Company takes heart as battery problem solved

Ottawa-based World Heart Corporation says it has solved the battery cell problem that was affecting its ventricular assist device known as the Heartsaver. World Heart spokesperson Dr. Tofy Mussivand said the battery-related failure was caused by a defect in the printed circuit board that controls power flow to the device's internal battery during recharging. World Heart says the device should be available for testing in January 2000.

The Heartsaver device operates using an external power supply; the internal battery is designed to allow the device to operate without the external power source for up to 90 minutes. The company says it expects to begin clinical trials in the first half of 2000, subject to Health Canada approval.

Research Update

Bolstering brain cells against stroke damage

A team of Canadian researchers has discovered a major mechanism by which cells are destroyed during stroke — a discovery that promises to pave the way for drugs that limit the brain damage suffered by patients (*Science* 1999;284:1845-8). By gaining an understanding of this critical chemical chain reaction, the researchers were able to derail it, thereby reducing the vulnerability of brain cells to stroke.

Dr. Michael Tymianski and colleagues at the Toronto Hospital–Western Division Neurosciences Centre found that a specific protein (PSD-95) causes calcium entering brain cells through receptors called NMDAs (*N*-methyl-D-aspartate) to bind with nitric oxide synthase (NOS) enzymes to form stroke-triggering free radicals. Eliminating or inactivating PSD-95, the research team discovered, makes brain cells more resistant to damage caused by lack of oxygen and glucose.

"The most significant aspect of this work is that now we recognize PSD-95, and molecules like it, as potential targets for drugs that treat stroke," said Tymianski, a neurosurgeon and a Medical Research Council of Canada clinician-scientist. "This is a novel target and is quite exciting for us from the point of view of therapeutic potential, as drugs that interfere with PSD-95 are relatively easy to make."

Tymianski and his fellow researchers are currently studying animals deficient in PSD-95 to find out if they are more resistant to stroke. From there, the team will design drugs that either suppress natural production of PSD-95 or prevent the protein from binding with NOS or NMDA. Once developed, such drugs will likely take 3 to 6 years to be approved for human trials.

"Only by understanding these principles can we move forward to develop rational therapies for stroke that will work," said Tymianski, who is also an associate professor at the University of Toronto. "We feel that we have brought the field a step closer to this goal. Based on this finding, we may be able to design drugs that target specific steps along the molecular pathways that lead to the destruction of brain cells after a stroke."

The research team from Toronto Hospital–Western Division has patented its discovery and is currently seeking an industry partner for future stages of the project. — *Greg Basky*, Saskatoon

Understanding how the gut reacts

A clue to intestinal inflammatory disease has been uncovered (*Nat Med* 1999;5:900-6). Feeding egg whites to mice genetically engineered to react to egg-white peptides had no effect until the mice were also given inhibitors of cyclooxygenase-2, which led to intestinal inflammation. Researchers found that cyclooxygenase-2-dependent arachidonic acid metabolites act as immunomodulators in the immune response to dietary antigens such as egg whites. Cyclooxgenase-2 therefore plays a key role in the intestinal immune system.

Long-term effects of childhood febrile seizures

Experiments in rats show that fever-induced seizures cause changes in the brain that last into adulthood (*Nat Med* 1999;5:888-94). After immature rats were subjected to heat-induced seizures, they experienced a selective presynaptic increase in inhibitory synaptic transmission in the hippocampus. These serious nerve alterations in the brain persisted well into maturity. The findings challenge the view that febrile seizures in childhood are benign. They also contribute to the debate about the causes of epilepsy later in life.

Starve a fetus, feed a sociopath

To test the theory that nutritional deficiency in the womb can lead to antisocial personality disorder later in life, researchers looked at more than 100 000 men in the Netherlands whose mothers were malnourished because of World War II food blockades during their pregnancy (*JAMA* 1999;282:455-62). The men were all given psychiatric examinations at age 18 before military service. Those exposed to severe maternal nutritional deficiency during the first or second trimesters had 2.5 times the risk of antisocial personality disorder. However, severe deficiency during the third trimester, or only moderate deficiency at any time in pregnancy, did not increase the risk.