Mechanical Pulmonary Ventilation
— A Source of Acute Lung Injury —

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On occasion new devices and techniques have been introduced to clinical practice that later have proven to be ineffective; others were found to have severe side effects that limited their usefulness to a select patient population.

This presentation will review the mechanical pulmonary ventilator. We consider the mechanical pulmonary ventilator safe, and effective. The widespread use of mechanical pulmonary ventilators over the past 30 years has greatly altered clinical care in patients with a variety of disease states.

But how safe are those devices themselves? We should want to agree that mechanical pulmonary ventilators are rather well engineered, and unlikely to break down and to malfunction. The question that I pose deals with the effects of mechanical pulmonary ventilation on lungs, and not to its ability to raise arterial blood Po2 or lower PCO2, or to improve on the appearance of the chest X-ray films. Any improvement in Po2 does not necessarily signify beneficial effects that ultimately lead to lung recovery; nor does clearing of the chest X-ray picture necessarily signify healing of the lungs.

The medical profession has embraced mechanical ventilation. A review of medical history shows that the polio epidemics of yesteryear were an important impetus to industry to provide ventilators that could do just that, i.e. ventilate the lungs. Lungs of patients with polio were presumably healthy, and results in the use of mechanical pulmonary ventilators in polio victims were mainly positive.

It is quite another matter to apply those newly developed mechanical ventilators to the treatment of patients with respiratory insufficiency, or frank respiratory failure. Those lungs differ greatly from healthy lungs of polio victims. To accomplish adequate alveolar ventilation, those lungs (both diseased and healthy lungs) could be ventilated by one setting alone, i.e. airway pressures were rather uniformly transmitted to both the diseased and the healthy areas of the lungs. Diffusely diseased lungs had no alternative, as only one ventilator can be used.

Past animal studies

Prior animal studies using the mechanical pulmonary ventilator were sporadic over the past 30 years. Aside from almost all lasting a few hours at best, the short term results agreed on the thing: normal animals can tolerate normal tidal volumes, airway pressures and rates for many days without untoward side effect; while even one hour of mechanical pulmonary ventilation at pressures of 28-40 cm H2O can produce either early (hours) acute life threatening pulmonary insufficiency, or a slow evolution in a disease process that lead to atelectasis, hypoxemia, and death. A review of world

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literature has shown no studies in long term mechanical pulmonary ventilation on healthy animals, and in whom intentionally elevated airway pressures were used to stimulate clinical picture of a patient on mechanical ventilation.

The ECMO study

The ECMO (Extracorporeal Membrane Oxygenation) study in the early seventies showed that patients with severe ARDS (expected mortality rate 90%) and who were also placed on extracorporeal membrane artificial lung did not recover any better from their illness, compared to a control group treated by state of the art ventilator care (less than 10% survival). Those results suggested to the participants of the study the irreversible nature of lung disease. Further progress, they concluded, depended on enhanced understanding of the pathophysiology of ARDS.

Our own conclusions differ greatly from the above opinion. We believed that continuing use of the mechanical ventilator while also using the membrane artificial lung was redundant; moreover, we felt that the mechanical ventilator itself may have been an important factor that contributed to both the evolution of the disease process (ARDS) and to the lack of lung healing.

Neurogenic lung disease

Of great interest to us was the evolution of acute lung failure in such diverse states as following head trauma, blood loss, exposure to high altitude, and following ingestion of certain drugs (such as aspirin) and while breathing spontaneously, unassisted by the mechanical ventilator. Those disease states can present major degrees of ventilation abnormalities, such as increase in tidal volume, minute volumes, and increase in respiratory rates. The model we chose to study in detail was lung disease due salicylate intoxication.

To avoid systemic effects, we injected 200mg of sodium salicylate into the cisterna magna of lightly sedated sheep. This resulted in a severe hyperventilation that reduced $P_{CO_2}$ to below 20 torr, with a corresponding rise in blood pH, and while systemic blood level for aspirin was not detectable using clinical toxicological methods. This response lasted perhaps one hour, and was sustained through repeated hourly injections of sodium salicylate.

During the following 12 hours, there was a progressive fall in $P_{O_2}$, total static lung compliance, and an increase in A-a gradient. At autopsy, the lungs exhibited severe atelectasis of over 30% of total lung surface, with great increase in minimum surface tension of saline lung lavage fluid.

On the other hand, animals injected with same amount of sodium salicylate but then paralyzed and ventilated at normal rates and tidal volumes with a mechanical pulmonary ventilator, maintained normal $P_{O_2}$, total static lung compliance, and had grossly normally appearing lungs at elective autopsy.

These studies suggest that maintaining normal tidal volumes, pressures, and respiratory rates with a mechanical pulmonary ventilator (in spite of the enhanced central ventilatory drive) as the single factor that prevented the evolution of acute lung disease. Our studies included other subgroups of this same model, all of which implicate altered respiratory mechanics due to a central cause as the offending agent.

Lung injury from mechanical pulmonary ventilation at high airway pressures
During mechanical pulmonary ventilation, the ventilatory drive is replaced by a machine, controlled by outsiders, the physicians and technicians. What is the proper thing to do? The great majority of physicians measure arterial blood gases, and then go on to adjust the ventilator to reach some predetermined values. The question is, does reaching those arbitrary blood gas values represent the end to itself, or is the healing of the lungs the ultimate goal.

Can the mechanical pulmonary ventilator induce lung disease in healthy lungs, and at what ventilator settings? The diseased lungs at some point of their disease process no doubt had areas containing healthy lung tissue, interspersed with areas of diseased lungs. Unfortunately, as stated earlier, the lungs must be ventilated as a single unit, it being not possible or practical to ventilate the various subunits of the lungs at different rates and volumes.

Earlier data by Greenfield et al had already suggested acute injury to lungs following some one hour of mechanical pulmonary ventilation at pressures of some 28 cm H2O in normal dogs. Rather, we were more interested in mechanical ventilation lasting for several days, and in exploring the effects of mechanical ventilation over time.

In sedated and paralyzed 20-30kg sheep, we ventilated their lungs in one series of animals at a peak pressure of 50 cm H2O, a value rather commonly found in ARDS. We used also subgroups of animals ventilated at low respiratory rates, high respiratory rates with added dead space, and with added CO2. Systemic arterial blood pH and Pco2 was always kept in the physiologic range. Invariably, serious deterioration of lung function, with impairment in blood oxygenation, fall in lung compliance, barotrauma, and a decrease in functional residual capacity was evident well before 48 hours of mechanical ventilation, and virtually all animals developed progressive respiratory failure and were sacrificed.

When similar studies were performed at peak pressure of 30 cm H2O, all animals were alive by 48 hours, with evidence of progressive deterioration in lung function. There was significant atelectasis involving multiple lobes of the lungs. The remainder of the lungs appeared heavy and red. The minimum surface tension of saline lavage lung fluid was highly abnormal.

These last two studies were in line what (perhaps) could have been predicted from the few studies conducted earlier by other investigators, except that we had extended them to a duration more in line found in hospital practice.

The overwhelming evidence points to an evolution of iatrogenic lung disease at airway pressures of 30 cm H2O and above, as seen in these animal models. It is highly probably that such injury process will also develop in man.

The lung injury mechanism based on our studies

We have shown that healthy lungs can be damaged during spontaneous breathing at large tidal volumes, or during mechanical pulmonary ventilation at pressures equal to or in excess of 30 cm H2O.

Our knowledge managing diseased lungs remains woefully inadequate. In our zeal to improve on blood oxygenation we may inadvertently have applied methods and techniques that have no basis in fact: the mere improvement in PaO2 does not necessarily imply an improved milieu for the lungs to heal. Frequently, it is quite the opposite.
The membrane artificial lung

Consider the potential that the membrane artificial lung can offer: such a device can remove part, or most, or all metabolically produced CO₂ from the body (and while also proving for some blood oxygenation), markedly reducing the need for high minute ventilation, high tidal volumes, and high airway pressures. Indeed, there would be no further need for the use of the mechanical pulmonary ventilator.

A rational approach for the future

The rationale for the use of the mechanical ventilator may start form experiments in the animal laboratory. We must establish the safety of mechanical ventilation in short and long term use, and delineate safe levels of use. We may find mechanical ventilation contraindicated in the sickest patients in whom we now consider it indispensable: it is possible that this patient population can best be managed with CPAP, while metabolically produced CO₂ is removed extracorporeally by a membrane artificial lung. Treating patients with less severely diseased lungs will likely undergo future reassessment.

The time has come to reassess the safety and the place of mechanical pulmonary ventilation in clinical medicine.

References


