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The NIH Record

World Health Officials Focus on AIDS

By Blair Gately & Lisa Datta

Dozens of NIH employees played a major role in the Third International Conference on AIDS held earlier this month at the Washington Hilton.

More than 7,000 physicians, researchers, epidemiologists, economists, government officials, and members of the news media gathered for the largest international scientific gathering to date on the growing AIDS crisis.

Among the topics at the 5-day conference were the search for a vaccine, the latest findings on the spread of AIDS, clinical trials for drug therapies, clinical management, and prevention and control of the disease.

Dr. George J. Galasso, Office of Extramural Research and Training, was the chairman of the conference's organizing committee. Dr. Kenneth Bridbord, Fogarty International Center, served as co-chairman.

"We worked for 2 years on the overall planning for the meeting, along with a number of other committees," Bridbord said.

Media relations for the conference, which was attended by 800 journalists, were coordi-

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Puts Them in DRRiver's Seat

DRR Trains Minority Scientists

By Michael Fluharty

Born and reared thousands of miles apart and separated by generations of cultural differences, Dr. Antonio Alegria, Dr. Kenneth Boutte, and Wilford Denetclaw grew up sharing a common interest: love of science. But thanks to their participation as students in the Minority Biomedical Research Support (MBRS) program, two have already earned doctorates in the biomedical sciences and all three have promising careers in biomedical research.

Denetclaw, a Navajo Indian working on his Ph.D. dissertation in cellular and developmental biology at the University of California at Berkeley, reflects their collective attitude: without the opportunities and support provided by the MBRS program, he's not sure he could become a research scientist.

Fifteen and Still Growing

Fifteen years ago this June Alegria and Boutte were among the first students in the MBRS

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Too Many Brain Cells Can Make You Dense

Scientists are Learning How Fewer Cells Make the Brain Work Better

By Leslie Fink

Biology shapes the brain sort of the same way Michelangelo sculpted the *Pieta*, according to a theory gaining popularity among neuroscientists. Michelangelo started with an ungainly chunk of rock and pared it down to articulating figures of infinite detail. Late in fetal development, biology takes a large conglomeration of brain cells and whittles out the most elaborate and precise communication network known.

This pruning process happens because, during development, our brains generate many more neurons—cells that carry out brain functions—than are good for us. During an early period of rapid cell growth, genetic signals tell neurons to grow and divide with apparent reckless abandon. "This results in a network that's not very functional," says NICHD neurobiologist Phillip Nelson. "Everything's connected to everything, and you have a poorly tuned system."

For the brain to work properly, many of these cells, and the connections between them called synapses, must die off—a slow process that generally starts around birth and lasts until we are about 6 or 7 years old. Studies have suggested that some brain abnormalities such as some forms of mental retardation result when the brain's pruning mechanisms go awry.

According to a report in the June issue of the *Journal of Cell Biology*, NICHD scientists have begun to learn how biology weeds out excess nerve cells and synapses to leave a tightly knit, functioning brain. The key, the report says, seems to lie not just in neurons but also in another type of brain cell called glia. Although glia cells have no direct nerve activity, they help support the brain's neuronal network. The new study suggests that a brain hormone and electrical activity of nerve cells stimulate glia cells to secrete substances that help decide which neurons shall live and which shall die.

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With Sister Mary Carl Malmstrom, director of the MBRS program at Xavier University, are John Harris and Richele Theodore. John, who is currently a graduate student in chemistry at Texas A&M University, helped conduct MBRS research in the area of x-ray crystallography while at Xavier. Richele, who will enroll at Texas A&M in the fall as a biochemistry graduate student, worked under the direction of Sister Mary Carl in research involving enzyme electrodes.

AIDS

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nated by NIH's Office of Communications, with the help of 85 volunteers from HHS information offices.

One of the most sobering predictions on the impact of the epidemic was that given by Dr. Jonathan Mann, director of the World Health Organization's (WHO) Special Programme on AIDS.

He said the WHO estimated up to 3 million new AIDS cases by 1991. Worldwide, the organization estimates that between 5 and 10 million people are currently infected with human immunodeficiency virus (HIV), the cause of AIDS.

"AIDS has created a worldwide emergency. Global AIDS control will require billions of dollars over the next 5 years," Mann said. "The disease has assumed pandemic proportions affecting every continent of the world, and further spread of the virus is inevitable. AIDS threatens all countries—there are no geographic 'safe zones' and no racial exemptions."

He emphasized the need for a global strategy to prevent and control the disease and outlined steps the WHO has taken, including formulating international research agendas, guidelines for public education, and a list of criteria for HIV screening programs.

The Public Health Service estimates that at least 1.5 million Americans are already infected with the virus.

At the conference, Dr. James Curran of the Centers for Disease Control predicted 270,000 cases and 179,000 deaths by the end of 1991.

In a session on the epidemiology of AIDS in the United States, Curran pointed out that the incidence of AIDS is different in some racial or ethnic groups. He said the rate of infection is three times higher in black and Hispanic communities than in white communities. He attributed the impact of AIDS on those groups to intravenous drug use.

Dr. Robert Gallo of the National Cancer Institute announced the discovery of a new related AIDS virus in Africa and predicted that others may be found. He said the original AIDS virus, HIV, however, remains the most virulent. The emergence of new viruses is ex-

pected to hamper research efforts to find a vaccine.

Dr. Samuel Broder of NCI reported on chemotherapy treatments of HIV infections, but cautioned against expecting too much from any particular drug.

He said the search for "the perfect drug"—one that will cure AIDS without serious side effects—should not hinder the development of "good" drugs which can prolong a patient's life or alleviate suffering.

Dr. Robert Walker of the National Institute of Allergy and Infectious Diseases presented the first study of the drug azidothymidine's (AZT) efficacy in treating AIDS patients at an earlier stage of infection. AZT has recently been approved by the Food and Drug Administration for the treatment of advanced AIDS patients with a history of pneumocystis carinii pneumonia, and patients with advanced AIDS-related complex (ARC).

FDA Commissioner Frank Young told a press conference that the agency is currently testing about 50 drugs to treat AIDS patients.

In addition to attending the scientific sessions at the conference, scientists from more than 50 nations attended poster presentations and roundtable discussions and viewed 60 exhibits by pharmaceutical companies, medical suppliers, health clinics and advocacy groups. □

BRAIN

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"We focused on the role of glia cells because, since they're in the business of keeping neurons happy, we thought they might release substances that affect neuronal survival," says NICHD's Douglas Brenneman, who headed the study. "I think we've got valuable information on how some substances participate in pruning back excess neurons to get the final, functional architecture of the brain."

To get a handle on how substances produced by glia cells might in turn regulate nerve cell survival, Brenneman and his colleagues first looked at a hormone known as vasoactive intestinal peptide, or VIP. Working neurons in the developing brain secrete VIP during electrical activity. Although scientists know VIP has several functions in the gut, the hormone was only recently discovered in the brain, and its role there is mostly a mystery.

But Brenneman and his colleagues got a clue from their earlier studies of VIP. They had exposed a mixture of mouse brain cells grown in a culture dish to a chemical that blocks electrical activity in nerve cells. Without electrical activity, nerve cells in the mixture died. The sci-

entists then added both the chemical and VIP to the cell cultures, and the nerve cells lived. VIP seemed to play some role in sparing nerve cells, even when their electrical activity had been blocked. Following that lead, the scientists began experiments to help them understand the links between electrical activity, VIP, and other conditions in brain cell cultures that influence nerve cell survival.

In the new study, the researchers grouped cells from the mixed cultures according to type. Then they added combinations of VIP and the blocking chemical to each of the different types of cell cultures. They found that, when treated with VIP, cultures containing only glia cells released a substance into the culture liquid that was later shown to prevent nerve cell death. Although the scientists have not yet identified this protective substance, and recognize that there may be more than one, these experiments suggest that the life or death of a neuron depends largely upon a survival factor produced by glia cells.

Cells Team Up

But neurons, electrical activity, and glia cells seem to team up during development to carve out a working brain. In many ways, says Nelson, it's a matter of natural selection. Survival of the fittest, whether in nightingales or neurons, is "the only way biology knows how to do it," he says. All of the neurons, the theory goes, compete for the survival substance released by glia cells. But some neurons may be in the wrong place, or may not be receiving the necessary environmental stimulation. These cells, according to Nelson and Brenneman, will die. Rather than "everything connected to everything" then, the remaining nerves regroup into a more specialized brain architecture.

In the human brain, the number of synapses is greatest at the time of birth and shortly thereafter. Then the pruning process gradually reduces the connections during our youngest years, when our brains generate a lot of electrical activity while taking in and dealing with an enormous amount of information. "This selective process goes on during what is probably the most important time during the development of the human nervous system," says Nelson. Because of the link between electrical activity in neurons, VIP, and survival factor(s) produced by glia cells, "information coming into the brain may determine what the person's going to have to work with for the rest of his or her life. It's an exceedingly important thing to understand." □

AmFAR Honors Gallo

Dr. Robert Gallo, NCI, received an award from Elizabeth Taylor, national chairwoman of the American Foundation for AIDS Research, at a fundraising banquet held on the eve of the AIDS conference.

He was honored, along with U.S. Surgeon General C. Everett Koop and Dr. Luc Montagnier of the Pasteur Institute, for his contributions to AIDS research.