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The mystery of SARS

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Abstract

The quest to understand SARS starts in the lungs of victims like Dr. Henry Likyuen Chan, 34, who contracted the illness in the Hong Kong hospital where he works. Chan's first few days as a patient are a blur. He had high fevers and was racked with coughs. Taking a shower felt like running a marathon. A colleague who called Chan to see how he was doing cried when she heard his wheezing gasps for breath. On day 10, when chest X-rays showed fluid in his lungs, Chan thought he was going to die.

Full Text

Headnote

As this strange new virus continues its spree, killing hundreds and infecting thousands more, scientists are working overtime, trying to keep people from harm

TORONTO WAS A CITY ON EDGE LAST WEEK. PEOPLE walked the streets as they always do, families went out to dinner and the Blue Jays game on Friday night drew thousands. But nobody was happy. The World Health Organization had declared the Canadian city-known for its pristine parks and friendly residents-a

hazard to public health, advising tourists not to visit after several SARS cases in other countries, including the Philippines, were linked to Toronto. In a furious attempt to reclaim the city's reputation, Mayor Mel Lastman praised Canadian health efforts and lashed out at the WHO. "Let me be clear," he told reporters. "It's safe to come to Toronto.' But the alert had set off global alarms. A Toronto girls' soccer team, on its way to Pennsylvania for a much-- anticipated exhibition match, was told it was no longer welcome. Player Katie Nizio, 16, had hoped to show off her skills and win a scholarship to college. "It was my one big chance," she says. "I was literally crushed."

From dashing the dreams of teenage athletes to forcing a stunning political fallout in China, severe acute respiratory syndrome, or SARS, is proving itself a formidable enemy at every level-medical, political, economic and even psychological. In Beijing, the government's Health minister and mayor were sacked, three hospitals shut down and 4,000 citizens suspected of exposure to the potentially fatal disease told to stay at home or in hospitals. A false alarm at San Francisco International Airport panicked travelers after a 50-year-old man suspected of having SARS was removed from a Northwest Airlines flight. In Hong Kong, only about 100 people turned up to ogle Qianlong porcelain at a Sotheby's cocktail party-the first major social event in weeks. The party normally draws hundreds in Manolos; last week's guests accessorized with paper masks.

In Britain, students returning to boarding school after spring break in Asia were quarantined in separate buildings or asked to spend an extra 10 days at home. Several dozen University of California students were called home from a study-abroad program in Beijing. A new Gallup poll reported that 43 percent of Americans are now worried about the disease-up one third from the week before. And in Los Angeles, politicians dined in Chinatown to counter rumors that you could get SARS from eating Asian food. Dr. Jonathan Fielding, the city's public-health director, made a point of eating wontons and chow mein at a press conference. "It's scarily reminiscent of the early days of AIDS," he says.

By late last week, there were more than 4,800 cases of SARS in 27 countries and 293 deaths-small numbers in the scheme of global threats. Many people couldn't help but wonder if health officials and the media were manufacturing hysteria over a microscopic bug, now that Iraq was no longer fodder for 24-hour cable news. But the insidious nature of the virus, its capacity to spread and kill, remained. And its lingering mysteries-how it's transmitted, why it's more virulent in some people than others, how it's best treated-have publichealth experts discernibly worried and unapologetic for erring on the side of caution.

In the United States, where the tally of "suspect" and "probable" cases is fewer than 300, with no deaths, there was still concern: Could the epidemic spread further? Why hasn't it? How worried should we be? The medical battle is being fought on multiple fronts: doctors are trying to diagnose, treat and contain the virus. Scientists are launching seek-and-destroy missions in petri dishes. And public-health officials are mapping strategies for drug and vaccine development. As with any new enemy, victory will not come easily-or quickly. "This is still a work in progress," said Centers for Disease Control and Prevention director Julie Gerberding last week. "We have a lot to learn."

The quest to understand SARS starts in the lungs of victims like Dr. Henry Likyuen Chan, 34, who contracted the illness in the Hong Kong hospital where he works. Chan's first few days as a patient are a blur. He had high fevers and was racked with coughs. Taking a shower felt like running a marathon. A colleague who called Chan to see how he was doing cried when she heard his wheezing gasps for breath. On day 10, when chest X-rays showed fluid in his lungs, Chan thought he was going to die. Now, six weeks later, Chan is 10 pounds lighter, but recovered. He is lucky: early in the course of his illness, hospital officials insisted he

check in for observation. That vigilance, a cocktail of drugs-including steroids, antibiotics and the antiviral Ribavirin-and a fighting spirit helped him through. "I am quite an aggressive person;' Chan says. "That is why I was determined to conquer SARS."

So, too, are the scientists. Thanks to technology and a spirit of global cooperation, the first genome of the virus that causes SARS was mapped by Canadian researchers in less than a week; soon after, it was identified as a coronavirus. Since then, more than a dozen sequences ofthe virus, decoded by labs from Singapore to Liverpool, have been posted on the WHO's Web site. All show slight differences in the string of about 30,000 bases that make up its blueprint, but researchers say that is not surprising. Coronaviruses are composed of single strands of genetic material called RNA, which has no built-in proofreading system to catch mistakes in replication. Every time the virus copies itself, it changes very slightly. "Coronaviruses mutate for a living," says virologist Mark Denison, of Vanderbilt University Medical Center.

The critical issue, then, is whether those mutations affect the severity of disease. So far, most people have recovered from SARS, but about 6 percent have died; researchers are desperate to know why. Scientists have learned from viruses such as the 1997 bird flu in China, which hopped to humans, that even a single change in the genetic code can mean the difference between a virus that sickens birds and one that can kill people. Experts suspect that the coronavirus mutations may explain why some people suffer more than others. But additional factors, such as the amount of virus in the body or a weakened immune system, could be to blame. And there may be different strains of SARS altogether-- viral siblings in the same genetic family, born at different times as the bug spreads. "I'd bet a bottle of champagne thatthere are" says virologist Robert Webster of St. Jude Children's Research Hospital in Memphis, Tenn.

The chameleonlike quality of a coronavirus makes coming up with accurate diagnostic tools all the more challenging. Right now doctors must rely on a checklist of symptoms-fever, dry cough-a history of travel to SARS hot spots or close contact with patients and chest X-rays to spot the disease. Public-health officials use two main tests to confirm the diagnosis: a blood screening, which looks for evidence of antibodies to the virus, and a polymerase chain reaction (PCR) test, which searches for its genetic footprint in saliva or cough residues. Experts caution that existing tests may have either false positive or negative results, and they are working hard to refine them.

An accurate diagnosis might have spared Mark Van Camp, 49, of Wichita, Kans., a difficult welcome home from China. In March, after he and his wife returned from adopting a baby girl in Guangzhou, Van Camp became sick and was diagnosed as Kansas's first suspect case of SARS. Even afterhe recovered and doctors concluded he probably had a bad case of pneumonia, his day-care provider said she wouldn't be able to mind his kids. And when Van Camp ran into his former physician and his wife at a local restaurant, the couple moved to another table. "That's the fear factor of SARS," he says.

The fear is that we don't know exactly how the virus spreads. While it's clear that it jumps from person to person through airborne droplets-a sneeze or a cough-experts suspect it may be transmitted fecally as well. In Hong Kong, residents who contracted SARS in a housing complex, Amoy Gardens, suffered severe diarrhea, and experts found coronavirus in feces and on an infected resident's toilet. Health officials concluded that the pathogen spread at least in part through breaks in the building's sewer lines. Worldwide, experts are also working hard to determine how long the SARS virus survives in the environment-on countertops or door handles-and whether that might contribute to its spread.

Treatment is another puzzle. The illness is caused by a virus, rather than a bacterium, so antibiotics are ineffective. Hong Kong doctors are using the antiviral drug Ribavirin, often in combination with steroids, but U.S researchers say the drug has no effect on the SARS virus in a lab. At the United States Army Research Institute for Infectious Diseases in Frederick, Md., scientists are conducting a treasure hunt for treatment. Every few days, a shipment of drugs collected from the National Institutes of Health and drug manufacturers around the world is delivered to a team of virologists led by John Huggins and Peter Jahrling.

Clad in gloves and respirator masks, the team bombards the SARS virus in plastic trays with whatever it can get its hands on: antiviral medications on the market for diseases like HIV, herpes, flu and hepatitis; anti-cancer agents, anti-inflammatories and anti-asthmatics, and more than 1,000 other compounds, including experimental drugs like cysteine protease inhibitors, which block some viruses from replicating. So far some interferon drugs look promising in early testing, but the medication can cause severe side effects, like depression and muscle pain.

Scientists may have to develop a new antiviral drug altogether, and biotech companies are eager to try out their latest inventions. "Every day, I get 20 to 30 e-mails from biotech start-ups telling me why their drug would work," says WHO virologist Klaus Stohr. The U.S. Department of Health and Human Services, meanwhile, is trying to lure vaccine manufacturers into the fight. Health Secretary Tommy Thompson held a recent meeting with Merck, Wyeth, Aventis Pasteur and other companies. About 70 people attended, including officials from the Department of Defense. "The message clearly was, 'This isn't business as usual'," says Dr. Bruce Gellin, director of the HHS's national-vaccine-program office.

With every step forward, new mysteries arise. Last week a Canadian virologist, Dr. Frank Plummer, questioned the link between the coronavirus and SARS altogether, announcing that he'd found evidence of the virus in only 40 percent of patients. The data are troubling, but other scientists say a number of factors could account for the finding, including weak or incomplete diagnostic tests. Halfway around the world in Hong Kong, doctors were reporting patients who tested positive for SARS-but had none of the classic symptoms. And then there's Sam Sun, a third-year law student in Beijing, who was cooped up in his dorm room after classes were canceled last week. "I'm worried," he said. "I don't know when this will end." The fact is, SARS may never be vanquished, but its lessons are preparing scientists for whatever comes next.

Sidebar
Health

Sidebar
The New Bug

Sidebar
SARS is the first new deadly disease in years that can easily pass from person to person. Here's what you need to know about its science and how it spreads.

Sidebar
THE VIRUS BEHIND THE EPIDEMIC

Sidebar
* The bug: Scientists think SARS is caused by a coronavirus, which is related to the virus behind the common cold.

* The source: The virus may have lived in livestock before jumping over to human victims. Here's how it could have switched hosts:

Sidebar

THE UNKNOWNS

Sidebar

* What causes SARS?The WHO points to the coronavirus, which was genetically sequenced three weeks ago. A few think other viruses may be involved.

Sidebar

* Why is SARS fatal for some and just a bad cold for others? The pathogen's genome varies, and some versions may be especially virulent. Or, the

Sidebar

sickest patients may simply be those

Sidebar

with already weak immune systems.

* How can we cure it? For the moment, we can't. Doctors are testing antivirals and other compounds.

Sidebar

* Is SARS here to stay?

Sidebar

Last week the CDC said the disease might prove ineradicable, permanently lurking

Sidebar

at low levels in the population. But the WHO thinks we might just beat it.

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