Atherosclerosis KOs anti-spasm fighter

Scientists last week reported the discovery of a mechanism by which atherosclerosis may trigger high blood pressure, heart disease and stroke. The key appears to be atherosclerosis's disruption of the production of "endothelium-derived relaxing factor" (EDRF), a substance that appears to prevent constriction of blood vessels. When atherosclerosis interferes with the supply of EDRF to muscle fibers inside vessel walls, segments of the vessel may rapidly open and close in a process called vasospasm, which could then lead to heart and blood-pressure-related problems.

Normal blood flow is maintained by interactions among the clot-inducing blood cells called platelets, the endothelial cells lining the vessels and the smooth-muscle fibers running beneath the endothelium. Scientists have known for several years that platelet secretions induce the endothelium to produce EDRF, which then acts to relax underlying muscle. If the endothelium is damaged, however, this three-step balance is lost and muscle fibers constrict.

Although EDRF's identity is incomplete, researchers earlier this year identified nitric oxide as a potential EDRF candidate, and there may be other, still-unknown secreted substances that similarly relax vessels. Studies in animals are confirming its importance in maintaining cardiovascular health. Reports from the annual American Heart Association meeting in Anaheim, Calif., suggest that reduced EDRF concentrations may lead to the intermittent pain experienced by some cardiac patients, as well as other symptoms associated with vessel and blood-pressure abnormalities. The most recent studies suggest that EDRF and atherosclerosis are linked in ways that could harm the patient.

Production of EDRF is "greatly impaired" in atherosclerosis, says Donald D. Heistad of the University of Iowa in Iowa City. He says atherosclerotic lesions inside the vessel walls impede EDRF production, and vessels tend to constrict and stop blood flow to tissues – with medical consequences that may be serious. "Spasm clearly is important in [problems associated with] the heart," says Heistad. "We suggest that it also may be important in transient ischemic attacks [minor strokes] in the brain."

To test the effects of atherosclerosis on the EDRF-mediated process, Heistad and his co-workers studied monkeys with normal blood vessels, early atherosclerosis or advanced atherosclerosis. Those with lesions had been fed fatty diets for 18 months prior to the study. The scientists found that even minor atherosclerotic changes in vessels impaired EDRF secretion. But if monkeys were given normal diets that lowered their cholesterol, endothelial production of EDRF was restored. This, says Heistad, could mean that a switch to low-cholesterol diets actually reduces vasospasms, rather than opening narrowed vessels as originally thought.

Because endothelial damage is a common denominator in this loss of vessel "relaxation," scientists at the meeting said that physicians evaluating a patient should consider endothelial damage caused by viruses, vessel transplantation and vessel catheterization during diagnostic testing. – *D.D. Edwards*

Fish oil takes a dive?

Changes in blood lipid, or fat, levels have been the driving force behind the current enthusiasm over fish oils as a convenient method to lower the risk of heart disease. Certain fatty acids in the oils called triglycerides apparently prevent blood clotting and lower lipid levels in the blood (SN: 10/19/85, p.252). Since that discovery, researchers have released some conflicting reports on fish oil's effectiveness, coupled with cautions on possible disadvantages of taking fish oil pills.

One negative effect may be an increase in the level of low-density lipoprotein (LDL), which carries cholesterol in the blood and contributes to fat accumulation, say scientists from the University of Kansas Medical Center in Kansas City, Kan. In a report presented at last week's meeting of the American Heart Association in Anaheim, Calif., William S. Harris said his group compared the effects of fish oil supplements to those made of safflower oil, in an experiment using patients with high triglyceride levels. The doses of fish oil given contained the amount of fatty acids found in 12 to 15 fish oil capsules. This is roughly equivalent to the fatty acid intake of the Greenland Eskimos, whose low incidence of heart disease first alerted scientists to fish oil's potential benefits. Despite the inconvenience of the fishy burps they developed while taking the oil, patients in the study benefited from the lowering by 40 percent of triglyceride levels, says Harris.

But the effect on lipoproteins wasn't so positive. While levels of high-density lipoprotein (HDL) – LDL's "good" counterpart – remained the same, LDL levels rose by about 16 percent. In view of LDL's link to heart disease (see p. 348), Harris says researchers should take a closer look at the relative risks and benefits of fish oil supplements. □

New connections may be memorable

It seems logical that the learning process would involve the construction of new circuitry inside the brain. Scientists have been hard pressed, however, to pinpoint learning-related anatomical changes in neural systems.

New research by Craig Bailey and his colleagues at Columbia University's College of Physicians and Surgeons in New York City strengthens the case for the nerve-circuit model of learning. Bailey last year presented the first solid evidence of learning-associated circuit formation in the slug-like "sea hare," *Aplysia*. This creature is a popular model for neurobehavioral experiments because its neural circuitry is well understood and because researchers can train it in ways that allow testing for short- and long-term memory.

The new research, presented last week in New Orleans at the meeting of the Society for Neuroscience, confirms previous evidence that the number of synapses, or neural interconnections, increases as *Aplysia* undergo training to respond to particular stimuli. Moreover, these synapses demonstrate an increased ability to secrete transmitter substances that are critical to nerve firing. The latest research shows for the first time that a gradual *decrease* in the number of synapses parallels the behavioral changes observed as an *Aplysia* eventually "forgets" how to respond to conditioned stimuli. The study suggests that nerve-circuit patterns are constantly changing as learning, remembering and forgetting occur.

"Learning," Bailey concludes, "may resemble a process of growth and differentiation," involving gene regulation, nerve protein synthesis and consequent rerouting of circuitry.

Meanwhile, William Greenough, of the University of Illinois College of Medicine in Urbana-Champaign, has been performing experiments to see if such neural changes are in fact due to learning. Some scientists have argued that the increased number of synapses might simply be due to a general increase in hormone levels or metabolism caused by the extra stimulation and handling that memory training involves. Working with rats, Greenough showed that given equivalent amounts of handling and exercise, rats that had to learn more complicated tasks developed more complicated neural connections.

The precise cellular processes involved in learning and memory are still not known. However, Greenough says, "The [learning-associated] mechanisms brain cells use may not be unique to memory. Natural processes that the cells use for other things may be coopted for use in memory." – *R. Weiss*