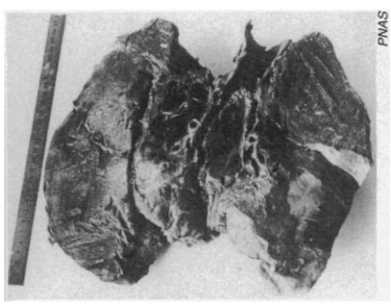
RANDOM SAMPLES

edited by IVAN AMATO

New Evidence in 1979 Soviet Anthrax Deaths

For 13 years, officials in the former Soviet Union have succeeded in concealing medical details of a 1979 anthrax outbreak in the southern edge of Sverdlovsk—a Russian industrial city now known as Ekaterinburg—in which 68 deaths were reported. One explanation blamed the outbreak on infected meat. But Western analysts suspected from the start that the epidemic was due to release of a biological agent from a nearby military facility known as Compound 19. Last May, Russian President Boris Yeltsin was quoted in *Komsomolskaya Pravda*, a Russian newspaper, as confirming that suspicion—but some ex-Soviet officials have continued to stick to the old story.

Now comes evidence—postmortem—from the victims themselves. Since 1979 two Russian pathologists—Faina A. Abramova and Lev Grinberg of Hospital 40 in Ekaterinburg—had been sitting on autopsy notes and specimens that they had hidden from official confiscation, according to pathologist David Walker of the University of Texas Medical Branch in Galveston. Last June, Walker was part of an investigative team assembled by Harvard University's Matthew Meselson, who has been studying the Sverdlovsk anthrax epidemic since 1980. And last week, Abramova, Grinberg, and Walker joined Olga Yampolskaya from the Botkin Hospital in Moscow to report the first detailed pathological evidence that the lethal agents indeed were inhaled (as from a military aerosol).



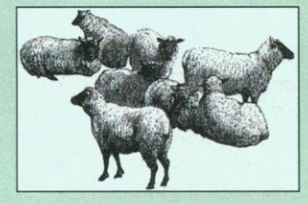
PNAS

Anthrax tracks. Lethal damage suggests biological weapon.

In the March 15 *Proceedings of the National Academy of Sciences*, the pathologists report that all 42 cases they examined showed a pattern of lesions in the thoracic lymph nodes, gastrointestinal tissues, and elsewhere that makes sense only if the victims had inhaled the anthrax bacillus, rather than merely absorbing it from food or across the skin.

The story does not end here, says Walker. Just days before he started work with Abramova and Grinberg (who now works in Walker's department at Galveston), officials in Moscow were still purveying the old party line. "There were weird things happening... and a lot of paranoia," he says. More of this story will emerge when Meselson and colleagues, who interviewed relatives of the victims and tracked down epidemiological evidence during the same June trip, publish their findings. "I think we will get to the bottom of this," Meselson says.

A Biotech Bonanza On the Hoof?



Somewhere in a pasture near Edinburgh, Scotland, is a prolific ram that has been siring some uncommon daughters. You wouldn't know it to look at them, but they are four-legged biotechnology factories. They make the usual wool, lanolin, milk—and in their milk, gobs of a substance that could be used to treat congenital emphysema.

The ram and his progeny are the first herd of sheep genetically engineered to produce a protein called alpha-1 antitrypsin (AAT). Humans ordinarily make their own AAT, which checks the action of elastase, an enzyme that can degrade lung tissue if unregulated. That's the case in congenital emphysema, in which AAT is missing or faulty; to replace it, patients are now treated with AAT derived from normal human blood plasma.

But the protein has remained scarce and expensive, says Martyn Breeze, spokesman and marketing director of Pharmaceutical Proteins Ltd., of Edinburgh, which hopes that the larger amounts of AAT available in the milk of its bioengineered sheep will help more patients breathe easier. The company began seeing results in 1991 with several transgenic ewes (*Science*, 4 October 1991, p. 35). But since a ewe-only club couldn't perpetuate AAT-making sheep, the project took on a more self-perpetuating quality when the company bred the transgenic ram. At a biotechnology conference in January, the company reported that the ram has already produced seven daughters that secrete at least 15 grams of AAT in each liter of their milk. Since each transgenic male could sire hundreds of such females, Breeze says, the path is open to having herds of AAT-producing sheep that could provide far more AAT than is possible using existing methods.

The company has yet to bring its product to clinical trials. But since AAT already is marketed in the United States, Breeze says his company doesn't expect regulatory obstacles. As for fears that any of the transgenic sheep might stray from the herd and mate with normal animals, Breeze says there's plenty of incentive to prevent that. Each year, "a single sheep will produce $100,000 worth of ATT," he says. "We don't want them getting away."

AIDS Conferees Get Berlin Assurance

Organizers of last year's international AIDS conference pulled the meeting out of Boston to protest U.S. immigration rules that prevent HIV-infected individuals from obtaining visas. The organizers of this year's conference, to be held in Berlin on 7-11 June, are coping with the fallout from a different kind of discrimination: the racial violence that has hit German cities in recent months.

A letter sent to journalists who registered for the conference states that in the wake of "recent violence against foreigners," concerns have been raised about the safety of guests in Germany. "We deeply regret and condemn the racist conflicts within Germany in the past few months," says conference chair Karl-Otto Habermehl, a virologist at the Free University of Berlin. But he adds, "The cosmopolitan open-mindedness and great tradition of tolerance which are so characteristic of Berlin have not been affected."

Habermehl told *Science* that he was asked by the World Health Organization, the International AIDS Society, and other nongovernmental groups to "inform the whole world" that people attending the meeting—which typically attracts more than 10,000 researchers—are not in danger. The recent violence, he says, stems from "very small extremist groups acting against people who come from abroad to work."

French Drug Developers Face HIV Fallout

Shock waves from the French contaminated blood scandal—which saw three senior physicians convicted by a Paris court last fall for failing to stop the distribution of HIV-infected blood clotting factors to hemophiliacs (*Science*, 30 October 1992, p. 735)—are still reverberating. Latest to be affected: French pharmaceutical companies planning clinical trials of drugs made by recombinant DNA technology or derived from human or animal tissues.

The blood scandal fueled widespread public anxiety about the safety of medicines, prompting the French health ministry last December to halt clinical trials involving "products of biological origin." Studies were to resume only when approved by a new 10-member panel of experts on viral

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contamination. Since then the weeks have rolled by without a green light for many of the stalled trials, and the drug industry has been up in arms.

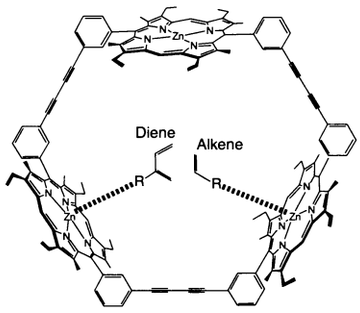
Industry sources are unwilling to speak on the record, but one senior executive last month said that the hiatus was seriously delaying the development of vaccines, monoclonal antibodies, and other medicinal products. Even a member of the new panel, who spoke to *Science* on condition of anonymity, criticizes the new procedure, blaming the health ministry for setting up the group of experts as a "panic reflex," before doing the groundwork to ensure that clinical protocols would be assessed quickly.

Jean-Hugues Trouvin, a Paris-Sud University pharmacologist who chairs the panel, defends the delays, arguing that it has taken time to devise a standard questionnaire about company procedures for excluding live viruses from their products. In any case, he says, the panel is now clearing the backlog. An initial 10 trials were approved when his group met on 24 February, and he hopes to review the remainder—up to 30 planned trials—within the next few months. Indeed, he argues, companies that have failed to return the questionnaires quickly now account for the majority of the delays.

Industry sources, however, remain worried that the new regulatory layer will continue to introduce lengthy delays. "We have no assurances" that protocols will be handled promptly in the future, complains one drug company executive.

Enzyme Pretenders Claim Some Success

Producing synthetic enzymes that catalyze reactions for which no natural enzyme exists has so far proved an elusive goal. But a Cambridge University team led by chemist Jeremy Sanders has taken another step in that direction, with the synthesis of a molecule that accelerates some 200-fold one of the most used reactions in synthetic chemistry. In the current issue of *Chemical Communications*, they describe a molecule that boosts the so-called Diels-Alder reaction, in which components known as a diene and an alkene react to form a six-membered carbon ring.



Wannabe enzyme. Loop of porphyrin molecules quickens reaction between ingredients held inside.

Although other groups have found compounds with similar properties, the Cambridge team's molecule—which consists of three porphyrin groups stitched into a cage-like structure that attracts a diene and an alkene and positions them in a reactive posture—is the first that has been purpose-built for the task. Indeed, the chemists even have been able to construct the cavity of their molecule so that the two reactants are brought together to make only the so-called *exo*-isomer, rather than the *endo*-form that dominates when the Diels-Alder reaction runs naturally.

That feat has impressed other researchers in the field. "It's novel and it's significant," says bioorganic chemist Andrew Hamilton of the University of Pittsburgh—although he cautions that the new molecule is still some way short of being a true synthetic enzyme. For one, nature's own enzymes accelerate reactions at rates that leave the Cambridge molecule far behind. Also, the synthetic enzyme pretender doesn't let go of the product, so it gets used up as the reaction proceeds. But Sanders is optimistic that he will be able to find a solution to that problem—perhaps by using slightly different reactants to yield a product with an unstable shape, which will rapidly flip to a stable form that pops out of the reaction cavity.

Millions for Memory Loss Research

Plenty of foundations have targeted their resources at specific diseases, but it's rare for one to take aim at the supposedly normal parts of getting old. But that's just where the Charles A. Dana Foundation is putting its money. Last month, David Mahoney, the foundation's head, announced that it has committed $8.4 million to establish the Dana Consortium on Memory Loss and Aging. And that's just for starters, says Mahoney.

The target isn't memory loss from conditions like Alzheimer's disease—the focus of most such research—but rather the forgetfulness usually blamed on a "normal" loss of neurons with age. But Mahoney and many of the researchers he will be funding aren't convinced that neurons always die off as you get older—or that memory loss is inevitable even if they do. By fostering a research synergy among neuroscientists and neuropsychologists, the foundation hopes to speed discoveries about the molecular events that underlie "normal" memory loss. In turn, that knowledge could spawn ways to "reduce, reverse, or prevent" it, the foundation suggested in a written statement.

The main consortium members include Columbia University College of Physicians & Surgeons, Harvard Medical School, Johns Hopkins University, the Mount Sinai School of Medicine, and the University of Pennsylvania. Specialists in positron emission tomography (PET)—an emerging brain imaging technique that shows promise for studying complicated brain functions—at the University of California, Los Angeles, and the University of Washington will join the effort.

"Each member of the consortium has strengths that others do not," remarks Guy McKann, who heads the Zanvyl Krieger Mind/Brain Institute at Johns Hopkins, a consortium member. "Each institute will be studying memory and aging in different populations with different tools," adds neuroscientist Marilyn Albert of Harvard Medical School.

The result, she hopes, will be a crisper picture of what happens in normal brains as they age. "We're beginning to have substantial evidence that neuron loss may not be" happening in normal brains, Alpert says. And that gives Mahoney hope that his foundation's money may end up helping to keep minds healthier longer.

Ten Most Cited U.S. Research Institutions in the Physical Sciences Between 1981-1991

Rank	Name	Papers	Citations	Impact
1.	Institute for Advanced Study, Princeton	1462	25,538	17.47
2.	Xerox Corp.	1619	26,516	16.38
3.	AT&T Corp.	10,340	169,031	16.35
4.	Harvard University	7049	110,760	15.71
5.	Princeton University	5593	85,423	15.27
6.	U. of California, Santa Cruz	1541	22,963	14.90
7.	IBM Corp.	8929	127,092	14.23
8.	U. of California, Santa Barbara	4583	64,744	14.13
9.	Caltech (including Jet Propulsion Lab)	9160	128,919	14.07
10.	University of Chicago	4781	65,203	13.64

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Top ten physics houses. When database experts at the Institute for Scientific Information toured and tallied references between 1981 and 1991 to thousands of physics papers, the research institutions listed above emerged as the ones whose papers were cited most often. The impact figure is calculated by dividing the total number of citations by the total number of papers counted for each institution. The journals searched covered physics, astrophysics, chemistry, geoscience, and mathematics.