

Scary-sounding new virus in the news? Here are the questions you should ask

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In the US, a dairy-farm worker develops itching, <u>blood-shot eyes</u>. In Australia, a <u>young girl falls ill</u> after a foreign holiday and is rushed to hospital. In Mexico, another man, already ill and bed-bound, becomes seriously <u>unwell and dies</u>. Each of these recent cases was caused by a different strain of influenza virus. In each case, it was an animal virus, which should not normally have turned up in humans at all. Should stories like this worry us?

When stories like this hit the news (and for <u>influenza viruses</u>, this happens quite often), journalists write to virologists and ask: How worried are you about this one?

The honest answer is that how any virologist really feels about a story depends on a lot of things, including our personalities: Some of us are natural optimists, while others tend to catastrophize. But our professional background does give us an idea of what to look for in a news story about a <u>novel virus</u>. When you next read about a novel virus in the news yourself, these are the questions that can help you decide how much of a worry it might be.

How far has it gotten?

This is usually the first question. It's actually really hard for a virus to adapt to growing well in a new host species. Even influenza viruses—basically bird viruses, but notorious for causing repeated human pandemics—only manage it every few decades.

For a virus, crossing into people from a different animal host is a staged process. (I'm writing "people," but it's the same logic if you're worried about a virus crossing between any two host species, say, <u>bird flu</u> adapting to spread in cattle.)



Have people been exposed to the new virus and developed immune responses, but with no signs of infection? If there has been a "spillover" infection of a human (whether or not this caused serious illness), is there any sign that the virus has adapted enough to spread onwards to other people? And if the virus is now spreading among people, is that spread still at a point where it can be contained?

How much do we know?

Surveillance is hard work that requires resources and cooperation, but it is hugely important in understanding and controlling outbreaks. So what do we look for?

Testing people for immune responses to a virus (serology) tells us who has previously been exposed. Sequencing viral genomes (from infected people or from the environment) tells us where the virus is now, and it also lets us work out how it is spreading and how it is changing.

We can do this because viruses mutate quickly. Lining up the differences in their genetic sequences lets us build family trees ("phylogenetic trees"), which we can use to reconstruct how the virus got to particular places at particular times.

Are we looking at one big outbreak or lots of separate outbreaks? Family trees can show us this. Looking at the changes in the virus's genome also lets us look for any telltale signs that it is adapting to a new species—assuming we understand the virus well enough to work that out.

What are we dealing with?

The better we understand a virus, the more we can anticipate what it might do next. For some very well-studied viruses, like the influenza



viruses, we know some of the genetic changes that are warning signs of adaptation to a new host species.

What else can we look for? We worry more about viruses jumping between similar <u>host species</u>, because this is easier for the virus to do. Influenza that's already in a mammal is closer to being able to infect us than influenza from a bird.

We can look at likely routes of transmission—a respiratory virus is likely to spread more quickly than a virus spread through sexual contact. We can also try to guess at the outcomes of infection—viruses that cause serious disease are concerning, but in terms of spread, we also worry about less serious cases, which could lead to people spreading the virus without realizing it.

However, viruses are tricky things, and in practice, it's really hard to predict what they will do.

The current outbreak of H5N1 influenza A viruses in cattle is a good example of this. An influenza A virus infecting cattle and then spreading through milk were both <u>huge surprises</u>. And while H5N1 is known to be capable of causing very severe disease, it seems that some cattle are carrying the virus <u>without serious illness</u>.

Experimental virology, in which animals and <u>cell cultures</u> are infected and studied under controlled conditions in secure laboratories, can be essential for understanding what a virus is really capable of.

Could it get worse?

Adapting to humans is hard for a virus, so anything that gives a virus more chances to pull this off is a concern. Sustained outbreaks are more of a risk than one-off cases.



We worry more about viruses in animals with close contact with humans. H5N1 spreading in North American cattle is more worrying than H5N1 spreading in South American <u>elephant seals</u>.

We worry about viruses taking shortcuts to adapting. For influenza viruses, this can happen in hosts like pigs that can pick up more than one virus at the same time and allow them to swap bits of their genome with each other.

And we worry about people doing anything that gives a virus more chances to get used to them. Things like <u>drinking unpasteurized milk</u> in areas where it could carry H5N1 influenza viruses, for example.

What would the worst case look like?

What would happen if things did get worse? Do we already have vaccines for this virus or one really like it? Is there the capacity for making large numbers of those vaccines and distributing them to <u>large numbers of people</u>? Do we already have antiviral drugs? Do we know what's needed to manage the symptoms caused by the virus effectively? Here, at least, it helps to face a virus like influenza that we've already been trying to fight for a long time.

The spread of a new strain of influenza virus around the world is just one of many viral threats, but the H5N1 strain of the virus has been doing a lot of things recently that cause us, as virologists, to watch it with concern.

While isolated cases can be devastating for the people involved, the bigger risk to society comes from viruses that spread—and H5N1 influenza is now spreading, in US cattle as well as in birds around the world. Importantly though, what it is not doing at the moment is anything that we would associate with it spreading among humans.



The current mood among virologists is definitely not what it was in--for example--February 2020, when it became clear that SARS-CoV-2 was spreading uncontrollably among humans. But bird flu is doing enough concerning things at the moment to make us pay close attention to it. Hopefully, if we do that, we can all prevent things becoming a lot more worrying than they are now.

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