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Henrik Enghoff and the Volumen Inefficax

J. F. Nunn and M. H:son Holmdahl

From the Division of Anaesthesia, Clinical Research Centre, Medical Research Council, London and the Department of Anesthesiology, University of Uppsala, S-750 14 Uppsala, Sweden

Concepts of the respiratory dead space were introduced during the latter part of the nineteenth century and have been continuously elaborated until the present time. A crucial stage in this development was the concept of the "volumen inefficax" by Henrik Enghoff in 1931 (5) and his suggestion in 1938 (6) that the P_{CO_2} of the arterial blood be substituted for the alveolar P_{CO_2} His contribution was overlooked at the time but, when rediscovered almost 10 years later, it was immediately hailed as a milestone in the understanding of respiratory function. Only at a later date was it realised that this essential advance had been made by Enghoff and, even to this day, many are unaware of his contribution.

The transition from the gill breathing of fishes to the air breathing of mammals involved the change from a highly efficient counter-flow exchange system to the less efficient tidal ventilation of the lungs. Such a tidal system carries the inevitable penalty of wasted ventilation of the dead space which, in an otherwise healthy subject, corresponds to the volume of the upper air passages from the terminal bronchioles to the mouth.

The earliest approach to quantification of the anatomical dead space was the measurement of the volume of the upper air passages by preparation of casts from post-mortem specimens of lungs (12) to yield a value for "den schädlichen Luftraum". The value so obtained was used to calculate the composition of the alveolar gas according to the Bohr equation (2):

$$\text{Alveolar } P_{CO_2} = \frac{\text{Mixed expired } P_{CO_2} \times \text{tidal volume}}{\text{tidal volume} - \text{dead space}} \qquad (\text{i})$$

All terms on the righthand side could be measured directly except for the dead space for which a value could be derived from post-mortem measurements,which had yielded volumes of the order of 140 ml.

The next landmark in this field was the discovery of the constancy of the

composition of the alveolar gas (8). It was then possible to sample alveolar gas and obtain a repeatable value for alveolar P_{CO_2}, the Bohr equation having been rearranged to indicate the value of the dead space:

$$\text{Dead space} = \text{tidal volume} \cdot \frac{\text{alveolar } P_{CO_2} - \text{mixed expired } P_{CO_2}}{\text{alveolar } P_{CO_2}} \qquad \text{(ii)}$$

It was found that the dead space of a resting subject was relatively predictable and (in millilitres) averaged rather more than twice the body weight (in kilograms). This factor was used in Radford's nomogram (14) which predicted correct ventilation as a function of body weight.

The rather simplistic view that the effective functional dead space was constant for a given patient was soon challenged with evidence that the dead space might be substantially reduced during hypoventilation. Rohrer (16) conducted an extensive study of the dead space in post-mortem lungs and brought into account considerations of the nature of gas flow in the bronchial tree. On theoetical grounds he reached the conclusion that laminar flow would reduce the effective dead space during shallow breathing and forecast that, at a tidal volume of 250 ml, the effective dead space would be only 33 % of its anatomical value. Henderson,Chillingworth and Whitney (9) used the axial flow of tobacco smoke through glass tubing to demonstrate that the effective dead space of the tubing could, in fact, be less than its geometric volume. Briscoe,Forster and Comroe (3) showed that some inspired gas could reach the alveoli of man during shallow inspirations of only 60 ml. A similar situation occurs during the shallow breathing of anaesthetized patients; Nunn and Hill (13) found values for "anatomical" dead space of less than 25 ml for tidal volumes below 250 ml. ("anatomical" dead space is here defined by the measurement technique described by Fowler (7) and is, in effect, the functional volume of the conducting air passages or "series" dead space.)

Interest in the reduction of dead space during hypoventilation was soon overshadowed by the question of whether the dead space was increased during hyperventilation, particularly during exercise. This led to one of the major controversies of respiratory physiology between Krogh and Lindhardt (11) on the one hand and Douglas and Haldane (4) on the other. The problem was fundamentally a matter of methodology. Douglas and Haldane used the alveolar P_{CO_2} for the measurement of dead space according to equation (ii) above and showed very large increases during exercise. Krogh and Lindhardt,however, used alveolar hydrogen concentration according to the method described by Siebeck (18) and found that the dead space was only slightly increased during exercise.

It was now clear that the discrepancy was due to the fact that, during short-

-term hyperventilation, particularly during exercise, there is an increased mixed-venous-to-arterial difference for P_{CO_2} but not for hydrogen, which is metabolically inert. The large P_{CO_2} gradient results in a rapid increase in alveolar P_{CO_2} during the course of a single expiration so that the end-expiratory P_{CO_2}, determined during the course of a prolonged expiration, may be in excess of the mean alveolar P_{CO_2}.

In those days, sampling of arterial blood was not considered to be a practical possibility and the alveolar P_{CO_2} was used as a substitute for arterial P_{CO_2}. Sampling of human arterial blood through the intact skin with a hollow needle was not reported until 1912 (10) and the first report of a series of arterial punctures in man was by Stadie in 1919 (19).

It was against this background that Henrik Enghoff in 1938 made his classical contribution "Volumen inefficax: Bemerkungen zur Frage des schädlichen Raumes" published in Upsala Läkareförenings Förhandlingar (6). Already in 1931 he had introduced the term "Volumen inefficax" as more explicit for the respiratory dead space which was estimated by physiological methods, and reviewed the problems of its measurement. In 1938 (6) he suggested that sampling of alveolar gas should be replaced by sampling of arterial blood and that arterial P_{CO_2} be used in place of alveolar P_{CO_2} in equation (ii) above. Using this approach, he found that the absolute value of the dead space was not a constant, but it was a relatively constant fraction of the tidal volume. He reported the mean value of the dead space/tidal volume ratio to be 34 %, and this remained fairly constant during hyperventilation and exercise. These observations have stood the test of time and 34 % would still be regarded as the normal value for the ratio today.

Enghoff´ s approach was used during anaesthesia by Nunn and Hill (13) who were able to impose a wide range of minute volumes on a series of unconscious patients. They obtained a mean ratio of 31.7% (standard deviation 8.6) during spontaneous respiration with a mean minute volume of 3.86 l/min. During artificial ventilation of the same patients the mean ratio was 31.8% (standard deviation 4.2) with a mean minute volume of 9.95 l/min. Mean values for the absolute dead space were 78 and 153 ml respectively.

It is sad to note that Enghoff´ s contribution was largely unnoticed, as were corresponding studies by Benzinger (1) and Rossier and Méan (17) who advanced the concept of deriving the alveolar P_{O_2} indirectly from arterial P_{CO_2} and the respiratory quotient. Such appears to be the fate of so much work published in European journals. Whatever the cause, there is no reference to any of these authors in the paper of Riley, Lilienthal, Proemmel and Franke (15) who in most people´ s eyes laid the post-war foundations of quantitative interpretation of changes in alveolar P_{CO_2} and P_{O_2}. They made the twin propositions

that the arterial P_{CO_2} be used as a substitute for the alveolar P_{CO_2} (echoing the views of Enghoff) and that the alveolar P_{O_2} be derived indirectly using a refinement of the equation proposed by Benzinger (1) and by Rossier and Méan (17). This was the basis of quantification of the Riley three-compartment model of the lung and, following the introduction of simple and reliable techniques for measurement of arterial blood-gas tensions, has made an enormous contribution to the elucidation of disordered lung function in diseased patients.

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