Rates of cardiac adverse events with trastuzumab in this trial were similar to those seen in the NSABP and NCCTG trials. All patients in the HERA trial will continue to be followed up for long-term safety and patients in the observation-only arm will be offered trastuzumab. Results regarding optimal trastuzumab duration (2 years vs 1 year) should be available in 2008.

Sledge reiterated the importance of investigating trastuzumab’s cardiotoxicity, including whether the adverse effects are completely or partially reversible. “We know virtually nothing about the long-term effects of [trastuzumab] on the heart,” he stressed. Nonetheless, he added, with NSABP/NCCTG and HERA results clearly indicating that adjuvant trastuzumab improves disease-free survival for women with HER2-positive breast cancer, the drug’s benefits far outweigh its risks. “There’s no question in my mind about this—biology has spoken, and we should listen,” he said. “But the price [of potential cardiotoxicity] is real and has to be discussed with patients.”

MORE TO BE DONE

The promising data from these monoclonal antibody trials have created a buzz among oncologists and cancer researchers, but they also caution that for most of the women participating in the studies, the new drugs provide a prolongation of survival, not a cure. Combining targeted therapies—a strategy similar to that used for treating patients with HIV—may someday prove to be the way to go, but life-saving drug cocktails for cancer have not yet been discovered.

New Human Retroviruses Discovered
Evidence That Cross-Species Leap Not a Rare Event

Bridget M. Kuehn

The path that HIV is believed to have traveled, from nonhuman primates in central Africa to the humans who have direct contact with them, may be a well-beaten one.

Cross-species transmission of retroviruses was once thought to be a rare event. Now, however, the discovery of two new primate retroviruses adds to the evidence that these viruses may be actively and frequently jumping the species barrier.

The new retroviruses, like several previously identified ones, were found among individuals in southern Cameroon who hunt, butcher, or keep monkeys or apes as pets. The research (a collaborative effort by researchers from Johns Hopkins University’s Bloomberg School of Public Health in Baltimore; the Centers for Disease Control and Prevention [CDC] in Atlanta; the Army Health Research Center in Yaounde, Cameroon; the Henry M. Jackson Foundation in Rockville, Md; and the Walter Reed Army Institute of Research, also in Rockville) was published in an early online edition of the Proceedings of the National Academy of Sciences (http://www.pnas.org) in May.

Whether the newly identified viruses, human T-lymphotropic virus (HTLV) type 3 and type 4, are pathogenic and can be transmitted among humans is not known. A second team of researchers has also identified the HTLV-3 virus (Calattini et al. Retrovirology. 2005;2:30). Related HTLV viruses are associated with disease to varying degrees and infection with the virus has spread to an estimated 15 million to 20 million individuals worldwide through sexual contact, from mother to child, or through exposure to contaminated blood through transfusions or use of injected drugs (Mahieux and Gessain. Rev Clin Exp Hematol. 2003;7:336-361). HTLV-1 has a long latency period and causes adult T-cell leukemia/lymphoma in addition to myelopathy/tropical spastic paraparesis and other inflammatory diseases in a small percentage of infected individuals. HTLV-2 is less pathogenic and has been associated with myelopathy/tropical spastic paraparesis.

“HIV has demonstrated that primate retroviruses that emerge in central Africa
can cause a global pandemic,” said Nathan Wolfe, ScD, an assistant professor at Johns Hopkins. He added that it is imperative to find out more about these newly identified viruses and to continue to monitor this population for emerging viruses.

The newly identified viruses also may have implications for blood safety. Typically, blood banks in central Africa do not screen for members of the HTLV-family of viruses, which could allow infection with the viruses to spread further. The researchers also found that currently available serological assays failed to distinguish HTLV-3 and HTLV-4 from HTLV-1 and HTLV-2, which may explain why the viruses were not detected earlier. The US Food and Drug Administration is using samples containing the newly identified viruses to test the sensitivity of current assays and the CDC is simultaneously working to develop more sensitive tests that can be used for broader populations, according to William M. Switzer, MPH, who leads non-HIV surveillance activities of the Laboratory Branch of the CDC’s Division of HIV/AIDS Prevention.

The researchers studied blood samples from more than 900 individuals from 12 rural villages in Cameroon. This group represents an interface where viruses from monkeys and apes are most likely to make the leap to humans because of activities such as hunting that bring them into contact with potentially infectious blood from the animals. By working with these individuals, the researchers hope to be able to identify emerging disease threats and to learn more about the process that allows viruses like HIV to cross the species barrier as well as how such viruses become pathogenic.

The investigators identified likely simian counterparts for the HTLV-3 virus as well as at least five strains of HTLV-1 they found in this population. No counterpart for HTLV-4 has yet been identified, but the researchers say it is likely to have a simian counterpart as well. Researchers from the team had also previously identified simian foamy virus, another primate retrovirus, in monkey and ape hunters from this region (Wolle et al. Lancet. 2004;363:932-937).

Continued cooperative efforts among scientists, villagers, and local officials are planned. The next steps will be to monitor infected individuals over the long term and to test for the viruses in individuals who come into contact with hunters. The researchers are also teaming up with scientists in the Democratic Republic of Congo on a long-term study of the emergence of other infectious diseases, such as Ebola hemorrhagic fever and monkeypox, in similar populations.

Team member Donald S. Burke, MD, also of Johns Hopkins, noted that such recent epidemics as SARS have occurred at interfaces between wildlife and humans and have spread globally. He said it is important to monitor the type of viral activity occurring in Cameroon to determine if there is a threat and to identify measures that will prevent the spread of infection with these viruses. “We need to consider emerging [disease] threats not just from a local or national level, but at a global level,” he said.

---

Scenarios for Stem Cell Creation Debated Panel Members Spar Over Ethical and Scientific Issues

Mike Mitka

While the President’s Council on Bioethics debated moral and scientific issues surrounding a number of potential scenarios for creating stem cells without destroying live embryos, real-world actions seemed to make the exercise almost irrelevant.

In the days following the May 12 release of the council’s white paper, “Alternative Sources of Human Pluripotent Stem Cells,” researchers from South Korea announced they developed an efficient method for creating embryos through cloning. (Their report was published on May 19 in an online edition of Science [http://www.sciencemag.org].) A week later, the US House of Representatives passed a bill that would loosen the prohibition of federal funding for research using new stem cell lines by allowing the use of excess embryos slated for destruction at fertility clinics. Still, with President Bush reiterating on May 24 that he would veto any bill easing the use of fertilized embryos, the council’s findings appear to be the current blueprint that would lead to federally funded stem cell research.

**SUGGESTED ALTERNATIVES**

The council considered four methods to possibly generate stem cells: using a dead embryo, biopsy of a living embryo to remove one or a few cells (blastomere extraction), creating biological artifacts resembling embryos (but incapable of developing into humans), and somatic cell dedifferentiation. Ultimately, the council formally gave ethical approval to only using dead embryos and cell dedifferentiation, although some council members dissented (http://www.bioethics.gov/reports/white_paper/index.html).

“Because the council is wholeheartedly committed both to the advancement of science for the betterment of humankind and to the defense of human freedom, dignity, and the value of human life, we are pleased to endorse these proposals as worthy of further