Partial liquid ventilation—turning back a PAGE on evolution

On an evolutionary time scale, liquid ventilation is not new. Land-dwelling vertebrates derived from fish 350 million years ago, and fish continue to breathe through a liquid medium. However, the ability to sustain mammalian respiration artificially by a liquid ventilation technique is generally accredited to work in the early 1960s, where mice were kept alive breathing hyperbaric salt solutions. The hyperbaric conditions were required in order that sufficient oxygen could be dissolved in solution to sustain cell respiration.

This was taken further by Clark and Gollan in 1966 when they described the use of silicone oils and fluorocarbons at atmospheric pressure in supporting the life of mice and cats receiving a liquid ventilation technique. Silicone oils were found to be too toxic to use in living creatures but the perfluorocarbons showed more promising characteristics. Perfluorocarbons (PFC) are a group of stable, inert, colourless and odourless liquids which are not soluble in either lipids or water. Oxygen, carbon dioxide and most other gases, however, are dissolved. The solubility of oxygen in PFC is of the order of 50 ml per 100 ml of solvent, and carbon dioxide 200 ml per 100 ml of solvent at atmospheric pressure (i.e. 20 and three times the solubility of each gas in plasma, respectively). They have a low predisposition to react with biological tissue. PFC may be derived from organic compounds (e.g. benzene) by replacement of carbon atoms (PFC) are dense although not appreciably more viscous than water. They therefore accumulate in the most dependent parts of the lung. This density implies that inflammatory debris “floats” on top of PFC and, as it were, is lavaged out of the alveoli. Furthermore, PFC have a low surface tension (for example Perflubron has a surface tension 18 dyn cm^−1). It has been speculated that Perflubron opened up previously collapsed segments in the most dependent parts of the lung making them available for gas exchange, that is expanding functional residual capacity. The surface tension reducing properties of PFC may help to keep the re-opened alveoli expanded, essentially a surfactant-like function. It was also argued that the density of the PFC displaced some blood to the non-dependent (better ventilated) portions of lung, optimizing ventilation/perfusion matching.

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The only problems resulting from Perflubron, according to Hirschl and colleagues, seemed to be mucus plugging, which was relieved by more vigorous suction. Pneumothorax occurred in five patients during PLV, but only in one who did not already have a chest drain for pre-existing pneumothoraces.

More general concerns with regard to the use of PFC include slow elimination from the body. A study in beagles showed traces of the PFC Caroxin-F in the lung (but also liver, kidney, spleen, heart, brain skeletal muscle and fat) 3 yr after 1-h exposure to liquid ventilation. Elimination of this PFC is primarily by evaporation and removal via the lymphatics. Not surprisingly therefore, the highest concentrations were noted in the lungs and associated lymph nodes. There was also an increase in serum alkaline phosphatase and cholesterol concentrations with an elevated peripheral white cell count, which returned to normal within a week. Follow-up platelet counts at 6 and 9 months were reduced significantly, although still within the normal range.13

Despite these findings, there were no histological structural changes in the lung, liver, spleen, kidney, heart or brain attributable to PFC. There is, however, understandable anxiety in using an agent which is retained in the body for so long, even if it apparently does no harm.

On an important practical note, the radiodensity of the PFC makes interpretation of chest radiographs difficult for several weeks after administration. It is also believed that deep sedation may be required.12 There is also the possibility (which is true of mechanical ventilation in general) that there may be impairment to venous return,12 although Hirschl and colleagues found no change in cardiac output.

Current knowledge suggests a clinical potential. It may be a means of providing some of the benefits of surfactant therapy (as yet still experimental in acute lung injury, compared with its established place in the treatment of immature, surfactant deficient lungs), in addition to applying a graded degree of PEEP where it is needed most in ARDS (in collapsed, dependent lung areas). By reducing inappropriate overdistention of the lung, this could limit iatrogenic lung damage.

Whether these theoretical benefits can be translated into reality depends on further research. Without further investigation into this form of therapy, we may be missing the opportunity of a useful novel adjuvant therapy to support the injured lung, to add to other novel treatments such as inhalation of nitric oxide and extracorporeal lung support.

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References