THE WALL STREET JOURNAL. ONLINE

April 23, 2005

HEALTH

Researchers Trigger Hibernation in Mice: Hints of Future Uses

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Staff Reporter of THE WALL STREET JOURNAL
April 23, 2005; Page B1

Maybe suspended animation isn't science fiction after all.

Scientists at the Fred Hutchison Cancer Research Center in Seattle put mice into an extremely low metabolic state simply by exposing them to a nonlethal concentration of the normally toxic gas hydrogen sulfide. Their findings appear today in the journal Science.

The team, led by molecular biologist Mark Roth, found they could cause the mice's oxygen consumption to fall by half in just five minutes. Over the course of six hours, their metabolic rates dropped 90%, and core body temperatures dropped to just a few degrees above room temperature. Returned to normal air and temperature, the mice recovered in two hours and exhibited no abnormal side effects.

Other research teams have induced a type of suspended animation in large mammals by forcibly cooling them to low temperatures. The Seattle work appears to be the first time scientists have pushed mammals into a natural, reversible state of hibernation. While the research reported is limited in scope and raises many questions, if the technique or one similar to it can be made to work in humans, the medical implications are profound.

For starters, the ability to ratchet down cell metabolism could have big implications for organ transplants. Almost as soon as they are removed from the body, organs such as hearts and kidneys start deteriorating. Reducing the tissues' oxygen consumption might make it possible to store organs longer or transport them over longer distances.

Farther out, putting critically injured or ill people into a suspended state might buy them extra time for emergency treatment. People with fevers of unknown origin might be suspended to give doctors time to find the right combination of antibiotics or antiviral drugs. Dr. Roth hypothesizes that suspended animation might even substitute for anesthesia or reduce the toxicity of radiation treatment for cancer.

"This work raises some really provocative scientific questions," says Patrick Kochanek, director of the University of Pittsburgh's Safar Center for Resuscitation Research. "It might represent a paradigm shift in thinking, that this isn't just the whole concept of Buck Rogers and that suspended animation isn't crazy."

The ultimate usefulness of Dr. Roth's technique is largely unknown. His three-person team experimented on 40 to 50 mice, none of which was suspended for longer than six hours. Dr. Roth declines to say whether he plans to test longer suspensions.

It isn't clear whether the mice's suspension led to neural damage, which can result from forcible-cooling experiments. Standard tests of mouse behavior, performed to assess possible damage from the procedure, found no effects, Dr. Roth says.

Equally uncertain is whether the hibernation technique will work when the mice have suffered traumatic injury -- an important question if suspension is to be useful in emergency medicine. And no one knows if induced hibernation will work the same way in larger mammals or in people. The researchers plan to explore the technique in trauma situations, although they haven't done so yet. Tests in larger mammals are farther off. Dr. Roth declines to discuss his plans in detail.

None of this is necessarily unusual given the guerrilla nature of the suspended-animation project at the research center informally known as "the Hutch." The iconoclastic Dr. Roth enjoys an unusual degree of freedom to pursue his own interests, although as a result he often works alone and without the full support and understanding of his colleagues.

"I try to do things that wouldn't get done if I'm dead," he says. His curiosity has led him to develop a diagnostic test for lupus and to explore new ways to detect cancer in a collaboration with chip-maker Intel Corp.

Several years ago, Dr. Roth grew fascinated with suspended animation after reading accounts of people who seemed to have frozen to death only to be revived. He decided to find out what triggered their hibernation-like states and plunged into largely unknown territory.

A few pioneers already had broken ground. Researchers at Dr. Kochanek's institute had succeeded in suspending pigs by cooling them quickly and then reanimating them. Their technique involved replacing the pigs' blood with a chilled saline solution, a complex and cumbersome procedure.

Dr. Roth suspected there might be a simpler way. He began experimenting with substances that depress metabolism, often with toxic effects. Early failures involved so-called heavy water, an isotope of ordinary water used to regulate nuclear reactions; tetrodotoxin, the poison found in pufferfish; and various other rat toxins. "It's not like there was a book you can find that says, here are things that might work better," he says.

Last year, his team found it could control the metabolic rate of simple worms, called nematodes, using a particular concentration of carbon monoxide. Similar work resulted in hibernation-like states in yeast and embryos of fruit flies and zebrafish. Carbon monoxide, however, wouldn't work on mammals -- or "fuzzies," as Dr. Roth calls them -- because of its toxicity in the bloodstream.

A documentary on caving inspired him to consider hydrogen sulfide, a toxic gas that sometimes belches out of the depths and can kill people instantly at high concentrations. Hydrogen sulfide is found in the human body, albeit in minute amounts. Dr. Roth hypothesized that it might block oxygen from a metabolic enzyme called cytochrome c oxidase, possibly triggering a suspended state. The researchers tried it in mice and, to their surprise, it worked.

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