SCIENCE NEWS of the week

Clues to Stimulating AIDS Immunity

Two new studies suggest that physicians may someday prevent or limit the immune decline seen in people infected with the AIDS virus (HIV) — either with a vaccine or by direct replacement of an immune-enhancing protein apparently depleted in infected individuals. While neither study promises immediate clinical applications, both yield important clues about the relationship between HIV and the immune system.

Researchers remain puzzled as to how the immune system in an HIV-infected person becomes so disabled, when only a small percentage of that person's immune cells harbor the virus. Ronald G. Crystal of the National Heart, Lung, and Blood Institute in Bethesda, Md., and his colleagues suspected that some of the immune failure could stem from a lack of a protein called glutathione.

Produced mostly in the liver and lungs, glutathione spurs certain T-cells to gobble up foreign invaders. The tiny protein also encourages B-cells to secrete more antibodies and serves as an antioxidant, protecting sensitive tissues from electron-stealing compounds that can damage DNA and lead to cell death.

In a study of 33 people, Crystal and his co-workers measured glutathione levels in the blood and lung fluid of HIV-infected, asymptomatic individuals and HIV-negative controls. Compared with uninfected subjects, the infected people had about one-third as much glutathione in their blood and two-thirds as much in their lung fluid, the researchers report in the Dec. 2 LANCET.

The study doesn't prove glutathione deficiency causes immune deficiency in HIV-infected individuals. "But from a logical point of view, it seems like a very reasonable hypothesis," Crystal says. He speculates that the deficiency in both blood and lung fluid — not noted with any other disease — may explain why most opportunistic infections in AIDS patients occur in the lungs.

Crystal's team has begun a pilot study with eight HIV-positive, asymptomatic individuals with the deficiency to test the safety — and ultimately the efficacy — of glutathione supplements. Because the compound breaks down quickly when taken orally and survives less than two minutes when injected intravenously, the researchers spray aerosolized glutathione into subjects' lungs.

They also hope to determine whether the deficit results from an HIV-triggered reduction in glutathione production or whether HIV somehow speeds the breakdown of the secreted product. Crystal notes that researchers in other laboratories are designing glutathione analogs that may show increased viability in HIV-infected tissues.

In other AIDS research, scientists this week reported development of a vaccine that protected monkeys against an AIDS-like virus normally fatal to those animals. Led by Michael Murphey-Corb of the Delta Regional Primate Research Center in Covington, La., a team of 12 university and corporate researchers made the vaccine from whole, killed simian immunodeficiency virus (SIV), which causes an AIDS-like syndrome in rhesus macaque monkeys. The vaccine resembles one described in August (SN: 8/19/89, p.116) by Ronald C. Desrosiers of the New England Regional Primate Research Center in Southborough, Mass., but appears more effective. The new vaccine prevented infection in eight of nine immunized rhesus monkeys injected with SIV doses up to 99 times those normally fatal to the monkeys. The ninth vaccinated monkey became infected when challenged with the live virus but has yet to show disease symptoms.

The work adds to the evidence that AIDS vaccines made from whole viruses may offer more protection than those made from isolated viral parts (SN: 6/17/89, p.375). The Louisiana researchers say they suspect that the delicate three-dimensional conformation of viral proteins — critical to any vaccine's ability to trigger an effective immune response — may be better preserved in their vaccine than in AIDS vaccines using individual viral components. They also wonder whether any single part of the AIDS virus will prove sufficient to stimulate a protective immune response. "Adequate protection may require multiple determinants, and these may be found on more than one viral protein," they write in the Dec. 8 SCIENCE.

"The pessimism shadowing the development of an AIDS vaccine is showing some signs of receding," comments Dani P. Bolognesi, a virologist at the Duke University Medical Center in Durham, N.C., in an accompanying editorial. However, he notes, unlike vaccines made from engineered viral elements, whole-virus vaccines carry the risk of containing small but deadly quantities of living virus. So while whole-virus vaccines may help researchers understand the subtle relationship between HIV and the immune system, such knowledge must ultimately be applied to other immunization approaches, Bolognesi contends. Moreover, he warns, given HIV's long and variable latency period between infection and disease, efficacy data on any human vaccines are bound to come slowly. — *R. Weiss*

Record-breaking reptile

The Lower Carboniferous period, lasting from 360 million to 320 million years ago, saw many important evolutionary changes in reptiles, amphibians and arthropods. Yet only a few tantalizing fossils remain to hint at what occurred.

Four years ago, paleontologists searching for fossils in a Scottish quarry found a cornucopia of Carboniferous amphibians and arthropods, including the oldest known amphibian and the earliest daddy longlegs spider (SN: 4/13/85, p.237).

The same quarry, called East Kirkton Limestone, has now yielded a 338-million-year-old reptile — almost 40 million years older than the previous record holder, reports Timothy R. Smithson of the Cambridge (England) Regional College. The almost complete fossil skeleton, 20 centimeters long, contains characteristic bones in the skull, spine and hind ankles that distinguish it from an amphibian, he says. Smithson, who also took part in the 1985 discovery, describes the specimen in the Dec. 7 NATURE.

"East Kirkton's been turning up some weird stuff," comments paleobiologist Nicholas Hotton III of the National Museum of Natural History in Washington, D.C. The 1985 amphibians "really revolutionized which goes where with respect to reptilian ancestry." Before that find, Hotton says, a group of primitive amphibians with reptile-like feet and skulls represented the most likely candidates for reptile ancestors, but near their temples they had well-defined "otic notches" — which reptiles lack — and their descendants retained that characteristic until they went extinct. Some of the East Kirkton amphibians, however, had no otic notches.

Having in hand the oldest known reptile may provide another clue to the mystery of how and when reptiles evolved, Hotton says.

From the pattern of its skull, Smithson has placed the ancient creature among the amniotes, an assemblage of reptiles, birds and mammals whose embryos feature an amniotic membrane. Further study of the specimen may help clarify the evolutionary relationship between amniotes and nonamniotes, he says. — *A. McKenzie*