The Great Flu

It's been a century since the world's worst influenza pandemic — could it happen again?

One hundred years ago this month, the 1918 influenza virus was just starting to spread. It would become the greatest public-health crisis of the twentieth century, claiming some 50 million to 100 million lives. The centenary has raised questions over whether such a severe flu pandemic could happen today, and whether the world is prepared.

There are few data points to go on — flu pandemics happen only three or four times a century — but one risk is certainly higher: 7.6 billion people share the planet in 2018, up from 1.9 billion in 1918. Feeding all those extra people has also meant a huge rise in livestock numbers, intensive farming and the numbers of animals being transported around the world. Scientists say that the genetic mixing and evolution of animal flu viruses is thus being amplified, increasing the chance of viruses gaining the potential to jump to humans and, if they can spread easily between people, causing a human pandemic. Our just-in-time global production systems and service economies are also exquisitely vulnerable to the quickly cascading disruption that a severe pandemic would cause.

The case-fatality rate in the 1918 pandemic was around 2.5% (compared with less than 0.1% in other flu pandemics), and a comparable or worse rate in a future pandemic cannot be discounted. There are two hypotheses to explain the 1918 strain's high lethality: cytokine storms and secondary bacterial infection. (In a cytokine storm, the body's immune system overreacts, causing tissue and organ damage, and even death.)

But in an intriguing 2008 paper (D. M. Morens, J. K. Taubenberger and A. S. Fauci *J. Infect. Dis.* **198,** 962–970; 2008), researchers went through data from almost 8,500 post-mortem records from the 1918–19 pandemic and discovered what doctors knew at the time, but which was subsequently forgotten — that most people in the pandemic probably died of secondary pneumonia from common bacterial pathogens.

Were this latter pattern to dominate in any severe future pandemic, the availability of antibiotics, which didn't exist in 1918, would dent death rates, provided that sufficient stockpiles were available. More broadly, the importance of robust public-health systems and surge capacity in hospitals as a basic bulwark against epidemic and pandemic threats of all kinds cannot be overstated. Yet health systems remain weak in many countries.

Speak to scientists, and they all agree on what must be the number one research goal for effective mitigation of any future pandemic: a universal flu vaccine. At present, the seasonal flu vaccine usually has to be updated every year or so to match the circulating virus strains — which are continually evolving — and these vaccines provide no protection against an altogether new pandemic subtype.

The 2009 swine flu pandemic showed that it takes months to start producing a vaccine against a pandemic flu virus. In many countries, substantial amounts of vaccine arrived only after the first wave of infection had already passed. Fortunately, the 2009 virus was relatively mild.

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A universal vaccine, ideally offering lifelong protection against all flu subtypes, would improve the effectiveness of seasonal flu vaccines and offer protection against novel pandemic threats. Even a vaccine that is around 75% effective in preventing disease symptoms would be a huge public advance, scientists reckon (C. I. Paules *et al. Immunity* **47,** 599–603; 2017).

A major international workshop on developing such a vaccine was held last year in Rockville, Maryland, and identified many research gaps — including the complexity of the immune response to infection and vaccination — and a road map for addressing them. Yet the United States, one of the largest flu-research funders, last year invested just US$75 million on universal flu vaccine research and development.

Whether the world will again ever see the likes of the 1918–19 flu pandemic cannot be reliably predicted, but given the stakes, it is best for society, as a whole, to plan for worst-case scenarios. And advocates rightly argue that the research and development of a universal flu vaccine — ultimately the only effective defence against future pandemics — merits a programme equivalent in scale to the Manhattan Project. ■

Annual report

Donald Trump has been in office for a year and the effects on science have been as bad as feared.

After a year of President Trump, scientists in the United States are doing their best in difficult circumstances, and *Nature* applauds them for it. It's increasingly clear that Trump has been just as bad for many aspects of science as we and others feared. Most crucially, the role of science and scientific advice in public life has been repeatedly undermined.

Writing after his election victory in November 2016, this journal tried to look on the bright side and suggested that Trump could yet "leave behind his damaging and unpopular attitudes and embrace reality, rationality and evidence" (*Nature* http://doi.org/bs57; 2016).

How wrong we were to be optimistic. After 12 months in office, Trump's impact on science can be neatly divided into two categories: bad things that people expected, and bad things that they didn't. The long list of items in the first category includes the US withdrawal from the Paris climate agreement, regulatory rollback across government (environmental agencies in particular) and the now record-breaking failure to appoint a science adviser. His administration has cut off funds to organizations abroad that promote public health but mention abortion, weakened restrictions under the Toxic Substances Control Act and censored the use by government agencies of phrases such as "evidence-based" and "climate change". Advisory groups, including one on HIV/Aids, have been disbanded, and scientists with Environmental Protection Agency grants have been banned from serving on the agency's advisory boards.

Turning to the second category, Trump's campaign rhetoric promised a travel ban on Muslims, but the full, chilling and chaotic details turned out to be much worse, and more divisive and disruptive, than even avowed opponents might have dared to suggest. Scientific organizations queued up to complain about the likely loss of talent.

There are also some bad things that critics expected Trump to do, but that have yet to come to pass. Budgets at key science and health agencies remain largely unmolested (although this is largely thanks to resistance in Congress to pledged cuts); bans on research using fetal tissue and embryonic stem cells have not emerged; and Obama-era programmes including the Precision Medicine Initiative remain in place for now.

One good thing has happened: Trump has triggered a surge of political activity by scientists motivated to oppose him. (And, of course, nations elsewhere, from China to France, are already stepping in to offer opportunities as US leadership slips.) Those who cherish the values of science should keep fighting. Scientists and politicians must continue to challenge the president's actions and seek to hold him to account. ■