of human fibroblasts to get the cells to shut down most of their genetic activity. Two days later, he added back a 10% serum solution. To see which genes were affected by the serum addition, Iyer purified mRNAs from subsets of the cells at various intervals during the next 24 hours, labeled the cDNAs made from those mRNAs with fluorescent dyes, and exposed each batch to the array. By monitoring which DNAs in the array bound the cDNAs, he and his colleagues were able to tell which genes were active at what times. With the aid of a computer program that examined the 500 most active genes, the researchers grouped those with similar activity patterns.

The computer program showed a coordinated response to serum by 28 genes known to be involved in controlling cell proliferation. The fastest to respond—some turning on within a few minutes after the serum exposure—were genes that make proteins that regulate the expression of other genes. These prodded the cells to copy their DNA and divide. Some of the active genes turned off within an hour; others remained active for several hours. A different subset of genes quieted down in response to serum, including those that keep the cell in a nondividing state.

But other sets of genes not involved in cell division also responded to the serum. Serum addition activated eight genes whose proteins elicit immune responses, 19 genes known to be involved in rebuilding damaged tissue, and a dozen whose proteins stimulate the growth of new blood vessels. The fibroblasts essentially reacted to exposure to serum in culture much as they would in the body if blood had seeped into a fresh skin wound. "If you look at the papers and the review articles [about the serum response model], everything is interpreted in terms of how [the results] fit into cell proliferation," Brown points out. "But that's not what the model was about."

Given that fibroblasts are known to help with healing, these findings are perhaps not surprising. Researchers "will be slapping their foreheads" for not having recognized it sooner, admits Stanford's Gerald Crabtree, and will see their work in a new light.

The work is also a taste of what is to come as researchers use microarrays to analyze gene expression in other mammalian systems. As Harold Varmus, director of the National Institutes of Health, pointed out last month in San Francisco at a meeting of the American Society for Cell Biology, "we will [eventually] be looking at the totality of gene behavior in individual cells, even [in] whole organisms" with microarrays. And that, he predicts, "is going to change our view of how life works." **–ELIZABETH PENNISI**

TOXICOLOGY

EPA Ponders Pesticide Tests in Humans

The volunteers drank corn oil spiked with a poisonous chemical as doctors watched for symptoms like sweating, headaches, and nausea. Inhuman torture or scientific necessity? That 1997 experiment was in fact performed legally on paid subjects in England by a commercial lab, but it is among several such experiments that spurred the Environmental Protection Agency (EPA) to convene an expert panel last month to lay the groundwork for its first-ever set of rules for testing the toxicity of pesticides on people.

How safe? Pesticides may be tested in humans as well as applied by them.

The panelists, who met on 10 and 11 December in Arlington, Virginia, wrestled mightily with the issue without pinning it to the mat. Some argued that pesticide experiments on humans might be permissible in the absence of alternatives such as studies of farm workers exposed to a pesticide on the job, although they insisted on a stringent ethical review of the experimental protocols. But others urged EPA to reject human data, especially from studies done merely to market a product. "I heard a lot of ethical and scientific concerns about those data," says Lynn Goldman, who stepped down on 31 December as head of EPA's Office of Prevention, Pesticides, and Toxic Substances, which hopes to issue draft regulations by this spring.

The current debate is an outgrowth of efforts to beef up protection against pesticide toxicity, which have spawned a backlash that could increase the number of tests done on humans. The agency now sets safe levels at one-hundredth the pesticide concentration found to have no effects on animals, partly on the assumption that humans might be more sensitive to the chemicals than lab rats. A 1996 law aimed at protecting children could lead to another 10-fold reduction in acceptable levels of toxicity. That further tightening has so concerned pesticide companies that some have proposed dumping animal-only tests in favor of direct tests in adult humans.

> **Human pesticide testing "makes me morally queasy, but not to the point where I'd say, 'ban it.'"**
>
> **—Arthur Caplan**

The EPA was already concerned about this possibility when the Environmental Working Group, a Washington, D.C.–based activist group, reported last July on the use of human volunteers in recent pesticide tests mostly in the United Kingdom. The publicity prompted EPA to check its own files, which contained the results of eight human no-effects studies—some recent, others decades old. In most cases, it was unclear whether the studies had been approved by an ethical panel called an Institutional Review Board, as required by a government-wide standard called the Common Rule. "We were terribly concerned ... because to observe no adverse effect levels, somebody's going to have to have an adverse effect," Goldman says.

Last month's panel, with experts on topics ranging from bioethics to toxicology, examined both the science and the ethics behind such testing. Several observers noted that many of the tests submitted to EPA included only a handful of subjects—too few to yield statistically significant results. If human tests are done, they "should be scientifically valid," said computational biologist Chris Portier of the National Institute for Environmental Health Sciences in Research Triangle Park, North Carolina.

At the same time, University of Rochester toxicologist Bernard Weiss pointed out that human data can offer valuable insights on topics such as toxicity mechanisms or individual sensitivity differences. Others noted that the tests, however unsettling at first glance, are similar to a Phase I clinical trial, where healthy volunteers are often used to test a candidate drug for side effects. University of Pennsylvania bioethicist Arthur Caplan says that human pesticide testing "makes me morally queasy, but not to the point where I'd say, 'ban it.' " Like other committee members, however, he emphasized that EPA should require companies to comply with the Common Rule, which is now applied only to agency-funded research.

To some panelists, however, the value to society of a new pesticide pales in compari-

CREDIT: S. C. DELANEY/EPA

son with the discovery of a new drug and, therefore, requires a higher standard. As Gary Ellis, who oversees human subject protection for the National Institutes of Health, put it, "The importance of knowledge to whom? Those interested in better growing of cotton in west Texas?" Considerations such as these caused at least one committee member to suggest that EPA reject any data involving human experiments.

The committee had hoped to prepare a recommendation during the meeting itself. But the 16 members decided instead to submit comments for a draft advisory report that would be sent to EPA by 1 January. The EPA plans to use the report in preparing a draft policy on human testing. Given the range of opinions already expressed, however, EPA officials can expect a lively debate during the comment period that follows its release.

–JOCELYN KAISER

EUROPEAN SPACE AGENCY

Flat Budget Keeps Space Science on Edge

Europe's space powers have postponed until spring a decision on the long-term science budget for the European Space Agency (ESA), although they have temporarily approved level funding and kept alive a planned Mars mission. The delay angers scientists who have been lobbying for an increase in the agency's new 5-year budget, which begins today. But some officials said they were heartened that agency officials didn't make further cuts in a budget that, since 1996, has lagged behind inflation.

Looking up. ESA's Bonnet sees budget as a "positive sign."

"I am disappointed," says Hans Balsiger, chairman of ESA's science program advisory committee. "I told the council that they can't keep patting us on the head, telling us how well we are doing and, at the same time, taking money out of our pockets." But Roger Bonnet, head of space science at ESA, is pleased with the decision to approve $3.5 million for Mars Express, a mission to orbit the planet that's planned for launch in 2003. "It is the first positive sign from council since Toulouse [an October 1995 meeting at which funding was capped for 3 years] that they are concerned about science. It does at least reverse the trend [of budget cuts]."

On 16 December, ESA's ruling council met in Paris to approve a 1999 space science budget of $408 million, including the earmark for Mars Express. Last year's budget was $407 million. But they deferred discussion of longer-term spending plans until a May meeting in Brussels of science ministers from the 14 member states.

CREDITS: ESA

On its way. ESA provides first increment for Mars Express orbital mission.

The delay is feeding anxiety among European space scientists, who have drawn up an ambitious agenda of exploration. Those missions—including an x-ray multimirror telescope and a cluster of instruments to study the Earth's magnetosphere to be launched in 2000, a gamma-ray laboratory in 2001, the Rosetta comet mission in 2003, and a far-infrared telescope in 2007—had counted on steadily rising expenditures. "If we get funding at the mid-1998 level and this [year's] increase is in line with inflation, we can just about do all of these missions," says Balsiger, looking ahead to the spring meeting. "If it is less, then we will have to cancel Mars Express."

The delay highlights the precarious level of support for space science throughout Europe. "We see problems in both the short term, 5 years, and the long term, 10 years," says Paul Merton, director of space science at the British National Space Center. Britain supports a budget that would keep pace with inflation, Merton says, but would like ESA to save money on its large missions to make room for the rest of the science program. In Germany, the new government is carefully reviewing its current level of expenditures on science. "The Social Democrats spoke favorably of basic research prior to the election but said nothing specific about space science," notes Manfred Ottobein, who oversees space and microgravity science at the German Space Agency. And French scientists don't want ESA programs to be hurt by their country's agreement with NASA to share the cost—still uncertain—of a sample return mission to Mars, says Phillippe Masson, a former science adviser to the government.

While scientists look to the spring ministerial meeting for salvation, some observers warn that even a modest increase may not solve the long-term problems facing European space science. "People are scrabbling for the last million Euros," says Roy Gibson, a former ESA director-general. "No program is worth doing if it is eroded every year by inflation." –HELEN GAVAGHAN

Helen Gavaghan writes from Hebden Bridge, U.K.

ASTROPHYSICS

Galaxies Seen at the Universe's Dawn

Astronomers from the State University of New York, Stony Brook, have won a race to the edge of the universe. After 3 weeks of working around the clock on infrared data from the Hubble Space Telescope, they may have shattered previous records for the most distant stars and galaxies, pushing the frontier of the visible universe to distances so great that they are seen just a few hundred million years after the big bang. "We knew other groups were working on the same data," says one of the astronomers, Ken Lanzetta, "so there was a lot of hurry."

Together with his Stony Brook colleague Amos Yahil, postdocs Alberto Fernandez-Soto and Sam Pascarelle, and students Hsiao-Wen Chen and Noriaki Yahata, Lanzetta analyzed data from a very small patch of sky in the southern constellation Tucana, where the Hubble gathered light for 10 straight days last October (*Science*, 27 November 1998, p. 1621). NASA released data from this observation, called Hubble Deep Field South, on 23 November. By 18 December, the team had published its results on the Internet (sbast4.ess.sunysb.edu /hdfs/home.html): a catalogue of 323 distant galaxy candidates, along with their redshifts—a measure of distance, and hence age. The farthest galaxy spotted previously has a redshift of 5.64, meaning that the expansion of the universe has stretched its light by a factor of 6.64. Lanzetta and Yahil now claim to have found 14 galaxies with redshifts of between 5 and 10, and another five candidates with redshifts larger than 10.

At a redshift of 10, galaxies are seen when the universe was only 9% of its current size and probably just a few hundred million years old. "We are getting back to a significant fraction of the age of the universe," says Yahil. "These are the last few percent to the big bang." If he and Lanzetta are right, galaxies and stars formed much earlier in cosmic history than most theorists had imagined.

There is a catch, however. Because the galaxies are extremely faint, Lanzetta and Yahil did not measure their redshifts from a spectrum—the usual procedure. Instead, they deduced redshifts by comparing each galaxy's brightness in measurements at different color