Preventing the next pandemic: Viral forecasting

Excerpted from a presentation by *Professor Nathan Wolfe*, School of Public Health, department of epidemiology, University of California at Los Angeles, and head, Global Viral Forecasting Initiative (GVFI), at a seminar conducted at the Duke-National University of Singapore Graduate Medical School.

The 1980s is the period commonly considered to be the beginning of the AIDS pandemic. However, from the perspective of prevention, the turning point was over by then. At least 100,000 cases of HIV had been established globally and the consequences were inevitable.

But the scenario might have been different had HIV been noticed earlier. Just as the Framingham Study identified the basic preventive risk factors for cardiology, we can find the equivalent of risks such as high blood pressure and high cholesterol for pandemics. The identification of earlier biological activities emerging in AIDS would have placed us in a better interventional position. This is where viral forecasting comes in.

HIV is the result of recombined monkey viruses that first spread extensively in chimpanzees, then into humans who hunted and butchered the animals. The animal-to-human transmission pattern is by no means unique to HIV, with similar phenomena in SARS, Ebola, yellow fever, and dengue, for example.

The idea of viral chatter is much like intelligence chatter, which monitors communications for unusual patterns that may be linked to terrorist events. Viral chatter refers to a constant process of animal viruses that become weakly adapted to humans, with some becoming transmissible by humans. A small number of these later become more strongly adapted to humans and a select few finally turn into an exclusive human agent that causes a pandemic. Viral forecasting involves the monitoring of numerous high-risk individuals exposed to animals, to identify the patterns associated with human transmissible agents that become exclusive human agents.

Simian foamy viruses provide an interesting model to understand how animal viruses emerge in human populations. They are present in almost every species of primate, with the exception of humans. To uncover whether foamy viruses had crossed over into humans, the Global Viral Forecasting Initiative (GVFI) looked for evidence of foamy virus in humans from 17 villages in Cameroon and the Democratic Republic of Congo.

This scrutiny uncovered 10 individuals with antibodies to foamy virus, demonstrating clear evidence of exposure, out of which, three were infected with distinct foamy viruses from different animals. Detailed behavioral data was available so we were able to identify their hunting technique as well as whether the animal exposure was through hunting, butchering or pet-keeping.

The data allowed us to understand that retroviruses are transmitted regularly under contemporary natural settings, and that hunting and butchering of non-human primates is

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associated with retrovirus transmission. Today, evidence of foamy viruses jumping over to humans has emerged in Bali, Indonesia, and India as well.

Like the foamy virus, human T-lymphotropic virus (HTLV) is associated with the primate virus, and has the potential to become a devastating pandemic. Different primates are associated with different types of HTLV, but simian TLV3 (STLV3) had no clear identification in human counterparts, until we uncovered that STLV3s had crossed over into humans, emerging as HTLV3. As all other forms of HTLVs are transmissible in humans, we paid close attention to HTLV3. We also found HTLV4, a completely distinct retrovirus.

This demonstrated that HTLV diversity is greater than previously imagined, and unknown HTLVs may be spreading. While screening assays have been utilized to keep HTLV out of blood banks, the fact remains that existing systems for detection and monitoring of human retroviruses are insufficient.

Indeed, the current pandemic of AIDS may lull us into a false sense of complacency. A rainbow of diversity in HIV strains currently exist in West Africa and 16 percent of the specimens we saw were unique or a recombinant of HIV. HIV-infected hunters stand a risk of being co-infected with another simian immunodeficiency virus (SIV). All it may take is for SIV to recombine with HIV and go through a few more replication cycles, to develop the necessary mutations to take hold in human populations, for another outbreak.

While the smoking gun of SIV moving over to HIV has not been identified, current evidence sufficiently debunks the conventional wisdom that animal to human transmission of viruses rarely takes place. Exposure to animals can lead to virus emergence as shown through widespread simian foamy virus introductions, ongoing HTLV emergence and the linkage between hunting and SIV antibodies. There is a tremendous amount of viral chatter, and there should be a capacity to have early warning systems.

Since GVFI was launched, the model of viral chatter monitoring started in Africa has been taken to the world. GVFI is currently working in the wet markets of China, which gave rise to SARS and H5N1, as well as other settings, to monitor emerging viruses and identify unknown viral threats. This initiative has become a decentralized collaborative that links scientists, provides lab connections, protocol and other resources. MI

Quality of life in heart failure not affected by defibrillators

Implantable cardioverter-defibrillators (ICDs) do not decrease quality of life for patients with stable heart failure, a study from Duke University Medical Center, US, has concluded.

The randomized trial involved 2,521 patients – all receiving optimal medical therapy along with either a single-lead ICD, amiodarone or a placebo. Physical functioning did not vary significantly between the groups at baseline, 3, 12 or 30 months, while psychological well-being was significantly improved in the ICD group at 3 and 12 months but not at 30. Receiving a shock in the month preceding assessment, however, was associated with a reduced quality of life. [*N Engl J Med* 2008 359(10):999-1008] MI

Spy games, heart studies and preventing pandemics

The Global Viral Forecasting Initiative (GVFI) is laudable not only for the work it is doing to try to prevent future pandemics, but also for the clash of diverse ideas that came together to form the initiative.

Wolfe and his colleagues applied the notion of monitoring communications for specific patterns that may indicate a terrorist attack – a notion developed in the intelligence community – and applied it to virology. They applied the idea of finding early risk factors for epidemics – much like the Framingham Heart Study identified hypertension and dyslipidemia as risk factors for cardiovascular events later in life – in a similar fashion.

GVFI highlights the benefit of looking beyond one's own area of expertise for inspiration. Research can often be inward-looking, with highly specialized experts within highly specialized fields turning to each other for new ideas. Inevitably "research silos" form. GVFI shows us just how important it can be to look beyond our silos.

- Ed