Huntington's: Defect in DNA repair?

Huntington's chorea, one of the most devastating neurological diseases, characterized by jerky movements, memory loss, rages and other symptoms of profound physical and mental deterioration, is caused by a dominant gene. This means that a person carrying the gene will develop the disease between the ages of 30 and 40 and has a 50-50 chance of passing the disease on. Huntington's is also known to be based on the premature death of neurons. This action's cause has been unknown, but a possible answer is provided in the October PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. The gene responsible could cause neuronal death by coding for a defect in DNA repair inside neurons. So report Dominic A. Scudiero, Sharon A. Meyer and Brian E. Clatterbuck of the Frederick Cancer Research Center in Frederick, Md., and Robert E. Tarone and Jay H. Robbins of the National Cancer Institute in Bethesda, Md.

In the past, metabolic abnormalities have been known for only two of the primary neuronal degenerative diseases characterized by premature death of neurons — xeroderma pigmentosum and ataxia telangiectasia. Patients with these diseases have cells that are especially sensitive to agents such as ultraviolet radiation and certain chemicals because of inherited defects in repair of DNA damaged by these agents.

Robbins, among other researchers, decided to see whether this might be the case as far as Huntington's is concerned. Last year he and others reported the first piece of evidence supporting this hypothesis: They found cells from Huntington's patients to be abnormally sensitive to ultraviolet radiation. Now Robbins and colleagues report a second piece of supporting evidence: They have found that cells from Huntington's patients are especially sensitive to chemicals that have an effect on cells similar to that of ultraviolet radiation.

They took fibroblasts (cells that grow in connective tissue and that are easy to culture) from six Huntington's patients, from seven patients with related diseases and from 13 healthy donors, cultured the cells, then exposed them to a chemical called MNNG that affects cells as does ultraviolet radiation. The cells' sensitivity to the chemical was then determined by measuring their ability to divide and form colonies. Compared to the cells from the healthy persons, those from all six Huntington's patients and from six of the seven other patients were found to be abnormally sensitive to MNNG. This finding, the scientists conclude, provides further evidence that a defect in repair of neuronal DNA damaged by ultraviolet radiation and related chemicals brings about the neuronal death underlying Huntington's as well as some related diseases.

The mechanism by which the gene that causes Huntington's exerts the defect in DNA repair is still unknown, Robbins told SCIENCE NEWS. But what is especially encouraging about the finding, he says, is that it represents a new direction in understanding neurological diseases like Huntington's. Robert Moore, chairman of neurology at the State University of New York at Stony Brook and chairman of the Medical and Scientific Advisory Board for the Huntington's Disease National Association in New York City, agrees. Although he doubts whether a defect in DNA repair will turn out to be the primary cause of neuronal death in Huntington's, he concedes that this is possible. The fact that Huntington's patients are especially sensitive to MNNG, Robbins and colleagues believe, may also eventually lead to the development of a test to screen persons who have Huntington's before the disease develops so that, if they desire, they can avoid reproducing and passing the disease on to their children. Such an assay is not currently available. —*J. A. Treichel*

Mental health cuts: A social dis-ease

"It's like an atomic blast," one National Institute of Mental Health employee told SCIENCE NEWS. "Initially it was like a volcano erupting, but now it's like an atomic blast with very few survivors."

The fallout of the Reagan administration's inaugural blast at the 1982 federal budget was still threatening victims last week as anxious agencies awaited final word from Congress about how deep the cuts would slash. At NIMH, the 23 percent reduction in staff that was compared to an atomic bombing was just one reflection of sharp shifts in policy regarding federal funding for mental health research.

At press time there was still confusion at NIMH (and on Capitol Hill) about exactly how deep the cuts in research would delve. A September proposal backed by the Reagan administration would authorize approximately $127 million for NIMH research — a 28 percent reduction from Carter's proposed budget for the same year. The Senate proposed a similar figure of $128.4 million; the House favored a milder cut, authorizing $150 million. While Congress and the President have spent months haggling over exact funding levels, the mental health agency has based expenditures since October on the $128.4 million figure.

This is one of a series of stories SCIENCE NEWS will run periodically on the impact of actual or proposed budget cuts on various areas of science.

"That [the 28 percent cut] is a bit of a thump because a good deal of our money is tied up in continuation costs," says P. E. Goody, NIMH budget officer. Because a typical grant issued at NIMH funds a project for three years, Goody explains, much of the money spent by the agency this year will be tied up funding grants initiated in past years. Only about $30 million is expected to be left to support new projects. "That's the lowest we've had in 15 years," he told SCIENCE NEWS.

"Social research" not explicitly tied to the promotion of mental health or the prevention of mental illness has been hit hardest by the budget reduction, says Lyle Bivens, deputy director for the agency's extramural research programs. But even projects in neurosciences with clear mental health relevance will feel the pinch in competing for fewer funds. "The pain is felt pretty much across the board," he said in an interview.

The word "social" picked up a special stigma in funding circles last spring when the Office of Management and Budget decreed that NIMH should phase out support of social research but did not spell out how the term should be defined. In a description of their new policy mailed to grant applicants in August, the NIMH officials judged the edict to mean that any research funded in the social sciences must have a strong mental health connection. But hard and fast rules for meeting that connection have not been detailed.

Rather than exclude whole areas of research from funding, the agency is evaluating each proposed study according to its specific link to mental health. However, some agency officials admitted that the distinction between fundable and nonfundable research is often fuzzy. For example, under the new criteria, a study of the divorce rates of offspring of divorced parents, although worthwhile research, would probably not be funded by NIMH, one grant evaluator says. But an investigation of the impact of divorce on the cognitive development of children could be approved for funding.

Some administrators worry that by demanding that all research proposals demonstrate immediate relevance to mental health, the new policy will retard growth in often fruitful basic research. They point to 1981 Nobel laureate Roger W. Sperry, a recipient of NIMH grants for 23 years, who initially studied the surgically split brains of animals. Follow-up studies of animals and humans whose brain hemispheres had been separated for treatment of epilepsy yielded detailed maps of the differing functions of right and left hemispheres. The work opened frontiers in understanding brain function that might have been locked shut two decades ago by shortsighted demands of relevancy in research, NIMH officials say. —*D. Franklin*