How oral vaccines could save Ethiopian wolves from extinction

One-Health focused mass vaccination programs could go wild in 2018

BY HELEN THOMPSON
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Deep in the Bale Mountains of Ethiopia, wildlife workers trek up above 9,800 feet to save some of the world’s most rare carnivores, Ethiopian wolves.

“It’s cold, tough work,” says Eric Bedin, who leads the field monitoring team in its uphill battle.
In this sparse, sometimes snowy landscape, the lanky and ginger-colored wolves (*Canis simensis*) reign as the region’s apex predators. Yet the combined threats of rabies, canine distemper and habitat reduction have the animals cornered.

Bedin and his colleagues, traveling by horse and on foot through dramatically shifting temperatures and weather, track these solitary hunters for weeks at a time. Team members know every wolf in most packs in these mountains. The team has vaccinated some wolves against rabies, only to have hopes dashed when the animals died of distemper months later.

“These guys work their asses off to protect these wolves,” says Claudio Sillero, a conservation biologist at the University of Oxford who heads up the Ethiopian Wolf Conservation Programme, of which the field monitoring team is an integral part. Down the line, humans stand to benefit from all this work too.

Sillero and his colleagues have been at this for 30 years. They’ve seen four major outbreaks of rabies alone, each leaving dozens of carcasses across the highlands and cutting some populations by as much as 75 percent.

Today, fewer than 500 Ethiopian wolves exist — around half of them in the Bale Mountains. A new oral rabies vaccine program aims to give the endangered animals a fighting chance. It may be their best hope for survival, Sillero says.

Later this year, if all goes well, oral vaccines hidden in hunks of goat meat will be scattered across wolf ranges and eaten by the animals. One dose every two years should bolster immunity against rabies among these iconic animals immortalized on several of their country’s postage stamps.

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Ethiopian wolves live in packs of up to 20 individuals. Packs meet up for morning, noon and evening socializing and border patrolling.

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**One Health**

Vaccinating endangered animals en masse in the wild is rarely attempted. Making the case for vaccination takes years of testing. And even when the case is strong for stepping in, the tools needed to vaccinate wildlife aren’t often available, says Tonie Rocke, an epizootiologist with the U.S. Geological Survey in Madison, Wis. On the opposite side of the globe from Bale, on North America’s Great Plains, Rocke’s lab is testing an oral vaccine to protect prairie dogs and endangered ferrets from plague.

A recent synergy has made these new oral vaccine efforts possible: improvements in vaccine technology (developed for humans and domesticated animals) and growing public and scientific interest in “One Health.” The conservation buzzword refers to efforts to help one species that also benefit others, including humans.
The researchers pushing for a green light in Ethiopia point to the one shining success in oral vaccines for wild animals, and to its One Health benefits. From 1978 to 2010, oral vaccines sprinkled across parts of Europe eliminated rabies in red foxes. Europe’s rabies cases in humans and other animals dropped by 80 percent from 1984 to 2014. But rabies is still common in certain parts of the world, including Ethiopia. Worldwide, more than 59,000 people die from the disease each year.

Successes on the plateaus of Bale and the prairies of North America could open the door for other vaccines to protect threatened species. Vaccines against Ebola in great apes and white-nose syndrome in bats are in the works.

But introducing vaccines into natural environments is a hard sell and can come with controversy and unexpected consequences.

Lay of the land

Over the last 20 years, two Ethiopian wolf populations have died out; another disappeared early in the 20th century, historical evidence suggests. Modern oral vaccines could save the remaining six populations from a similar fate.

A last resort

To the average U.S. vet or dog owner, vaccination is a no-brainer. But for endangered species, the stakes are high. Some conservationists are reluctant to intervene with disease-preventing vaccines in the wild, says Karen Laurenson, an epidemiologist and veterinarian with the Frankfurt Zoological Society.

Disease has its place in ecosystems. It can control population levels and put pressure on species to develop natural resistance, says Laurenson, who started working with the wolf project in the mid-1990s. Using a vaccine to take a disease out of the mix could leave a population vulnerable to future outbreaks should the vaccine become ineffective or stop being used. In an ecosystem with multiple power players, one vaccinated predator could gain an unnatural advantage over its competitors.

Some vaccines also bring direct risks. Injectable vaccines often require trapping the animal — a costly endeavor that’s stressful and dangerous for both wild animals and the humans doing the vaccinating. Oral vaccines could be scooped up and eaten by other animals. Plus, for an oral or injectable attenuated vaccine, which contains a living but harmless version of a virus, there’s a slim possibility that evolutionary pressure could eventually drive the virus, now distributed through the population, to become lethal again.

Because room for error is slim for a species on the brink of extinction, most instances of vaccine use have been limited to emergency responses during ongoing outbreaks.
Projects that don’t go well can have lasting repercussions. In 1990, researchers tried to vaccinate some packs of endangered African wild dogs (Lycaon pictus) in Tanzania and Kenya against rabies, assuming the disease was behind a recent dip in numbers. Every dog in the study died. The stress of getting vaccinated, shot by dart from a distance, may have made the dogs more susceptible to disease, though that theory was never proven. The incident increased skepticism about vaccines and caused some African countries to tighten vaccine regulations. “It left a terrible legacy,” says veterinarian Richard Kock of the University of London.

The long game

The uphill battle faced by Sillero’s team involves more than the challenges of canvassing the Ethiopian highlands. Making a case to government officials that oral vaccines are necessary conservation tools took decades of fieldwork, genetic testing and meetings upon meetings. “The credit really goes to Claudio and the others for persisting,” Laurenson says. “Even when the doors have been shut, sometimes they’ve kept banging.”

Sillero arrived in Ethiopia in 1987 to study the wolves. A rabies outbreak hit in late 1989. Just as it does in dogs and humans, the disease attacks a wolf’s brain, causing aggressive behavior and, eventually, death. Canine distemper appeared in 1992. Marked by severe diarrhea, vomiting and coughing, the disease appears to hit wolves harder than dogs, Sillero says. The Ethiopian packs have faced four more major flare-ups of rabies and two of distemper. Two of the eight populations of wolves he came to study have gone extinct in that time.

On alpine plateaus across Ethiopia, local monitors like Muzeyen (pictured) follow the ups and downs of every pack, staying on the lookout for potential disease outbreaks.

“This is a human-caused problem, not a natural dynamic,” Laurenson says. Each year, shepherds and farmers move higher up into the wolves’ habitat, bringing grazing livestock. These people also bring domesticated dogs — the primary carriers of rabies and canine distemper (SN Online: 9/30/16). In one area of Ethiopia, wolf habitat shrunk by 34 percent from 1985 to 2003. Islands of wolf populations persist in remote highland areas surrounded by oceans of free-ranging dogs.

Vaccinating the wolves was plan B, after the lower-risk approach of vaccinating domestic dogs didn’t cut it. Because the dogs roam far and wide, dog vaccination programs didn’t reach enough animals to generate prolonged protection and prevent outbreaks in wolves. “I’m sure we were improving the situation and reducing the chance of spillovers in wild carnivores, but we weren’t preventing them altogether,” Sillero says.

Going with oral vaccines was plan C. In 2003, the government approved use of an injectable vaccine only in response to outbreaks. Sillero’s team first had to collect samples and send them to international labs...
to confirm that an outbreak was happening. The researchers were always behind. An oral option that proactively protects the animals started to sound like a smart way to go.

**Deliver the dose**

On paper, the wolves look like good candidates for an oral vaccine intervention. Few other animals brave the highlands habitat, so the odds are low that a vaccine distributed in bait would get eaten by the wrong creatures. And not vaccinating is arguably riskier than making the effort. Consecutive rabies and distemper outbreaks recently cut one of the smallest known wolf populations down to two individuals, Sillero’s team reported in December in *Emerging Infectious Diseases*.

The Ethiopian team chose to test an oral rabies vaccine, called SAG2, that had been used successfully in red foxes. Twenty million baits had been dropped across Europe with no vaccine-induced rabies cases or reported deaths. SAG2 also passed safety tests in a slew of different species, including African wild dogs. “That work was absolutely fundamental,” Laurenson says.

Researchers tested oral rabies vaccines hidden in raw goat meat, boiled goat intestines and dead grass rats. Raw goat meat (shown) enticed wolves the most.

Getting the vaccine into the animals is the trickiest part. Animals have to bite into the bait to puncture an internal packet that contains the vaccine, rather than swallow the bait whole. “You've got to make the bait such that the [wolf] would chew it,” says Anthony Fooks, a vaccine researcher who runs a U.K. government lab that handles sample tests for the wolf project.

So Sillero and his team launched a series of pilot studies of an oral SAG2. “We set up cafeteria-type experiments, with different baits and delivery methods,” Sillero says. The researchers dropped 445 baits in locations around Bale. Hiding the vaccine in goat meat and distributing the goods at night worked better than other options, the team reported in 2016 in *Vaccine*. Of 21 wolves trapped a couple of weeks later, 14, or 67 percent, carried a biomarker showing the vaccine was in the wolf’s system. Of those, 86 percent had developed immunity against rabies. The impact on other wildlife was low: Only a few raptors snatched up vaccines meant for the wolves.

With all that data in hand, Sillero’s team finally won over Ethiopia’s Wildlife Conservation Authority in December, receiving an official thumbs-up to move forward. This month, 4,000 vaccines arrived; the mass vaccination program could get off the ground this summer.

It’ll be the first mass oral vaccination program to target an endangered species in the wild. The basic plan: Distribute the oral vaccines at night once every two years, vaccinate at least 40 percent of a chosen wolf population and use motion-sensing cameras to see if each pack’s high-ranking males and females — the primary pup producers — take the bait. It’s important to keep the top producers healthy.
vaccinated, so they can survive outbreaks and breed pups the next season.

Drones and peanut butter

Having a readily available oral vaccine for the wolves was a lucky break for the researchers in Ethiopia. A research team in the United States had no such luck. Tonie Rocke and her colleagues had to develop their own oral plague vaccine for prairie dogs. The team devised a raccoon poxvirus that produces plague proteins once inside the prairie dog body. The proteins train the immune system to fight the plague-causing Yersinia bacteria.

Saving plague-ridden prairie dogs (Cynomys spp.) is an indirect way to protect the real target: an endangered predator, black-footed ferrets (Mustela nigripes) of the Great Plains. The ferrets survive on a diet of mostly prairie dogs and had nearly gone extinct in the 1970s due to centuries of habitat loss, prey declines and plague.

Endangered black-footed ferrets (left) catch plague from eating sick prairie dogs, which in turn catch the disease from fleas. Peanut butter–flavored oral vaccines delivered near prairie dog homes across the Great Plains could give the ferrets a shot at a comeback — and even save some at-risk prairie dogs (one at right, holding bait).

On top of captive breeding and reintroduction programs to keep the ferret species afloat, the U.S. Fish and Wildlife Service traps and vaccinates wild ferrets directly. But it’s not enough.

Rocke and her colleagues went ahead and developed a peanut butter–flavored oral plague vaccine. They distributed it by drones and four-wheelers in small test plots in seven states to limit prairie dog carriers. (Plague can threaten prairie dog populations too, so everybody wins.)

Last June, the researchers published the results of these successful small-scale field trials in EcoHealth. A prairie dog’s odds of surviving in plague-ridden areas just about doubled. And the peanut butter pellets were as good at reducing plague levels as traditional insecticides that kill plague-carrying fleas. It’s unclear just how many prairie dogs in colonies need to be vaccinated to protect the ferrets from plague.

Getting the vaccine approved wasn’t as tortuous as it has been in Ethiopia. Collaborators at Colorado Parks and Wildlife already had a cheap way to make the baits, and in 2017, Colorado Serum Company licensed the product through the U.S. Department of Agriculture.

This year, Rocke hopes to conduct larger-scale field trials to determine the levels of immunity required for success in a mass vaccination. Ultimately, the application will be limited — just selected populations of prairie dogs that are either in ferret territory or endangered themselves, such as the Utah prairie dog (C. parvidens). Plague infects a handful of humans and domesticated animals each year as well, and the team is looking into using the vaccine in areas where humans spend time, like national parks.

SPECIAL DELIVERY Normally, plague vaccine baits might be delivered on foot — dropped by hand in the vicinity of
Encouraging others

Success for one species could be good news for others. Similar preventative strategies might work in other threatened animals, including other members of the dog family dealing with rabies and ungulates like zebras at risk of catching anthrax while grazing. Researchers are testing preventative vaccines to protect wild Hawaiian monk seals from a seal-specific distemper virus.

Oral vaccines aren’t the only nontraditional delivery method. Rocke’s lab is working on a topical vaccine against white-nose syndrome, which threatens bats (SN Online: 3/31/16), and one to combat rabies in common vampire bats (Desmodus rotundus). Vampire bats in particular nuzzle each other during social grooming. “It’s an easy way to get the vaccine distributed amongst members of the colony,” Rocke says.

In October in PLOS Neglected Tropical Diseases, her lab reported that the vaccine works in captured big brown bats (Eptesicus fuscus), but it still hasn’t been tested in vampire bats, key rabies carriers in South America. Rocke and colleagues hope to start trials in vampire bats this year in Mexico and Peru.

Great apes can fall victim to some of the same pathogens as humans, such as measles and Ebola. In March 2017 in Scientific Reports, a research team published successful lab tests of an oral vaccine against Ebola in captive chimpanzees (Pan troglodytes). The vaccine relies on the rabies virus to deliver Ebola proteins that elicit an immune response in chimps, but it hasn’t been tested in the field yet.

Such a vaccine should be used selectively, Kock says. Vaccinating great apes against Ebola in preserves where the animals might encounter human carriers makes sense. But vaccinating gorillas across large forests in the Congo “is just silly,” he says.

Protecting isolated species on the brink of extinction is where vaccines could do the most good. Endangered Amur tigers (Panthera tigris altaica) have been hit hard by canine distemper, their numbers falling to around 500 individuals in their Siberian habitat. Vaccines have been debated as a potential option and injectables have been tested in captive tigers.

Sillero doesn’t expect to see any oral options developed against distemper in the future, because there’s not a big economic incentive. Unlike rabies, the disease doesn’t cause problems in humans. So he’s working with the shots available. Genetic analyses of locally circulating distemper strains published in July 2017 suggest the injectable distemper vaccines should work for the Ethiopian wolves, Fooks says. Sillero’s team is testing one in the field now. Preliminary data suggest the shot elicits a good immune response.

Vaccines are becoming more accepted among conservation scientists. Efforts to orally vaccinate great apes like mountain gorillas against Ebola might follow a similar field-testing template to that set out by the wolf project.
What's good for the wildlife

Greater awareness about the overlap of human, livestock and wildlife health on shared lands underlies many of these projects. Ethiopia has one of the highest rabies death rates among humans in the world, and lowering the disease prevalence in any animals that humans come in contact with has benefit.

“This will have positive impacts for the threatened animals, for the welfare of domestic dogs and livestock, and for the health and finance of the human community,” Sillero argues. The One Health mind-set is also behind programs run in a few areas of Ethiopia’s northern highlands, to teach local farmers how to build more efficient stoves that require less firewood, and thus, less foraging in wolf territory.

“Vaccination and eradication of things like rabies ... needs a whole of society approach,” Kock says. “It cannot be done piecemeal.”

For Ethiopia’s impending oral vaccine launch that has been so many years in the making, Sillero is optimistic. But he’s still holding his breath.

“I have to see the wolves taking up the baits before I can congratulate the team,” he says. “But I think we’re nearly there.”

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Citations


T. Rocke et al. Sylvatic Plague Vaccine Partially Protects Prairie Dogs (Cynomys spp.) in Field Trials. *EcoHealth*. Published online June 22, 2017. doi: 0.1007/s10393-017-1253-x.


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**Further Reading**


