Research Update

Mounting a defence against Alzheimer's disease

Research being carried out at McMaster University in Hamilton, Ont., and elsewhere is considering a potential new direction in treating Alzheimer's disease and other neurodegenerative conditions. McMaster neurologist Michel Rathbone reports that the new method "enhances the brain's ability to defend itself against noxious things."

The treatment involves the use of purines, chemical compounds that have been found to have trophic effects on the brain after damage to the brain and spinal cord (*Alzheimer Dis Assoc Disord* 1998;12[Suppl 2]:536-46). Some purines — guanosine and guanosine triphosphate — stimulate the astrocytes to produce neuronal growth factor and several other growth factors. The effects of guanosine are important because they remain elevated for long periods after injury to the brain.

Rathbone says that natural and synthetic purines enhance memory in both old and young mice, stimulate astrocytes in the brain and protect hippocampal neurons in vitro from exposure to high concentrations of glutamate.

Natural guanosine is present in all cells but it cannot be given therapeutically because it is broken down in the stomach. Two synthetic purine compounds — propentofylline and neotrofin — are undergoing clinical trials in humans for the treatment of Alzheimer's disease. According to Rathbone, propentofylline mimics the trophic effects of guanosine, but to a lesser extent than neotrofin.

Neotrofin, which is given orally, crosses the blood–brain barrier and has not been shown to have any side effects. The first phase I trial of this drug was carried out in Hamilton by Rathbone and geriatrician Willie Molloy with a sample of 10 elderly patients.

Another clinical trial of neotrofin has been conducted by Leon Thal of the Alzheimer's Disease Consortium in the US and the University of California, San Diego, and funded by the National Institute on Aging (*Soc Neurosci Abstr* 1998;24:1217 [abstract]). In the study, Thal found that the drug produced no side effects and was well tolerated, with indications of beneficial effects on memory and speed of processing. — © *Marvin Ross*

Research news . . .

Fat? Fidget!

Research into why some people who overeat gain weight and others don't has found that such simple activities as fidgeting and maintaining posture can burn off 10 times more fat in some people than in others (*Science* 1999;283:212-4). In an experiment, healthy, nonobese volunteers were fed huge amounts of energy-rich food. Two-thirds of the subsequent increase in energy expenditure was due to so-called "nonexercise activity thermogenesis" — regular daily activities that consume energy and are a major way of keeping fat off some people. By contrast, people who do not increase their daily activities after eating large amounts of food gain fat more readily.

Forget the fibre?

A massive study of almost 90 000 women conducted over 16 years indicates that the amount of fibre in a diet has no effect on the risk of benign or malignant tumours of the colon and rectum (*N Engl J Med* 1999;340:169-76). The researchers took into account age, established risk factors and total energy intake, and also reanalysed the data to exclude women who had changed their fibre intake during the study period. However, there appears to be no difference in the rate of adenomas or cancer among those who ate the highest versus the lowest amounts of fibre.

Drug stops body from absorbing fat

A drug that keeps the body from absorbing about a third of the fat that is eaten, and helps patients lose weight and keep it off, sounds like another outrageous claim from the diet industry. But orlistat appears to be the real thing (*JAMA* 1999;281:235-42). More than 1000 obese people from across the US participated in a randomized, double-blind, placebo-controlled trial lasting more than 2 years. All participants also followed an energy-reduced diet. Those taking orlistat lost an average 8.76 kg in the first year, whereas those taking placebo lost 5.81 kg. The participants who received orlistat in the first year were reassigned to orlistat or placebo in the second year, and those taking orlistat regained less weight (3.2 kg for those taking 120 mg 3 times a day, and 4.26 kg for those taking 60 mg) than those taking the placebo (5.63 kg).