Researchers gain traction in race against pandemics

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Is another pandemic on the scale of the 1918 influenza pandemic inevitable, or can research and prevention head off another deadly transmission of animal viruses to human populations?

This was among the questions considered at "A Dangerous Leap: Animal-to-Human Transmission of Disease," a panel of experts in epidemiology and microbiology convened on Nov. 9 for the 13th annual Dorothy N. Stratton Lecture on Critical Issues.

Visions of pandemic bird flu may "send a chill up our spine," said moderator Lee Gehrke, Hermann von Helmhotz Professor of Health Sciences and Technology at MIT. But he wondered whether the issue been blown out of proportion.

The panel discussion at the Wong Auditorium, chaired by Gehrke, who is also a professor at Harvard Medical School, featured guest speakers Megan Murray, assistant professor of epidemiology in the Harvard School of Public Health; Michael Farzan, assistant professor of microbiology and molecular genetics at Harvard Medical School; and Adolfo Garcia-Sastre, professor of microbiology at Mount Sinai School of Medicine in New York City.

Garcia-Sastre led off with a summary of his research into the HA influenza strain, which is carried by birds and caused the 1918 influenza epidemic. This pandemic killed more than 20 million people worldwide and more than 600,000 in the United States. He noted that while flu

vaccines give us reasonable protection against B, H3 and H1 virus strains, "if the H5, H7 or H9 strains can master human-to-human transmission, the human population has no immunity."

His group at Mount Sinai Hospital has synthetically reproduced the 1918 virus, using genetic material gleaned from lung-tissue samples preserved in paraffin by the U.S. military as well as samples preserved in bodies deposited below the permafrost line in a mass grave in the remote Inuit village of Brevig Mission, Alaska. (In Brevig Mission, the postman delivered the virus along with the mail, and within a week all but eight of the village's 80 inhabitants had perished.) Garcia-Sastre's group has determined that the glycoprotein and polymerase genes are those responsible for virulence of the 1918 flu strain.

Science gains speed in response

Farzan discussed how the severe acute respiratory syndrome (SARS) corona virus, which normally affects only birds, "learned" to infect humans. He recapped the course of the outbreak that occurred earlier this decade, from the first cases in November 2002 through the World Health Organization global health alert issued in March 2003 at the peak of the epidemic, through its attenuation over the following year. By March 2004, it was clear that the virus has lost much of its lethality. His group, therefore, focused on studying the minute differences between the early, virulent strain of the SARS virus, and the later strain, which was far less lethal, causing a "mild, flu-like disease."

He noted in particular how extremely rapid the scientific response to this outbreak had been: By April 2003, researchers had identified the pathogen as a corona virus; by May, they had isolated the virus and proved its lethality in macaques, and another group had determined the entire 27,000 base-pair genome. Farzan noted, "A lot of what happened here reflects the sequencing technology…a natural outgrowth of the

scientific effort, the Human Genome Project."

His group concluded that the difference between the very deadly strain of the SARS virus and the far milder, later strain was the shift of two amino acids in the so-called spike (S) proteins that allow the virus entry into the cells. One change made it easier for the virulent strain to infect human cells, and the other made it much more effective once it had broken in.

Murray closed the program with a discussion of three epidemics caused by animal-to-human disease transmission. The first discussed was the 1911-1912 pneumonic plague epidemic in China, in which fleas from infected rats spread the plague among workers living in crowded conditions at Manchouli, a railroad boomtown in the western part of the country. Manchouli also happened to be the native territory of the tarbigan, a marmot in which the bubonic plague bacillus is endemic and whose pelts had become highly valuable due to a global fur shortage.

Murray then outlined the 1999 encephalitis outbreak in Malaysia. This epidemic, caused by the Nipah virus, was traced to pig urine and from there to the droppings of fruit bats, which had flocked to farms and orchards after being forced out of their native habitat by ferocious wildfires. These fires, mostly attributable to illegal logging, affected much of Southeast Asia in 1999.

Finally, Murray discussed the origins of the human immunodeficiency virus (HIV) epidemic. There is general agreement that HIV derived from the simian immunodeficiency virus (SIV), but debate rages as to how the crossover occurred and why it did so now, when humans and apes have been coexisting in Africa for millennia. Current theories now focus on the opening of labor camps in the central African forests. There the eating of bushmeat (ape flesh), mass "health care" dispensaries that reused hypodermic syringes and the recruitment of prostitutes to service

the laborers, who were far from their home villages, may have created a "perfect storm" in which the transmission of SIV to humans was facilitated.

Each of the epidemics was the result of "coinciding social, economic and political upheavals"--the fur shortage and railroad boom in China, the deforestation and fire in Malaysia and the opening of labor camps in the African forest--rather than a simple, random pathogenic jump from animal to human.

The Dorothy N. Stratton lecture series is sponsored by the MIT Women's League in honor of Kay Stratton, wife of the late Julius Stratton, who was president of MIT from 1959 to 1966.

Source: MIT