Measles Virus Reveals Its Killing Ways

Despite the introduction of a relatively effective vaccine in 1963, measles remains a killer. An estimated 1 to 2 million children worldwide, most of them in developing countries, die each year after contracting the infectious disease.

Scientists now report that they have finally discovered a crucial detail of how the measles virus exacts its deadly toll.

Investigators have long known that, like the AIDS virus, the measles virus kills indirectly, weakening an infected person's immune system so that he or she becomes more susceptible to other pathogens. It's those secondary infectious agents, which may cause pneumonia, diarrhea, or other diseases, that can prove fatal, especially in countries with poor medical care.

The measles virus appears to make people vulnerable to other infections by preventing immune cells called monocytes and macrophages from manufacturing a molecule vital to a strong cellular immune response, report Christopher L. Karp of the Johns Hopkins Medical Institutions in Baltimore and his colleagues in the July 12 SCIENCE.

The researchers had initially focused their attention on other immune cells called lymphocytes. While the ability of these cells to proliferate and react to infection was clearly diminished in measles patients, the investigators found that the measles virus did not concentrate its attack on the cells.

"The lymphocytes were being affected, but they were not infected," says Diane E. Griffin, a report coauthor also from Johns Hopkins.

Griffin and her colleagues found that the measles virus incapacitates lymphocytes by attacking monocytes and macrophages. These immune cells have a number of roles, such as producing interleukin-12 (IL-12), a molecule needed to trigger a strong lymphocyte response.

The investigators discovered that the measles virus dramatically decreases the amount of IL-12 made by monocytes and macrophages. The virus "doesn't even have to infect the cells. All it has to do is interact with their measles receptor. That shuts down the ability of those cells to make IL-12," says Griffin.

The measles receptor is a cell surface protein called CD46. Apart from inadvertently allowing the measles virus access to cells, CD46's best-known function is to snare a few of the immune system proteins known collectively as complement. The complete complement system forms complexes that attach to and kill bacteria and other pathogens. CD46 prevents similar attacks on the body's own cells by not allowing the complement proteins to form these complexes.

The new research, says Griffin, indicates that CD46 responds to the measles virus by sending signals into the interior of the immune cell, including one that prompts it to reduce IL-12 production.

Griffin notes that she and her colleagues have shown only that the measles virus lessens IL-12 output in laboratory-grown monocytes and macrophages. To confirm that this phenomenon takes place during an actual measles infection, the investigators need to examine the immune cells of infected people.

"We're looking for a large measles outbreak," says Griffin. The investigators are trying to set up monitoring programs in Zimbabwe and Zaire, for example.

Administering IL-12 to people with measles may offer one option for preventing secondary infections, acknowledges Griffin. But, she warns, IL-12 is a powerful drug that can produce severe side effects, including death, if injected throughout the body (SN: 6/17/95, p. 375). A safer option for measles patients, says Griffin, might be to develop a drug that prevents CD46 from telling cells to stop making IL-12.

Investigators are also curious as to whether other viruses weaken the immune system by using CD46. Karp suggests that part of the immunosuppression seen in AIDS patients, including the diminished capacity of immune cells to make IL-12, may result from the tweaking of CD46 by complement proteins bound to the AIDS virus. "There's a lot of tantalizing hints but no direct data yet," he says. — *J. Travis*

Signs of altered bonds in squeezed ice

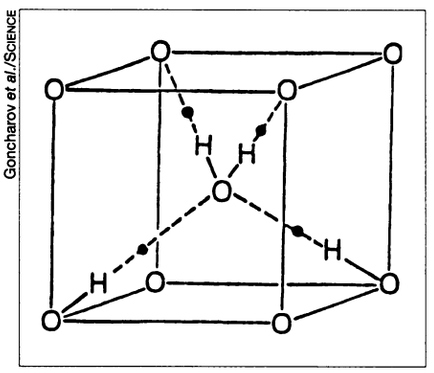
The hydrogen bond—an attraction between a hydrogen atom in one molecule and an atom belonging to another molecule—plays a crucial role in determining the characteristics of water and the microscopic structure of ice.

Theorists have predicted that a sufficiently high pressure can alter the bonding in ice, transforming the material from a molecular solid in which hydrogen bonds hold water molecules in place into an ionic material made up of oxygen and hydrogen ions (protons). In this transformation, the strong, covalent bonds that normally link two hydrogen atoms to a single oxygen atom in a water molecule would become indistinguishable from the hydrogen bonds that link neighboring molecules.

Now, a team of researchers has obtained experimental evidence that for the first time pinpoints the transition in ice from covalent molecular bonding to complete hydrogen bonding. Alexander F. Goncharov and his colleagues at the Carnegie Institution of Washington's Center for High-Pressure Research in Washington, D.C., report their findings in the July 12 SCIENCE.

Goncharov and his coworkers loaded ordinary ice into a small hole in a stainless steel gasket between two diamonds. They pushed the diamonds together to squeeze the sample (SN: 7/6/96, p. 6).

At pressures greater than 2 gigapascals (20,000 times atmospheric pressure), water exists in a form known as ice VII. In this structure, the oxygen atom of each water molecule is hydrogen-bonded to four of the water molecule's eight nearest neighbors, producing a tetrahedral arrangement.



In ice VII, hydrogen (H) atoms are strongly bonded (solid lines) to an oxygen atom (O) of the same water molecule and weakly bonded (dashed lines) to oxygen atoms of neighboring water molecules. Increasing the pressure decreases the distance between adjacent oxygen atoms, and hydrogen atoms end up positioned midway (solid circles) between pairs of oxygen atoms.

At 60 GPa, measurements of the infrared light reflected by the compressed ice indicated a distinct change in the vibrations of water molecules. The observed transition "provides evidence for symmetric hydrogen-bonded states in ice," the researchers conclude.

They also found a similar transition, at a pressure of 70 GPa, in the ice phase of heavy water, in which deuterium atoms replace hydrogen atoms. — *I. Peterson*