such phenomena as a transition from a nonmetallic to a metallic state.

The Meissner effect provides an independent and more stringent test of superconductivity because it is harder to mimic when the measurement is done correctly. When a metal in a constant (dc) magnetic field is cooled to below its superconducting transition temperature, it expels all magnetic flux lines from its interior. This effect shows up as a large negative magnetic susceptibility below the transition temperature. In addition to the published ac susceptibility measurements, dc measurements on samples taken to the Los Alamos National Laboratory indeed exhibited the expected large negative susceptibility.

Useful superconductors in large-scale applications must retain their properties not only at high temperatures but also in the presence of high magnetic fields and while carrying large electrical currents. The first measurements of the maximum or critical field at which the new Y-Ba-Cu-O compound remains superconducting suggest a critical field at 0 K as high as 180 tesla. In comparison, the critical field of lanthanum-copper-oxygen material containing either strontium or barium is estimated to be at least 60 tesla at 0 K. The presence of a high transition temperature and critical field does not necessarily imply a high critical current, however. The previous holder of the record for critical field, the compound $PbMo_6S_8$, has had disappointingly low critical currents.

It is too soon for theorists to have developed models for the new superconductor. The standard Bardeen-Cooper-Schrieffer theory of superconductivity contains two aspects. The first is that the superconducting state consists of electrons bound together in pairs known as Cooper pairs. The second is that the binding occurs by means of an interaction between electrons and lattice vibrations that generates an attractive force between the electrons involved. The transition temperature is the temperature at which thermal energy is sufficient to break up the Cooper pairs.

Stronger attractive forces between electrons than the electron-lattice vibration interaction can generate may be necessary to explain transition temperatures as high as 94 K. Several proposals for ways to produce such forces, including the magnetic interaction described by Anderson in this issue of *Science*, exist in the literature. ■

ARTHUR L. ROBINSON

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Clinical Trials Planned for New AIDS Drug

U.S. researchers seek FDA approval to start testing peptide T in AIDS patients while the Swedish government has okayed a randomized controlled trial

A new anti-AIDS drug, which may prevent the AIDS virus from entering cells, is about to be tested in Sweden in a randomized, controlled, clinical trial. At the same time, researchers at the National Institute of Mental Health have applied to the Food and Drug Administration for permission to begin a 1-month phase one trial, which tests toxicity only. If that trial is successful, the group wants to follow it immediately with a randomized controlled trial in the United States.

Candace Pert

The Swedish investigators, led by Lennart Wetterberg of the Karolinska Institute, gave the drug, known as peptide T, to a group of four near-terminal AIDS patients last October. This was not meant to be a scientific study—the drug was given on a compassionate basis, Wetterberg explains. But the four men showed no ill effects during the month they received peptide T and, in fact, their symptoms abated. Their conditions have declined since the peptide was withdrawn, and the Swedish government has given Wetterberg and his colleagues permission to give these men the drug again for a period of 6 months. At the same time, the group will start testing peptide T against placebo in 36 AIDS patients.

Peptide T is the only potential anti-AIDS drug that is thought to work by preventing the virus from entering cells. Candace Pert of the NIMH, in whose lab it was discovered, explains that "it came out of left field and it sounded to some people too good to be true." But, she continues, other investigators are becoming convinced. "Skepticism is changing to excitement," she remarks.

Samuel Broder of the National Cancer Institute, says "the important thing is that there are data that suggest peptide T can interfere with binding [of the AIDS virus]. It is an interesting hypothesis and it can be tested at the clinical level. The clinical trial methodology will determine if it is useful."

Dean Mann of the cancer institute, who says that his preliminary data do not indicate that the peptide blocks the AIDS virus from attaching to cells, says he nonetheless has a "gut feeling" that peptide T prevents the AIDS virus from growing in cells. Pert's data indicate that when cells are treated with peptide T, the AIDS virus no longer replicates in them, although she did not measure viral binding directly.

The discovery of peptide T, says Pert, "came out of my lab's 15 years of studying peptides and peptide receptors and mapping receptor patterns in brains." Since AIDS patients often have neurological problems, including dementia, memory loss, and depression, Pert and her colleagues decided to look for evidence that the AIDS virus infects brain cells. When the AIDS virus infects lymphocytes, it enters the cells through the T4 receptor. So Pert and her associates decided to look for T4 receptors in the brain.

They and others found the T4 receptor in the brain, but what was most intriguing was the pattern of the distribution of the receptor. It looked to Pert, Joanna Hill and the others in the group exactly like the pattern of neuropeptide receptors, such as the opiate receptors which Pert and her colleagues had studied extensively. "As soon as we saw the pattern, we knew it was a neuropeptide receptor," Pert says. There was a great deal of binding in the amygdala, for example, the walnut-sized portion of brain that is just below the ears and that is "hard-wired with deep-seated emotional patterns—sex and violence," Pert explains. All neuropeptides bind in the amygdala, she says.

Pert and her associates then decided to try

to make a peptide that binds to the AIDS virus receptor. Since the binding data indicated that a naturally occurring neuropeptide binds to the receptor, they began by looking for such a peptide. To do this, they searched a computer data bank, looking for sequences shared by the AIDS virus and other known substances. The computer found an octapeptide from the viral coat which matched up with a segment of the coat of Epstein-Barr virus. They called this AIDS peptide peptide T because it contains four threonines. Then Edward Ginns of NIMH "thumbed through books" and found that the peptide also is part of vasoactive intestinal peptide, or VIP, a 28 amino acid peptide that acts on the gut and the central nervous system.

They then looked at the sequences of all known AIDS virus isolates and discovered that a pentapeptide within the original octapeptide remains constant. "It is a mini-constant region within a hypervariable region," says Pert. Moreover, they learned that this pentapeptide prevents the replication of the AIDS virus in lymphocytes, presumably by preventing the virus from entering cells. It also binds to brain—including monkey brain and human brain obtained after autopsy—in the same pattern as the antibodies against the AIDS virus receptor.

When the researchers gave peptide T to rats and monkeys, they found that it seemed nontoxic and that it entered the animals' brains. In fact, says Peter Bridge, they "never found an LD_{50}", which is the dose that kills 50% of the animals receiving the drug. Standard toxicological studies of drugs always include an LD_{50} as an indicator of a drug's lethal dose.

In Sweden, says Wetterberg, the AIDS patients who received peptide T had no ill effects. The only adverse effect occurred when a nurse doubled the rate at which a patient was being infused with the drug. The patient's blood pressure dropped from 120 to 90. The patient, however, "did not feel anything. He had no subjective side effects," Wetterberg says.

Although the Swedish study was not meant to be a scientific test of the drug, Wetterberg says he was encouraged by the way the patients improved when they took it. Their lymphocytes increased in number and the virus' effects on their brains, as measured by nuclear magnetic resonance, declined. One patient had a severe case of psoriasis as a result of his AIDS infection and his lesions cleared up entirely after four weeks of treatment. The psoriasis has now returned, Wetterberg says. The patients have been off the drug since the end of October.

If indeed peptide T is relatively nontoxic, its apparent safety seems paradoxical since it is derived from VIP, which has definite physiological effects. VIP in large doses causes an increase in blood pressure and also causes diarrhea, for example. But Michael Ruff and his colleagues from the NIMH speculate that these known effects of VIP may be caused by a different part of the molecule than peptide T.

When VIP was first sequenced, says Ruff, investigators noticed that it has a natural cleavage site about 13 or 14 amino acids from its carboxyl terminus. They suggested that perhaps VIP normally is split up and that the two sections of it have different actions. This hypothesis was not pursued, however, until the NIMH investigators came upon peptide T. Ruff, Ginns, and their colleagues are looking to see if a 12-amino acid fragment of VIP exists in nature and, if so, what it does. Although VIP apparently binds to the brain, no one has any idea what it does there.

Wetterberg speculates that the normal function of VIP in the brain may be a clue to the AIDS-associated dementia and other neurological problems. The AIDS virus, he says, may bind to VIP receptors in the brain and prevent VIP from acting as a neuropeptide. Peptide T may overcome this effect of the AIDS virus.

Although the Swedes are testing peptide T alone against placebo, they and the NIMH group think that if the drug is successful it may eventually be given along with an anti-viral agent, such as azidodeoxythymidine, or AZT. Peptide T does not kill the AIDS virus and patients may retain active viruses which may enter cells as soon as peptide T is withdrawn.

Of course, peptide T, promising as it looks, has not yet been scientifically tested in humans and it could still turn out to be a disappointment. Although the theory that led to the drug is attractive, the real test will be the clinical trials. ■ GINA KOLATA

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Manic-Depression Gene Tied to Chromosome 11

A dominant gene causes this psychiatric disorder in 60 to 70% of those who inherit it

A group of researchers from the Massachusetts Institute of Technology, the University of Miami School of Medicine, and Yale University School of Medicine has found a genetic marker for manic-depression—a piece of DNA so near the manic-depression gene that it is inherited along with the disease-causing gene. This is the first genetic marker for a mental illness and the investigators stress that it is expected to lead to a new understanding of the biochemistry of manic-depression and also to new treatments. "We see this as a landmark study," says David Pauls, one of the study investigators.

At the same time, two other groups report that they have failed to find the marker in other populations of patients with manic-depression, indicating that there is more than one gene that predisposes to this mental illness. The three groups report their results in the 26 February issue of *Nature*.

The new study indicates that at least some cases of manic-depression are caused by a dominant gene on the tip of the short arm of chromosome 11. Although the researchers do not yet know what the manic-depression gene is, they are intrigued by the fact that at least one gene in this region of chromosome 11—the tyrosine hydroxylase gene—is involved in the synthesis of the neurotransmitter dopamine. Dopamine is thought to be involved in the genesis of manic-depression.

Yet, at least in the case of manic-depression, the gene is not necessarily destiny. Only 60 to 70% of those who inherit the gene get the disease, and investigators speculate that some as yet unknown environ-