Biomedicine

Putting the squeeze on anesthetics

Modern surgery would be unthinkable without anesthetics. Yet after more than a century of their use, the detailed molecular mechanisms of these compounds — how and where they act biochemically — remain a mystery. Solving this mystery might result in new anesthetics that are safer and more effective than existing compounds.

One possible approach to the problem is inspired by an intriguing observation, first documented 40 years ago, that the effects of general anesthesia can be reversed by putting an anesthetized animal in a pressure chamber and subjecting it to 100 or so atmospheres of pressure. Researchers don't yet understand this pressure phenomenon, but Patrick T.T. Wong, Harold Jarrell and their colleagues at the National Research Council of Canada in Ottawa, Ontario, have made an encouraging start. With a powerful experimental tool, Wong's group may be able to home in on how pressure influences the potency of *local* anesthetics. Whether or not this will lead to a better understanding of how general anesthetics work remains to be seen.

According to Jarrell, researchers believe that the ultimate targets of many local anesthetics are the proteins in the membrane channels that regulate the passage of sodium ions into and out of nerve cells. Some anesthetics may block this flow, thereby preventing the nerve cell from sending a pain message to the brain. However, scientists are unclear about the details of this interaction and, most important, the extent to which the membrane as a whole may control an anesthetic's access to the channel proteins.

As for the effects of pressure on local anesthetics, some researchers hypothesize that pressure alters the structure or shape of the channel proteins so that they are not able to effectively interact with the anesthetic molecules. Another school of thought focuses on the cell membranes, whose lipid structure is reorganized at high pressures. This reorganization may squeeze the anesthetic out of the membrane or else constrain its movement; either event would make it difficult for the anesthetic to reach channel proteins.

While it is still too early in the game to say which of these ideas is correct, Wong and his colleagues have at least taken a first step toward elucidating the behavior of isolated membranes and anesthetics under pressure. Writing in a recent (Dec. 29) BIOCHEMISTRY, they report that they have performed lab experiments in a high-pressure vessel and obtained "the first direct observation of the expulsion from [artificial membranes] of a local anesthetic, tetracaine, by pressure." In addition, they have demonstrated the same pressure-induced expulsion of tetracaine from natural, inactivated nerve membranes, showing that the artificial membranes serve as good models for their natural counterparts.

While these observations are consistent with the "squeezing-out" pressure theory, Jarrell cautions that "it remains to be seen if they are truly important in terms of the pressure-reversal phenomenon." For that, the researchers are starting to investigate functioning nerve cells — to see, for example, whether the tetracaine's ejection from the cell membrane influences the nerve's ability to send signals. And according to Wong, the group will also study how pressure alters proteins and their interactions with tetracaine.

Wong says his laboratory is the only one in the world that can perform such high-pressure studies, using a high-pressure infrared spectrometer for studying biological systems in aqueous solutions, which he recently developed. The use of pressure, he says, enhances some molecular interactions, enabling researchers to learn about the sites, types and strengths of bonds and other structural details that might not be as discernible at atmospheric pressure.

Earth Sciences

Seismic sail through the Andes

Dragging a 2-mile-long streamer that holds thousands of underwater microphones, seismologists aboard the research vessel *Robert D. Conrad* are cruising in the waterways that weave through the extreme southern portion of the Andes Mountains. They are attempting to use underwater explosions to get at the roots of a longstanding puzzle about the origin of the southern mountains in that range.

Every 20 seconds, air guns towed behind the ship will go off, sending sound waves through the water and down into the earth's crust. The microphones on the streamer will detect waves that reflect off irregularities in the crust, thereby producing a sonic picture of the Andes' innards, says chief investigator John C. Mutter of the Lamont-Doherty Geologic Observatory in Palisades, N.Y. This underwater seismic technique is often used out in the open ocean, but scientists are only beginning to bring the technology into enclosed waterways. These surveys will help geologists understand why the mountains are as large as they are, says Mutter.

Seismic techniques conducted on land are a common geological tool for probing into the earth. But marine techniques can be cheaper and easier than land-based studies, especially in a remote and rugged area like the Andes. In one day, marine seismologists can map the same amount of area that it would take a land crew three months to cover.

Smallest fossil reptile

Paleontologist Martin Sander has found what may be the smallest known skeleton of an extinct reptile species, he reports in the Feb. 12 SCIENCE. Measuring 51 millimeters long, or slightly more than 2 inches, this 230-million-year-old member of the *Neusticosaurus* species reached only 22 percent of the average adult length. *Neusticosaurus* was an aquatic reptile that frequented warm coastal waters.

The skeleton is curled up and displays many undeveloped features. This indicates that the animal was an embryo, which makes it an extremely rare fossil find, says Sander, a paleontologist at Zurich University in Switzerland. The embryo fossil will help detail the growth patterns of *Neusticosaurus*. In addition, scientists can use the fossil to discern evolutionary relationships between *Neusticosaurus* and other reptiles.

The embryo may fuel the debate over the possibility that some ancient reptiles, including some dinosaurs, gave birth to live young. It is believed that most extinct reptiles laid eggs, a process confined to land. But paleontologists have found one species, a fully aquatic porpoise-like creature, that gave birth to live young in the water. Sander suggests that *Neusticosaurus* may also have borne live young because the fossil embryo was found in sediments that were miles offshore, and it is not clear how an egg could be carried that far from land.

Storms at the bottom of the sea

The dark abyss at the bottom of the ocean was thought to be quiet and almost totally at rest, with sediments slowly raining down and accumulating at a rate of about 1 millimeter per century. But photos taken in the 1960s shook that peaceful image by revealing signs that the sediments often shift position after they are on the bottom. Now, for the first time, scientists have observed the infrequent "storms" along the ocean floor that rearrange the sediments, report Thomas F. Gross of the Skidaway Institute of Oceanography in Savannah, Ga., and his colleagues in the Feb. 11 NATURE. Over the course of a year, meters stationed on the seafloor off Nova Scotia detected five occasions when currents at the bottom surged, sending the top millimeter of sediments awhirl. Photos from underwater cameras showed that these storms erased animal tracks and created ripple marks in the sediments