HIV also kills developing white blood cells

It's bad enough that the AIDS virus attacks mature white blood cells, rendering them useless for the body's defenses. But now two research teams have discovered that HIV also destroys young immune-system cells before they have a chance to develop. Their reports in the June 24 NATURE support the notion that HIV does its dirtiest work in lymphoid tissues (SN: 3/27/93, p.196).

White blood cells called T cells mature and proliferate in the thymus, a small organ that sorts through these cells, destroying those that might attack the body's own tissues. To study whether HIV can infiltrate this T-cell nursery, the two groups implanted human fetal liver and thymus tissue into mice that lack the ability to mount any sort of immune response. In these SCID-hu mice, so called because of their severe combined immunodeficiency defect and their human tissue, the liver makes precursor cells that move to the thymus and develop much as they do in a person.

At the University of California, Los Angeles, School of Medicine, Grace M. Aldrovandi and her colleagues treated a dozen SCID-hu mice with either no virus, inactivated virus, HIV from children with AIDS, or HIV cultured in the laboratory. Seventeen days later, they analyzed the T cells in each thymus implant by staining and sorting through these cells.

In mice that got no active virus, 80 percent of the stained T cells showed both CD4 and CD8 receptors – indicating immature cells – while most of the rest of the cells took up only the CD4 stain. Mice with HIV from children had lost most of the doubly stained cells as well as most of the CD4 cells, the typical HIV targets, the UCLA group reports.

Next, the UCLA researchers injected a much lower dose of different viral strains into additional mice. The T cells disappeared more slowly, and it seems the immature cells were destroyed first, followed by CD4 cells, says Jerome A. Zack, who heads the UCLA group.

Analyses of viral genetic material in these different cell types revealed that the immature cells tended to harbor five to 10 times as much virus per cell as other cells, says Zack. Immature cells divide rapidly, thus providing a way for the virus to replicate rapidly, he adds.

Also, an infected thymus looks different from an uninfected organ, which contains clearly defined rim and core regions. Because so many cells had died in the infected tissue, the researchers had trouble distinguishing the two regions under a microscope, they note.

At SyStemix, Inc., in Palo Alto, Calif., Mark L. Bonyhadl and colleagues also observed that HIV infection spread through the thymus, wiping out most CD4 and immature cells within five weeks. Electron and light microscopy revealed that many cells seemed to undergo programmed cell death (SN: 11/21/92, p.344). HIV may subvert this normal process in the thymus by triggering destruction in cells that otherwise would have been spared, says immunologist Joseph M. McCune of SyStemix.

Both research teams caution that they do not know how well these results translate to AIDS in humans, but they expect the SCID-hu mouse will prove useful for studying HIV in living organisms and may help scientists understand how HIV harms the immune system. *– E. Pennisi*

Sleep-disorders quiz awakens interest

An easily learned interview technique may enable mental health clinicians and researchers to diagnose sleep disorders more accurately and to distinguish primary sleep problems from those brought on by other psychiatric conditions, according to a study in the June AMERICAN JOURNAL OF PSYCHIATRY.

A research team at Albert-Ludwigs University in Freiberg, Germany, developed the interview approach for sleep disorders based on the latest *Diagnostic and Statistical Manual of Mental Disorders* (DSM), published by the American Psychiatric Association. Clinicians currently lack a standard interview method for identifying sleep disorders.

"Development of a structured interview for sleep disorders fills a critical gap in our field," write psychiatrist Charles F. Reynolds III of the University of Pittsburgh School of Medicine and his colleagues in an accompanying editorial. "It is *potentially* a useful clinical instrument for the office-based screening of patients with sleep disorders, as well as for sleep research."

Much controversy surrounds the definition of sleep disorders. The DSM divides these conditions into two general categories: disturbances in the amount, quality, or timing of sleep, such as insomnia; and abnormal events that occur during sleep, such as repeated nightmares or sleepwalking. Many sleep-disorders specialists criticize DSM for ignoring physical ailments linked to sleep problems, and some prefer an alternative classification system that lists nearly 70 sleep disorders.

The German researchers, headed by psychologist Elisabeth Schramm, devised a 20- to 30-minute interview with questions covering physical health, drug use, mental health, and signs of sleep disorders adapted from DSM. Interviewers then fill out a symptom summary sheet.

A total of 68 people attending one of three sleep-disorders clinics participated in the study. Twelve clinicians, 10 of whom specialize in sleep disorders, conducted the interviews. Volunteers were interviewed twice over a four-day period, each time by a different clinician.

Clinicians almost always agreed on diagnoses of sleep disorders, as well as on which participants suffered from sleep difficulties related to mental disorders such as depression.

For 27 of 30 volunteers attending one clinic, the researchers confirmed diagnoses of sleep disorders with overnight observations in a sleep laboratory and physiological measures – including brain waves, respiration, and leg movements – obtained during sleep.

The German study contains several limitations, Reynolds and his coworkers assert. For instance, the ability of clinicians who do not specialize in sleep disorders to use the new interview successfully remains uncertain.

Moreover, the failure to gather physiological data on all participants raises the possibility that some were misdiagnosed and may have had an underlying, unrecognized problem, such as sleep apnea or leg twitching, the Pittsburgh scientists argue. *– B. Bower*

Clinton backs scaled-down space station

President Clinton last week endorsed a scaled-down, simplified version of Space Station Freedom. The proposed station will combine two of the cost-cutting alternative designs that NASA unveiled on June 8 after a three-month effort (SN: 6/19/93, p.389).

The President ruled out a third option, whose design differed most radically from the original Freedom.

In the next 90 days, NASA and its foreign partners in the space station program will determine the orbiting laboratory's final configuration. They will also decide whether NASA should park the station in a higher-inclination, "international" orbit to make it more accessible to other spacefaring nations, most notably Russia, according to administration officials.

At the same time, NASA will redesign itself: Clinton has directed the agency to implement internal cost-cutting measures, including a 30 percent reduction in the space station workforce. These cuts will affect NASA employees as well as private contractors involved in the space station program.

When completely assembled – sometime around the turn of the century – the

redesigned space station will have cost $16 billion, administration officials said. The original design of Space Station Freedom would have cost $25.6 billion.

In a June 17 announcement, the President cited the station's potential contribution to the continued economic prosperity and scientific prowess of the United States. "I strongly believe that NASA and the space program represent important investments in that future," Clinton said. He also noted the space station's potential for promoting international cooperation.

The President's preferred design for the station is most like NASA's option A, which maintains Freedom's modular configuration: pressurized chambers attached to a central backbone with solar panels mounted at either end. To reduce costs, NASA engineers gave option A simpler electrical and computer systems, shortened its backbone, and made cost-saving changes to the modules in which the station's four-person crew will work and live for extended periods.

The redesigned station will also incorporate features of option B – a more complex, Freedom-derived version of the space station – to enhance the laboratory's capabilities.

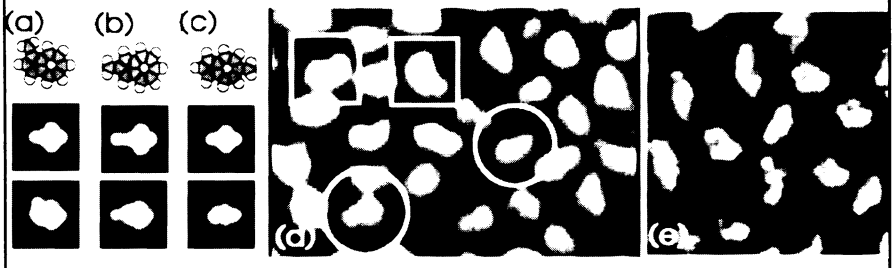
Option A differs from the original Freedom blueprint largely in the amount of electrical power and shelf space it can supply for experiments and equipment. For example, option A offers an average of 31 kilowatts of power per orbit, compared to Freedom's 34, and has seven fewer "racks" for instruments and experiments.

Despite these differences, an independent panel advising the President on space station options declared option A "fully capable" of meeting the basic goals of the space station program. The advisory group, chaired by Charles M. Vest, president of the Massachusetts Institute of Technology, examined the advantages and disadvantages of the space-station design options.

Although administration officials refuse to specify which elements of option B will make it into the new design, the Freedom-derived "alpha joints" are likely candidates for Clinton's hybrid space station. The alpha joints are movable solar-panel mounts that would ensure an unwavering supply of electricity regardless of the laboratory's orientation toward the sun, which changes throughout the year.

Without the joints, NASA would have to shift the station's position periodically with onboard thrusters to maintain power levels. But these shifts would apply forces to the station, possibly compromising experiments that require a "microgravity" environment, says Daniel E. Hastings, a professor of aeronautics and astronautics at MIT. Hastings and other members of NASA's Space Station Advisory Committee worked closely with the agency during the three-month redesign effort. *– D. Pendick*

Shape of things to come: Molecular STM



IBM Research

The scanning tunneling microscope's (STM) needle-like probe enables researchers to image the electron clouds surrounding atoms. Making sense of those images, however, requires detailed calculations that predict the shape of electron clouds for individual atoms. The task is even more difficult for molecules.

Now, a team led by Vickie M. Hallmark and Shirley Chiang at IBM's Almaden Research Center in San Jose, Calif., has come up with a simple calculation technique that provides accurate shapes of the electron clouds surrounding molecules deposited on platinum. They used this prediction method along with high-resolution STM to distinguish among closely related chemicals called isomers – molecules containing the same number and kinds of atoms but built in different geometric arrangements.

As part of a report in the June 14 PHYSICAL REVIEW LETTERS, the group looked at three isomers of monomethylazulene (a-c, top). They calculated the shape of each isomer's electron cloud using a conventional technique (a-c, center) and their new approach (a-c, bottom). In an STM image of a mixture of molecules (d), they marked isomer a with a square and isomer b with a circle; the image of isomer c is shown at right (e). The shapes predicted by the new calculations – which include the influence of the platinum substrate – more accurately reflect those seen in the high-resolution STM images, Chiang and Hallmark assert. This advance brings researchers a step closer to using STM to track the reactants, intermediates, and products of chemical reactions on metal surfaces.

Prolonged nursing and the risk of bone loss

Women who nurse their infants for six months or more lose a significant amount of the mineral calcium from their bones, according to a new report. Although most women make up for that loss shortly thereafter, researchers speculate that such bone loss may put certain new mothers in jeopardy of potentially crippling fractures later in life.

Lactation, or the production of milk, requires a tremendous amount of calcium to ensure that nursing infants form a strong skeleton. But previous investigators disagreed on whether some of that bone-building mineral comes from maternal bone. So epidemiologist MaryFran R. Sowers at the University of Michigan in Ann Arbor and her colleagues decided to take a closer look at the bones of nursing mothers.

The researchers recruited 98 healthy women during the last months of their pregnancy. They measured bone density two weeks after delivery and again at various points after childbirth.

The team discovered that women who nursed their babies for six months or longer showed an average loss of bone density of 5.1 percent from the lower spine and a loss of 4.8 percent from the top of the leg bone. "That's actually a lot of bone," Sowers says.

Women who bottle-fed their infants from birth or breastfed for less than a month showed no such loss, the team reports in the June 23/30 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

Sowers says the bone loss was not explained by differences in age, diet, or physical activity. Indeed, she notes, most of the women in the extended lactation group consumed large amounts of dietary or supplemental calcium.

For most healthy women, any bone mass lost during nursing will quickly be recovered. Moms who weaned their babies between six and nine months of age had recovered all of their lost bone a year after the baby's birth. Women who nursed beyond nine months had not yet rebuilt that lost bone.

The average U.S. woman nurses her baby for just three months and thus is unlikely to lose significant amounts of bone. Yet Sowers worries that teenage mothers and women who are malnourished may lose a critical mass of bone during lactation. This might put them at risk of developing osteoporosis – a bone-robbing disorder – after menopause.

"This isn't to say that women shouldn't breastfeed," says Stephen P. Heyse of the National Institute of Arthritis and Musculoskeletal and Skin Diseases in Bethesda, Md. Young women should make sure they get enough calcium to build strong bones before they get pregnant, he adds. *– K.A. Fackelmann*