crobe's diabolical modus operandi.

Using a tissue culture system in which the microbe causes the same type of damage as in humans, the researchers found that two toxic substances produced by *B. pertussis* work together to kill the ciliated cells. One of those molecules, tracheal cytotoxin (TCT), has long been a suspect, but the other, endotoxin, is somewhat of a surprise. It is usually known for causing widespread immune system stimulation, which can lead to shock. "This is different," says Drusilla Burns, a microbiologist at the Food and Drug Administration's Center for Biologics Evaluation and Research in Bethesda, Maryland. "Endotoxin is not normally associated with specific pathology."

Even more surprising, the two toxins do not launch a direct attack on the ciliated cells. Instead, they work together to incite neighboring cells to produce a noxious molecule, nitric oxide (NO), which kills the ciliated cells by an as yet unknown mechanism. "This work might explain some of the pathology of *pertussis*," says Ferric Fang, a molecular biologist at the University of Colorado Health Sciences Center in Denver. And, he adds, it might also "provide strategies for intervention."

Such strategies are badly needed. In developed countries, vaccination largely holds whooping cough in check, but the incidence of the disease in adults appears to be increasing; in nondeveloped countries, *B. pertussis* still kills from 300,000 to 500,000 people every year. And although antibiotics eliminate the bacteria, by the time the characteristic cough develops, the microbes are often already gone, having set a cascade of destructive events in motion. Drugs that inhibit NO production might allow the tracheal epithelium to recover more quickly.

Earlier work by Goldman's group had shown that NO is involved in the attack on the ciliated cells and suggested that TCT acts as a trigger. But when the team tested whether TCT causes epithelial cells in cultured hamster tracheal tissue to activate production of an enzyme called inducible NO synthase (iNOS)—which makes NO—they got what Goldman describes as a "surprise result." TCT had no effect at all on iNOS production in epithelial cells. The researchers concluded that something in addition to TCT may be required to coerce the epithelium to produce NO.

Goldman and Flak suspected that this coculprit might be endotoxin, because the team had previously uncovered another case of TCT-endotoxin cooperation, in preventing the growth of a single type of respiratory epithelial cell in culture. It prompted the researchers to add endotoxin along with TCT to their culture system. The combination worked.

Because not all the cells in the tracheal epithelium are ciliated, the team wondered whether the ciliated cells themselves or their neighbors produce the NO. As Goldman recalls asking, "Are the ciliated cells committing suicide, or are they being assisted by other cells in the epithelium?" Further studies provided an answer: TCT and endotoxin induce the nonciliated, mucus-secreting cells to produce the toxic gas.

Goldman notes that both TCT and endotoxin are made by many other bacteria in addition to *B. pertussis*, although most of the other microbes recycle TCT rather than release it. "You've got almost an ironic situation," he says, "where you have this extraordinary specificity of pathology and of nitric oxide production" spurred by two extremely common molecules. Endotoxin and TCT might collaborate to kill other ciliated cells in the body as well. Work by Raoul Rosenthal's group at Indiana University School of Medicine in Indianapolis and collaborators suggests that *Neisseria gonorrhoeae* destroys ciliated cells of the reproductive tract using these same two molecules.

The researchers do not yet understand how NO kills the ciliated cells without harming the secretory cells that produce it. But, as Goldman points out, the strategy might be "exactly what [*B. pertussis*] needs," because it allows mucus to accumulate while eliminating the normal way for expelling it. The result is a hacking cough—an ideal way to transfer the bacteria from one person to another.

Many questions remain about how both NO and the TCT-endotoxin partners produce their effects. Researchers also need to find out whether *B. pertussis* operates the same way in humans. This might be addressed, says Erik Hewlett, a *B. pertussis* expert at the University of Virginia, Charlottesville, by seeing whether the iNOS expression patterns in trachea specimens from children who died from whooping cough mimic those seen in Goldman's experiments. If so, it might indicate that *B. pertussis* is putting its subversive tactics to work in environments other than the culture dish. **–EVELYN STRAUSS**

CREDIT: DSG

RESEARCH FUNDING

House Panel Cuts Space Science, NSF Budgets

Two weeks ago, NASA's leaders were popping champagne corks to celebrate the 30th anniversary of the "giant leap for mankind" on the moon and the recent launching of the x-ray telescope Chandra. Then last week, the atmosphere in NASA's Washington, D.C., headquarters turned funereal: On 26 July, the House Veterans Affairs–Housing and Urban Development (VA-HUD) appropriations subcommittee cut $1.4 billion, or more than 10%, from NASA's current budget. This carved a massive $640 million slice out of space science, threatening future Mars missions and the

ScienceScope

High-Tech Whipping Boy A federal program that funds high-risk industrial R&D is back in the congressional doghouse. Last week, House appropriators voted to zero out the 2000 budget of the Department of Commerce's Advanced Technology Program (ATP). House Science Committee chair James Sensenbrenner (R–WI) then piled on, calling reform efforts at ATP "a sham."

After much prodding from Congress, ATP in 1997 rewrote its rules to fund only those R&D proposals at companies that failed to secure private money for projects. But according to a new report from the Government Accounting Office, ATP officials still review initial proposals in which the prospects for private sector funding aren't spelled out.

ATP project for making semiconductor chips.

To Sensenbrenner, that means the reforms aren't working. ATP associate director Marc Stanley, however, says the program hews to its new line: Regardless of which projects ATP ends up reviewing, only those shunned by corporate financiers get federal dollars. The Senate has given ATP an easier go, allotting the program $226.5 million, nearly the full White House request; a House-Senate conference later this year will resolve the differences.

Darwin-Free Biology Kansas authorities are poised to approve a new set of science standards that eliminates most references to evolution. The decision is expected on 11 August, when the Kansas State Board of Education meets to approve wording of a text that has been the focus of a prolonged public battle.

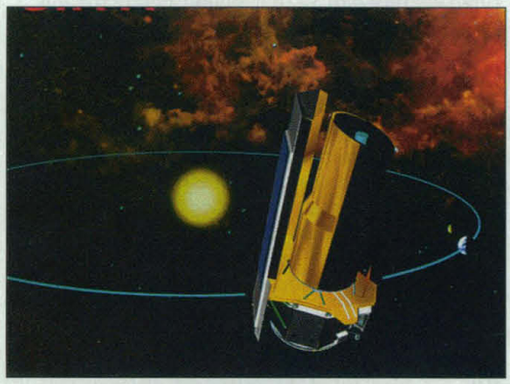
Several members of the 10-member elected board have fought to keep evolution out of the document, which will be the basis for statewide achievement tests. Religious fundamentalists on the board have recruited a six-member majority in favor of a version that deletes most references to evolution from the biology curriculum, says John Staver, director of the Center for Science Education at Kansas State University in Manhattan and co-chair of the committee that drafted the standards. If approved, the curriculum will leave individual school districts free to decide whether to include evolution in biology classes. "It's a sad day for public education and an embarrassment for the state of Kansas," Staver says.

Space Infrared Telescope Facility (SIRTF), scheduled for launch in 2001. In the same bill, the subcommittee proposed a $25 million cut (a reduction of 0.7%) in the budget of the National Science Foundation (NSF), with an $8.5 million (0.3%) increase for research.

A few days later, though, the full House appropriations committee repaired some of the damage. It added back $400 million to NASA's budget, rescuing SIRTF and the Mars missions, yet leaving NASA's total appropriation about 7% below the current level. No one mended the hole in NSF's budget, and researchers were left wondering where this turbulent process will leave them in the fall.

The cuts were necessary to stay within spending caps Congress adopted in 1997, which neither Congress nor the White House is willing at this stage to lift. "The allocation [for the fiscal year 2000 budget] was significantly lower than last year's budget, so we needed to find money," a subcommittee staffer told *Science*. Because the subcommittee didn't want to cut housing programs and intended to boost spending for veterans' medical care—both in the subcommittee's jurisdiction—"we only had limited choices, and NASA was our first choice," he adds.

Space scientists are still reeling. Carl Pilcher, science director for Solar Systems Exploration at NASA, says many felt the subcommittee's message was: "You're done; finish what's on your plate, close the shop, turn off the lights, and go home." Pilcher calls the vote "the most severe cut in NASA's 40-year history." Planetary scientist Steven Squyres of Cornell University in Ithaca, New York, the chair of NASA's Space Science Advisory Committee, agrees. The initial proposal "was a going-out-of-business budget for space science. Except for missions that are well on their way to the launch pad, it would have effectively zeroed out all future missions," he says.



Threatened. NASA's infrared space telescope SIRTF was cut by one House panel and rescued by another.

To repair the initial cuts in NASA's budget, the full appropriations committee shifted $400 million from the Corporation for National and Community Service (Americorps) to NASA. "I'm absolutely delighted about the $400 million, especially since it all goes into space science," says Squyres. But others fear that killing the national service corps will invite a presidential veto.

And although SIRTF survived, other space projects are still endangered. The "faster, cheaper, better" Explorer astronomy missions and the Discovery planetary missions, for instance, would be reduced by $60 million each. In addition, CONTOUR, a $50 million comet mission, would be canceled altogether. And the Research and Technology account would lose $100 million. Louis Friedman, executive director of the Planetary Society, warned in a statement that "the remaining cuts are still draconian and will throw NASA into turmoil."

NSF came through the ordeal clinging to a survival budget, but with future plans in tatters. Its strategy of bundling much of its requested $218 million increase into the Administration's multiagency $366 million information technology initiative was shot down by both the subcommittee and the full committee. The legislators gave NSF only $35 million of its $146 million request in that area and nothing for a requested $35 million terascale computer. Members were put off by the initiative's size, and they feared that any competition for the new machine would favor NSF's two existing supercomputer centers at the University of California, San Diego, and the University of Illinois, Urbana-Champaign. "Even if they had the money, they'd have wanted to phase it in," explains a House aide. "They also didn't want to let the haves get even further ahead."

Next, the VA-HUD bill moves to the floor of the House, where a vote could occur before Congress begins a recess this weekend. Although space science supporters may try to seek changes, "appropriations bills are hard to overturn," a Capitol Hill source says. "Right now the odds are with the bill passing" in the House. Then the process will begin all over again in the Senate, giving science lobbyists another chance. Says Squyres, "I don't think I've made my last visit [to Washington, D.C.] this summer."

–MICHAEL HAGMANN

With reporting by Jeffrey Mervis.

CELL BIOLOGY

Gene Linked to Faulty Cholesterol Transport

From a secluded island off the coast of Virginia in the Chesapeake Bay comes a genetic treasure that lay buried for centuries in the inhabitants and their descendants. This population carries a rare hereditary disorder, called Tangier disease—after the name of the island—characterized by a defect in cholesterol management that leaves the patients with yellow tonsils, oversized spleens, and scant amounts of the heart-protective high density lipoprotein (HDL) cholesterol in their bloodstreams. In the August issue of *Nature Genetics*, three groups now report that they have nabbed the gene at fault in Tangier disease—a discovery that not only sheds light on this condition, but may also lead to a better understanding of a much more common genetic deficiency that carries a high risk of heart attack.

The gene identified by the three groups, which were led by Michael Hayden of the University of British Columbia in Vancouver, Gerd Schmitz of the University of Regensburg in Germany, and Gerd Assmann of the Westlischen Wilhelms University in Münster, Germany, encodes a member of a large family of proteins that shuttle molecules into and out of cells. Although this particular family member, known as ABC1 (for ATP-cassette binding protein 1), had been unearthed before, researchers had not yet pinned down its exact function.

The new work suggests that ABC1 transports cholesterol from inside cells to the cholesterol-enveloping proteins waiting outside to carry it as HDL cholesterol particles to the liver for recycling back to cells in the body. Christopher Fielding of the Cardiovascular Research Institute at the University of California, San Francisco, who co-authored a *Nature Genetics* "News and Views" item on the three papers, notes that it's been 25 years since researchers learned how cholesterol gets into cells via the LDL receptor. But, he says, "this is the first time we know anything about how it comes out."

Even more promising is the finding by Hayden's team that defects in the *ABC1* gene also pop up in patients with familial HDL deficiency syndrome (FHA), a disorder characterized by low blood levels of HDL cholesterol and a high risk of coronary disease. That result could be "a bonanza," says cardiologist Dennis Sprecher of the Cleveland Clinic in Ohio. "There are piles of low HDL syndromes," he notes, and the new discovery raises the possibility of developing drugs that protect against heart attack by targeting ABC1 and thus increasing HDL cholesterol levels in the blood.

CREDIT: JPL/NASA