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National Institutes of Health

Symposium on Animal Use in Research Slated

The National Institutes of Health has scheduled a 2-day national symposium on "Imperatives in Research Animal Use: Scientific Needs and Animal Welfare." It will begin 9 a.m. Wednesday, Apr. 11, in the National Academy of Science Auditorium (2100 C Street, N.W.) in Washington, D.C.

The purpose of the symposium—as the inaugural event in a comprehensive educational program—is to build a wider consensus among the scientific community and general public concerning Public Health Service policies for the humane care and use of research animals.

More than 600 scientists and concerned members of the public from throughout the United States will attend.

Speakers at the first session will focus on the rationale for involving animals in research. Dr. Donald S. Fredrickson, vice president of the Howard Hughes Medical Institute, and former NIH Director, will be the keynote speaker.

Clinical applications of recent animal research will be illustrated by physicians and their patients who have benefited from animal studies. This panel will be moderated by

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Cancer Prevention Awareness Drive Launched: Secretary Heckler Stresses Diet, No Smoking

Reduced smoking and improved diet—including more fiber and less fat—are two key changes in American lifestyle that the National Cancer Institute says could help cut cancer deaths in half by the year 2000.

Health and Human Services Secretary Margaret M. Heckler, in announcing NCI's new Cancer Prevention Awareness Program on Mar. 6, said, "Too few Americans realize the simple truth that cancer is usually caused by the way we live, and its risks can be reduced by the choices we make."

Mrs. Heckler said at least 95,000 lives a year could be saved through cancer prevention. This figure represents about half of NCI's new goal of reducing cancer deaths by 200,000 by the turn of the century.

Some 75,000 lives could be saved by less smoking; another 20,000 lives could be saved through improved use of cancer treatments.

Only a decade ago, scientists understood little about the role personal habits and the environment played in causing cancer, and Americans had little information on what they could do to prevent cancer.

Today it is known that up to 80 percent of cancer cases may be linked to "lifestyle and

HHS Secretary Margaret M. Heckler and NCI Director Dr. Vincent T. DeVita, Jr. answer reporters' questions during the Mar. 6 press conference on cancer prevention awareness in the ACRF auditorium.

environmental factors," Mrs. Heckler said.

"We now know that the most important causes of cancer are the ones we can control or influence," she said. "We are not always at the mercy of our environment."

The new Cancer Prevention Awareness Program is a major Federal effort to increase public awareness of the possibilities for cancer prevention, challenging Americans to learn what they can do every day to control their own cancer risks.

Based on the most recent scientific infor-

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New Virus Uncovered as Cause of SAIDS By Science Teams From NINCDS/U. Cal.

A new virus that causes an often fatal monkey disease called simian acquired immune deficiency syndrome, or SAIDS, has been identified by a team of scientists from NINCDS and the University of California at Davis.

The investigators used the new virus, which was isolated from the blood of diseased monkeys, to transmit SAIDS to healthy rhesus monkeys.

SAIDS resembles human acquired immune deficiency syndrome, or AIDS, the lethal disease that primarily affects male homosexuals and intravenous drug abusers in the United States.

In a process that scientists believe may be similar to the destructive process in AIDS, SAIDS disables the monkey's immune system causing victims to die from malignancies or infections they would normally fight off.

"An understanding of the monkey disease may be particularly important for learning about human AIDS," says Dr. John L. Sever, chief of NINCDS's Infectious Diseases Branch. "Right now there is no animal model for AIDS—no one has been able to transmit human AIDS to experimental animals for study."

Dr. Sever heads the Institute's SAIDS research team, which also includes Drs. Maneth Gravell and William T. London.

Also collaborating in the discovery were scientists from NIAID, St. Jude Children's Research Hospital, Memphis, Tenn., the NCI Frederick Cancer Research Facility, Frederick, Md., and the University of California at San Francisco. Partial support for this research was provided by an interagency agreement between NHLBI and DRR.

The group recently reported in *The Lancet* and *Science* that they had identified the new SAIDS virus as a type D retrovirus.

A related retrovirus, classified as type C, causes a T-cell leukemia in humans. Some scientists suspect the type C virus as the cause of human AIDS.

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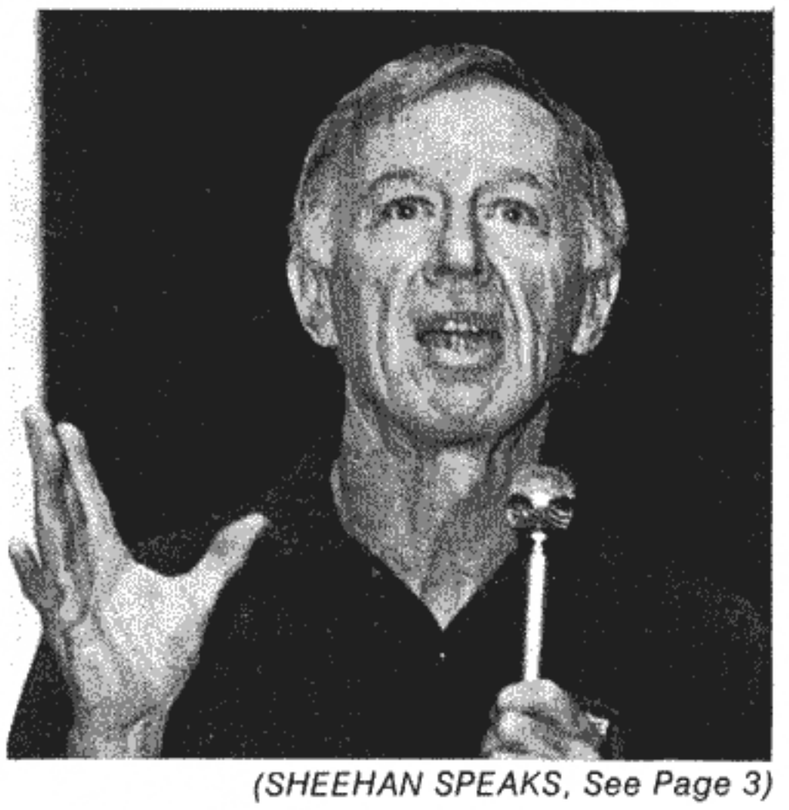

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New Hypothesis Proposed to Explain Liver Failure–Brain Malfunction Link

Clinicians over the last several decades—and perhaps as long as the past 100 years—have been immensely interested in an apparent link between liver and brain function.

When diseases of the liver cause liver failure, distinct neurological symptoms occur, from disturbances in sleep patterns and personality changes to coma.

Several theories have been proposed to explain the link in liver/brain function. Three of these theories have received much attention.

When the liver shuts down or its function is impaired, several substances which can affect the function of the brain—but are normally cleared by the liver—accumulate in the blood and may eventually cross the blood-brain barrier into the brain.

Ammonia Hypothesis

One hypothesis suggests that accumulation of ammonia (a normal waste product that typically is disposed of easily) may be the cause of neurologic problems associated with liver disease.

Another suggests that the additive effects of ammonia, mercaptans, and fatty acids affect the functioning of the brain.

The third hypothesis, termed the false neurotransmitter hypothesis, suggests that the substances that normally conduct nerve transmission in the brain (neurotransmitters) are reduced, while "false" neurotransmitters increase.

The overall effect of this upset balance is thought to lead to the neurological problems evidenced in liver disease/failure.

Now researchers in the Liver Unit, NIADDK—Drs. E. Anthony Jones, S. Chris Pappas, and Peter Ferenci—propose a different hypothesis, with supporting data to explain the functional relationship between the liver and the brain.

This hypothesis has been termed the true neurotransmitter or GABA hypothesis. GABA, gamma-aminobutyric acid, is the principal substance that causes inhibition of neural function in the mammalian brain.

True Neurotransmitter

This hypothesis suggests that increased levels of GABA in the blood, together with an increased sensitivity of the brain to GABA, eventually leads to neurologic dysfunction.

Using a rabbit model of liver failure, the investigators examined visual evoked potentials (VEPs). VEPs are the averaged recorded brain responses to multiple light pulses by an animal undergoing certain treatments.

The investigators found that the VEPs in liver coma were very similar to those caused by stimulation of the GABA neurotransmitter system, whereas responses to ammonia and ammonia with other toxic substances were different.

Supporting Data

Other supporting data indicate that GABA in the bloodstream can cross into the brain during liver failure, though under normal circumstances it does not. It is produced by bacteria in the gut, and brain receptors of GABA increase when liver failure induces coma.

While these results are exciting and encouraging, research continues to strengthen the hypothesis.

With the development of new drugs, it eventually may be possible to counteract the inhibitory brain effects of GABA in coma due to liver failure. □

Minority College Students Introduced to NIH Research

The National Institute of Allergy and Infectious Diseases recently sponsored a two and one-half day program "An Introduction to Biomedical Research" designed to alert college juniors and graduating seniors to the opportunities for minority students in biomedical research at NIAID as well as other research centers at NIH.

While at the conference, students heard a series of lectures by members of the NIAID staff, were interviewed by NIAID scientists, and took a tour of the hospital and laboratory facilities on the NIH campus.

Students from the United States and Puerto Rico were recommended by their deans and professors to attend this program.

To be eligible, students must be interested in science and have some courses in the physical, chemical, biological, mathematical or behavioral sciences. Some also are involved in ongoing research projects at their universities.

Of the 52 students attending the conference, at least 20 individuals will be offered summer employment in NIAID laboratories, located either in Bethesda or in Hamilton, Mont. □

On Pregnancy and Smoking

Facts About Pregnancy and Smoking, an illustrated brochure, describes the effects of cigarette smoking on the developing fetus.

The booklet presents the findings of the National Institute of Child Health and Human Development-supported research on how maternal smoking affects newborns, contributes to more premature births and small and underweight infants, and increases the incidence of respiratory and cardiovascular problems and perinatal deaths among newborn babies.

The brochure graphically shows the path smoke travels via the mother's mouth, lungs, bloodstream, placenta and umbilical cord to the fetus. It also gives some other sources of information for pregnant mothers and health care providers on the subject of pregnancy and smoking.

Single copies of *Facts About Pregnancy and Smoking* may be ordered free of charge from NICHD's Office of Research Reporting, Rm. 2A32, Bldg. 31, NIH, 9000 Rockville Pike, Bethesda, MD 20205. □

Reason is God's gift; but so are the passions: reason is as guilty as passion.—*Cardinal Newman*

SAIDS

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Retroviruses differ from most viruses because they contain a special enzyme called reverse transcriptase, which is necessary for the virus to replicate or make copies of itself. This replication enzyme provided the key link in discovering the cause of SAIDS.

To find the SAIDS virus, scientists at NINCDS and the DRR-supported California Primate Research Center at the University of California at Davis had been following an elaborate scheme of experiments.

From these experiments the investigators knew the SAIDS agent was infectious; they knew it was transmitted by blood; and they knew it was small. The evidence pointed to a virus.

But the virus proved elusive. The scientists took plasma—the liquid component of blood—from diseased monkeys and tried to grow the SAIDS agent in laboratory-cultured cells. Many viruses are easy to detect in culture because they kill the cells they infect.

The SAIDS agent, however, grew in the cultured cells without killing them, making the virus hard to spot. It wasn't until the scientists checked their infected laboratory-grown cells for reverse transcriptase—the enzyme that characterizes retroviruses—that the SAIDS agent was uncovered.

The scientists isolated the virus from their cultures, purified it, and injected it into a new group of healthy rhesus monkeys. When these monkeys died of SAIDS a few weeks later, there was little doubt the virus caused the disease.

But even more evidence surfaced. About the same time that the NINCDS/Davis team and their colleagues published their results, an independent group of scientists at the DRR-supported New England regional Primate Research Center in Southborough, Mass., similarly reported that they had isolated a type D retrovirus from monkeys with SAIDS. However, their reports did not include the successful transmission of the disease to healthy monkeys.

"With the evidence from our group and the New England group, we are quite sure that the new retrovirus causes SAIDS," Dr. Gravell says. "But there is a slight possibility that the purified virus innoculated into the test monkeys could have contained a contaminating virus that was not detected."

Though the case appears closed on the SAIDS culprit, scientists still face the ultimate challenge—finding the cause of AIDS. "Now that we have identified the cause of SAIDS, we believe that similar techniques may help us find a virus in humans with AIDS," Dr. Sever says.

The NINCDS investigators also want to find out how the new virus destroys the ability of the monkey's immune system to fight disease. "We hope this information will help explain the disease process in human AIDS as well," Dr. Sever says.

In addition, the scientists are working on ways to prevent SAIDS in rhesus monkeys, which are used throughout the country in medical research that can not be done on humans. Approximately 6,000 rhesus monkeys born annually in breeding colonies in the United States are potential SAIDS victims.

—Lynn Cave □