

The race to mimic complex natural molecules



How the mind maps the world



The perils of inbreeding

countries to share knowledge and technology, and cooperative research to tackle problems of global dimensions.”

In the absence of firm aid commitments, a group of African delegations came up with the self-help plan to devote a portion of the Third World debt relief from the G8 to science and education. “We hope this will allow African governments to devote more resources to research and education,” said Ahmadou Lamine Ndiaye, rector of Senegal’s Gaston Berger University.

Ethics was another hotly debated issue, in large part due to the proposal by Joseph Rotblat—a physicist who won the 1995 Nobel Peace Prize for his work as founder of the Pugwash Conference, which pressed for nuclear disarmament—that all young scientists be required to take an oath, similar to the Hippocratic Oath taken by physicians. He suggested it include the line: “I will not use my education for any purpose intended to harm human beings or the environment.” While UNESCO’s Mayor told *Science* that he favored the concept, many scientists at the conference—including U.S. Nobel laureate Paul Berg and German biologist Hubert Markl, president of the Max Planck Society—said such an oath would have only symbolic value. “The Nazi doctors who committed atrocities at the concentration camps had taken the Hippocratic Oath,” Markl told *Science*. In the end, the conference documents did not specifically back Rotblat’s proposal, but urged young scientists to “adhere to the basic ethical principles and responsibilities of science.”

One issue that all delegates seemed to agree on was the need for a rapprochement between science and society. Indian plant geneticist M. S. Swaminathan told the conference that, despite its great advances during this century, science has failed to address many human needs in the developing world. “The formidable power of science and technology can benefit mankind only if we know how to temper it with humanism.” He called for “information empowerment” by connecting the Third World to the Internet and giving the poor greater access to scientific advances.

As the bleary-eyed delegates headed home from Budapest, some recalled that the noble goals of the last such conference—held in Vienna in 1979—had not been fulfilled (*Science*, 11 June 1999, p.1760). And they vowed this time around to make sure the Budapest framework goes somewhere. “The follow-up is the most important aspect

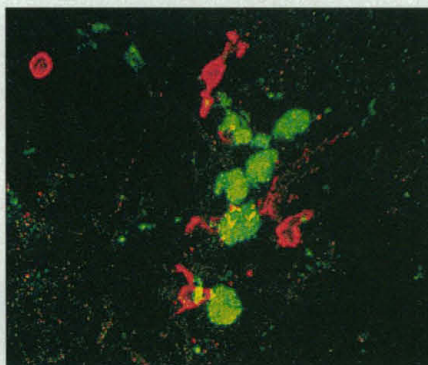
of the conference,” said Mayor. He said UNESCO would establish a network to meet regularly to evaluate the conference follow-up and recommend ways to implement the resolutions. “We want the Budapest conference to be more effective in the long run” than was the Vienna meeting, said Indian scientist M. G. K. Menon, a former ICSU president. Added Mohamed Hassan, a Sudanese mathematician who directs the Third World Academy of Sciences and is president of the African Academy of Sciences: “We want to send a message to the world’s countries: support science, because it is in your interest.” —ROBERT KOENIG

With additional reporting by Daniel Clery.

## NEUROBIOLOGY

### An Immunization Against Alzheimer’s?

Immunization, once largely limited to fighting infectious diseases, is finding surprising new targets. Researchers have recently learned that some cancers can be eliminated by cranking up the immune system with vaccines, and now, new findings raise a startling possibility: someday immunizing people to prevent or even reverse the mental devastation of Alzheimer’s disease.



**Cleanup operation.** Microglia, the brain’s scavenger cells (red), and amyloid plaques (green) in the brain of an immunized mouse.

One hallmark of Alzheimer’s is amyloid plaque, a protein deposit that builds up in the brains of those with the disease. A team at Elan Pharmaceuticals in South San Francisco reports this week in *Nature* that, in mice genetically engineered to develop an Alzheimer’s-like condition, immunization with  $\beta$ -amyloid ( $A\beta$ ), the protein fragment that forms the plaque, reversed or prevented

plaque formation and neural damage.

The finding “raises the possibility that immunization with  $A\beta$  may eventually be used as a treatment, or prophylactically, for Alzheimer’s disease,” says Alzheimer’s researcher Peter St. George-Hyslop, of the University of Toronto. “If so, this would be an absolutely tremendous result.” Alzheimer’s researcher Sam Sisodia of the University of Chicago agrees, but adds: “One has to exert caution [in thinking] about using this strategy for therapeutics. Things could work differently in humans.” One big question mark, notes St. George-Hyslop, is that even if immunization prevented plaque formation in humans, no one is certain yet that plaque actually causes Alzheimer’s symptoms.

Even so, plaque made up of  $A\beta_{42}$ , an abnormal-length fragment of a normal cellular protein, has been a central focus of Alzheimer’s research. It is an early and consistent feature of the disease, and while it hasn’t been proven to cause the symptoms, many researchers think multiple lines of evidence strongly suggest that it does.

Several labs have bred transgenic mice that produce  $A\beta$  and develop plaques and neuron damage in their brains. Although they don’t develop the widespread neuron death and severe dementia seen in the human disease, they are used as models for its study. Dale Schenk, vice president of neurobiology at Elan, wondered whether immunization with  $A\beta$  might produce antibodies that would prevent plaque formation in the mice. The antibodies would have to cross the blood-brain barrier, but “we knew [from prior work] that everything from the blood gets into the brain at some level,” says Schenk, so he thought it was worth a try.

Schenk’s team injected the mutant mice with  $A\beta$  at a young age, before plaque formation had begun, and found that those mice never developed plaque or neuron damage. When they immunized older mice that already had plaque in their brains, the plaque—and the signs of disease—largely went away. In the brains of these mice the team found evidence of an immune response: bits of remaining amyloid that were dotted with antibodies, and microglia, the scavenger immune cells of the brain, chock-full of amyloid protein they had cleared away.

The presence of antibodies on the remaining plaque means that the antibodies successfully crossed the blood-brain barrier, says neurologist Lawrence Steinman, who studies immune-brain interactions and amy-

loid at Stanford University Medical Center. Once there, he says, it's easy to see how they could block amyloid molecules from sticking together in plaques. "If the amyloid protein is bound to an antibody, there is no way it can form these aggregations," he says. What's more, Sisodia notes that recent studies in mice showed that when amyloid deposition is halted by killing neurons that secrete A $\beta$ , existing deposits diminish over time. "The idea that you can ... get rid of [amyloid] is not inconceivable," he says. Researchers agree they'd like to see the immunization results repeated. They may not have long to wait, as at least one other group is rumored to have similar results.

But will the approach work in humans? Mice aren't a perfect mirror of human physiology, Steinman notes. In particular, he worries whether in humans "there is enough of a breach of the blood-brain barrier to allow this to happen." And St. George-Hyslop cautions that the protein precursor to A $\beta$  is found in many cell types, so immunization might induce a harmful autoimmune response in nonbrain tissues.

Allaying concerns about autoimmune reactions may require further animal testing. But by the end of the year, Elan hopes to start clinical trials of the therapy on Alzheimer's patients. Those trials could yield a verdict not only on this therapeutic approach but also on the importance of plaque in Alzheimer's disease. "The bottom line of this all," says St. George-Hyslop, is that "we will know quite clearly what the true role of extracellular A $\beta$  is in Alzheimer's disease. We will either get a brilliant treatment, or we will get some powerful insights that modify how we think about the disease."

—MARCIA BARINAGA

#### SCIENCE POLICY

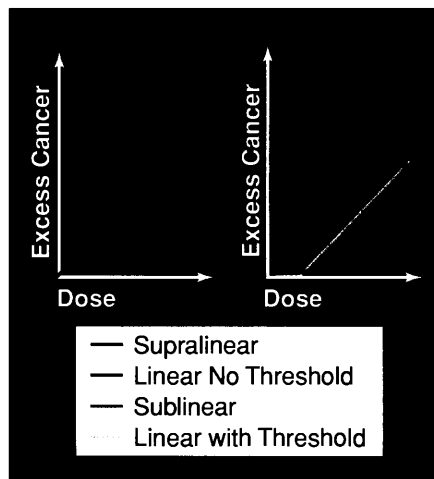
## NRC Pulled Into Radiation Risk Brawl

A festering feud over possible health risks of low radiation levels has blistered into public view. But instead of assailing each other, two bitter foes are unloading on the National Research Council (NRC) for assembling what they claim is a biased panel to weigh radiation risks. In response, the NRC last month canceled the panel's first meeting and agreed to review its composition. "We're just taking a breather," says radiation biologist Evan Douple, director of the NRC Board on Radiation Effects Research.

The nasty decades-long dispute centers on the risk posed by ionizing radiation from sources such as medical isotopes and spent nuclear fuel. A range of federal agencies have set exposure standards for the general public and for workers—standards based on accepted risk levels that the government

tasks the NRC to review every several years. Billions of dollars are at stake: Stricter standards could increase the amount that agencies and industries must spend to clean up radioactive waste and protect workers.

Arriving at safe levels of radiation exposure is hard because little data exist on how low doses—less than 10 Roentgen equivalent man (rem) a year—affect health. (Annual U.S. exposure from all sources is 360 millirem). For years researchers have derived estimates mainly from cancer rates among 50,000 Japanese atom bomb survivors who received



**Venomous debate.** Groups disagree on which model best fits the data on low-dose radiation and cancer risk.

acute doses of more than 500 millirem. Current exposure regulations are based on the Linear No-Threshold (LNT) model, which uses a straight line to extrapolate the Japanese data to zero: It assumes no safe cutoff, and that doubling the dose doubles the risk.

The bone of contention is whether the LNT reflects reality. Some experts believe that population studies in regions with high background exposure—from radon or uranium deposits—suggest that radiation is harmless below a certain dose. Others point to data—including cellular studies—hinting that low doses may pose an even greater cancer risk, proportionally, than higher doses (see figure). At the request of several agencies, the NRC organized the latest panel on the Biological Effects of Ionizing Radiation to look at what model best fits the data.

But the 16-person committee that the NRC unveiled on 10 June, chaired by Harvard epidemiologist Richard Monson, drew an angry response. The panel "is completely skewed" toward people who favor relaxed standards, claims Dan Hirsch of the Committee to Bridge the Gap, a nuclear watchdog group in Santa Cruz, California. His organization and 73 other groups and individuals claim in a 22 June letter that most panelists have published studies or opinions

## ScienceScope

**Dying Flame?** The Department of Energy's (DOE's) fusion program is dangerously close to flickering out, says an advisory panel.

In March, Energy Secretary Bill Richardson appointed a task force led by physicist Richard Meserve, a Washington, D.C., attorney, to examine DOE's \$230 million fusion portfolio. Battered by budget cuts, DOE's "vibrant and valuable" fusion work "is now subcritical," the panel states in a draft report scheduled for release today. All it would take to get the effort back on track, the panel suggests, is a gentle management shake-up and a budget increase of less than \$20 million a year to fund a handful of promising research projects.

The report is "mostly a pat on the back" for DOE, says Stephen Dean of Fusion Power Associates in Virginia. More-critical reviews could come later this year, when a National Academy of Sciences committee and another DOE advisory panel offer their advice on fusion's future.

**Blood Money** Scientists could get an extra \$25 million over the next 5 years to study youth violence. In the wake of the Columbine High School shootings, House and Senate lawmakers have passed anti-crime bills calling on the National Institutes of Health to spend the funds—which would come on top of more than \$50 million the agency already pumps into related work each year.

The American Psychological Society had pushed for a \$100 million boost for studies on violence prevention, peer



**Columbine High School.**

pressure, and other issues. But the lower figure is fine with executive director Alan Kraut, who calls it "a big first step."

There are still some hurdles to clear before the cash arrives. Later this year, House and Senate negotiators must agree on a final version of the crime bill—but talks could bog down over controversial provisions, including several on gun control. And even if the bill passes, Congress must still come up with the money in the 2000 budget, now under discussion.