces and clearly not by Fowler's airway deadspace.[11] The true $V_{D_{phys}}$ can, however, be estimated if shunt fraction is known, but this requires pulmonary artery catheterization in order to measure venous P_{CO_2}. Of the simpler clinically feasible methods, only the Bohr–Enghoff deadspace increases with increasing severity of V/Q mismatch. When alveolar P_{CO_2} is increased by any mechanism, $P_{a_{CO_2}}$ calculated by Koulouris' method does not agree well with average alveolar P_{CO_2}.

To respiratory physiologists, these results should be intuitive, but confirmation by Tang and co-workers is welcome. Non-invasive respiratory measures only provide limited information, and the differences between them and invasive measures have caused much confusion. The misleading similarity between the plot of carbon dioxide against volume, and the more familiar plot of carbon dioxide against time, has induced some to confuse $V_{D_{Bohr}}$, the deadspace measured by inserting end tidal F_{CO_2} into the deadspace equation, with $V_{D_{aw}}$, the 'Fowler' deadspace. Thus any alveolar deadspace is included, and $V_{D_{aw}}$ is overestimated.[12] An equally misleading use of the end tidal value is to use this as a surrogate for $P_{a_{CO_2}}$, thus replacing the Bohr–Enghoff equation with the original Bohr equation, and underestimating the alveolar and physiological deadspaces.[13]

Tang's work also emphasizes the drawbacks of Cumming's alternative SBT-CO_2 plot,[4] also used by Koulouris, which presents the accumulated expired carbon dioxide volume, rather than F_{CO_2}, against expired carbon dioxide. However, this adds no new information to that available in the standard Fowler plot, as it is derived from the same observations. Delineation of $V_{D_{aw}}$, the first step necessary for any division of the physiological deadspace into its components $V_{D_{aw}}$ and $V_{D_{alv}}$, is not improved. Further, the Cumming plot is less easy to grasp, and its pictorial representation of the alveolar deadspace is less helpful. Koulouris and colleagues attempted to extract more information out of Cumming's method than was there in the first place: it not possible to divine $P_{a_{CO_2}}$ from it in patients with lung disease. Similar claims to those of Koulouris and colleagues have been made by others,[14] based on limited experimental and correlational evidence.

Tang and colleagues also confirm the important effect of intrapulmonary shunting on gas exchange. By the 1980s, it was clear that the R–L shunting of cyanotic heart disease caused a large arterial-end tidal P_{CO_2} difference. Some thought that intracardiac shunting caused poor perfusion of the lung,[15] but this is not a necessary condition. Tang shows nicely that increasing intrapulmonary R–L shunting causes large arterial-end tidal P_{CO_2} differences, confirming clinical observations.[10] A clinically relevant observation is the strong relationship between impaired arterial oxygenation as indicated by pulse oximetry and the arterial-end tidal P_{CO_2} difference.[16]

These facts may explain why the 'new' message, that increased deadspace in ARDS independently predicts outcome, may be none other than the 'old' message that arterial oxygenation is impaired by shunting. Indeed, concentrating on factors that could obstruct pulmonary capillaries or increase ventilation/perfusion ratios, in other words factors that could increase deadspace, as discussed by Nuckton and his colleagues,[2] shows that these authors failed to consider how shunting can also impair carbon dioxide elimination. Impaired carbon dioxide elimination may well be a good marker of early lung damage, but perhaps only because it is less affected by variables such as PEEP (indeed, carbon dioxide elimination could be made worse by PEEP) and $F_{I_{O_2}}$, which act to obscure the message from arterial hypoxaemia, than any intrinsic capacity to signal disturbed gas exchange. Disturbed gas exchange will impair carbon dioxide evolution and oxygen uptake in equal measure: and R–L shunting increases the measured deadspace.

Tang and co-workers also confirmed that Bohr's deadspace, obtained from substituting $F'_{E_{CO_2}}$ in the deadspace equation, has another of the drawbacks of a 'non-invasive' measure. The Bohr deadspace does not reveal the parallel deadspace of pulmonary embolism, where the SBT-CO_2

has a flat phase III and a very large a-A gradient, a feature recognized since the experiments of Severinghaus and Stupfel.[13]

Although measurements of SBT-CO_2, and physiological and alveolar deadspace are not yet widely available at the bedside, clinical measurement of the respiratory deadspace is beginning to establish itself. The study of Nuckton and colleagues[2] suggests that deadspace measurement may be a robust index of gas exchange impairment, and a good prognostic index, whatever the mechanism may be.

There are several other uses for SBT-CO_2. In the diagnosis of pulmonary embolism, the shape of SBT-CO_2 combined with a large alveolar deadspace is almost pathognomonic.[17] Bohr's deadspace to tidal volume ratio, and the slope of the phase III can distinguish patients with asthma from patients with emphysema who have the same degree of airways obstruction.[18]

Given the abstract nature of the deadspace concept it is perhaps not surprising that from time to time blind alleys will be entered, and 'will-o'-the-wisps' pursued. Analysing exhaled carbon dioxide alone is unduly optimistic: Tang and colleagues have done valuable service by showing that arterial blood is generally necessary to fully understand impaired carbon dioxide elimination, and even with an arterial sample, we can be misled by unwarranted assumptions.

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