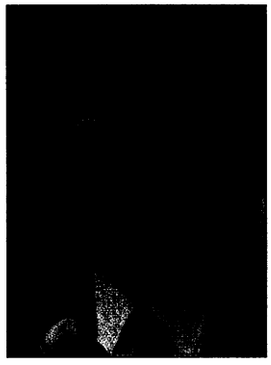
Fisheries, which hopes to receive money to speed up work on sequencing and analyzing the rice genome. "The Millennium Projects are emphasizing areas where additional spending is needed," adds Leo Esaki, a Nobel Prize–winning physicist and former president of the University of Tsukuba. But others are more cautious in their praise. "In some cases, it's hard to tell just what's included," says an official from the New Research Centers Planning Office of RIKEN (the Institute of Physical and Chemical Research) outside Tokyo, which has proposed five Millennium Projects.



Scientific help. Prime Minister Obuchi hopes Millennium Projects will boost economy.

Obuchi caught the scientific community off guard in August when he asked each agency to nominate research-oriented projects to address social and economic needs in three broadly defined categories: information technology, the aging of society, and the environment. The projects, ideally involving cooperation among government, industry, and academia, are intended to boost the nation's technological prowess and address pressing societal needs. Priority areas for projects of up to 5 years include such goals as connecting all primary and secondary schools to the Internet, creating a paperless government by 2003, enhancing the skills of older workers, reducing the use of dioxin and PCBs, and developing fuel cell–powered cars.

Although some scientists worried initially that the awards would circumvent established selection procedures, most agencies ended up nominating projects from among those already in the pipeline in the hope of moving them forward or freeing up funds for other projects. Officials also coordinated their proposals to ensure that everyone would get a piece of the pie. "I think we have almost gotten what we wanted," says Nobuhiro Muroya, deputy director of the Science and Technology Agency's Planning and Evaluation Division. The three categories also proved remarkably flexible, with rice genome work fitting within the "needs of an aging society."

In addition, the Millennium Projects will pad Japan's R&D bottom line. Without them, projected science spending would remain relatively flat, at $30 billion for the fiscal year beginning on 1 April. But crediting the entire $2.4 billion to science would mean an annual increase of more than 8%.

The uncertainties surrounding the projects pose some problems for planners. At RIKEN, for example, it's not clear how much money will go to two projects on the list: a new institute to focus on cell development, differentiation, and regeneration; and a project to study single nucleotide polymorphisms, subtle genetic variations that distinguish human beings that may lead to drugs tailored to an individual's characteristics (*Science*, 9 July, p. 183). Officials also hope to get some money for a new research center to focus on plant genetics and genomics, including 50 new positions.

Another uncertainty stems from the fact that Obuchi has invited the public to submit ideas before the list of projects is finalized in December. Just how the public will participate is up in the air, however. Muroya says a telephone hot line is a possibility. Any suggestions will be reviewed by the Council for Science and Technology, the nation's highest science advisory body, which is chaired by the prime minister.

–DENNIS NORMILE

OBESITY RESEARCH

Leptin Not Impressive In Clinical Trial

Like a promising starlet with her first box-office flop, the hormone leptin, which made a stunning debut 5 years ago as a potential weight-loss drug, has met with disappointment after the conclusion of its first clinical trial in humans. On a positive note, the results, which appear in the 27 October issue of *The Journal of the American Medical Association*, show that some study participants given leptin lost more weight than controls. The differences were statistically significant, however, only in obese subjects given the two highest leptin doses.

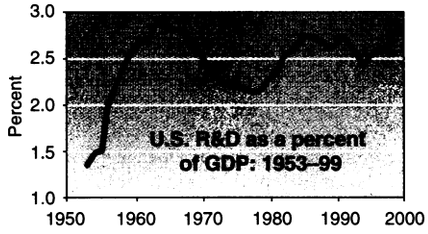
And because it's a protein, the hormone had to be injected, which produced redness and swelling severe enough to cause subjects to drop out of the study early. What's more, some obese volunteers cheated on their required diets. As a result, they gained weight despite receiving the drug. "I was not very impressed," says Jeffrey Flier, a longtime leptin researcher at Harvard Medical School in Boston. "Leptin, given the way the researchers gave it to a group of people with a common variety of obesity, is relatively ineffective in most of them."

There still may be hope for leptin as a diet therapy, however, if researchers can uncover what made the few individuals who responded to the drug more sensitive; it could enable them to identify patients likely to benefit. But that sort of finding, even if it comes soon, will still leave the majority of obese individuals—an estimat-

ScienceScope

Upwardly Mobile A strong economy has pushed the share of U.S. resources devoted to research to the highest level since the race-to-the-moon boom of the 1960s. This year the United States will spend 2.79% of its $88 trillion gross domestic product (GDP) on R&D, concludes a new National Science Foundation report (NSF 99-357, at www.nsf.gov/sbe/srs). The $247 billion investment extends a 6-year uptick and erases an earlier decline that had triggered dire warnings of a loss of U.S. leadership in science. The most recent figures keep the United States close to Japan's 2.92% and comfortably above Germany's 2.3%.

This year's $20 billion, 8.8% spending boost is fueled by industry, which funds 68% of the U.S. scientific enterprise. Meanwhile, the federal government's spending share slipped to 27%, the lowest percentage since NSF began collecting data in 1953. "It's a reflection of good economic times," notes NSF's Steve Payson. If industrial investment remains strong, he says, next year's figures could beat the 1964 record of 2.87% of GDP.



Minority Report The National Institutes of Health (NIH) already has too many institutes and centers, according to NIH director Harold Varmus. But his lack of enthusiasm for subdivisions hasn't stopped Congress from proposing more. This week Senator Ted Kennedy (D–MA) planned to throw his legislative weight behind a bill to create a new Center for Research on Domestic Health Disparities, which would study health problems of particular concern to minorities.

Kennedy's bill is expected to mirror one proposed in the House on 30 June by Representative Jesse Jackson Jr. (D–IL). Jackson's bill (HR 2391) calls on NIH to fund research that aims to find out why ethnic minorities and "individuals in underserved communities" are likely to die earlier than whites of diseases such as cancer, diabetes, and AIDS. Jackson has already signed up 70 co-sponsors, including members of the Asian, black, and Hispanic caucuses. But neither bill is expected to make much progress this year.

Contributors: Jeffrey Mervis, Constance Holden, Eliot Marshall

CREDIT: KATSUMI KASAHARA/AP; GRAPH SOURCE: NSF/DIVISION OF SCIENCE RESOURCES STUDIES

ed one-third of the U.S. population—to struggle with therapies that don't really seem to work.

The story of leptin has had as many ups and downs as a chronic dieter's bathroom scale. First discovered in 1994 by a team led by Jeffrey Friedman at The Rockefeller University in New York City, the appetite-suppressing hormone hit the headlines accompanied by pictures of mice that were grossly overweight as a result of leptin gene mutations. Rockefeller University subsequently licensed the human version of leptin to the biotech firm Amgen Inc. of Thousand Oaks, California, for an initial fee of $20 million, and researchers scrambled buoyantly toward the hope of using the hormone as a wonder diet drug.

One sign of trouble came, however, when researchers learned that most obese human patients do not have depleted leptin levels in their bloodstreams. In fact, the heavier the person, the higher the levels. Still, that did not rule out the idea that leptin might work as an obesity therapy. Patients with adult-onset diabetes make insulin, but develop a resistance to the hormone that can sometimes be overcome by insulin injections. Hoping for something similar with leptin, a team led by Mark McCamish at Amgen devised a clinical trial designed to quickly test its safety and efficacy in humans.

Investigators at six sites recruited 54 normal and 73 obese volunteers, who were assigned to receive injections either of a placebo or of leptin at one of four different doses. Obese volunteers were also instructed to diet. After 4 weeks, when the drug appeared to be safe, the obese volunteers were given the choice to go the full 24 weeks planned for the study. Forty-seven completed the study, the rest having dropped out either because of problems with injection sites or noncompliance with the diet or the injections.

At the end of the trial, individuals in the highest dose group had lost a mean weight of 7.1 kilograms as compared to 1.3 kilograms lost by the controls, who were given no drugs. "Our data show that there is not an absolute leptin resistance in this group of [obese] people," says study co-author, nutritionist Steven Heymsfield of St. Luke's-Roosevelt Hospital Center in New York City.

That may be true, say other researchers, including Flier, but a close look at the numbers shows that only patients in the highest two dose groups had significant weight losses compared to those taking the placebo. And even then, several in those groups actually gained weight during the study. "It's looking very much as if there is no real effect except in a subset of patients," Flier says.

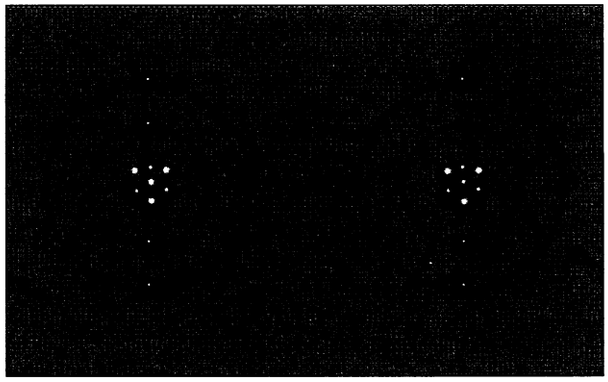
The Amgen team now plans to try to identify exactly what factors made those people more responsive to leptin. If successful, says Heymsfield, "one could screen people beforehand for certain markers and then know the probability of responding would be much higher." He notes that researchers at Addenbrooke Hospital in Cambridge, U.K., reported in the 16 September issue of *The New England Journal of Medicine* that leptin did cure the obesity of a youngster found to have defects in his leptin gene. Such mutations are rare, however, and until researchers learn to identify people with more common types of obesity that respond to leptin, the drug is not likely to appear in pharmacies. **–TRISHA GURA**

Trisha Gura is a writer in Cleveland.

GEOCHEMISTRY

Tweaking the Clock of Radioactive Decay

Certainty, it seems, is on the wane. The sun may rise tomorrow on schedule, and the seasons may pass as they always have. But radioactive decay—the pacemaker of geologic time—can no longer be called precisely "clocklike." Says geochemist Douglas Hammond of the University of Southern California (USC) in Los Angeles: "Everybody always assumes radioactive decay to be totally independent of temperature, pressure, and chemical form. It seems there are some exceptions."



Atomic cannibalism. Beryllium-7 decays by capturing one of its own electrons, transforming a proton into a neutron. Because chemical bonds affect the electrons' behavior, the decay rate of beryllium-7 can depend on its chemical form.

In the 15 September issue of *Earth and Planetary Science Letters*, geochemist Chih-An Huh of the Institute of Earth Sciences of the Academia Sinica in Taipei reports that the decay rate of beryllium-7 varies, depending on its chemical form. Creationists hoping to trim geologic history to biblical proportions will be disappointed—the variations seen so far are much too small, just a percent or so, to affect Earth's overall time scale. Still, the variability in beryllium decay will prompt those who want to trace out fine divisions in the earliest reaches of time to take a close look at their pacemakers.

Theoreticians long ago anticipated some variability of radioactive decay. The decay of beryllium-7, for example, should depend on the density of electrons at the nucleus. That's because it transforms itself into lithium-7 by capturing one of its own electrons, turning one of its protons into a neutron, and emitting a gamma ray. When a change in chemical bonding subtly rearranges the electrons and increases an electron's chance of finding itself at the nucleus, the odds are better that it will be captured and the beryllium will decay.

In the last few years, German researchers have demonstrated the converse of this effect: a surge in the decay of rhenium-187, which emits an electron rather than capturing one. When Fritz Bosch and his colleagues at the Gesellschaft für Schwerionenforschung in Darmstadt, Germany, stripped away all the electrons from rhenium nuclei, something that might happen in a star's harsh interior, its half-life plummeted from 42 billion years to 33 years. But, until now, researchers have detected only tiny variations (or none at all) in the decay rate of beryllium and other atoms under Earth-like conditions.

Undismayed, Huh applied the latest technology to the problem. He used an extremely sensitive but stable gamma ray spectrometer to monitor the decay of beryllium-7 (which has a half-life of about 53.3 days) in the form of the hydrated ion, the hydroxide, and the oxide—chemical combinations common in the environment. Thanks to an unprecedented precision of ±0.01%, he could see that the half-lives of the three forms were 53.69 days, 53.42 days, and 54.23 days, respectively. The 1.5% range is "probably quite real," says geochemist Teh-Lung Ku of USC. "Although the idea has been around quite a while, this time [the researchers] will be able to show it more convincingly."

It remains to be seen how important the effect will be in dating geologic samples. Beryllium-7 is used to gauge the rate of erosion or sediment deposition over weeks to months. Except perhaps in studies aspiring to the highest possible resolution, the decay variability due to chemical form is likely to be swamped by other uncertain-

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