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**You pay a price when you fool with mother nature.**

W R Hayden

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### You Pay a Price When You Fool with Mother Nature

William R. Hayden<sup>1</sup>

Critical-care physicians, in the never ending search for lifesaving technology, discovered long ago that many deaths occurred as a result of heart and/or lung failure. Much to the consternation of these aggressive and well-meaning physicians, the deaths continued to occur, albeit at a reduced rate, even after the introduction of ventilators, hyperbaric oxygen chambers, heart surgery, and drugs that dilate the pulmonary vascularity (pulmonary vasodilators), reduce intravascular volume (diuretics), and improve the pumping action of the heart (pressors). Some of the diseases that killed these patients were seen by these physicians, and rightly so, as acute illnesses, which, if given more time for healing, might resolve. All that was necessary was a machine that could take over the function of the heart and/or lung (a heart-lung machine) and could be connected to the patient while the underlying condition ran its course. The challenge was different than that faced by cardiac surgeons. Support would be required for days, or possibly weeks, rather than the few hours necessary for most bypass procedures.

The use of a heart-lung machine for severe respiratory failure (high oxygen requirement, high ventilator pressures, and high predicted mortality) in adults was studied in the 1970s and found to offer no advantage over standard care (1). Ninety percent of the patients died in both the experimental and control groups. The technology was termed *extracorporeal membrane oxygenation* (ECMO).

ECMO requires that venous blood be drained from the body through a large-bore catheter placed most commonly in the central but occasionally in the peripheral venous system. A mechanical pump (technically an artificial heart) pushes the blood through a silicone membrane oxygenator (artificial lung) and a warmer before returning the oxygenated and warmed blood to

either the venous circulation (V-V ECMO) or to the arterial side of the circulation (V-A ECMO).

The concept is an easy one to understand. However, the practical application of this technique requires an investment in staff, equipment, and attention to detail exceeds even that required for most other complex technologies. Providing ECMO for one patient requires a team of four to six physicians, one of whom, on a rotating basis, must be in the near vicinity of the patient at all times. In addition to the usual 1:1 nursing ratio, there must be a specially dedicated ECMO pump technician to pay constant attention to the extracorporeal life support system. These specially trained technicians are nurses, respiratory therapists, or pump technicians from the cardiovascular operating rooms. The entire team needs special training and coordination to provide this kind of care on an around-the-clock basis for an average of 5 to 7 days and occasionally up to 3 weeks per patient. ECMO costs \$5,000 to \$10,000 per day.

Major complications occur and are associated with both the severity of illness requiring ECMO and the ECMO process itself. Heparin anticoagulation may result in major hemorrhage into surgical wounds, the brain, and the chest. Constantly stressed plastic tubing may rupture, spewing blood everywhere. Electrical power failures stop the pump and the thrombogenic membrane oxygenator clots and requires replacement. Stopcocks under constant pressure occasionally shoot like minirockets off into ICU space.

The readers of this piece might be asking why any sane person would want anything to do with such a procedure. The answer lies in what we observe immediately after initiating ECMO. Previously hypoxic, shocky patients on maximal ventilator and pressor therapy immediately become well oxygenated and hemodynamically stable. Oxygen is reduced to low concentration,

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ventilator pressures can be reduced and, in most cases, pressors can be discontinued. Blood oxygen and pH levels normalize. Blood pressure stabilizes. The patient stays alive.

Pediatricians, knowing that "children are not little adults," and being of independent mind, began using ECMO in the 1980s in the neonatal intensive care units for respiratory illness specific to neonates. Happily, the survival rates for very severe cases of pneumonia due to meconium aspiration, sepsis, and the neonatal respiratory distress syndrome improved in newborns weighing more than 2.5 kilograms (2). Eighty to ninety percent of neonates survived ECMO who previously would have had a 20% probability of survival. Approximately 5,000 neonates have been attached to the ECMO circuit in the last 10 to 15 years. About 4,000 survived. Without ECMO, 1,000 would have lived. Three thousand or so children are alive now who would not have been if ECMO had not been used. Well over 50% of these children are developmentally normal.

Observing the success in the nursery, pediatric critical-care physicians recently reported the use of ECMO in older children with cardiopulmonary failure caused by severe viral pneumonia, hydrocarbon ingestion, pulmonary infarctions, and cardiac dysfunction after cardiac surgery. Although only a small number of patients have been so treated, it seems that approximately 50% of the children survive, mostly intact (3).

Although the above commentary conveys an overall positive attitude about extracorporeal life support, to be honest, I need to express the ambivalence I and others feel about procedures like ECMO. True controlled studies of ECMO are rare and the technology has been established more on positive experience than on scientific merit. There are some who go so far as to say that ECMO is not of benefit. At the very least, most believe that ECMO should not be approved for any new indications without controlled studies.

The paper in this issue of *AJNR* demonstrates exactly why new procedures need to be studied in detail by every means possible. Brunberg, Kewitz, and Schumacher (4) have shown a pattern of central nervous system abnormality that is characteristic of venovenous ECMO and distinct from the patterns seen when venoarterial ECMO is used. Subarachnoid space enlargement, ventricular dilation, hemorrhage, and regions of low brain attenuation appeared on early CT scanning in their patients. These abnormalities occur infrequently with V-A ECMO.

We should expect pathology (to pay a price) when new technology alters the natural or usual course of a disease (when we fool with mother nature). Not only are the patients extraordinarily ill, but the procedures themselves have the potential to alter a patient's physiologic state. In the case of ECMO, blood flow is changed from pulsatile to nonpulsatile, large-bore catheters obstruct venous drainage of the upper body including the central nervous system, anticoagulation is necessary, and the tissues of various organs have been injured by the pre-ECMO state (hypoxia, shock, acidosis).

Much credit should go to institutions like the University of Michigan for their detailed studies of ECMO and follow-up of the patients they have managed. Detailed imaging studies and developmental follow-up will sooner or later help determine which of the different methods of ECMO will cost the least in terms of brain injury.

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