when little or no active viral production can be detected in blood cells. Fauci's group is trying to explain the disparity between blood and lymph tissue by studying follicular dendritic cells, or FDCs. Lymph nodes are filled with an intricate lattice of FDCs, which filter and trap HIV and other viral particles. As HIV disease progresses and the immune system collapses, the FDC "architecture drops out" of the lymph node and it can no longer trap virus, says Fauci, releasing HIV into the blood.

If the deterioration of the FDC network is linked to the immune system collapse seen in AIDS, it is obviously critical to understand that process. Yvonne Rosenberg, an immunologist at the Henry M. Jackson Foundation Research Laboratory in Rockville, Maryland, is using a primate model to try to explain how the network falls apart. Rosenberg has been investigating lymphoid organs like the gut and spleen from macaque monkeys infected with HIV's simian relative, SIV, and she finds what she calls "a nice correlation" between the disruption of the FDC lattice and the infiltration of white blood cells bearing on their surface immune-system receptors designated CD8—though it's still unclear to her how the CD8 cells are damaging the lattice.

Extending one of the themes of the conference—the relationship between blood and lymph tissue in AIDS—Rosenberg is now questioning the common wisdom about white blood cells bearing the CD4 marker (whose depletion is the hallmark of HIV disease) in blood and lymph. "The assumption has been that if CD4 goes down 50% in the blood, it goes down 50% in the [lymph nodes]," says Rosenberg. "That's just not true."

She found that in her monkeys, the levels of CD4 cells vary in a much more complex pattern. As the ratio of CD4 to CD8 cells declines in the blood, the ratio remains stable in the lymph nodes. Only much later does the fraction of CD4 in the lymph nodes decline—and it is then that immunological trouble really begins. This pattern leads Rosenberg to suspect that initial declines in CD4 cells in the blood are deceptive. CD4s, she thinks, are not disappearing altogether, they're only being sequestered in the lymphoid tissue. If so, this pattern could have some major implications for clinical treatment of HIV disease, since it raises the possibility that to prevent onset of AIDS, researchers should focus on preventing the decline of CD4 levels in the lymph nodes, not in blood.

As many of the presenters at Keystone did, Rosenberg raised as many questions as she answered. Still, a clearer picture is finally emerging of how much HIV there is in the bodies of infected people and where most of it resides. And that means researchers are finally getting a firmer handle on the chain of events that is set in motion by the stealthy entrance of HIV.

–Jon Cohen

MEETING BRIEFS

Chemists Gather in Denver to Get the Big Picture

The Rockies were hidden by clouds, but "Welcome ACS" signs were visible all over the Mile High City from 28 March to 2 April. No wonder the city's boosters were cheering: More than 10,000 scientists, purveyors of laboratory equipment, and other chemophiles had flooded into Denver to take in a vision of chemistry's intellectual scope that was wide enough to compensate for the missing scenic grandeur. In just a tiny sampling of the roughly 4800 presentations, chemistry appears in guises ranging from the most basic molecule making, through cleanup strategies for major environmental challenges, to forensic methods for unraveling a historical mystery.

Mass Spec on the Little Bighorn

June 25, 1876, was the ultimate disaster for General George A. Custer and his men—that much is certain. Beyond that, however, says military archeologist Douglas Scott, there's "more myth than reality" to the generally accepted story of how Custer and more than 200 cavalrymen lost their lives at the hands of Sioux and Cheyenne warriors during the Battle of the Little Bighorn in southern Montana. For a decade Scott, colleagues at the National Park Service's Midwest Archeological Center in Lincoln, Nebraska, and volunteers have been trying to penetrate the cloud of myth. They've now enlisted a new, high-tech ally: accelerator mass spectrometry for analyzing the chemistry of old bones.

Even before chemistry entered the picture, traditional forensic evidence—bullets, cartridges, and other artifacts—had led Scott to some provocative findings. For one, he said, "we found evidence for over 45 types of firearms" among the Sioux and Cheyenne, many far superior to those available to Custer's men. The researchers also argue from the pattern of bullets and spent cartridges on the battleground that, contrary to a common image of Indians swarming over Custer's men, "it looks like there were many well-armed Cheyenne and Sioux" firing from protected positions.

Scott is hoping the bones harbor an equally striking tale. As he told his ACS audience, he and his colleagues are analyzing skeletal remains both from the battleground and from the 10 of Custer's men who were buried as unknown soldiers in the Custer Battlefield National Cemetery. They're searching for subtle chemical differences that should reflect what the men ate in their final weeks.

Using accelerator mass spectrometry, which can detect and precisely measure trace amounts of elements in a sample, Scott's team is measuring ratios of elements such as zinc, strontium, and calcium. Because different foods leave their own elemental signatures in bones, the group's analysis may be able to distinguish bones of officers, who may have eaten diets rich in meat, from those of the enlisted men, who ate more hardtack. Even among enlisted men, differences in mess hall diet might make it possible to tell members of different companies from one another.

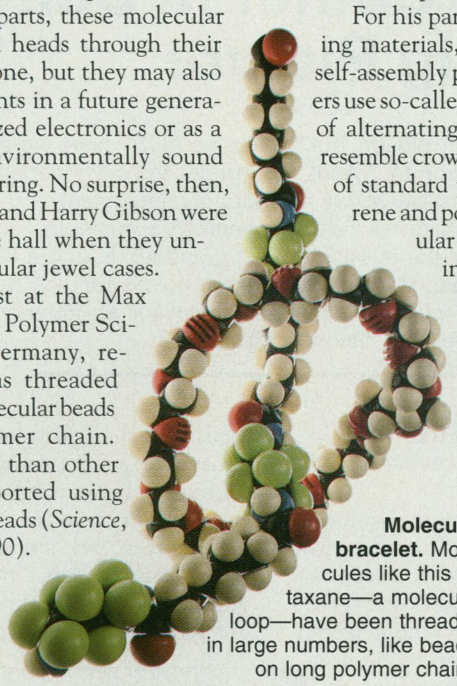
BETTMANN ARCHIVE

Custer's last stand. Old bones hint that the battle was less chaotic than historians had imagined.

If so, how bones with different elemental signatures are scattered around the battlefield could help reveal details about the choreography of the battle. Already, says Scott, his team's analysis may have found subtle differences in the elemental ratios between different clusters of remains, suggesting that "we might be seeing [members of] company mess units" who fought and died together. That could mean that the battle was less chaotic than had been thought. Still, the evidence so far won't be enough to dispel all the confusion among historians over Custer's last fight. The "preliminary evidence is tantalizing, but the meaning is not yet clear," Scott says.

The Molecular Bead Game

Imagine threading tiny beads onto a necklace. Now imagine shrinking the necklace by a factor of, oh, 10 million, at which point its thread and beads reach the dimensions of molecules. Now you've got an idea of what polyrotaxane chemists are up to. Like their large-scale counterparts, these molecular necklaces can turn heads through their aesthetic appeal alone, but they may also serve as tiny elements in a future generation of molecule-sized electronics or as a means to more environmentally sound polymer manufacturing. No surprise, then, that Gerhard Wenz and Harry Gibson were able to fill a lecture hall when they unpacked their molecular jewel cases.



Molecular bracelet. Molecules like this rotaxane—a molecular loop—have been threaded in large numbers, like beads, on long polymer chains.

GIBSON ET AL.

Wenz, a chemist at the Max Planck Institute for Polymer Science in Mainz, Germany, reported that he has threaded about 120 of his molecular beads onto a long polymer chain. That's plenty more than other chemists have reported using other threads and beads (*Science*, 12 February, p. 890). Gibson, a polyrotaxane maker at the Virginia Polytechnic Institute and State University, is up to about 15 beads. In both cases, the move to more beads has edged molecular necklaces from intriguing mechanisms toward new materials.

The secret to stringing these necklaces is finding the right match of beads and threads so that they assemble themselves in solution. Wenz, for example, chose beads made of cyclodextrins (CDs)—groups of sugar molecules chemically cinched into a loop. The outsides of the resulting loops have many electrically polarized sites that attract water molecules; as a result they readily dissolve in water. The insides of the rings, however, are hydrophobic (water-avoiding), which makes them apt to form liaisons with other hydrophobic structures.

That's just what the cyclodextrins find along the threads—polymers that have hydrophobic segments alternating with shorter hydrophilic nodes. As Wenz sees it, once a bead happens to slip onto the end of the string, it tends to hop along from segment to segment, and other beads follow suit. After letting the self-assembly proceed for a while, Wenz's team caps the ends of the polymer thread with slightly smaller CD molecules, to keep the larger beads from sliding off again. In one case, Wenz reports, the process yielded a molecular necklace that had nearly one in four of its hydrophobic segments occupied by a CD bead.

If even more beads could be slipped onto the necklace, Wenz said, they would be close enough together so that he could chemically join them to form a tube. And if the chemical links between beads could be made conductive, the tubes could be used as tiny molecular wires, he noted. Or, Gibson adds, they might function as molecular sieves, which could be exploited for chemical separations.

For his part, Gibson chose other starting materials, and he exploits a different self-assembly process. He and his co-workers use so-called crown-ethers (whose loops of alternating carbon and oxygen atoms resemble crowns) as the beads and a variety of standard polymers including polystyrene and polyacrylonitrile as the molecular threads. And his necklaces, instead of forming when the beads slide onto already completed threads, take shape as the polymers themselves form: Shorter polymer segments link together into a string, snagging beads in the process.

Though Gibson's necklaces are sparser than Wenz's, they elicit an eye-opening personality change from the host polymers. Take polyacrylonitrile. Normally it dissolves only in harsh and hazardous solvents. But when camouflaged within crown ethers, the polymer dissolves even in methanol, a relatively gentle solvent. That effort suggests that polyrotaxanes, by opening a more benign processing route for industrially important polymers, may turn out to be clean as well as decorative.

For Dirty Dirt, a Gentle Cleaner

A gentle extraction technique already proven for coaxing caffeine from coffee, flavor essences from spices, and nicotine from tobacco may now be headed for bigger, meaner jobs. Supercritical fluid extraction (SFE), in which substances as mild as water or carbon dioxide become powerful solvents, was the subject of about 40 presentations at the ACS meeting. A recurrent theme: turning SFE loose on some of the country's ugliest cleanup problems, such as contaminated soils at the Hanford Nuclear Reservation and toxic pits left by turn-of-the-century gas works.

Gentle though it often is, SFE seems to have what it takes, groups at the Westinghouse Hanford Co. in Washington and the University of Akron reported at the meeting. The technique, which relies on fluids at temperatures and pressures that put them in a strange limbo somewhere between the liquid and gaseous states, also has marked advantages over existing cleanup techniques, Westinghouse chemist Timothy Moody argued. Conventional soil remediation methods rely on organic solvents, which can themselves be environmental bugaboos, or high-temperature stripping steps that cook contaminants out of the soil but also "kill" it by massacring its beneficial microorganisms. The soil is left clean but infertile.

At the Hanford Nuclear Reservation, where the Department of Energy used to make plutonium for nuclear weapons, Moody will have ample opportunity to see whether SFE is actually an improvement over conventional methods. Though Moody is leaving it to others to worry about the tons of radioactively tainted water, soil, gas, and sludge there, Hanford is also a chemical nightmare, filthy with dumped diesel fuel, polychlorinated biphenyls, and other organic contaminants. To get them out, the Westinghouse researchers plan to make use of carbon dioxide at a pressure of several hundred atmospheres and a temperature of 70 degrees C.

In that form (for reasons chemists still don't understand) CO_2 becomes a powerful extractant. In tests using soil samples weighing about 500 grams from Hanford, Moody and his colleagues found that the supercritical CO_2 extracted more than 99% of the diesel fuel and 97% of the polychlorinated biphenyls. The researchers are now building a pilot plant to study the best conditions for treating soil loads more like the 50 to 100 tons per day that will have to be processed in a full-scale cleanup of the bomb-making site.

Chemical engineer Brian Kocher of the University of Akron adds that SFE could also help to clean up some older messes: several thousand "town gas sites" all over North America, where coal was turned into gas for lighting and heating in a process that was standard until around 1930. The gasification process left behind a residue of hydrocarbons, including carcinogenic polycyclic aromatic hydrocarbons (PAHs), and the disposal was casual. "The toxic liquids were dumped in unlined pits," Kocher said.

The moist, clay-rich soils in much of the Midwest and the East Coast, where many of the gasworks are located, rule out CO_2 as the supercritical fluid because it would more readily dissolve into the soil than make off with the toxics. Instead, Kocher and his colleagues are testing a water-based method, which requires higher temperatures—around 375°C—at 200 atmospheres of pressure. In early tests, the engineers found the supercritical water extracted 99.47% of the PAHs from small, 20-gram samples. "This process returns the contaminated soil to the environment with residual contaminant traces less than those found in clean soil," Kocher said at a press conference. The high temperatures needed for water-based SFE, however, sterilize the soil, unlike Moody's milder CO_2-based method.

Once they've tested out the technique on a larger scale, Kocher and his colleagues envision mobile SFE units that could scrub dirt at the sites that need it most.

–Ivan Amato