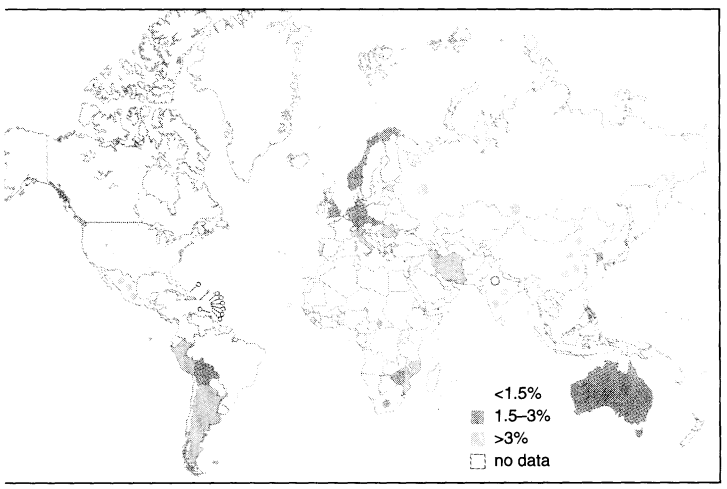
INFECTIOUS DISEASE

Drug-Resistant TB on The Rise

Tuberculosis is back with a vengeance. Once nearly vanquished by antibiotics, at least in the developed world, tuberculosis resurged in the late 1980s and now kills more than 2 million people a year—second only to AIDS among infectious diseases. Especially frightening is the emergence of drug-resistant strains. The wake-up call came in the early 1990s, when New York City was hit with an epidemic in which about 9% of cases were resistant to two or more TB drugs. The outbreak took years—and cost $1 billion—to quell. But global trends in resistant TB, though the subject of considerable speculation, have been unknown.



Tough bugs. Prevalence of TB cases resistant to two or more frontline drugs (data collected 1994–99).

Now, the World Health Organization (WHO) has some answers, and they are grim. Drug-resistant TB is rampant and appears to be spreading, WHO concludes in its most comprehensive report to date. Said WHO Director-General Gro Harlem Brundtland: "This report confirms our worst fears." WHO warns that these resilient strains could cripple the economies of developing nations and could erupt in Western countries as well.

Scientists blame the rise of resistant strains on a history of drug misuse. Sometimes doctors do not prescribe the proper course of treatment, which involves taking a mix of drugs for up to 6 months. Understandably, some patients fail to comply. And in many poor or war-torn countries, drugs are not always available.

WHO's new report covers 72 regions and has statistics on 28% of known TB cases. In three of the 28 areas for which data were available from a 1997 WHO survey, the prevalence of drug-resistant TB has skyrocketed. In both Germany and Denmark, it climbed by 50% since 1996, to 10.3% and 13.1% respectively. New Zealand fared even worse—resistance more than doubled to 12%.

Experts agree that treating TB properly from the outset can prevent the rise of resistant strains. The best weapon is a strategy called Directly Observed Treatment, Short-course (DOTS), in which health workers make sure that patients swallow every pill over the long course of treatment. The problem is, only 21% of TB patients around the world received DOTS in 1998. And for TB strains resistant to two or more drugs, known as multidrug-resistant (MDR) TB, conventional drugs and DOTS don't work. Instead, health workers must rely on second-line drugs that are less effective and more expensive. Treatment can cost up to $250,000 per person and take 2 years—well beyond the reach of many poor countries.

Now that MDR TB has arisen, these strains are spreading through communities. The problem is particularly severe in six regions—Estonia, Henan Province in China, Latvia, the Ivanovo and Tomsk regions in Russia, and Iran—where between 5% and 14% of first-time TB cases are multidrug resistant. The spread of resistant strains has ignited intense debate over whether it's best to spend scarce resources on treating the widespread susceptible strains or on tackling MDR strains. One thing that's clear, however, is that the problem is a devil of our own making. Resistance is "almost an inevitable consequence of bacterial evolution and human nature," says molecular epidemiologist Peter Small of Stanford University. "The bug wins again." **–ERIK STOKSTAD**

CREDIT: (LEFT) WHO

PUBLIC HEALTH

Bat Researchers Dispute Rabies Policy

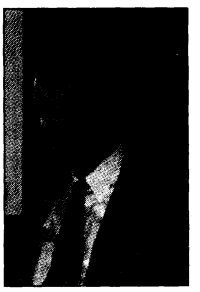
How noticeable is a bat bite? That seemingly esoteric question is center stage in a dispute over the small risk of catching rabies from bats. Based on some puzzling human rabies deaths, public health officials, including the Centers for Disease Control and Prevention (CDC) in Atlanta, recommend that in some circumstances people exposed to bats get rabies shots, even if there's no evidence of a bite. Bat researchers counter that the animals don't attack and leave stealth bites and

ScienceScope

Slight Rebound The National Science Foundation's (NSF's) flagship program to support graduate students is struggling to find talented underrepresented minorities after phasing out a special effort to attract them. The new class of 850 fellows, announced last week, contains 89 minority students pursuing Ph.D.s in science, mathematics, and engineering. Although that's a bit more than last year's crop of 76, the number is a far cry from the 175 minorities who earned the 3-year fellowships in 1998, the last year in which NSF held a separate competition for Hispanics, African Americans, and Native Americans (*Science*, 16 April 1999, p. 411). In addition, the number of minority applicants continues to fall, down 25% in 2 years, while the number of whites and Asians applying has held steady.

NSF officials hope a larger annual stipend, up $1000 this year to $16,200 toward a goal of $18,000, will boost demand. They also invited applicants to write about "any impediments" to a degree, says Susan Duby, head of graduate education, and asked reviewers to ponder NSF's role in serving underrepresented groups. "We're making more of an effort," says Duby, "but we haven't seen the payoff yet."

Resisting TB The effort to beat tuberculosis resistance is getting a boost. The Bill and Melinda Gates Foundation last week announced that it is giving $25 million to a new consortium of foundations, international organizations, and pharmaceutical companies called the Global Alliance for TB Drug Development. The groups will put the funds to use to come up with new drugs and test their efficacy in clinical trials.



And more help may be on the way. On 24 March, U.S. Representatives Sherrod Brown (D–OH, pictured) and Connie Morella (R–MD) introduced a bill that would boost anti-TB spending from $35 million to $100 million to establish effective TB programs, especially in nations that suffer most from the disease.

Contributors: Pallava Bagla, Michael Balter, Jeffrey Mervis, Erik Stokstad

that the policy sparks unwarranted fear of bats. The "infinitesimally small risk" of rabies from bats, says bat researcher Thomas Kunz of Boston University, has been blown "out of proportion."

After years of grumbling about the effects of CDC's stance, participants in the annual North American Symposium on Bat Research—which after 30 years of meetings has recently been organized into an official scientific society—are releasing a statement next week to address what they see as bad science and bad press on the issue. The researchers "find no credible support" for what they call "the undetected bite hypothesis" and argue that "it should not drive public policy."

Baffling bats. A rabies viral strain linked to eastern pipistrelle bats has killed humans, but these bats are rarely seen near people.

Federal health officials, however, are unapologetic for what they see as a cautious stance concerning a frightening if rare disease. Of the 27 rabies deaths in the United States in the 1990s, 20 were traced to viral strains associated with bats, the rest to canine strains. Current federal immunization guidelines, established by an advisory committee to CDC, say that rabies vaccination "is appropriate even in the absence of a demonstrable bite, scratch, or mucous membrane exposure in situations in which there is reasonable probability that such contact occurred (e.g., a sleeping person awakens to find a bat in the room …)." "I think our message is pretty reasonable," says Charles Rupprecht, chief of the CDC's rabies section.

Bat researchers say that this advice is based on a faulty premise. CDC maintains that only one of the recent deaths "had a definite history of a bat bite," implying that the others may have been the result of undetected or unreported bites. But bat researchers insist that a nip from a bat wouldn't go unnoticed. It's "not a bad bite, but it gets your attention," says biologist Thomas A. Griffiths of Illinois Wesleyan University in Bloomington.

Bat researchers agree that there's good evidence of a bat on the scene in all but a few of the cases of bat-associated rabies. They argue, however, that some victims may have been bitten but died before reporting a bite, or were bitten long ago and forgot the encounter, as apparently happened in some canine rabies deaths. In the few cases with no evidence of bats at all, a cat might have killed a rabid bat, then transmitted the virus to a person, says Denny Constantine, a retired rabies researcher with the state of California and CDC. Supporting that idea is the fact that these deaths were caused by a virus linked to two species rarely seen around people.

The federal guidelines have sparked overreaction, observers say, such that many people get rabies shots—costing an average of $2000 a series—after simply being in the same room with a loose bat. "What has happened in many places is people have gone beyond [the CDC guidelines]," says Stephen Frantz, a disease-vector specialist with the New York State Department of Health. In 1998, for example, to comply with state and federal guidelines, 52 boys at a summer camp in New York were vaccinated against rabies after a bat flew through their cabins.

The bat researchers' statement warns that such overreaction can have "negative consequences for bats," many of which are endangered or in rapid decline, notes Merlin D. Tuttle of Bat Conservation International in Austin, Texas. Whenever a species is made out to be a public health threat, says Kunz, it counters conservation efforts. Declared Tuttle at a bat research symposium last October in Madison, Wisconsin: "This has set back conservation efforts by about 2 decades."

—CHRISTINE MLOT

Christine Mlot is a science writer in Madison, Wisconsin.

2001 BUDGET

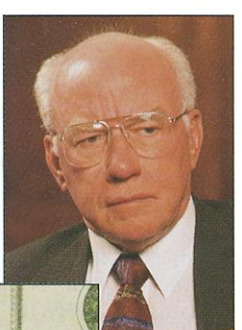
Austerity Push Begins A Bumpy Ride for R&D

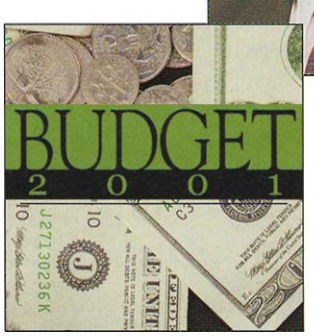
A booming economy, an enthusiastic president, and a supportive Congress should provide science and technology with safe passage through the turbulent annual budget cycle. That's the conventional wisdom. And while many budget watchers predict that science will eventually prevail, a bitter partisan battle now under way over government restraint in an era of surpluses is giving R&D advocates a collective case of the jitters. "It's going to be ugly," bemoans one congressional aide.

The weapon of choice among conservative Republicans in their battle against increased government spending is the budget resolution, a measure that sets overall funding limits within the one-third of the $1.8 trillion budget funded at Congress's discretion. Conservatives such as Senator Phil Gramm (R–TX) want to adhere as closely as possible to spending caps imposed when the government ran an operating deficit, while Democrats and the Administration argue for the need to increase spending on education and other domestic programs (*Science*, 11 February, p. 952).

The House took the first step down the 2001 budget road last week, narrowly passing a plan that would set discretionary spending well below the president's request. The Senate is still struggling with its version, which must be reconciled with the House in a process that Republican leaders have vowed to complete next month.

The House figure of $596 billion for discretionary spending exceeds Gramm's demand for a freeze at this year's level of $586 billion, and it is $45 billion over the scheduled cap. But Clinton requested $625 billion. And not only did the House cut the total, it also wants to boost the defense budget—which takes up slightly more than half of all discretionary spending. That will make it even tougher to fund the vaunted 17% increase for the National Science Foundation (NSF) and boosts for other civilian R&D agencies. "I think everyone should prepare for a bumpy ride again," warns Representative Jim Walsh (R–NY), who chairs the panel that funds NSF, NASA, and the Environmental Protection Agency.





Priority. Rep. Ehlers pleads for boost in researsh spending.

Even NASA's modest 3% requested boost could be in trouble. Representative Alan Mollohan (D–WV), ranking minority member on the panel, says his subcommittee "will have a hard time preventing another round of cuts in NASA's budget" despite strong support for its mission. The panel's priorities will be to fund hefty increases in housing and veterans' medical care, says aide Frank Cushing, who adds, "we need [more] dollars." The combination of increased defense spending and the push for more education funding will make it doubly difficult to repeat the 15% boosts of the past 2 years for the politically popular National Institutes of Health (NIH). And election-year politics may result in another year of legislative gridlock for the NIH appropriations bill. "We're paralyzed," complains one aide.

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