APIC Conference: Infection prevention in an era of emerging pandemics

‘Imagine how the world might have been different had we identified this epidemic early.’

By Gary Evans, Executive Editor

What if HIV had been detected in the small human populations where it first appeared, African bushmeat hunters who were likely infected with the novel retrovirus decades before it struck the United States and spread globally in the 1980s? How many of the 25 million people who have died of AIDS would have remained uninfected because the virus had been identified by scientists in the field?

This tragic, tantalizing question was among the provocative issues raised by Nathan Wolfe, PhD, founder of the Global Viral Forecasting Initiative, recently in Fort Lauderdale, FL at the 40th annual meeting of the Association for Professionals in Infection Control and Epidemiology (APIC). Frequently cited as one of the rising stars in infectious diseases, the virologist warned some 4,000 infection preventionists that they will continue to see pandemics arising from animal reservoirs, taking full

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advantage of unprecedented paths into susceptible human populations.

“The connectivity we have as a global population is really just massive — there is no way to overstate this,” Wolfe said. “We have habituated to the world we live in, but if we go back 100 years — certainly 200-300 years — we lived in a world where by and large communities were separate, people didn’t travel a tremendous amount and there wasn’t the potential for communicable diseases like we have on the planet right now. “

As a result, a person infected with some novel virus anywhere in the world could be sitting in an emergency room just about anywhere else on the globe within a very brief span of time. To cite two current examples, countries throughout the world are on alert for cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Influenza A (H7N9) emerging in China.1,2 Though there is still some question about the definitive animal reservoir for these viruses, the SARS coronavirus that emerged in 2002-2003 was traced back to a reservoir in Chinese horseshoe bats, with palm civet “cats” acting as intermediate hosts. While bats are suspected as the reservoir for MERS-CoV, other animals including camels are also being tested. For H7N9, 77% of the first 126 cases were exposed to live birds (chickens or ducks).

Essentially all influenza viruses are of avian origin, though animals like pigs can serve as a mixing vessel for bird and human viruses to intermingle and mutate.

**Pan t. troglodytes**

We now know that HIV can be traced back to a specific chimpanzee reservoir, crossing into humans as they hunted and butchered the animals in central Africa.

“We forget because we get our meat clean and prepackaged — you would never know there was blood in an animal from the meat you buy at the grocery store — but this is one of the most biologically intimate kinds of interfaces that exist,” he said. “It is a mechanism by which many viruses can cross into human populations.”

Researchers found that the natural reservoir for HIV is Pan t. troglodytes chimpanzees3 in Cameroon, an area where Wolfe does much of his current field work. Surprisingly, the viral jump

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between species may have occurred as long as a century ago in central Africa. How did it go undetected for so long? Let history be the judge, he said, warning that the verdict will not necessarily be kind.

“They are going to say that this was a group that really tried very hard, but despite all of their technology fundamentally missed something completely under their nose,” Wolfe told APIC attendees in the closing keynote of the conference. “It took us many, many decades, until 1981 to identify the AIDS syndrome. It took us until 1983 to identify the virus that caused AIDS. Amazingly, it took until 1986 before the president of the United States even used the word AIDS in public. This was for ridiculous political reasons, but if we think back we can imagine how the world might have been different had we identified this epidemic early.”

Indeed, perceptions and demonization of the so-called “gay cancer” — the whole sexual politics issue that undermined early prevention efforts — could have been completely different.

“If we had identified HIV in central Africa somewhere in the 1950s or 1960s it would have fundamentally changed things,” Wolfe said. “Even if it was a small number of individuals and you barely found it. For example, you would have known that it was transmitted primarily heterosexual in central Africa. That information alone would have changed the political status of this epidemic when it hit the United States in the 1980s. Who would have guessed that would have been a benefit of finding these things early, but I always ask people to think that there are a million positive things we can get by recognizing these phenomena early. It’s almost impossible to think of any negative impact.”

Before the next pandemic emerges there will be someone in the field looking for the etiological agent, very likely Wolfe or one his colleagues and collaborators in the global forecasting initiative. By following sentinel populations like African hunters they are discovering novel retroviruses and are poised to sound the alarm should a virus capable of sparking a pandemic emerge. The global risk of these pathogens is somewhat counterintuitive, as high mortality viruses like Ebola that burn through populations and then disappear are much less threatening than something like the novel H1N1 pandemic influenza virus that appeared in 2009. Though lightly regarded by the general public, H1N1 did something that would be impossible for Ebola in its present form — it infected 1 billion people in one year, he said. The implication that it could be nearly as transmissible but more virulent next time was left unspoken but clearly understood.

**The undiscovered country**

While we understandably focus on such “nasty actors,” Wolfe reminded that we are discovering more and more about “beneficial microbes” that protect and improve our quality of life. IPs are well aware of this symbiosis, knowing, for example, that wiping out commensal bacteria in the gut via antibiotics opens a door for pathogens like *Clostridium difficile* to emerge as enteric infections.

The microbial world is so vast and uncharted it remains largely an undiscovered country for future biologists and virologists.

“We think of ourselves as having explored both poles and all of the oceans,” Wolfe said. “We think we know Earth, but it when it comes to the microbial world it’s really like we are in the 17th century. We really understand very little about what’s around us. It really sort of evokes this alien world.”

For example, Wolfe showed an electron microscopy slide of what appeared to be a cell infected by viruses, a common arrangement in the microbial world. In actuality, he explained, this was a large virus infected by smaller ones, so-called “sputnik” viruses that had penetrated their viral cousin like so many parasites. “This was only discovered two or three years ago, and to me it serves to remind us of how much is still completely unknown in this world,” Wolfe said.

A photograph of an impoverished African hunter with a dead primate strapped on his back flashed on the screen, a testament to the ragged line between animal viruses and man.

“What we really see from this is that we are talking about a situation of profound poverty,” he said, noting that an emerging pandemic would affect much of the globe “and yet we are leaving the responsibility to address this on a small population of some of the poorest people in the world. I believe this is one of the fundamental issues of our time even though we don’t recognize it.”

Wolfe has tramped through jungle and village to ask these hunters for blood samples, finding in the first four or five years of the project that “nearly a half dozen individuals in this population were infected with novel retroviruses. Given the global cost of the AIDS pandemic how is it possible that new retroviruses are coming into the human population and we are not aware of it?”
The fire next time: Hard work, luck may prevent pandemic

‘God gave Noah the rainbow sign, no more water but fire next time.’

African-American spiritual

By Gary Evans, Executive Editor

Despite all the accolades and academic honors, Nathan Wolfe, PhD, is disarmingly down to a very different Earth — one teeming with microbes that are ever interacting with animals and man.

In the world of Wolfe’s work, we are but a few viral mutations away from the next pandemic of infectious disease, perhaps the index case is even now spiking a fever on an inbound plane. And despite our revered national and international public health institutions — the armies of epidemiologists at the CDC and the WHO — we actually know very little about what happens next. Our collective fate may be in the bloody hands of a destitute African hunter skinning a freshly killed baboon to bring his family a few precious pounds of protein.

This is the hot zone for pandemic emergence, whether Wolfe and colleagues are looking for the next retroviral plague or listening to “viral chatter” that may signal an emerging respiratory virus like SARS or a sudden antigenic shift in a novel strain of influenza. It is the work of a far-flung network called the Global Viral Forecasting Initiative, which he founded in 2008 after leaving the security of a life-time tenured position in the world of academia.

“My colleagues thought I was crazy,” he says. “Sometimes you have to take risks.”

**REFERENCES**


**Why did SARS arise and vanish so quickly?**

We sat down with Wolfe recently in Fort Lauderdale, FL shortly before he delivered the closing keynote at the 40th annual conference of the Association for Professionals in Infection Control and Epidemiology (APIC). In an interview with *Hospital Infection Control & Prevention*, we asked Wolfe about his field work and his recently published book, *The Viral Storm*, in which he predicts that we will see more and more pandemics and emerging infectious diseases.

Q. We have two new emerging infections on the radar right now, the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Influenza A (H7N9) in China. Both of these seem to have a transmission problem in humans — they seem to have high mortality but very little human transmission. Is the primary concern that they will mutate and become more transmissible?

A. “There are two variables — how many people does it kill or harm and how easy is it to transmit from one individual to the other. And both are obviously important features, but something that is very highly transmissible can kill fewer people [but do] more damage. Some strains of Ebola will kill upwards of three-quarters of the individuals that they infect. Compare that to something like human papillomavirus (HPV) and the impact it has on global populations. Though it doesn’t kill in as dramatic a way — it takes a lot of time — it has so much more of a huge impact on global public health. Some of the particular variants of HPV cause cervical cancers. It spreads silently but it ends up being a huge killer because it is so transmissible. It is estimated that roughly one of three sexually active adults are infected with one or another [form of] HPV. So sometimes our instincts as to what’s most risky can be sort of counter to the reality of these things.

For the novel coronavirus and H7N9, it is in the early days for both of them in terms of estimating mortality and determining transmissibility. I think it is a very important point to make that these kind of viruses have a lot of capacity to mutate and swap genes around in recombination and assortment. That means that the virus that you see today is not necessarily the same virus that you are going to see in weeks or months.”

Q. The original SARS coronavirus in 2002-2003 seemed to have a lot of the classic pandemic characteristics and it did emerge. Why did it vanish in a relatively short period of time and why
hasn’t it come back?

A. “Well, I do think that our public health system responded in a fairly strong way to SARS. But also probably there was some good luck. Some people have postulated that the timing of the outbreak relative to seasonal fluctuations in respiratory virus season [worked in our favor]. We don’t fully understand why it is — it probably has to do with the density of human populations in the Northern Hemisphere in relation to the seasons — but there really are these seasonal effects. The Northern Hemisphere’s winter is when you see really the most important respiratory virus season in the world. You get a little bit in the Southern Hemisphere during their winter, but there is some postulation that SARS ‘second peak’ was at the wrong time. It was the end of the respiratory virus season. Some folks argue that had it come along a little bit earlier we might still be living with the virus.

The second question is how come it hasn’t reared its head again. The way that we think about these things is that there is this constant process by which these viruses are ‘pinging’ at human populations from the animal reservoirs that they come from. The events that we see are an incredibly small percentage of the events that are occurring. So it may very well be that there has been zoonotic transmission of SARS from animals to humans, but until we are really doing the right kind of surveillance we might be missing them.”

Q. Many outbreaks have been discovered by astute clinicians looking at a single unusual case or by infection preventionists and health care epidemiologists trying to prevent patient infections. How do these IPs fit into your model of pandemic prevention?

A. “To me the infection preventionists are really at the frontline of this. That is kind of where the rubber hits the road and from our perspective we have an incredible respect for that kind of work and recognize its huge importance. They will continue to be very important. As you said, clinicians have played very important roles in identifying these outbreaks. As a biologist I am focused on these microbial populations, both the bad actors and the good actors. I think as we identify more and more of the positive sides of the microbial world it may very well be that IPs and other folks that are members in APIC might be in a perfect position to not only stop the nasty ones but also try to promote some of the positive ones.”

Measles outbreaks continue as retracted study echoes

‘You can’t undo fear.’

Infection preventionists must raise a “common voice” in support of the measles/mumps/rubella (MMR) vaccine to overcome the misplaced fears and false information that have led to recurrent outbreaks in unvaccinated populations, an IP urged recently in Fort Lauderdale, FL at the 40th annual meeting of the Association for Professionals in Infection Control and Epidemiology (APIC).

“You can’t undo fear very well,” said Patricia Stinchfield, MS,RN,CPNP, director of infection prevention and control at Children’s Hospital and Clinics of Minnesota. In describing the massive disruption and chaos her hospital and community faced after a measles outbreak began among an unvaccinated group of people from Somalia in 2011, Stinchfield warned that similar unvaccinated groups in other states are only one exposure away from infection.

“It’s sort of like the perfect storm,” she said. “You get a group of people and they choose not to be vaccinated for whatever reason. They live closely together, [but] they’re out in the world and the community. If they have one single exposure it goes through that community like a match on tinder.”

Indeed, a recent measles outbreak among an unvaccinated Jewish community in New York City resulted in some cases of pneumonia, hospitalizations and one miscarriage, according to published reports. Interestingly, the index case in the New York outbreak was a visitor from the United Kingdom, where a large measles outbreak in Swansea, Wales has prompted UK officials to begin a mass MMR vaccination campaign.

The outbreak described by Stinchfield and subsequently reported by the Centers for Disease
Control and Prevention began on March 2, 2011 when the Minnesota Department of Health confirmed measles in a nine-month-old infant in Hennepin County. In the following month, investigation of contacts and heightened surveillance revealed a total of 13 epidemiologically linked cases. Seven of the 13 cases were of Somali descent. Eight patients were hospitalized. Vaccination status was known for 11 patients: five were too young to have been vaccinated, and “six (all of Somali descent) had not been vaccinated because of parental concerns about the safety of the MMR vaccine,” the CDC reported.

Stinchfield showed a slide of a young child with measles infection so severe he was attached to various medical devices in an intensive care unit bed. The child survived and his mother — who turned down the MMR vaccination for him — insisted the photo be shown to underscore the severity of measles, she said.

**A rare retraction**

In 1998 the British journal The Lancet famously published a since-retracted “study” that fueled fears that the MMR vaccine may cause autism. The article was retracted by the journal in 2010 after years of controversy and criticism from the medical community. The journal published the following statement in retracting the article:

“Following the judgment of the UK General Medical Council’s Fitness to Practise Panel on Jan 28, 2010, it has become clear that several elements of the 1998 paper by [Andrew Jeremy] Wakefield et al are incorrect, contrary to the findings of an earlier investigation. In particular, the claims in the original paper that children were ‘consecutively referred’ and that investigations were ‘approved’ by the local ethics committee have been proven to be false. Therefore we fully retract this paper from the published record.”

Wakefield issued the following statement at the time of the retraction: “The allegations against me and against my colleagues are both unfounded and unjust and I invite anyone to examine the contents of these proceedings and come to their own conclusion. In fact, the Lancet paper does not claim to confirm a link between the MMR vaccine and autism. Research into that possible connection is still going on.”

In any case, the damage done continues to echo on the Internet, where concerned parents may find a wealth of misinformation circulated by anti-vaccine groups. The fear continues, though there are “two dozen great studies” showing no link between MMR vaccine and autism, Stinchfield says.

“[The study] has been retracted and is known to be false information, but that myth really still prevails. A lot of people still believe it; they’re worried about it” she said. “Sometimes people say, ‘I see autism all over the place, and I don’t want a child with autism. I really don’t ever see measles and how bad can it be? It’s a rash, they have a runny nose, they have a fever — it’s going to end, whereas autism is for their whole life.’ But there is no relationship [between MMR vaccination and autism].”

Thus, hospitals and public health officials must remain vigilant for outbreaks of a highly contagious airborne disease that had already been declared eradicated in the U.S. A single case entering a hospital emergency room can set off an outbreak response that includes time-consuming and disruptive follow-up of patients and health care workers. Stinchfield did not have a cost estimate for managing the measles outbreak at her hospital, but previous investigations have tallied staggering sums. For example, a single imported case of measles ultimately cost two Arizona hospitals some $800,000, with much of the expense related to ensuring the immunity of employees and furloughing workers.

Hospitals typically require new employees to receive two doses of the MMR vaccine or show proof of immunity. People born before 1957 may be presumed to be immune, according to CDC guidelines — although in the event of an outbreak, the CDC recommends that healthcare workers born before 1957 receive two doses of MMR.

**REFERENCES**


