

Concern as revived 1918 flu virus kills monkeys

The 1918 influenza virus, which killed some 50 million people worldwide, has proved fatal to macaques infected in a laboratory. The study follows *Nature's* controversial publication¹ of the virus's sequence in 2005, alongside a paper in *Science* that described the recreation of the virus from a corpse and its potency in mice².

Some scientists question the wisdom of reconstructing such a deadly virus. Do the benefits outweigh the risks?

Those who carried out the macaque study say yes, as a better understanding of how it acts in a system similar to humans' will help scientists treat future pandemics. The study was carried out in the biohazard level 4 labs of the Public Health Agency of Canada in Winnipeg. Yoshihiro Kawaoka of the University of Wisconsin-Madison and his colleagues infected macaques

with the 1918 virus or a contemporary flu strain³. Whereas the contemporary virus caused mild symptoms in the lungs, the 1918 flu spread quickly throughout the respiratory system and the monkeys died within days. The damage parallels reports of human patients in 1918.

The team reports that the 1918 virus caused the monkeys' immune systems to go into overdrive, causing immune proteins to be expressed at abnormally high levels and attack the body — what immunologists call a cytokine storm.

The research suggests that 1918 flu might work in a similar way to other viruses, such as West Nile, that can also cause a massive auto-immune reaction. This suggests a route towards treatment, says Michael Gale, a virologist at the University of Texas Southwestern Medical Center. Drugs that target over-zealous immune responses, such as those that control an immune protein called interleukin-6, are being developed for other diseases. Tweaked versions might work for pandemic flu.

But despite the promise of treatments, the results echo what had already been found in mice, and Gale feels there is a more important issue to be addressed. "The pathogenesis is interesting," he says. "But the key question is: how was it spread so efficiently?"

A team at the Mount Sinai School of Medicine has already started to investigate. Peter Palese is working with Adolfo Garcia-Sastre and Jeffery Taubenberger, who first reconstructed the virus, to find out how it spreads.

Working with ferrets, they have found that a change of only one or two amino acids in the flu sequence is enough to stop transmission. They will publish the result in *Science*. Identifying which sections of the genome are responsible for transmission "has huge predictive value for whether strains will become pandemic or not", says Guus Rimmelzwaan at the World Health Organization's National Influenza Centre in Rotterdam, the Netherlands.

The next move for Kawaoka's team is along similar lines — they will be swapping sections in and out of the virus to establish exactly which bits make it so lethal.

But the latest results haven't assuaged everyone's concerns. Richard Ebright, a bacteriologist at Rutgers University, New Jersey, believes the virus should never have been recreated.

"The key implication is that the material is now present in at least two locations," he says. The new study, he argues, increases the risk that the virus could escape and sets "a dangerous precedent" for other labs to follow.

Ebright argues that publishing the study in *Nature*, when similar research on more mundane pathogens regularly appears in lower-impact journals, could in itself increase the proliferation risk, if it tempts research groups to work on high-risk pathogens simply to get more recognition. Similar views were expressed off the record by other scientists. Ritu Dhand, *Nature's* chief biological sciences editor, defends the decision to publish, arguing that because the 1918 virus is not like other flu viruses, gaining insight into what makes it so virulent in humans is of scientific interest.

Gale agrees that understanding the 1918 flu strain better could have huge public-health benefits. But he says there might be better ways to study this, and admits that some research might be driven as much by historical interest as by the potential health benefits.

Jens Kuhn, a virologist at Harvard Medical School who advises on arms control, also feels divided. "Everything I say, I make 'enemies' on one or the other side," he says. "I am torn sometimes between the two worlds." ■

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1. Taubenberger, J. K. et al. *Nature* **437**, 889–893 (2005).
2. Tumpey, T. M. et al. *Science* **310**, 77–80 (2005).
3. Kobasa, D. et al. *Nature* **445**, 319–323 (2007).

ON THE RECORD

“Who wants an ugly, stupid kid? I mean, come on.”

Jennalee Ryan, head of 'embryo brokerage' the Abraham Center of Life, which offers test-tube embryos created from attractive and intelligent egg and sperm donors, and which is being investigated by US officials.

SCORECARD



Human drugs

The US Food and Drug Administration gave the green light to just 18 new drugs in 2006, an eight-year low...



Dog drugs

...although it has just approved Slentrol, the first drug to battle canine obesity.

NUMBER CRUNCH

50% is the reduction in greenhouse-gas emissions over the past five years claimed last week by budget airline Ryanair, the self-styled "greenest, cleanest airline".

50% is the emissions reduction that the airline was originally going to claim per passenger, as revealed by an earlier leaked version of the same press release.

300% is the actual increase in the airline's overall emissions, owing to vastly increased passenger numbers.

SHOWBIZ NEWS

Christmas visits to the American Museum of Natural History shot up 20% relative to the previous year, after the release of Ben Stiller comedy vehicle *Night at the Museum*.

Sources: AP, Bloomberg, FDA, Science Blog, BBC Newsnight

