Genetic Link to Depression: Experts Claim Immunity

Behavioral scientists have believed with growing conviction over the last decade that serious depression is at least partially inherited. But if placed before a judge or jury, the evidence presented thus far would have been found almost totally circumstantial. Statistical studies, particularly involving families with twins, have strongly suggested a genetic component to what is called clinical depression — where the person becomes depressed regardless of his or her life circumstances.

The nature of the genetic link, however, has remained a mystery. Now, scientists at the University of Rochester and the University of Toronto report they have pinpointed the marker of a gene that makes "a major contribution to susceptibility to depressive illness." The gene is located near the HLA (human leukocyte antigen) site on the sixth chromosome. Because the HLA site carries information about the body's immune system, the discovery suggests that certain forms of depression may involve a breakdown in the brain's immune responses.

The finding represents the most convincing evidence to date that the affective disorders — unipolar illness (depression) and bipolar illness (manic-depression) — have some hereditary basis, said University of Rochester geneticist Lowell R. Weitkamp. "I was convinced of a genetic component to depression before we started the study, but our results are more convincing [than previous studies] because we're talking about a specific chromosome region," he told SCIENCE NEWS. The report, by Weitkamp and psychiatrist Harvey C. Stancer and colleagues at the University of Toronto, was published in the Nov. 26 NEW ENGLAND JOURNAL OF MEDICINE.

The researchers studied blood samples of members of 41 families with more than one member suffering from diagnosed depression. Weitkamp and his colleagues personally studied 20 families; data on the rest were taken from recent medical literature. In a complex series of cross-matchings, the scientists found that depressed offspring shared the same HLA genes and inherited the HLA marker from their *well,* non-depressed parent significantly more often than would be expected by random chance.

A number of previous studies have failed to conclusively establish such a link, Weitkamp said, primarily because they tried to trace the transmission from the *depressed* parent to the depressed child. But since the unaffected parent may be simply a "carrier" of only one or two depression-linked genes — as opposed to the affected parent, who probably transmits several more such genes — it is easier to recognize and trace specific markers passed on by the non-depressed parent, Weitkamp explained. "We're not saying it is *only* the unaffected parent that does the transmitting," he said in the interview, "it's just easier to study that type of transmission." The same type of phenomenon was discovered in inheritance studies of diabetes mellitus, he noted. (In 1979, a California researcher reported he had found a mutant brain protein that was a genetic marker for depression [SN: 1/13/79, p. 20]. That study, however, was widely criticized and has yet to be verified.)

The implication of a non-depressed adult as a possible carrier of a depression-related gene points up a major caveat in the study: Genetics appear to dictate only a predisposition to the disorder. "You can have susceptibility and never show the disease," Weitkamp said. Whether or not such an individual actually develops depression, he said, seems to depend on the "environment — and that can mean anything from the totally biological environment to the totally psychological one ... I just don't know."

Whatever the exact ingredients of this disorder that affects 1 to 2 percent of people in the United States, these latest findings might eventually open the door to a new era of genetic counseling. "If this turns out to be true, then it's a large jump toward pinning down the site of at least one type of depression," said Robert Hirschfeld, chief of the Center for Affective Diseases at the National Institute of Mental Health. Weitkamp is applying for an additional NIMH grant to study an additional 100 families. "We want to compare one sibling to another and find out how precise we can be in predicting high and low susceptibility," Weitkamp said. The geneticist says that eventually such an ability to predict could lead to "genetic counseling and people making decisions" about whether or not to have children.

Weitkamp found that the same genetics appear to be common to both unipolar and bipolar depression. Whether a person develops one or the other seems to be due to other factors, he said.

Exactly why the HLA region would be related to depressive disorders "is not immediately evident," brain researchers Steven Matthysse of Harvard University and Kenneth K. Kidd of Yale University write in an accompanying editorial in the Nov. 26 NEW ENGLAND JOURNAL. But they suggest that in a process similar to that at work in the neuromuscular disease myasthenia gravis, a depressed person might produce some type of antibodies that block certain neurotransmitter receptors in the brain. In assessing the Weitkamp study, they say: "This finding will certainly elevate the mood of researchers who study depression." —*J. Greenberg*

Cancer survival rate increases

Is the 10-year war on cancer being won? National Cancer Institute Director Vincent T. DeVita Jr. has been claiming for some time that it is. A year ago, for instance, he reported that 41 percent of patients with serious cancers were being cured (SN: 1/3/81, p. 13). Now he reports that the figure is 45 percent to 50 percent.

DeVita based his estimate last year on a summary report published in 1976 that showed that 41 percent of white cancer patients studied had or were expected to survive five years. This 41 percent in turn derived from statistical analyses conducted at three hospital-based cancer registries — the California Tumor Registry in Berkeley; the State University of Iowa Hospital in Iowa City, and Charity Hospital of Louisiana in New Orleans — and at one population-based registry — the Connecticut Tumor Registry in Hartford. (The latter examined the cancer experience of all patients diagnosed in a specific geographic area.)

Then, a few months ago DeVita estimated, on the basis of published clinical trial results, medical research literature and on the assumption that physicians are now applying what scientists have learned during the past decade to be the best possible cancer therapies, that 45 percent of the patients diagnosed with serious cancers in 1980 were being cured. (He excluded skin and cervical cancers, which are nearly 100 percent curable.)

And now, for the first time, five-year survival statistics from NCI's Surveillance, Epidemiology and End-Results Program (contributed by population-based registries in Connecticut, New Mexico, Utah, Atlanta, Detroit and Seattle-Puget Sound) have become available. And as DeVita reports, they show that 45 percent of patients of all races and both sexes diagnosed for cancer in 1973 or 1974 have been cured, assuming that a five-year survival represents a cancer cure. In fact, DeVita says, because patients diagnosed for cancer since 1973-1974 are probably living even longer than those diagnosed at that time, about 50 percent of all patients with serious cancers are probably being cured today. So the message, he concludes, "is clear: Patients with cancer are living longer now than ever before."

— *J. A. Treichel*