New Culprits Cited for Schizophrenia

Some pregnant women experience an immune reaction that presents dangers to their unborn children. Scientists now have evidence suggesting that this reaction raises sharply the rates of schizophrenia in such offspring by young adulthood.

If confirmed in further investigations, the discovery may indicate that fetal brain damage caused by the mother's immune response underlies some cases of schizophrenia.

A related study provides preliminary evidence that severe malnutrition in the early months of fetal development may also contribute to schizophrenia.

The reports, both in the January ARCHIVES OF GENERAL PSYCHIATRY, add new twists to the theory that disruptions in fetal brain development promote schizophrenia (SN: 12/16/95, p. 406).

"Perhaps the most important clinical implication of [these] studies is that some forms of schizophrenia may be preventable," states Richard Jed Wyatt, a psychiatrist at the NIH-NIMH Neuroscience Center at St. Elizabeths Hospital in Washington, D.C., in an accompanying comment.

The immunity investigation focused on women's antibodies to the Rhesus (Rh) D antigen. RhD is a substance in the blood capable of provoking strong immune reactions. An RhD-negative mother can become sensitized to RhD-positive blood through miscarriage, abortion, or delivery of an RhD-positive child. In later pregnancies, RhD-positive infants draw intensified responses from the mother's immune system. These reactions can result in anemia, jaundice, and brain damage in the child.

J. Megginson Hollister, a psychologist at the University of Pennsylvania in Philadelphia, theorized on the basis of observations of her own family that this biological mismatch between mother and child contributes to schizophrenia. Hollister's RhD-positive sister, the second-born of their RhD-negative mother, experienced medical complications at birth and suffers from schizophrenia. Hollister and her brother, in contrast, are RhD-negative, encountered no birth complications, and remain free of psychiatric disorders.

Hollister and her coworkers consulted comprehensive Danish medical and psychiatric records for 1,867 men born between 1959 and 1961 in Copenhagen. Of that number, 535 were Rh incompatible (RhD-positive individuals born to RhD-negative mothers) and 1,332 displayed Rh compatibility (any other mother-child RhD combination).

Through 1994, the schizophrenia rate for all Rh-incompatible men reached 2.1 percent, compared to 0.8 percent for Rh-compatible men. Among second- and later-born men, an even greater excess of schizophrenia emerged (2.6 percent for Rh compatibles versus 0.8 percent for Rh incompatibles). First-born men in each of the two groups displayed similar schizophrenia rates, 1.1 percent for the Rh incompatibles and 0.7 percent for the Rh compatibles.

The full extent of fetal medical conditions related to Rh incompatibility in the Danish sample is not known, the researchers note. However, the records show that one Rh-incompatible man in five received blood transfusions shortly after birth, one in four was born with high concentrations of bilirubin (a substance that can cause jaundice) in the blood, and two in three suffered from jaundice shortly after birth.

Independent studies of Rh incompatibility and schizophrenia are under way, according to Hollister's group. If the finding holds up, it raises an important caution for current work aimed at cornering genes involved in schizophrenia, they contend (SN: 11/4/95, p. 292).

Genes determine whether an individual possesses RhD-positive or RhD-negative antigens, so Rh incompatibility probably clusters in some families. If schizophrenia also runs in these families, they might be identified as bearing a genetic predisposition to schizophrenia, whereas in fact their genes expose them to Rh incompatibility and its attendant dangers.

The introduction nearly 30 years ago of maternal treatment for Rh incompatibility may have inadvertently helped to lower the incidence of schizophrenia, Hollister suggests.

In the second study, Ezra Susser, a psychiatrist at the New York State Psychiatric Institute in New York City, directed a review of medical and psychiatric records of people born in western cities of the Netherlands from 1944 through 1946. Residents of these cities endured severe famine in late 1944 and early 1945 because of a Nazi blockade of ports and other supply routes.

People conceived at the height of the famine later displayed about twice the schizophrenia rate of people conceived at other times during the study period, including the early months of the famine, Susser and his colleagues report. Moreover, this pattern held for both men and women, the researchers contend.

In the famine's worst months, individuals consumed from 500 to 1,000 calories daily, about one-quarter to one-half the recommended numbers, much of it from bread and potatoes. Deaths from malnutrition skyrocketed during that time.

Further research is needed to determine whether a heightened risk of schizophrenia stems from general effects of malnutrition or from specific dietary losses, Susser asserts. — *B. Bower*

Fake fat gets FDA's okay

Last week, the Food and Drug Administration approved the use of olestra, a synthetic fat substitute, but only in snack foods. Procter & Gamble, the Cincinnati-based creator of olestra, has given it the trade name Olean. A compound of fatty acids and sugar, olestra is neither absorbed nor digested in the body and therefore contributes no calories to foods (SN: 1/27/96, p. 61).

Announcing the action, FDA Commissioner David Kessler acknowledged olestra's shortfalls. "Olestra may cause abdominal cramping and loose stools in some individuals, and [it] inhibits the body's absorption of certain fat-soluble vitamins and nutrients," he says. FDA states that it will require Procter & Gamble to label all foods containing olestra with a warning of those ill effects.

Nevertheless, the agency decided that olestra is safe.

Procter & Gamble, which introduced Crisco shortening in 1911, plans to test-market a line of olestra-containing foods, such as potato chips, cheese puffs, and club crackers, during the next few months. Eventually, the company will put Olean in a broad variety of snack products, says spokesperson Wendy W. Jacques. She says foods made with Olean have the "great taste" of real fat without the added calories.

Yet critics have denounced FDA's action on olestra.

"I find it incredible that Dr. Kessler would certify this food additive as safe," says Michael Jacobson, executive director of the Center for Science in the Public Interest, a consumer group based in Washington, D.C.

Jacobson notes that many prominent scientists have warned FDA of olestra's ill effects, including its ability to rob the body of key nutrients called carotenoids. Researchers have reported evidence that carotenoids, which are found in fresh fruits and vegetables, protect against certain cancers and other serious diseases. — *K.A. Fackelmann*