he says, the blast can spread "like a fire through a field of dry grass." The fungus has a harder time finding a compatible host in a mixed environment.

Martin Wolfe, a plant pathologist and research director of the Elm Farm Research Center, an organic farming research center in Hamstead Marshall, Newbury, U.K., supports the approach but notes that the mixture must be tailored to local growing conditions. "This is a useful tool," says Wolfe, who has written a commentary in the same issue. "But you can't just rush in and plant together anything you like."

The message from Zhu's study appears to be spreading through Yunnan Province, where this year 40,000 hectares were planted in the mixed pattern, he says. The payoff, he adds, is easy to measure for farmers: "more rice and more money." **–DENNIS NORMILE**

MICROBIOLOGY

A Weak Link in TB Bacterium Is Found

Easily the most successful human pathogen in the world, the bacterium that causes tuberculosis infects one-third of the world's population. Often acting in deadly combination with AIDS, TB kills 2 million to 3 million people per year, more than any other infectious disease. The secret of the pathogen's success is that it can linger undetected in the lungs for decades, hiding from the macrophages that aim to chew it up and spit it out. Now a team of researchers has uncovered a vulnerability in this resilient bug that suggests new ways to starve it out of its bolt-hole.

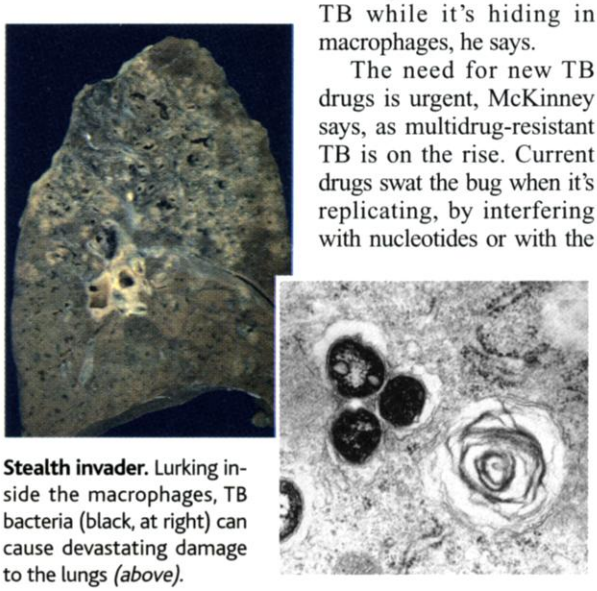
When *Mycobacterium tuberculosis* infects a person for the first time, it proliferates for a few weeks until the immune system marshals its defenses. The two then reach a stalemate, says John McKinney of The Rockefeller University in New York City, part of a four-institution team reporting its findings in the 17 August issue of *Nature*. This persistent state—the pathogen population doesn't increase, but the immune system can't get rid of the bacteria already ensconced—can last a lifetime, with the person suffering no obvious ill effects. But in 10% of those infected, TB will erupt into full-blown disease in response to various stresses or if the immune system is compromised.

During its latent days inside macrophages, the bacterium is stuck with a restricted diet: It eats carbon from lipids via a pathway called the glyoxylate shunt present in bacteria and plants. The TB bacterium also builds amino acids via the oft-memorized Krebs cycle, explains McKinney, but "we went after the glyoxylate shunt because it's the only [pathway the bacteria use for metabolism] not found in humans." Working with William Jacobs Jr. at the Albert Einstein College of Medicine in the Bronx, he created a knockout *M. tuberculosis* that lacks an enzyme called isocitrate lyase (ICL) that is critical for this pathway. Study collaborator David Russell of Cornell University in Ithaca, New York, discovered that ICL levels are elevated in *M. tuberculosis* when it's in its latent phase. Normal TB bacteria burrow into macrophages in mice and make themselves at home indefinitely, but McKinney's altered bacteria that can't produce ICL were wiped out by the animals' immune system.

"One of the things we don't understand is how *M. tuberculosis* can sit around in tissue for years or decades," says Jo Colston, an expert on microbial pathogenesis at the National Institute for Medical Research in London who was not involved in the study. "Obviously, if you can hit a protein that enables [the bacterium] to survive, that represents a potential therapy target."

McKinney and colleagues are searching for such compounds. In a second publication in the August issue of *Nature Structural Biology*, they describe the protein structure of ICL. They also identify two compounds that smother the active end of ICL and shut down the enzyme, thus preventing it from playing its part in the glyoxylate shunt. X-ray crystallographer James Sacchettini of Texas A&M University in College Station, a collaborator on both publications, says his group, working with research sponsor Glaxo Wellcome in the United Kingdom, will screen hundreds of thousands of additional compounds. Those that stymie ICL have potential to serve as drugs that can starve TB while it's hiding in macrophages, he says.

The need for new TB drugs is urgent, McKinney says, as multidrug-resistant TB is on the rise. Current drugs swat the bug when it's replicating, by interfering with nucleotides or with the

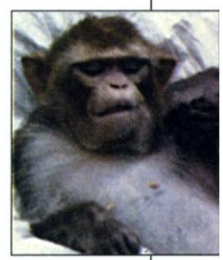


Stealth invader. Lurking inside the macrophages, TB bacteria (black, at right) can cause devastating damage to the lungs *(above)*.

CREDITS: (LEFT TO RIGHT) IMAGE FROM WEBPATH, COURTESY OF EDWARD C. KLATT; DAVID G. RUSSELL/CORNELL UNIVERSITY

ScienceScope

Defining Distress Plans by the U.S. government to change the way researchers characterize pain and distress in lab animals is drawing reaction from biomedical and animal-rights groups. In July, the U.S. Department of Agriculture (USDA) asked for comments on the new guidelines, which are supposed to help researchers spot and lessen discomfort in lab animals. Among other things, the plan defines "distress" as stress that has "negative effects on [an animal's] well being."



Last week, the Federation of American Societies for Experimental Biology (FASEB) said it would prefer a different definition, adopted by the National Research Council in 1992. It describes stress as "an aversive state in which an animal ... shows maladaptive behaviors." FASEB also wants practical rules that rely on the "professional judgement" of researchers and veterinarians.

The Humane Society of the United States and other groups, however, want USDA to adopt a Canadian-style scheme that ranks pain and distress into several categories, based on common lab procedures. "We need a scale with very clear-cut markers," says John McArdle, director of the Alternatives Research & Development Foundation of Eden Prairie, Minnesota. Other ideas may still surface, as USDA will receive comments until at least 8 September.

Orange Alliance At the urging of Senator Tom Daschle (D–SD), the National Institute of Environmental Health Sciences (NIEHS) is trying to team up with Vietnamese scientists to conduct studies of the health and environmental effects of dioxin. The chemical, implicated as a cause of cancer and other disorders, was present in the defoliant Agent Orange, which U.S. forces sprayed widely during the Vietnam war. Today, some Vietnamese carry tissue concentrations of dioxin that are up to 20 times higher than those found in people living in the United States.

This week, NIEHS gathered a group of epidemiologists and toxicologists in Monterey, California, to discuss research strategy and the resources needed to perform epidemiological studies in Vietnam. Later this year, NIEHS scientists plan to meet with their Vietnamese counterparts, with joint studies set to begin in 2002. "That is, assuming the Vietnamese are interested," says NIEHS's Chris Portier.

Contributors: Erik Stokstad, David Malakoff, John MacNeil

building of new cell walls, but they can't really harm the TB bacterium while it's inside the macrophage. As a result, even the most potent medications have to be taken for 6 months. Most people don't finish the whole course, a practice that promotes drug resistance. A treatment regimen that lasts only 2 weeks would greatly reduce that problem, says McKinney. But that will require a drug that kills *M. tuberculosis* while it's resting inside the macrophage. **–LAURA HELMUTH**

PLANETARY SCIENCE

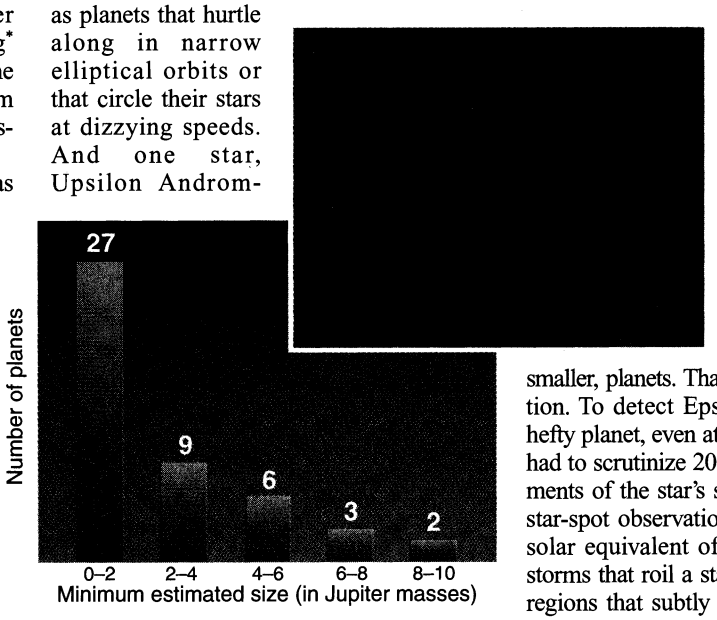
Newfound Worlds Hint At Hard-Knock Life

The art of planet hunting took a big step toward becoming a science last week, when three teams of astronomers announced nine newly discovered planets orbiting other stars. Headline grabbers from the meeting* included the lightest known "exoplanet," the one closest to Earth, the one farthest from its parent star, and the second extrasolar system to contain more than one planet.

To scientists, though, the real news was not novelty but numbers. As the roster nears 50, extrasolar planets are ceasing to be curiosities and turning into data. "They are coming in bunches now, and we can start to do real science," says astrophysicist Debra Fischer of the University of California, Berkeley. The expanded sample offers scientists the first real evidence that stars are fecund breeding grounds for worlds. But it also hints that the planetary nurseries may be hellish places to grow up. Some astronomers now suspect that most of the planets they can detect are veterans of ancient combat against hordes of rivals for a handful of stable orbits.

Until recently, astronomers had no clue that such celestial arenas existed. Inside our own solar system, planets trace out neatly spaced, near-circular orbits, with small, rocky bodies near the sun and cold, gaseous giants farther out. It's an arrangement that seems to have coalesced directly from the swirling pancake of leftover gas that encircled the newborn star. The first trace of mayhem came 6 years ago, when Michel Mayor and Didier Queloz of the Geneva Observatory in Switzerland spotted evidence of an exoplanet in the wavering light of 51 Pegasi. The planet was far too faint to be seen by telescope; picking an exoplanet out of the glare of its star is "like trying to find a firefly in the glow of a nuclear explosion," says Geoff Marcy, a planet-hunter at the University of California, Berkeley. Instead, Mayor and Queloz looked for indirect evidence of tiny stellar wobbles triggered by the gravitational tug of the planet. As the star oscillates toward Earth, its light Doppler-shifts to higher frequencies, analogous to the rising pitch of an approaching train whistle. By timing the shifts in frequency, the Swiss astronomers could infer the shape and period of the presumed planet's orbit and estimate its mass.

The planet they turned up was unlike anything astronomers had ever imagined. Its mass, half that of Jupiter, and circular orbit seemed ordinary enough. But the planet's location, a tenth as far from its star as Mercury is from the sun, was all but impossible to explain. Doppler searches of other stars added more "hot Jupiters" to the exoplanetary zoo, along with new oddities such as planets that hurtle along in narrow elliptical orbits or that circle their stars at dizzying speeds. And one star, Upsilon Andromedae, harbors three Jupiter-sized planets locked together in a fierce gravitational wrestling match.



Downsizing. The prevalence of lightweight exoplanets suggests that Epsilon Eridani's Jupiter-sized companion *(inset)* may herald smaller worlds to come.

The nine newly unveiled planets continue the trend. In light from Epsilon Eridani, only 10.5 light-years from Earth, Marcy's team found evidence of a Jupiter-sized body with an orbital radius of 478 million kilometers, the largest of any known exoplanet. Around a star called HD 83443, Mayor's team turned up a second planet, half as massive as Saturn, making it the second multiple-planet system outside our own.

Astrophysicists are still struggling to make sense of the extrasolar bestiary, but they will venture a few conclusions. Stars appear to be prolific planet factories, they believe, with lighter bodies outnumbering heavier ones. If the pattern holds, droves of even smaller planets are awaiting discovery. For another thing, multiple planet systems are probably common. Right now, the 49 known exoplanets are scattered among 46 different stars. But at the conference, Fischer presented evidence—tiny leftover fluctuations in the data—that suggests many of the apparent loners might have partners in their cosmic dance.

Some of those shadow partners could make the waltz of the planets look more like a mosh pit. The three planets orbiting Upsilon Andromedae, for example, are poised on the brink of chaos; if the system had even one more planet, interplanetary gravitational forces would tear it apart, sending planets shooting out into interstellar space. Astrophysicists say that such gravitational powder kegs are in a state called dynamic saturation. "If more systems are dynamically saturated, it probably means that planets formed in bunches and then shook out later," Fischer says. The star-hugging orbits and tight ellipses of many exoplanets, she adds, may be the remnants of such violent shake-outs.

So far, such ideas are still informed hunches. To confirm them, astronomers will need to track down more, and smaller, planets. That won't be easy, they caution. To detect Epsilon Eridani's relatively hefty planet, even at close range, astronomers had to scrutinize 20 years' worth of measurements of the star's spectrum and 34 years of star-spot observations. Star spots, the extrasolar equivalent of sunspots, are magnetic storms that roil a star's surface, creating cool regions that subtly alter the star's spectrum. On a young, magnetically active star like Epsilon Eridani, cycles of high and low star-spot activity can create a "false Doppler shift" that mimics or fuzzes the effect of stellar wobble. "I'd say there is a 75% chance that it is real," Marcy says about the purported planet.

The same problem stymies astronomers looking for low-mass planets. The solution is new methods and equipment, such as NASA's planned Space Interferometry Mission (*Science*, 25 September 1998, p. 1940) or the ground-based Large Binocular Telescope under construction in Arizona, which combine information from multiple telescopes to achieve the power of one much larger telescope. The Large Binocular Telescope will also incorporate flexible adaptive-optics mirrors to remove atmospheric distortions. Astronomers hope such devices will provide them with a firsthand glimpse of these rough-and-tumble planetary nurseries.

–MARK SINCELL

Mark Sincell is a science writer in Houston.

* International Astronomical Union 24th General Assembly, Manchester, United Kingdom, 7–18 August 2000.

CREDITS: (LEFT TO RIGHT) G. MARCY; R. MILLER