

# Fear gone viral

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If you were paying attention to the flap over two recent flu experiments involving ferrets, you may have come away with the impression that scientists all but waved a red flag in front of terrorists and said, "Here's a perfect biological weapon - help yourselves."

But there's really not much cause for alarm.

Here's the background. In December, the National Science Advisory Board for [Biosecurity](#) asked the premier science journals Science and Nature to redact key information from two papers scheduled for publication, one by University of Wisconsin [virologist](#) Yoshihiro Kawaoka and the other by a team at Erasmus Medical Center in Rotterdam, the Netherlands, led by Ron Fouchier.

Both groups used strains of highly virulent H5N1 [avian flu](#) that had been engineered to make them communicable to ferrets, though not in a way that ferrets could easily pass the [virus](#) among one another. Researchers used nasal swabs to infect a ferret, and once it was infected, they took a nasal swab from it and infected the next ferret. By the end of a chain of 10 or so ferrets, the virus had mutated to become transmissible through respiratory droplets alone, meaning it could be far more easily passed from one animal to another, even when they were in separate cages.

Now, the biosecurity board has asked the journals not to publish the exact nature of the mutations, so that terrorists couldn't use the "recipe" to produce a deadly, transmissible human flu that could, in the words of a New York Times editorial, "kill tens or hundreds of millions of people

if it escaped confinement or was stolen by terrorists."

The fallacy in all this is that it's not the exact "recipe" - the [molecular changes](#) - needed to turn a non-transmissible mammalian virus into a transmissible one that's so important here. It's the method by which the mutations were accomplished. And that method - passing the virus from ferret nose to nose - has been known for quite a while. Daniel Perez at the University of Maryland, for example, published a paper in 2009 describing the same technique using a low-pathogenic virus.

It might be hard to perform the initial molecular tweaks that made the flu something to which ferrets were susceptible, but the crucial step of causing the virus to evolve so that it was more easily transmitted was simple. These scientists created a disease factory for ferrets - essentially what farmers in Asia do by cramming 5 million chickens together.

"It's not rocket science," says Adolfo Garcia-Sastre, an influenza researcher from Mount Sinai School of Medicine in New York.

The justification for creating a ferret disease factory was to study how such mutations could evolve in nature and trigger a pandemic. The experiments, said Perez, help scientists to know what to look for.

But the idea that these laboratory-created mutations could now pop up together in some Asian chicken and launch a lethal pandemic is implausible. That's not how evolution works. Evolutionary biologist Paul Ewald of the University of Louisville predicted in 1993 that packing chickens in factory farms would allow the evolution of lethal chicken viruses. And that's exactly what happened: Chicken viruses evolved that killed chickens. Even H5N1, which eventually evolved so it could transmit to humans, remained a far better chicken virus than a human one. Though it certainly infected - and killed - many humans around the globe, it never developed into an effective human virus, which is why it

has never caused the kind of global pandemic initially feared.

None of this is to say, however, that the ferret experiments weren't important. What they showed is how quickly natural selection can transform a virus.

"You put selection pressure on the system for increased transmissibility, and you quickly get the outcome that you expect to get," says Ewald. Influenza has a high mutation rate, and natural selection then picks the most transmissible of the viral strains that mutations generate, pushing the virus toward ever-greater transmissibility. This is what makes the ferret experiments with highly virulent H5N1 so alarming to contemplate.

But to become a world-destroying pandemic, a virus would need a so-called human disease factory in which to refine its mutations. Virologist Vincent Racaniello of Columbia University considers the entire ferret flu frenzy a massive overreaction. As he points out: "Ferrets are a good model for influenza, but they are a model - they don't duplicate every aspect of influenza as it occurs in humans."

The 1918 flu, which killed 50 million people worldwide, was formed in the massive disease factory of the Western Front of World War I. Why was it a disease factory? Because soldiers were crowded into close quarters that were the perfect environment for the flu to mutate into something highly virulent. When a soldier got deathly ill, there was no place to move him, and he remained packed tightly in among the other soldiers.

The 1918 flu virus eventually lost its virulence as the conditions that gave rise to it abated. When a virus depends on a mobile host to transmit it, as normal human flu viruses do, there's a limit to its virulence. Once humans aren't crowded so tightly together, it's the milder strains of

viruses that natural selection favors, because transmission is more easily accomplished if the infected person feels well enough to be out in public sneezing and coughing instead of taking straight to a sickbed where few other people are likely to be infected.

Ewald also argues that an accidental or deliberate release of H5N1 ferret flu could not have anything like the same impact as the 1918 pandemic. That flu was carried all over the world by perhaps a million people who had just left "virus factories" and were now harboring a virulent, transmissible virus. That wouldn't be the case now. "It might be a nasty event, but it would be small," says Ewald.

The ferret experiments were important but hardly a revelation. And they certainly didn't create world-threatening virus strains. Evolution - with help from disease factories - had already demonstrated how to create transmissible and lethal diseases. Rather than trying to suppress scientific information, government biosecurity experts might do better to focus their efforts on putting an end to factory farming.

**More information:** *Wendy Orent is the author of "Plague: The Mysterious Past and Terrifying Future of the World's Most Dangerous Disease." She wrote this for the Los Angeles Times.*

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