

LYME DISEASE

Patients Scarce in Test Of Long-Term Therapy

by 20% to \$696 million. That figure constitutes 6% of the country's overall defense budget, its highest share ever, and reflects the government's attempt to beef up indigenous military technologies.

Two related sectors also fare well. Space research is scheduled to rise by 16%, to \$439 million. The increase will fuel a program to develop a booster for the country's new geosynchronous communications satellites and to create a second launch site. Atomic energy programs will receive a 32% boost, to \$384 million, and funding for nuclear power plants, including a prototype fast breeder reactor, will also rise. The Bhabha Atomic Research Center in Mumbai, India's leading laboratory for nuclear weapons research as well as for civilian-related projects, gets a 33% hike, to \$134 million. In addition, the Department of Atomic Energy announced a new National Center for Applied Mathematics and Radiophysics at the Tata Institute for Fundamental Research in Mumbai, although no details were available at press time.

On the civilian side, the department of science and technology, which funds academic research, is receiving an 18% hike, to \$164 million, and the department of biotechnology's budget will rise by 9%, to \$30 million. Civilian electronics garnered a 33% increase, to \$52 million, reflecting India's push to compete in world markets. The budget for agricultural research and education is slated to rise by 26%, to \$303 million, with the largest increases going for research on wheat, rice, and pulses.

Some of the loudest applause is coming from CSIR, which runs a chain of 40 laboratories catering to the needs of industry. Its 30% boost, to \$199 million, is the largest in its 50-year history. "For the first time, our R&D budget is looking healthy," says Mashelkar, who singled out for praise a tripling of its \$1.25 million program to find commercial applications for biologically active agents in plants.

The new budget also contains new initiatives in grassroots innovations, vaccines, and biodiversity. A \$5 million foundation is being set up to encourage small inventors to pursue commercialization of their ideas, along with a national registry to recognize the achievements of those without the means to apply for patents. The vaccine initiative is most likely to benefit efforts to develop vaccines against rotavirus and cholera, which are already undergoing clinical tests. A new National Biore-sources Board is expected to consolidate under one roof all research related to biore-sources and to expand survey and taxonomic activities. "This would put India in a very strong position to exploit the age of biology in the next century," says Manju Sharma, secretary of the department of biotechnology.

—PALLAVA BAGLA

Scientists are having trouble enrolling enough patients in a \$4.2 million study to test whether long-term antibiotic treatment is effective against chronic symptoms of Lyme disease. Ironically, while researchers were discussing this problem in a suburb of Washington, D.C., last week, officials in Connecticut—ground zero for the disease—held a hearing to increase pressure on insurance companies to cover extended Lyme disease therapy.

About 13,000 U.S. citizens get tick bites each year that transmit a corkscrew-shaped parasite (*Borrelia burgdorferi*) that causes inflammation and joint pain—Lyme disease. But medical experts differ on how to treat very long bouts of arthritis, fatigue, and memory loss that some patients experience—a syndrome known as Chronic Lyme Disease (CLD), which is a controversial diagnosis.

The current study, run by a team led by Mark Klempner of the Tufts University



Recruiting. Study director Mark Klempner seeks victims of Lyme parasite (above).

School of Medicine in Boston, offers CLD patients a 90-day course of antibiotics. It's the largest study of its kind, aiming to bank 45,000 tissue samples for future research (*Science*, 13 October 1995, p. 228). But, as its leaders revealed in an interim review last week, patient recruitment is lagging.

After a year of advertising, says Klempner, only 57 subjects had been enrolled. The goal is to get 260 by the time the study ends in 2 years. More than 1200 people have expressed interest, and 700 have come in for screening. But only one in 10 who appear in the clinic fits the study's strict criteria.

A patient is enrolled in the double-blind placebo study, funded by the National Institute of Allergy and Infectious Diseases (NIAID), only after testing positive in a blood antibody test for *Borrelia* or having evidence of a tick bite rash. Patients who have received extensive intravenous antibiotic treatment are ex-

cluded, as are, for ethical reasons, those who have never received any treatment. The criteria are designed to focus selectively on CLD. Once enrolled, patients are randomized into a placebo or treatment group. The treatment group gets 30 days of intravenous ceftriaxone followed by 60 days of oral doxycycline.

On 25 February, Klempner asked a gathering of NIAID project managers, members of an advisory panel, and patient advocates for ideas on how to speed up enrollment. But he also offered an encouraging note: Many CLD patients have a distinctive enzyme in their spinal fluid that's been seen before in patients with neuroborreliosis—when the organism invades the central nervous system. The enzyme, he suggested, might be useful as a disease marker.

After the meeting, Klempner and NIAID Lyme program director Philip Baker said they would not relax study criteria to get more patients. That would wreck the protocol, Baker said. Instead, at extra cost, NIAID will add a recruitment site in Connecticut to existing sites in Boston and New York, and possibly others in New Jersey and Maryland. Klempner also sought help from advocacy groups such as the controversial Lyme Disease Foundation (LDF) of Hartford, Connecticut.

Karen Vanderhoof-Forschner, chair of LDF, which has questioned conventional CLD therapy, agreed to open LDF's membership to recruitment. In addition, Klempner says, some physicians who specialize in CLD may cooperate. Vanderhoof-Forschner told *Science* that she thought some eligible candidates had not volunteered for the study because they are suspicious of the researchers. But it's also possible, Klempner concedes, that there aren't as many CLD patients as expected.

That possibility might surprise the attorney-general of Connecticut, Richard Blumenthal. One day before Klempner solicited ideas to enroll more patients, Blumenthal held a hearing in Hartford to help people seeking reimbursement for long-term antibiotic therapy for Lyme disease. "Most insurance companies will not cover treatment of longer than 4 weeks of intravenous antibiotics," Blumenthal says, "despite the judgment of treating physicians" that the drugs should be provided. Blumenthal is drafting a bill to "mandate" insurance coverage for what the doctor orders.

Meanwhile, Klempner says that his team will try to "remove barriers" to enrollment. Conducting free screening clinics "within the walls of advocacy organizations," he says, should provide access to a new cohort of patients.

—ELIOT MARSHALL

