ECOLOGY

Australian Pest Control by Virus Causes Concern

Australia has a problem with European imports. No, not a flood of cut-price Michelin tires or Gucci loafers—rabbits and foxes. Soon after the British brought the English rabbit (*Oryctolagus cuniculus*) and European red fox (*Vulpes vulpes*) to the island continent in the mid-1800s (the rabbits for food, the fox to be hunted) people realized they'd made a mistake. The rabbits multiplied like—well, like rabbits, and began munching and burrowing in farm fields, pastures, and forests, leaving a trail of ruined crops and environmental destruction. The predatory foxes, meanwhile, turned their voracious attentions on native animals. So far, they've been implicated in the extinction of 20 species of local marsupials.

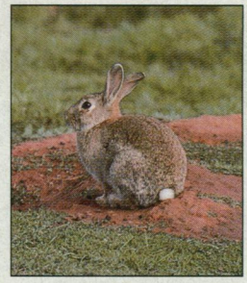
A. G. WELLS/FRPS, EFIAP, AAPS

Australians have tried to stop them, but after 110 years and more failed control attempts than anyone cares to count, Aussies are ready to try a new—and controversial—method of attack: using a genetically engineered virus to go after the pesky animals before they are even conceived. The Cooperative Research Centre for Biological Control of Vertebrate (VBC) Pest Populations (a government and university consortium) plans to release genetically redesigned viruses that will sterilize most foxes and rabbits by tricking the females' immune systems into attacking male sperm.

Even those who are carrying out the project are concerned about this venture into unknown territory. "No country has ever tried to manage a pest species on this scale or in this way before," says Mark Bradley, a reproductive immunologist and project leader of the VBC's fox program. "It raises questions across disciplines, from virology to immunology to the animals' social behavior and ecology. And we're trying to answer them all." Answers to these questions are crucial, since critics of the project aren't pleased with the idea of releasing live, infectious viruses. "We're concerned about a live vector that might get into other species and has the potential to travel abroad," says Bob Phelps of the Australian Gen-Ethics Network, a citizens' watchdog group. On the other hand, if the project is successful—and safe—it could provide a model for wiping out pests in other fragile, threatened habitats such as Hawaii and New Zealand.

The plan for the rabbits has raised critics' hackles, since it involves modifying a live, infectious myxoma virus. The virus, which only infects rabbits and hares, was first brought to Australia from Europe by scientists 40 years ago in an early effort to eradicate the rabbits. Although the virus initially felled 99% of the rabbit population, some rabbits proved resistant, and the virus itself later mutated into a benign form and the rabbits rebounded. But VBC researchers are again trotting out myxoma to create their immunocontraceptive, this time as a "Trojan Horse," says Michael Holland, leader of the rabbit program. By inserting one of the rabbit's sperm proteins into the virus, the team hopes to trigger an immune response in female rabbits—essentially tricking their immune systems into producing antibodies against the sperm proteins at the same time that they produce antibodies against the viral proteins. These antibodies will mark any sperm they later encounter as an invader to be destroyed.

M. P. BRADLEY/CSIRO



M. P. BRADLEY/CSIRO

Pest control. Australians plan to use viruses to sterilize the red fox *(above)* and the rabbit *(right)*, saving endangered marsupials like the numbat *(top left)*.

Last year, the Australian government's biotech watchdog agency, the Genetic Manipulation Advisory Committee (GMAC) approved in vivo laboratory tests of the VBC's first recombinant myxoma virus—although this is not a contraceptive, but a test-recombinant to demonstrate that the virus can be successfully tinkered with. Ron Jackson, a molecular virologist in Holland's group, inserted the gene for the hemagglutinin (HA) protein of the influenza virus into the myxoma virus, then injected the recombinant into laboratory rabbits. "We wanted to demonstrate that the myxoma virus will accept foreign DNA, and that the rabbits will produce antibodies to the antigen—which they do," says Holland.

The next step is to insert a rabbit sperm antigen into the myxoma virus. And that step isn't too far away, according to the researchers. "We've identified our first sperm candidate and are cloning that gene now," says Holland, who hopes to receive GMAC approval to put it in the virus within the next year for laboratory testing.

On the fox side of the combined program, researchers have for the moment chosen to forego developing a live viral vector. "We haven't yet identified a fox-specific virus," Bradley says, explaining that without such a virus the chances of inadvertently sterilizing dingoes (Australia's wild dog) and domestic dogs are just too great. Instead, his team is evaluating two approaches, both of which involve hiding the immunocontraceptive in bait. In the first approach, Bradley intends to package fox sperm proteins in biodegradable microspheres; the second strategy involves engineering a recombinant vaccinia virus that contains a gene that produces a fox sperm protein. Once the foxes are inoculated, they should make antibodies against the proteins.

The key aspect of the program is the simultaneous sterilization of both species, Bradley and others believe. Since the rabbits are the main item on the foxes' menu, any sudden population crash in the rabbits will force the foxes to seek alternative fare—the likely choices being small, endangered marsupials such as the numbat (*Myrmecobius fasciatus*—a squirrel-like insectivore), the woylie (*Bettongia penicillata*—a rodent-like creature that hops on its hind legs), and the black-footed rock-wallaby (*Petrogale lateralisn*—a sort of miniature kangaroo). Even with the rabbits still around, foxes have done a lot of damage to these animals, but in regions cleared of foxes, ecologists have found, marsupial populations readily bounce back.

But many critics contend that the project could take other, unexpected bounces. Perhaps the most disturbing possibility, and the one that has been raised by members of the VBC's citizens' advisory board and researchers at the World Health Organization, is that the redesigned myxoma virus could escape Australia and sterilize rabbit populations elsewhere. "This could be very useful for Australia, but Australia is not a separate part of the world," says Michel Aubert, a virologist and epidemiologist at France's Ministry

of Agriculture in Nancy. "The main proof of this is that rabbits and the myxoma virus are not native there. So, if the rabbit and virus have traveled to Australia, you could say their return ticket has already been bought."

The researchers at the VBC contend, however, that while myxoma proved a faulty weapon in their earlier rabbit wars, it has never escaped—not even to New Zealand. Nor has the virus ever infected species besides rabbits and hares. Researchers contend that new myxoma strains have tremendous difficulty establishing themselves in new areas and that they tend to be pushed out by local varieties. Hugh Tyndale-Biscoe, the director of the VBC, believes that the team's "biggest problem will actually be getting the thing to take in the rabbit, not stopping it."

But playing with animal populations raises questions that go beyond concerns about researchers' ability to control a virus. Even with immunosterilization, the foxes will only reach a certain reduced population level—although what that level might be, and whether it will be low enough to stimulate a resurgence of marsupials, is currently unknown. That leads to another worry. In some habitats, foxes live in groups that have several females, but only the dominant female breeds. What if the sterilization somehow alters the foxes' social structure so that subdominant females begin bearing litters? Would that trigger a population boom, following the initial bust?

Such unanswered questions make the Australian plan a gamble. In the hopes of reducing the odds, and further understanding the animals' reactions to population flux, the researchers have begun field experiments using surgically sterilized animals to mimic the hoped-for effects of the immunocontraceptives. But they have every intention of going forward with the program once the data come in and GMAC gives its approval. By 1995, they hope to have permission to put the recombinant virus in a lab rabbit for testing.

If the doubters can be silenced, and the scheme works, then it might be adapted for controlling non-native species that are devastating environments such as Hawaii, where feral pigs are wreaking havoc, and New Zealand, where introduced possums are causing trouble. The U.S. Department of Agriculture is cosponsoring an international conference on immunocontraception in wildlife management in Denver in October; the Australians will be there to present their research. But if the plan doesn't work, and pest populations start to explode after crashing or the virus gets out from down under, Australians could be facing a new ecological crisis just as severe as the one they're trying to end.

–Virginia Morell

COSMOLOGY

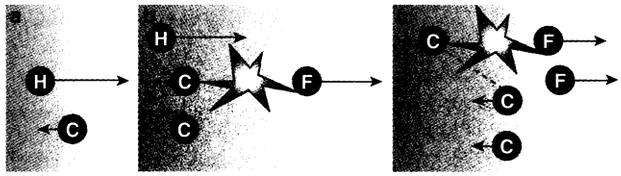
Hot and Cold Dark Matter on Tap

Lately, cosmologists have been turning the birth of the universe into a computer video game. They populate space with various sorts of particles, set the cosmic density and other parameters, then run a movie of the Big Bang and the subsequent expansion. The winning simulation is the one that blows up to look something like the observed cosmic macrostructures—"walls" and "filaments" of galaxies—and does so with as few never-before-seen particles or other arbitrary, ad hoc ingredients as possible. Now a team from the Canadian Institute for Theoretical Astrophysics has devised a way to boost the standing of a favorite strategy.

The innovation involves a modification of a key ingredient of the simulations: "dark matter," hypothetical, invisible particles that contribute their gravitational pull to creating structure in the universe. Many cosmologists can swallow the idea of one type of mystery particle, but the simulation that comes closest to recreating the structures seen in today's universe requires not one but two types of dark matter: "hot" particles that move near the speed of light and "cold" particles that move far more slowly. In this week's *Physical Review Letters* Nick Kaiser, Robert Malaney, and G. Starkman propose a remedy for this distasteful requirement: They add just one mystery particle, which does the job by spontaneously breaking down in two stages to create a hot and cold cosmic cocktail.

To get the needed bang out of a single particle, it has to be both massive and unstable. The original candidate of such a monster emerged in 1991, when several groups thought they saw signs of a new kind of neutrino, with a mass of 17 kiloelectron volts instead of the unmeasurably small mass of ordinary neutrinos (Science, 18 December 1992, p. 258). Cosmologist Jes Madsen of the University of Aarhus suggested that this particle might break down into hot and cold dark matter.

By now, "the 17 kev neutrino is dead," admits Kaiser. But that doesn't mean that some type of heavy neutrino is out of the question. His group speculates that the newborn universe was aswarm with massive neutrinos that, within the first second after the Big Bang, could have broken down in two steps, the first step creating the cold matter, the second, the hot.



Chain reaction. In the newborn universe, the cold dark matter particles (C) released—along with a byproduct (F)—by the decay of heavy neutrinos (H) might have triggered successive decays.

The first step is called "neutrino lasing" because it creates cold particles in a chain reaction analogous to the way a laser makes photons. In a laser, a group of atoms must be pumped into an energized "excited" state. When one randomly breaks down to a more stable form, it emits a photon that triggers other atoms to break down. As this cascade continues it ultimately releases many photons with precisely the same energy. In neutrino lasing, the heavy neutrino acts as the excited atom, and it breaks down into a more stable neutrino-like particle and a hypothetical dark matter particle, of unspecified type, which like a laser's photons triggers emission of more dark matter particles.

The lasing step emits dark matter of the cold variety, explains Kaiser, for the paradoxical reason that the newborn universe is so hot that the heavy neutrinos move at close to the speed of light. When the fast neutrinos decay, "the situation is rather like what would happen if one exploded a grenade on the back of a rapidly moving truck." To an observer on the roadside, he says, the grenade fragments that sprayed out behind the truck might appear to move much slower than the truck itself.

The lasing makes all the particles come out with the same energy as the one that sets off the cascade, so one cold particle could produce a whole swarm of clones. The hot matter comes out later, when the universe cools too much to sustain the remaining population of heavy neutrinos. These break down, without lasing, into hot dark matter.

This two-stage scenario, says Fermilab cosmologist Michael Turner, is "a very cute idea." But he points out that the best mixed dark matter models require a 70-30 mix of cold to hot matter, while the Canadians' recipe yields at most a 50-50 ratio. And Turner says he isn't even sure of the premise of mixed dark matter in the first place. Turner prefers unadulterated cold dark matter—which doesn't come out quite as well in the simulations but is simpler, requiring fewer fancy ingredients and preparation methods. Besides, he says, it might be close enough. "We've learned over the last decade," he says, "that computer simulations are less reliable than we thought."

–Faye Flam