

VIROLOGY

Australia Fends Off Critic of Plan to Eradicate Rabbits

infractions by any employer whose work force is made up of at least 20% H-1B workers. That could include many university programs if officials classify individual departments or research grants as "employers." The investigations, which could be initiated even if no complaint had been filed, could bring normal departmental business to a standstill as administrators scramble to provide records and documentation, says Sands.

Still, another part of the Specter amendment is "certainly good for educational institutions," says Catheryn Cotten, international adviser at Duke University and its medical center. The language, first proposed by Senator Paul Simon (D-IL), would give universities more flexibility in setting an appropriate wage scale for foreign workers. That way, biologists at universities, for example, would not be locked into the higher wage scales paid by industry, as sometimes happens. With the Specter amendment, says Cotten, "we're not required to, in some cases, pay aliens more than we pay citizens."

Compared to a month ago, the immigration bill "certainly seems to be going in a more rational direction," says Chicago's Schramm. But some scientists who find themselves competing for jobs and fellowships with foreigners disagree. The original Simpson bill "encouraged employers to look down the street, in their own state, in their own country for workers" rather than going abroad, says Jennifer Cohen, a former researcher at Los Alamos National Laboratory who is teaching physics at Shippensburg State College in Pennsylvania. Cohen—who is also an organizer of the Network of Emerging Scientists, composed of researchers who are "emerging" into the job market after completing their degrees or being laid off from earlier jobs—says the Simpson bill is "the best thing we've seen at this time."

Day, for his part, says the universities' stance is partly "self-serving." Universities "want to have access to [foreign students]," says Day, because the students are reliable sources of tuition money. Schramm responds that Day's assertions "show a lack of understanding of how a research university works." In most cases, he says, "a faculty member's research grant would pay the tuition whether the [doctoral] student is foreign or domestic."

"What we're really concerned with," says Schramm, "is getting the best possible students to do the best possible research—independent of where they come from." Whether that attitude will have to change should become clear over the next few weeks on the floors of the House and Senate.

—James Glanz

GEE LONG, AUSTRALIA—Last spring the Australian government began a 2-year biological warfare experiment with a potent, imported virus. The target: wild rabbits, which have spread economic and ecological disaster throughout Australia. The plan was to study the natural course of the Rabbit Hemorrhagic Disease (RHD) virus, also known as Rabbit Calicivirus Disease, among a quarantined population of rabbits on tiny Wardang Island off the South Australia coast. If the deadly experiment was a success, the next step would be a large-scale release targeting the country's estimated 300 million feral rabbits, descendants of a dozen animals brought from Europe almost 150 years ago.

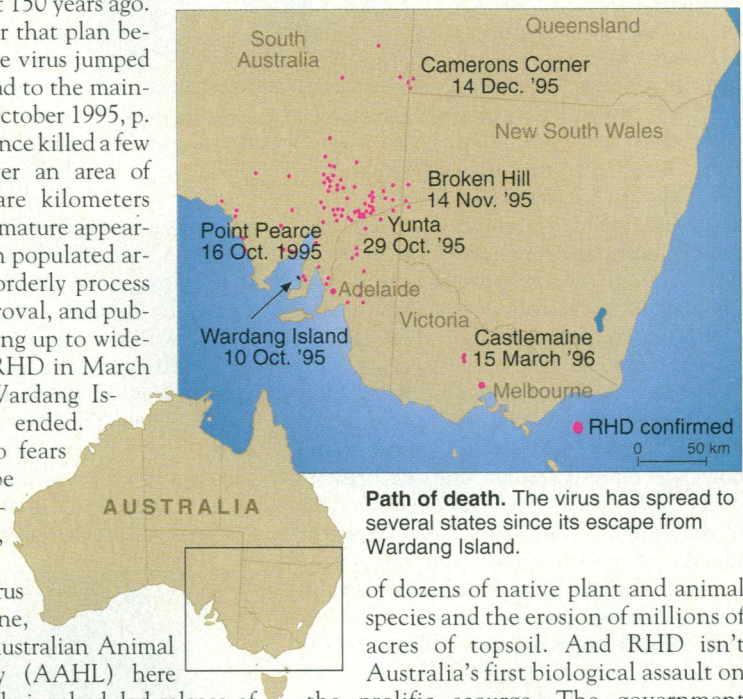
But last October that plan began to unravel. The virus jumped the fence and spread to the mainland (*Science*, 27 October 1995, p. 583), where it has since killed a few million rabbits over an area of thousands of square kilometers (see map). The premature appearance of the virus in populated areas precluded an orderly process of evaluation, approval, and public education leading up to widespread release of RHD in March 1997, after the Wardang Island experiment ended. And it has led to fears that RHD might be capable of infecting other animals, and even humans.

Now that the virus is out of quarantine, scientists at the Australian Animal Health Laboratory (AAHL) here want to move up their scheduled release of large quantities of RHD throughout the country, in the hope that it will deal a knockout blow before the rabbits have developed immunity. Three government regulatory bodies are expected to decide shortly whether it is safe to go ahead. John Anderson, minister of primary industry and energy, says that the government plans to proceed as early as next month if the Biological Control Authority, the Environmental Protection Agency, and the National Registration Authority approve RHD virus as a biological control agent.

As the government weighs the pros and cons, caliciviruses—an obscure research field with a relative handful of experts—have been elevated to a topic of intense public debate. Standing virtually alone in one

corner is virologist Alvin Smith of Oregon State University, an expert on caliciviruses, who accuses government scientists of moving too quickly into field trials without sufficient understanding of the virus. Lined up against him, by his own count, are some two dozen government agencies that have voiced support for using the RHD virus, along with a host of prominent virologists who discount Smith's warning of possible cross-species infection.

The stakes are high: The rabbits' ravenous appetite results in an estimated \$115-million-a-year loss to the native wool and meat industries, along with the decimation



Path of death. The virus has spread to several states since its escape from Wardang Island.

of dozens of native plant and animal species and the erosion of millions of acres of topsoil. And RHD isn't Australia's first biological assault on the prolific scourge. The government scored a temporary victory in the 1950s by releasing the myxomatosis virus, but its deadly punch weakened over time.

Smith, who has spread his message via press releases, Internet postings, interviews, and letters to top officials, says he chose to enter the fray in December after being angered by the "positive tone" of a local newspaper account of the virus's escape. "I thought I knew something about calicivirus that other people didn't know," he told *Science*. His initial press release warned that the Australian government is "playing with dynamite" because, he says, it hasn't demonstrated that the virus won't cross into other species, a charge that was repeated last month on the Australian *60 Minutes*. His

critique has fed stories in the Australian media about a "biological time bomb" that threatens public safety.

Not surprisingly, government officials have been quick to rebut Smith's charges. Within 24 hours of his first press release, for example, Keith Murray, head of the AAHL conducting the experiment, issued a statement "correcting misinformation by an overseas veterinarian." In addition, virologists around the world say Smith's attacks are off-base and that the science behind the trial is solid. They say they're not surprised the virus has been confined to the European rabbit (*Oryctolagus cuniculus*) because there's no reason to think RHD affects other animals.

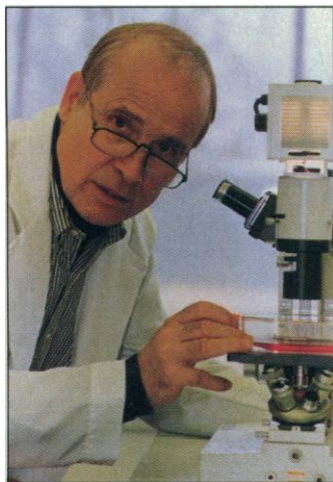
Smith is one of a small number of researchers working on caliciviruses, a family of small RNA viruses. Of the five groups based on genetic makeup and replication strategies, Smith has worked most extensively on marine caliciviruses, in particular San Miguel Sealion Virus (SMSV). His lab found that SMSV is capable of jumping to other species, something he believes is relevant to RHD. "There are many things we don't yet understand about calicivirus," Smith says. "But their hallmark is that they are not host-specific."

But several prominent virologists reject his claims. "The Australians have done an incredible amount of work to prove this virus does not represent some untoward risk to other species," says Frederick Murphy, dean of the school of veterinary medicine at the University of California, Davis, and former director of the U.S. National Center for Infectious Diseases in Atlanta. "Smith's idea that all caliciviruses behave like SMSV is speculation without any data. That's not the way taxonomy works. You have to regard each virus separately, and the data on the rabbit virus is that it's not infecting [other animals]." AAHL scientists inoculated 28 different animal species with the RHD virus and found no evidence of infection, for example. In addition, there have been no reports of human infection in rabbit-consuming countries, even after natural outbreaks of the disease in Mexico, China, and Europe killed millions of rabbits.

Retired virologist Frank Fenner, a recent recipient of the Copley Medal of the Royal Society for a lifetime of work in the field that includes chairing the committee on global eradication of smallpox, notes that each virus is unique, with host cell surface receptors that determine its specificity. SMSV has a

structure with "a naturally broad host range," he says. "It isn't that it suddenly changed its nature to infect other animals."

Smith has repeatedly criticized Australian scientists for proceeding to field trials despite the failure of scientists around the world to grow the virus in vitro. (The virus is grown in rabbits and then harvested and processed for use as a biological agent.) And he

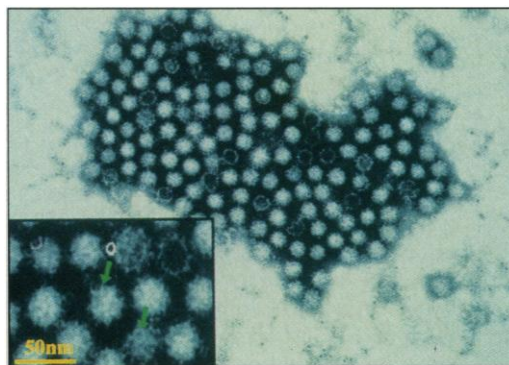


Explosive talk. Calicivirus expert Alvin Smith says officials are "playing with dynamite."

says that the dosage used in animal tests to measure their susceptibility to infection was too low to rule out a reaction at a higher level. "A thousand infective doses is a pretty pitiful, small, infective dose for any virus you're dealing with, actually," says Smith, who says he regularly gives dosages a thousand times higher.

But Michael Studdert, a virologist at the University of Melbourne and a member of an international taxonomy panel on caliciviruses, says that "if any of the target species had been susceptible, [the level used] would have been a reasonable dose." AAHL's senior veterinary virologist, Harvey Westbury, adds that if dosages are too high, researchers can artificially "force a response" from any test animal without causing actual infection.

Westbury says the failure to get the RHD virus to grow in cell culture isn't a valid reason for delaying field tests: "Undoubtedly, in vivo is preferable to in vitro for testing the susceptibility of an animal to a virus." Notes Fenner, "You'll find that viruses can infect cultured cells for a number of different spe-



The killer. The calicivirus's name comes from the cuplike projections on its surface. Shaded areas are complete virions.

cies, but they won't infect the intact animal."

AAHL officials admit that they have been slow to publish dosage data and that they failed to anticipate the escape of the virus. They still cannot identify what caused it to

leave the island, although bush flies feeding on rabbit carcasses are suspected. And they plead guilty to a bit of spin control: They acknowledge that attempting to use the term Rabbit Calicivirus Disease instead of RHD, to make the virus seem more innocuous, was an ill-conceived public relations ploy. But semantics aside, they defend the science underlying the trial. "We stand by our investigations and conclusions," says Murray.

Even scientists and organizations that Smith suggested *Science* should contact shy away from endorsing his arguments. "At this point there is no evidence that the agent has affected people clinically, nor has it affected other species," says virologist James House of the U.S. Department of Agriculture's Plum Island (NY) animal disease lab. The lab has even invited Smith to work with the RHD virus in its Level 3 containment facility—the only place in the country where such research could be done—but Smith says that he "wouldn't want to burn a year on it" because the virus is not a problem in the United States.

At the same time, Rockefeller University virologist Steve Morse says the inability to predict which species a virus can infect by looking at its genetic makeup prolongs the debate. "There's no evidence that it can [affect more than one species]," he says. "But it's still anyone's guess as to how this all will turn out," adds Morse.

If the regulatory bodies give their approval, the government has two primary options: observe the natural progression of the escaped virus, or speed up the process by releasing massive amounts of the virus, along with an aggressive campaign of traditional control measures such as hunting, trapping, and destroying rabbit warrens. Because feral rabbits are Australia's number one pest, the scales seem to be tipped in favor of intervention. "We have to weigh the [potential] risk of a virus which might cross over to other species against the inevitability of losing more of our native species," says ecologist Brian Cooke of the Commonwealth Scientific and Industrial Research Organization (CSIRO).

In the meantime, Smith's campaign—including press releases, interviews, and letters to the prime minister and other high officials—has drawn a sharp responses from his scientific colleagues. "The [virus's] escape from Wardang Island got the media in a frenzy," says Studdert. "But one didn't expect the same reaction from our scientific colleagues." Smith is unrepentant, however: "There needs to be more discussion of this, and I'm just bringing this to everyone's attention."

—Dan Drollette

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