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AIDS' effect on brain studied

Newly published studies on AIDS shed light on connections between the brain and immune system.

Progressive degeneration of the central nervous system, with or without the presence of immune deficiency, is being seen in more and more individuals infected by the AIDS virus, HIV. Indeed, a growing number of cases are being seen in which brain degeneration leading to death is the only manifestation of infection by the virus. As in the case of immune dysfunction, however, the mechanism of this process within the living patient is still obscure.

Some of this obscurity was clarified by a recent report in the *Journal of Experimental Medicine* by scientists at the Institute for Immunology in Munich, West Germany. Using monoclonal antibodies, these scientists were able to detect the CD4 molecule, the characteristic surface receptor of the so-called T-lymphocytes, on the surface of brain cells. Not only was the molecule detected on the cells of the supporting network of the brain, known as glial cells, but also on the actual neurones, or nerve cells.

In a related study in the May 1987 issue of *The Journal of Infectious Diseases*, scientists at the Baylor College of Medicine in Houston, Texas, demonstrated HIV virus in the brain tissue of five of seven patients with progressive encephalopathy (brain degeneration).

Using electron microscopy, the researchers found the virus in two types of glial cells, known as astroglia and microglia, as well as in brain capillaries. Virus was found in the lumens of the capillaries, as well as in gaps between the cells which line the capillaries, and in the spaces between adjacent brain cells. No virus was reported in the neurones themselves.

Infection of the glial cells would have a devastating impact on the brain even if the actual nerve cells were not infected. The astroglial cells or astrocytes, so called because of their star-shaped form, are intimately connected to the small capillary blood vessels of the brain and form part of the "blood-brain" barrier which controls which substances and nutrients in the blood will gain access to the nervous tissue.

The microglial cells are responsible for producing the myelin sheath which surrounds the long processes of the neurones, known as axons. These axons are the equivalent of electrical wires and the myelin sheath is the equivalent of the insulation which prevents short-circuiting of the nervous impulses. Destruction of the microglial cells would result in degeneration of the myelin sheaths of the nerves, known as demyelinating disease, which is one of the characteristic forms which AIDS encephalopathy takes.

In the Houston study, the majority of virus replication appeared to take place in the microglia, even though astrocytes and neurones also appear to contain the CD4 receptor. This would seem to indicate that something other than the CD4 receptor may be necessary for infection of a cell and production of virus by that cell.

One indication that this is true is an article in the May 2 issue of the medical journal *Lancet*. In this article, researchers at St. Mary's Hospital Medical School in London describe the relationship of inherited variations in a cell surface molecule to susceptibility to HIV infection and the subsequent risk of developing AIDS.

The surface molecule, known as group specific component (GC) exists as three genetically distinct forms which can be distinguished by the speed with which they migrate in an electric field. These are known as Gc 1 fast (Gc 1f), Cc 1 slow (Gc 1s), and Gc 2. Individuals can either be homozygous, i.e., they have two identical molecules, or heterozygous, in which case they have two of the three types.

The study consisted of examining 203 homosexuals at risk of infection or infected with HIV, 50 randomly selected homosexuals and 122 male heterosexual healthy seronegative controls. Of patients with active AIDS, 30.2% were homozygous for Gc-1f, and patients with other manifestations of HIV infection were also more likely to have Gc-1f. On the other hand seronegative, symptomless homosexual contacts of AIDS patients lacked Gc-1f and 25% of them were homozygous for Gc 2. Not one AIDS patient was homozygous for Gc 2. Progression to AIDS in infected individuals was strongly correlated with presence of Gc 1f, and negatively correlated to Gc 2.

The group specific component is a binding site for vitamin D and is apparently close to the CD4 molecule. The difference between the various Gc molecules is related to the presence or absence of sialic acid, which appears to be related to viral binding and entry into cells. One epidemiological support for the role of this surface receptor in AIDS development is the fact that in Central Africa the Gc 1f gene predominates in the indigenous population.