Biomedicine

Corticosteroids can't counter caustics

The standard therapy for children who have consumed caustic chemicals provides no real benefit, a new study demonstrates. With no alternative treatment available, the finding underscores the need for preventive measures such as expanding the use of childproof packaging and improving safety education, researchers say.

Each year, an estimated 26,000 U.S. children under 6 years of age ingest corrosive chemicals — mostly household products such as detergents and drain openers. A cascade of tissue-destroying reactions typically ensues for two to three weeks, in some cases ultimately requiring esophageal replacement.

The corticosteroid prednisone has remained the treatment of choice for the past few decades, although several studies have questioned its use. In the most thorough analysis yet of prednisone's value in childhood corrosive injury, Kathryn D. Anderson and her colleagues at Children's National Medical Center in Washington, D.C., used fiber-optic viewers to track esophageal healing in 60 children who had ingested caustic materials. About half had been treated with prednisone. In terms of lasting damage or need for esophageal replacement, the untreated group healed as well as the treated group, the researchers report.

The finding is sobering, says Frederick H. Lovejoy of Children's Hospital in Boston. "Corrosive injury to the esophagus in children is a completely preventable disease," he notes in an editorial accompanying the research report in the Sept. 6 NEW ENGLAND JOURNAL OF MEDICINE. The new study, he says, "has removed any false security derived from believing that an effective medical treatment exists."

Dopamine receptor genes found, cloned

Scientists have plucked from human cells two genes that guide production of molecular switches important in schizophrenia and Parkinson's disease. With the genes in hand, the researchers have grown cultured cells engineered to contain the switches, which respond to a chemical messenger called dopamine. The feat promises to simplify studies of the switches' functions and speed development of new drugs.

For years, neuroscientists and psychologists have been frustrated by their lack of tools to investigate dopamine, a neurochemical intimately involved in such diverse functions as motor coordination and the experience of pleasure. Dopamine shortages in certain brain regions cause Parkinson's disease, but nobody knows why these shortages occur. And while some schizophrenia drugs tweak the dopamine system, scientists still don't know why these drugs help.

In 1988, researchers isolated and inserted into cultured cells the gene for a cell-surface receptor called D2, which responds to dopamine by inhibiting certain chemical reactions inside cells. Now, in the Sept. 6 NATURE, three separate research teams say they've cloned a related protein, D1, that responds to dopamine by stimulating, rather than inhibiting, those same cellular reactions. The teams were led by Allen Dearry at the Duke University Medical Center in Durham, N.C., Olivier Civelli of the Oregon Health Sciences University in Portland, and Brian F. O'Dowd of the University of Toronto.

And in the Sept. 13 NATURE, Pierre Sokoloff and his colleagues at INSERM in Paris, France, report cloning a third, previously unrecognized dopamine receptor gene, which they call D3.

Researchers say experiments on cultured cells bearing the newly cloned genes could simplify laboratory investigations of the molecular mechanisms underlying Parkinson's and schizophrenia. They add that cultured cells engineered to bear both stimulatory and inhibitory dopamine receptors could provide new insights into dopamine regulation and aid in the development of new drugs to alter dopamine's activity.

Chemistry

Ivan Amato reports from Washington, D.C., at a meeting of the American Chemical Society

Wiring enzymes to sense biochemicals

Devices that quickly measure a target compound in a solution teeming with thousands of different chemicals entice scientists and businesspeople alike. Enzymes — nature's own chemical manipulators — offer one strategy for making such picky sensors. Scientists have long sought to emulate enzymes' ability to bind and rearrange specific molecules. Now, Adam Heller of the University of Texas in Austin and his colleagues have begun tailoring a new class of biosensors by attaching certain electron-juggling enzymes to hair-thin carbon electrodes, using polymers as connecting "wires." One of their more promising experimental models apparently measures blood glucose levels more rapidly and precisely than existing diagnostic tests.

Making a glucose sensor, they find, can be as simple as immersing a carbon fiber into two solutions: first into a polymer solution of polyvinylpyridine molecules studded with osmium-containing groups, and then into a bath of glucose oxidase, a commercially available enzyme. "Two dips produces a useful electrode," Heller reports.

Molecules of the stringy polymer squiggle into crevices of the overlying enzyme molecules. When the resulting biosensor contacts a sample, such as a drop of blood, glucose molecules oxidize by giving up an electron. The osmium-centered relay stations hurriedly pass the electrons, like hot potatoes, to the carbon surface. The electrical signal reaching the carbon electrode is proportional to glucose levels in the sample.

This diagnostic system, already under evaluation in a French hospital and German medical school, could mean big business since millions of diabetics monitor their blood glucose levels every day.

Hints of a biological role for silicon

With every sip of tapwater, humans swallow trace amounts of dissolved silicon. Though no one has identified a specific cellular or biochemical function for silicon, chemist J. Derek Birchall of Imperial Chemical Industries in Runcorn, England, says he has found a candidate role that might even have implications for Alzheimer's disease. The toxicologic and chemical evidence he has assembled suggests that silicon — present in body tissues as silicic acid — binds to aluminum, reducing that metal's toxic potential.

In the 1970s, researchers observed that young rats and chicks fed silicon-deficient diets gained too little weight and developed abnormalities in bone, cartilage and other tissues. Replenishing their diets with silicon reversed these trends.

Birchall and his colleagues reported in NATURE last year that young salmon suffered gill damage and died within 48 hours of being placed in water that contained toxic levels of aluminum and scant silicic acid. But in aluminum-laden waters with high levels of silicic acid, all fish survived without obvious gill damage. The researchers proposed that silicic acid prevents systemic absorption of aluminum by preventing it from binding to gills.

Even when present in low levels, silicon- and aluminum-based oxides and hydroxides eagerly combine in a solution to form aluminosilicates, which are also commonly found in soil minerals, Birchall found. He suspects that this coupling effectively imprisons — and thus detoxifies — the aluminum.

Birchall now suggests a possible connection between Alzheimer's disease and silicon levels in the body. Scientists have detected abnormally high concentrations of aluminum in the autopsied brains of Alzheimer's patients, but no one knows whether the metal is a cause or effect of the disease, he notes. To help resolve this ambiguity, Birchall proposes comparing the amounts of silicon and aluminum ingested by Alzheimer's patients.