# Viral Exposure Boosts Schizophrenia Risk

For about a month in the fall of 1957, Helsinki, Finland, was swept by a serious Type A2 influenza virus epidemic that is estimated to have infected two-thirds of the population. Thanks to the meticulous record-keeping of the Finnish government, researchers now have established that people who were exposed to the worldwide epidemic while in their second trimester of fetal development have an increased risk of hospitalization for schizophrenia.

"A basic risk for schizophrenia seems to occur when there is some kind of fetal trauma during the second trimester," says psychologist and research director Sarnoff A. Mednick of the University of Southern California in Los Angeles. "It is not so much the type of stress as it is the timing of stress during gestation which is critical in determining the risk."

But, importantly, he and his colleagues report they have found a link between second-trimester exposure to a specific virus and the adult diagnosis of schizophrenia. Longstanding theories of an "infection connection" in some cases of schizophrenia have generated more debate than data (SN: 11/30/85, p.346). The Finnish study, which will appear later this year in ARCHIVES OF GENERAL PSYCHIATRY, was generated by the researchers' ongoing, 24-year study of Danish children with schizophrenic mothers. Children who developed schizophrenia in adulthood and had an excess of birth complications also tended to have been born during periods of increased viral infections (January, February and March) in crowded Copenhagen.

For the county encompassing Helsinki, the investigators tracked all children born in the nine months immediately following the 1957 epidemic who were hospitalized before the age of 26 in one or more of the county's eight psychiatric facilities. These 216 "index" individuals were compared with 1,565 "control" children born in the same county in the corresponding months of the previous six years, and who were hospitalized for psychiatric disorders before 26 years of age.

Nearly 36 percent of the index patients exposed to the epidemic during their second trimester of fetal development were diagnosed as schizophrenic by Finnish psychiatrists. In contrast, about 22 percent of both control patients and index subjects exposed to the epidemic in the first or third trimester of fetal development received diagnoses of schizophrenia; the rest had a variety of psychiatric diagnoses. The "second-trimester effect" held for both males and females, and independently in each of several of the psychiatric hospitals.

Moreover, for the entire Helsinki population, the rate of hospital diagnoses of schizophrenia per 1,000 Helsinki live births for second-trimester exposures was around 1 percent, twice the rate for first- and third-trimester exposures.

There is no direct evidence that pregnant women actually sufferred a viral infection during the epidemic, notes Mednick, and psychiatric admissions beyond 26 years of age have not been examined. Nevertheless, he says, the study adds to "sparse evidence" implicating other second-trimester disturbances with an increased risk of adult schizophrenia. For instance, Finnish researchers previously found that when pregnant women learned of their fathers' deaths during the second trimester, the offspring later showed an elevation in psychotic disorders including schizophrenia.

Infections and other disturbances during the second trimester may interfere with the migration of brain cells to structures in the cortex, the brain's outermost layer, says Mednick. A combination of these influences and a genetic predisposition may produce different forms of schizophrenia, he adds. The Danish study has identified birth complications, poor parental supervision and placement in public institutions as additional risk factors.

Further work needs to examine whether second-trimester vulnerability occurs over a limited period of perhaps a few days, says Mednick. He plans to repeat the influenza study in Denmark, where extensive population data are also available. *– B. Bower*

# New class of antibiotics confirmed

It was quite by chance that Alexander Fleming in 1928 discovered penicillin. Since then, many antibiotics have been developed, but the serendipitous route of discovery has changed very little. Antibiotics are to this day being patiently sought in naturally occurring substances such as tropical plant extracts and soil molds.

In recent years, however, as molecular biologists have become more proficient at making customized biochemical compounds, interest in "rational drug design" has increased. Rather than looking for naturally occurring drugs – or modifying already-discovered ones – scientists are attempting to craft extremely specific molecules that are capable of killing pathogens without harming the human host.

The first successful synthesis of a rationally designed antibiotic was reported by Swedish researchers in late June of this year. Now scientists working independently at Abbott Laboratories in Abbott Park, Ill., report success with a similar "designer" drug. Tests have so far been restricted to laboratory cultures of disease-causing bacteria. But the research confirms the potential of this new class of antibiotics and provides some encouraging details about how effective the drugs are apt to be.

Robert Goldman and his co-workers report in the Sept. 10 NATURE the synthesis of a potent antibiotic that is effective against an important class of disease-causing microbes – the gram-negative bacteria. Gram-negative bacteria cause a large number of diseases, including gonorrhea, cholera, meningitis and a variety of dysenteries.

"Even penicillin-resistant, erythromycin-resistant and tetracycline-resistant organisms are still sensitive to this compound because it's an entirely different metabolic pathway that's being affected," Goldman told SCIENCE NEWS. The compound inhibits an enzyme inside the bacterial cell that is crucial for the production of lipopolysaccharide – an important component of the bacterial cell membrane. The resulting defective membrane leaves the bacteria unable to reproduce, while rendering them up to 10 times more susceptible to standard antibiotics.

The synthesis of such a specific inhibitor is the culmination of years of research in which the critical bacterial enzyme – CMP-KDO synthetase – was identified, isolated and eventually cloned. Using nuclear magnetic resonance, scientists determined its structure in 1985. On the basis of that information, they designed an inhibitor to mimic the enzyme's natural target, or substrate.

"It's a very straightforward competitive inhibitor of the enzyme," Goldman says. "When the inhibitor [drug] binds to the active site of the enzyme, the enzyme has no access to the real substrate. But the enzyme can't do anything with the inhibitor, so it just sits there, dead."

Moreover, he says, the targeted enzyme "is unique to gram-negative bacteria, so you don't have to worry about inhibiting some analogous pathway in the human."

Encouraging as the research is, work remains to be done before the drug will be ready for clinical trials. Most impor-

tant, Goldman says, improvements need to be made in the peptide delivery system that carries the drug into the bacterial cell. Because the inhibitor does its duty *inside* the bacterium, but is itself incapable of penetrating the bacterial membrane, it requires a carrier molecule to get it across. Currently, researchers are binding the drug to tiny peptides that are naturally capable of crossing that membrane. Once inside the bacterium, intracellular enzymes cleave the molecular complex, releasing the drug.

"The peptide gets the compound in sort of like the Trojan horse, and then you clip off those amino acids to release that warhead molecule," Goldman says. However, the carrier peptides now being used do not penetrate all gram-negative bacteria equally well. So although all gram-negative bacteria contain CMP-KDO synthetase – and are theoretically susceptible to the enzyme inhibitor – not all of them are equally vulnerable to the invading antibiotic. Other peptide carriers may prove more invasive for a broader spectrum of bacteria.

A second problem is that peptide carriers tend to be very short-lived in the human body. Improvements are needed, Goldman says, "so that the compounds will stay around long enough to do their job." *– R.Weiss*

## Alzheimer's update

As recently as March of this year, genetic studies were pointing to the likelihood that a single genetic defect responsible for overproduction of amyloid protein in the brain might be the cause of the hereditary form of Alzheimer's disease (SN: 3/21/87, p.188). Two new studies, however, provide strong evidence that the gene coding for amyloid production is not the same gene that is responsible for the hereditary form of Alzheimer's – even though the genes are neighbors on chromosome 21, and even though the two syndromes often coexist.

The two multicenter international studies, one led by C. Van Broeckhoven from the University of Antwerp, Belgium, and the other by James F. Gusella from Harvard University, followed familial inheritance patterns of the two syndromes using new genetic markers. Their findings, reported in the Sept. 10 NATURE, suggest that the two genetic defects are inherited independently.

Although the studies don't rule out some kind of link between amyloid plaques in the brain and Alzheimer's disease, the direction of causality remains unclear. It's likely, two of the researchers told SCIENCE NEWS, that either syndrome can be caused by any of a number of genetic or environmental factors.

"It's a very heterogeneous disease," one researcher sighs. "Talk to me again in about a year." □

## Seeking aneutronic nuclear fusion

"Aneutronic" is a word that has not yet made its way into the dictionaries. It refers to processes of thermonuclear fusion that produce few or no neutrons. In energy-producing fusion reactors, aneutronic processes would have advantages in both safety and in ease of gathering the energy released. However, this breed has had low priority in the fusion research program funded for the last 40 years by the Department of Energy (DOE) and its predecessors. Now something of a push toward them seems to be developing.

Last week, the Committee on Advanced Fusion Power of the National Research Council's Air Force Studies Board issued a report advising the Air Force that research on aneutronic fusion processes is worth supporting as a possible answer to Air Force requirements both for electric current and for propulsion. As the report was issued, many of the interested scientists were gathered at the International Symposium on Feasibility of Aneutronic Power, meeting at the Institute for Advanced Study in Princeton, N.J.

The report was generally well received, although some people, particularly Bogdan Maglich of AELabs in Princeton, thought it too pessimistic in predicting how many years it would take to bring about practical aneutronic reactors.

Conventional fusion requires confining atomic nuclei at high density and high temperature. The easiest conditions of confinement and temperature, and therefore the ones sought first by the mainstream fusion program, are those for fusion of deuterium and tritium. However, the energy released in such a fusion is carried away by neutrons – dangerous, penetrating particles, which will yield their energy only by the inefficient means of heating something.

But in an aneutronic reaction (for example, deuterium and helium-3), the energy comes off with protons. Protons can be converted directly into electric current, or they can generate power in the form of radio waves. Protons are not very damaging or dangerous and so minimal shielding is necessary. However, in the jargon of the DOE, these substances are called "advanced" fuels, because the confinement and temperature conditions necessary for them go beyond those for deuterium-tritium.

Proponents of aneutronic fusion say that to the DOE "advanced" means far in the future or even in the hereafter. But Bruno Coppi of the Massachusetts Institute of Technology argues that experimentation with deuterium and helium-3 could be done in some current mainstream experiments – MIT's Alcator, for example. "You could make with today's technology an experiment that burns deuterium and helium-3," he says. However, it lacks funding. Quoting the Swedish physicist Hannes Alfvén, one of the grand old men of this kind of physics, Coppi says that there seems to be "a conspiracy not to do fusion."

Instead of depending on more or less random encounters of nuclei that have been heated to overcome their repulsion for one another, as the mainstream experiments do, aneutronic systems like Maglich's "migma" use the principle of colliding beams, directing the nuclei into intersecting orbits, where they are more likely to encounter each other. "Our position is that the whole concept of heating to achieve collisions is obsolete," he says.

The most recent migma experiment, Migma III, achieved confinement conditions that rival those of conventional experiments, and did it without the disruptive instabilities that plague conventional experiments (SN: 3/9/85, p.151). Migma IV, to be built in Palatka, Fla., in collaboration with the University of Florida at Gainesville, will attempt to increase the density of nuclei in the center of the experiment to 300 billion, 10 times that of Migma III, reaching the "space-charge limit," the point where electric repulsions will prevent further crowding. It will test whether neutralizing some of the charge by introducing electrons will permit higher densities, and it will also test predictions that the resulting plasma should be stable under these conditions.

If deuterium-helium-3 fusion works out as a source of power, it will require a continuing supply of helium-3. (Deuterium can be obtained from sea water.) Although helium-3 is rare on earth, George Miley of the University of Illinois in Urbana-Champaign notes that it is "one of the most plentiful fuels we can find in the universe." But we will have to go off the earth to get it.

On earth, the immediate source is radioactive decay of tritium, a by-product of nuclear fission reactors. According to Miley and the National Research Council, by the year 2000 we can obtain about 600 kilograms of helium-3 from tritium decay. This would run a 200-megawatt power plant for 20 years, "not enough for an economy," says Miley.

Scientists would have to go to the moon and mine helium-3, which the solar wind generates on the lunar surface. Ultimately, when space travel is sophisticated enough, says Miley, we could get it from Jupiter.

*– D. E. Thomsen*