Breaking the Ice:

An Anesthesiologist Searches for Medical Clues in the Antarctic

Walk into Warren Zapol's office at the Massachusetts General Hospital (MGH), and you immediately recognize signs that a polar scientist is in residence. Framed photographs on the wall show research teams bundled up in red parkas; in one photo, Zapol and a flock of emperor penguins cavort on the sea ice. Zapol has led nine expeditions to Antarctica and although his "day jobs" as head of the department of anaesthesia and critical care at MGH, and Reginald Jenney Professor of Anaesthesia at Harvard Medical School, preclude more frequent travels, he has maintained a deep connection to the Antarctic, which he calls "the most beautiful place in the world."

This article is adapted from an article by Susan Cassidy in *Harvard Medical Alumni Bulletin*, Winter 2001, and supplemented with information from the 2010 ASA John W. Severinghaus Lecture on Translational Science by Warren M. Zapol, M.D., as published in *Anesthesiology* 2011; 114:771–781.

On his first trip to Antarctica in 1974, Zapol's research centered on measuring the blood pH of fish. But he quickly shifted his attention to one of the South Pole's warm-blooded creatures, the Weddell seal *(Leptonychotes weddelli),* which weighs 770 to 880 pounds and is about 6 feet long. While a human who can swim unaided to a depth of 20 meters and stay submerged with three to four minutes of breath-holding is considered an expert diver, that ability pales in comparison to the behavior of this seal, which has the amazing ability to dive deeper than 500 meters and stay underwater for more than 90 minutes. The animal has developed adaptations that allow it to withstand the intense pressure of deep-sea diving, not to mention the lack of oxygen and the extreme cold.

The challenge facing Zapol was to determine what physiologic and biochemical strategies the Weddell seal has evolved, and whether such information could be deployed in treating human respiratory failure. Zapol points out that one of the greatest dreams in medicine is to find a way to shut down metabolism when the body cannot supply oxygen and eliminate waste products, particularly during acute heart attacks and strokes. "If you knew how to shut down metabolism, much as the seal can, you could preserve the brain and the heart from injury."

Diving Virtuoso

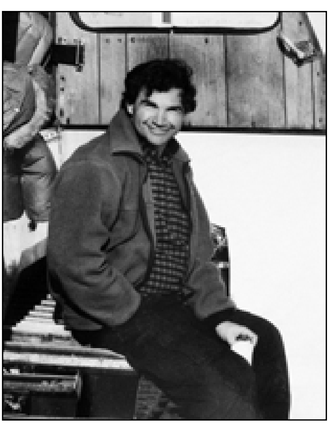
During a dive, the seal must provide its tissues with oxygen, limit buildup of carbon dioxide in the blood, and avoid various ills of extreme pressure, such as nitrogen narcosis—what divers call "rapture of the deep." And if the nitrogen tension in blood and tissues becomes too great as the seal swims to the surface, the result can be "the bends," a condition that may lead to blocked vessels in the brain and spinal cord, paralysis, and even death.

So, how do Weddell seals overcome these obstacles? Laboratory studies have provided some important clues. Human divers depend on their lungs for oxygen storage, but seals do not. Storing twice as much oxygen per kilogram of body weight as humans, they concentrate it mainly in the blood. Another adaptation is bradycardia. Further, some of the seal's tissues stop functioning during a dive; others switch to anaerobic metabolism.

Yet to fully understand the adaptations that allow Weddell seals to penetrate to such depths and stay submerged so long, field studies were required. "Forcing a seal confined in a laboratory to put its face underwater does not necessarily evoke the same response as a dive undertaken freely in the sea." So, on six occasions, Zapol and his team headed to the National Science Foundation's research station on the shore of Antarctica's McMurdo Sound to study the behavior of the seals in the wild.

Wild Discoveries

McMurdo is 800 miles from the South Pole on the shores of Ross Island, an active, 12,448-foot-high volcano covered with ice, snow and glaciers. Zapol and his colleagues generally made their trips during the Antarctic spring in October and November. At that time, temperatures average minus 18 degrees Celsius and the sea ice is beginning to break up, yet is still thick enough to allow planes to land directly on it. The researchers lived and worked on the ice itself.



Warren Zapol in 1985 relaxing on a Trackmaster vehicle on the sea ice off McMurdo Station, Antarctica.

To allow the scientists to understand metabolically what happens when a seal dives, Roger Hill, Ph.D., then a physicist and pulmonary circulation research fellow at Zapol's MGH laboratory, designed, developed and programmed software and built a battery-operated diving microcomputer that could be glued to the seal's dorsal fur. It was programmed for predetermined seawater depths and diving times to record heart rate, body temperature, and swimming velocity; it also commanded a pump to draw blood samples.

Young male seals were gathered from colonies near the shore and sledged to the study site about 5 miles offshore. A 3-foot-diameter hole was drilled through the sheet of ice roughly 6 feet thick, in an area that had no nearby cracks through which the seal could surface. The seals were briefly anesthetized with 1 gram of intramuscular ketamine followed by halothane via a to-and-fro system, a 25-liter reservoir bag, and a carbon dioxide absorber. Catheters were inserted and the computer was attached; when the seals recovered from the anesthesia, they entered the hole and swam away.

For shelter against the elements, the research team used a small hut on skis that was towed across the ice to the desired location and positioned so that a hole cut out of the bottom of the hut was over the hole in the ice. The hut also housed a computer to retrieve data from the diving computer when the seals returned to breathe. Another small hut formed the research team's living quarters.

The researchers soon learned that the seals' diving responses did not match what they had seen in the laboratory. Ninety-five percent of the seal's voluntary dives were short feeding dives, lasting less than 20 minutes; the animal would head straight down for its prey, the Antarctic cod, and then resurface. Only 5 percent of the dives lasted longer than 20 or 30 minutes, these longer dives occurring when the seal was exploring new territory or escaping from predators.

Through these free-diving seals in their natural habitat, it was determined that the "diving reflex"—the profound circulatory redistribution brought about by selective systemic vasoconstriction and vagal bradycardia—was a natural phenomenon and *not* due to the stresses of the laboratory. The longer dives of 200 to 300 meters were characterized by bradycardia, with little variability of heart rate, that remained present until the seal resurfaced. On the shorter trips, the seal's heart rate would quicken and slow in accordance with its swimming speed. In the laboratory, even short dives had evoked the response typical of a long dive. The reason? "In the laboratory, the seal doesn't know how long it will be submerged, so it prepares for the worst." Moreover, the seal's arterial oxygen tension dropped to 20 to 30 mmHg, concentrations lower than those estimated in exhaled gas from humans summiting Mount Everest. Seals' muscle is extremely rich in myoglobin, which slowly desaturates as it releases large stores of oxygen into the circulation, thus enabling the long dives.

Zapol also focused on two of the seal's great secrets: the extension of the diving reflex from its use of the spleen as a storage tank for red blood cells (RBCs), and its ability to collapse its lungs. It was estimated that the Weddell seal stores about 60 percent of its RBC supply in the spleen (humans store less than 10 percent). "The seal's spleen appears to be something of a contractile scuba tank in its ability to store and release RBCs needed for bouts of diving," discharging about 20 liters of packed RBCs into the circulation, thus giving the seal added circulating RBCs to rapidly take up oxygen when it briefly breathes air at the surface during a series of dives.

From their studies, the team also learned that the seals' lungs collapse at the beginning of each dive. This collapse decreases buoyancy, making it easier for the seal to descend, and limits the amount of nitrogen that can enter the blood during a dive. As they descended, the seals' blood nitrogen concentrations increased to three to four times higher than those at the surface, equivalent to about 30 meters of seawater pressure. However, the increase of blood nitrogen stopped with further descent and then concentrations actually declined, confirming that the seal's lung completely collapses with each dive below 25 to 50 meters, thus ceasing the uptake of nitrogen from alveolar gas into the blood. In fact, the seal's lung becomes airless, resembling a fetal lung. "When people go for a long dive, they breathe in, to fill up their lungs. Seals do the opposite; they breathe out when diving to help collapse their lungs. It's such a smart technique. We found that out early when we measured the amount of nitrogen in their blood and noted that it didn't rise to the levels that a human scuba diver's would rise to." Thus, the seal is able to remain alert during deep dives, allowing it to find and capture its prey without succumbing to nitrogen narcosis.

The Weddell seal studies provided major insights into mammalian adaptations for diving, but so far have not resulted in breakthroughs in treating human respiratory failure. In contrast, Zapol's pioneering landmark work with inhaled nitric oxide would change the therapy for newborns with persistent pulmonary hypertension as well as other causes of hypoxic respiratory failure, as well as for children undergoing cardiac surgery and adults having left ventricular assist devices implanted. However, as a result of the seal studies, Dr. Zapol and his team of skillful scientists were honored by the U.S. Board on Geographic Names, which named a glacier in Antarctica after him! The Zapol Glacier can be found at 78 degrees south, 85 degrees west.