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EDITORIAL

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# Pulmonary oxygen consumption

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I am indebted to Dr. Michelle Hayes for drawing my attention to some of the papers here reviewed.

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Most of the oxygen consumption of the lung is not reflected in the systemic arterial-to-mixed venous oxygen content difference, but it is included in the quantity measured by analysis of respired gases (spirometry or indirect calorimetry). Therefore, the validity of the Fick method of determination of cardiac output depends on the oxygen consumption of the lung being small enough to be ignored. The classic paper by Light [1] showed that the oxygen consumption of an infected lung is certainly not negligible and can be measured as the difference between the total oxygen consumption measured by spirometry and the quantity measured by the "reverse Fick method".

Jolliet and colleagues [2] list seven sets of data from patients with acute respiratory failure or sepsis syndrome which, together with their own series, yield a mean "pulmonary oxygen consumption" of the order of 60 ml $min^{-1}$ (or about 35 ml $min^{-1}$ $m^{-2}$). This would seem convincing evidence of a greatly enhanced oxidative activity in the infected lung, comparable to the normal oxygen consumption of the brain. Furthermore, many of these studies have used the theoretical figure of 1.39 ml $g^{-1}$ as the oxygen-combining capacity of haemoglobin instead of the measured values of 1.31 ml $g^{-1}$, which is surely more relevant to the problem in hand. Gregory's value of 1.31 was derived after many years of painstaking research with the Van Slyke apparatus calibrated against standard reagents [3], and its general recognition is long overdue. Adoption of 1.31 instead of 1.39 reduces the calculated reverse Fick value for oxygen consumption by about 6%, and calculated "pulmonary oxygen consumption" would be increased in a typical study by about 10 ml $min^{-1}$.

There are two notes of caution in the assumption that the oxygen consumption of the lung is being measured by these techniques. Hanique and colleagues [4, 5] have recently studied large numbers of patients with infected lungs and reported only very small differences between the two methods of measurement of oxygen consumption. Furthermore, Jolliet and colleagues [2] list seven sets of data from patients before and after cardiopulmonary bypass (to which I can add another recent study [6]), all of which show "pulmonary oxygen consumptions" almost as high as in patients with infected lungs. It is hard to see why oxygen consumption of the lung should be so greatly increased in such patients. Unfortunately, it is very difficult to collect a large series of patients with uniform and well-defined pulmonary pathology and even more difficult to study a control series of completely normal human subjects.

If the enhanced oxygen consumption of infected lungs is real, then it is reasonable to take the view that this reflects the response of neutrophils and macrophages to infection. It is well known that these cells proliferate and are apparent in broncho-alveolar lavage (BAL). Both types of cells use oxidative metabolism, which would be increased in accord with greater numbers and phagocytosis. This hypothesis was explored by Jolliet and colleagues [2] who, rather surprisingly, found no correlation between pulmonary oxygen consumption and BAL cellularity.

It has long been known that neutrophils show an enormous increase in oxygen consumption during the "oxygen burst" associated with the formation of oxygen-derived free radicals. Some years ago, the present writer suspended samples of human neutrophils in saline and observed the $PO_2$ of the stirred suspension [7]. There was a barely perceptible change in $PO_2$ over control periods lasting 5 h, until a suspension of IgG-coated latex particles was

added. After a latent period of 15 s, the $PO_2$ fell from 18 kPa to zero in 3 min. Phagocytosis and degranulation were confirmed by electron microscopy. From this simple experiment it may be calculated that the average enhanced oxygen consumption was of the order of $150 \times 10^{-12}$ ml $min^{-1}$ per activated neutrophil. If the average pulmonary oxygen consumption of the lung in the studies outlined above (say 60 ml $min^{-1}$) is entirely explained by activated neutrophils, it would require a cell count of about 130000 cells $\mu l^{-1}$ on the basis of a lung volume of 3 l. This seems rather high, although it is hard to find data on cell counts under such conditions.

This hypothesis is open to test. The production of oxygen-derived free radicals does not involve the formation of carbon dioxide, and the respiratory quotient related to this process would therefore be zero. It should be possible to measure carbon dioxide production simultaneously by spirometry and reverse Fick. Subtraction should then indicate the carbon dioxide production of the lung which, when divided by the pulmonary oxygen consumption, should yield the respiratory quotient of the lung. If this were found to be low (say less than 0.5), it would be evidence for free radical production. Provided that sufficient accuracy could be achieved, this might hold promise for a relatively non-invasive measure of pulmonary-free radical production. Spirometric methods can measure carbon dioxide production with great precision [8, 9], and the challenge would be measurement of the carbon dioxide production by the reverse Fick method at the required level of accuracy.

The belated revival of interest in direct measurement of oxygen consumption has been of special interest in the continuing saga of the dependence of oxygen consumption on delivery in critically ill patients. Hanique et al. [4] have added to the impressive list of 15 studies reviewed by Russell and Phang [10], showing that delivery dependence was seen only when oxygen consumption was measured by the reverse Fick method and not when measured by spirometry. The presumption is that the dependence shown with the reverse Fick method is an artefact of mathematical coupling of shared variables, particularly cardiac output, but may also in part be directly caused by drugs used to increase cardiac output. Spirometric measurements can be easily and absolutely calibrated against combustion of butane or alcohol [8, 9], which is more than can be said for the reverse Fick method.

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