Health

Forty percent of people with coronavirus infections have no symptoms. Might they be the key to ending the pandemic?

New research suggests that some of us may be partially protected due to past encounters with common cold coronaviruses.

Cycling fans wearing protective face masks watch the riders arriving prior to the start of the one-day classic cycling race Milan-San Remo in Milan on Saturday. (Marco Bertorello/AFP via Getty Images)

By **Ariana Eunjung Cha**

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When researcher Monica Gandhi began digging deeper into outbreaks of the novel coronavirus, she was struck by the extraordinarily high number of infected people who had no symptoms.

A Boston homeless shelter had 147 infected residents, but 88 percent had no symptoms even though they shared their living space. A Tyson Foods poultry plant in Springdale, Ark., had 481 infections, and 95 percent were asymptomatic. Prisons in Arkansas, North Carolina, Ohio and Virginia counted 3,277 infected people, but 96 percent were asymptomatic.

During its seven-month global rampage, the coronavirus has claimed more than 700,000 lives. But Gandhi began to think the bigger mystery might be why it has left so many more practically unscathed.

What was it about these asymptomatic people, who lived or worked so closely to others who fell severely ill, she wondered, that protected them? Did the "dose" of their viral exposure make a difference? Was it genetics? Or might some people already have partial resistance to the virus, contrary to our initial understanding?

[Teens and covid-19: Several studies suggest adolescence could mark a turning point for how the virus affects youths — and their ability to spread the pathogen.]

Efforts to understand the diversity in the illness are finally beginning to yield results, raising hope the knowledge will help accelerate development of vaccines and therapies — or possibly even create new pathways toward herd immunity in which enough of the population develops a mild version of the virus that they block further spread and the pandemic ends.

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"A high rate of asymptomatic infection is a good thing," said Gandhi, an infectious-disease specialist at the University of California at San Francisco. "It's a good thing for the individual and a good thing for society."

The coronavirus has left numerous clues — the uneven transmission in different parts of the world, the mostly mild impact on children. Perhaps most tantalizing is the unusually large proportion of infected people with no symptoms. The Centers for Disease Control and Prevention last month estimated that rate at about 40 percent.

Those clues have sent scientists off in different directions: Some are looking into the role of the receptor cells, which the virus uses to infiltrate the body, to better understand the role that age and genetics might play. Others are delving into face masks and whether they may filter just enough of the virus so that those wearing them had mild cases or no symptoms at all.

The theory that has generated the most excitement in recent weeks is that some people walking among us might already have partial immunity.

Asymptomatic novel coronavirus cases

Summary of testing studies from around the world showing the share of people who tested positive for the coronavirus but had no symptoms

COHORT	TESTED	PERCENT POSITIVE	SHARE OF INFECTIONS THAT WERE ASYMPTOMATIC
Diamond Princess cruise ship passengers and crew	3,711	19.2%	**46.5%**
Boston homeless shelter occupants	408	36.0	**87.8**
New York City obstetric patients	214	15.4	**87.9**

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USS Theodore Roosevelt aircraft carrier crew	4,954	17.3	**58.4**
Japanese citizens evacuated from Wuhan, China	565	2.3	**30.8**
Charles de Gaulle aircraft carrier crew	1,760	59.4	**47.8**
Los Angeles homeless shelter occupants	178	24.2	**62.8**
King County, Wash., nursing facility residents	76	63.2	**6.3**
Arkansas, North Carolina, Ohio and Virginia inmates	4,693	69.8	**96.0**
New Jersey university and hospital employees	829	4.9	**65.9**
Indiana residents	4,611	1.7	**44.8**
Argentine cruise ship passengers and crew	217	59.0	**81.3**
San Francisco residents	4,160	1.8	**52.7**
Tyson Foods Springdale, Ark.	3,748	12.8	**94.6**

Sources: Annals of Internal Medicine, Tyson Foods THE WASHINGTON POST

Summary of testing studies from around the world showing the share of people who tested positive for the coronavirus but had no symptoms (Tim Meko)

When SARS-CoV-2 was first identified on Dec. 31, 2019, public health officials deemed it a “novel” virus because it was the first time it had been seen in humans who presumably had no immunity from it whatsoever. There’s now some very early, tentative evidence suggesting that assumption might have been wrong.

One mind-blowing hypothesis — bolstered by a flurry of recent studies — is that a segment of the world’s population may have partial protection thanks to “memory” T cells, the part of our immune system trained to recognize specific invaders. This could originate from cross protection derived from standard childhood vaccinations. Or, as a paper published Tuesday in Science suggested, it could trace back to previous encounters with other coronaviruses, such as

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those that cause the common cold.

"This might potentially explain why some people seem to fend off the virus and may be less susceptible to becoming severely ill," National Institutes of Health Director Francis Collins remarked in a blog post this past week.

On a population level, such findings, if validated, could be far-reaching.

What antibody tests can teach us about potential coronavirus immunity

Antibody testing has garnered the attention of many researchers and government officials in the fight against the coronavirus outbreak. (John Farrell, Jonathan Baran/The Washington Post)

Hans-Gustaf Ljunggren, a researcher at Sweden's Karolinska Institute, and others have suggested that public immunity to the coronavirus could be significantly higher than what has been suggested by serology studies. In communities in Boston, Barcelona, Wuhan and other major cities, the proportion of people estimated to have antibodies and therefore presumably be immune has mostly been in the single digits. But if others had partial protection from T cells, that would raise a community's immunity level much higher.

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This, Ljunggren said, would be “very good news from a public health perspective.”

[Asked and answered: What readers want to know about coronavirus]

Some experts have gone so far as to speculate whether some surprising recent trends in the epidemiology of the coronavirus — the drop in infection rates in Sweden where there have been no widespread lockdowns or mask requirements, or the high rates of infection in Mumbai’s poor areas but little serious disease — might be due to preexisting immunity.

Others say it’s far too early to draw such conclusions. Anthony S. Fauci, the United States’ top infectious-disease expert, said in an interview that while these ideas are being intensely studied, such theories are premature. He agreed that at least some partial preexisting immunity in some individuals seems a possibility.

And he said the amount of virus someone is exposed to — called the inoculum — “is almost certainly an important and likely factor” based on what we know about other viruses.

But Fauci cautioned there are multiple likely reasons — including youth and general health — that determine whether a particular individual shrugs off the disease or dies of it. He also emphasized that even those with mild illness may have lingering medical issues.

That reinforces the need, in his view, for continued vigilance in social distancing, masking and other precautions.

“There are so many other unknown factors that maybe determine why someone gets an asymptomatic infection,” Fauci said. “It’s a very difficult problem to pinpoint one thing.”

Immune memory machine

France's President Emmanuel Macron talks last month in Brussels with German Chancellor Angela Merkel, Finland's Prime Minister Sanna Marin and Sweden's Prime Minister Stefan Lofven in their first face-to-face summit since the coronavirus outbreak. (John Thys/Pool/Reuters)

News headlines have touted the idea based on blood tests that 20 percent of some New York communities might be immune, 7.3 percent in Stockholm, 7.1 percent in Barcelona. Those numbers come from looking at antibodies in people’s blood that typically develop after they are exposed to a virus. But scientists believe another part of our immune system — T cells, a type of white blood cell that orchestrates the entire immune system — could be even more important in fighting against the coronavirus.

Recent studies have suggested that antibodies from the coronavirus seem to stick around for only two to three months in some people. While work on T cells and the coronavirus is only getting started — testing T cells is much more laborious than antibody testing — previous research has shown that, in general, T cells tend to last years longer.

One of the first peer-reviewed studies on the coronavirus and T cells was published in mid-May in the journal Cell by Alessandro Sette, Shane Crotty and others at the La Jolla Institute for Immunology near San Diego.

The group was researching blood from people who were recovering from coronavirus infections and wanted to compare that to samples from uninfected controls who were donors to a blood bank from 2015 to 2018. The researchers were floored to find that in 40 to 60 percent of the *old* samples, the T cells seemed to recognize SARS-CoV-2.

“The virus didn’t even exist back then, so to have this immune response was remarkable,” Sette said.

[U.S. coronavirus map: Tracking cases and deaths]

Research teams from five other locations reported similar findings. In a study from the Netherlands, T cells reacted to the virus in 20 percent of the samples. In Germany, 34 percent. In Singapore, 50 percent.

The different teams hypothesized this could be due to previous exposure to similar pathogens. Perhaps fortuitously, SARS-CoV-2 is part of a large family of viruses.

Two of them — SARS and MERS — are deadly and led to relatively brief and contained outbreaks. Four other coronavirus variants, which cause the common cold, circulate widely each year but typically result in only mild symptoms. Sette calls them the “less-evil cousins of SARS-CoV-2.”

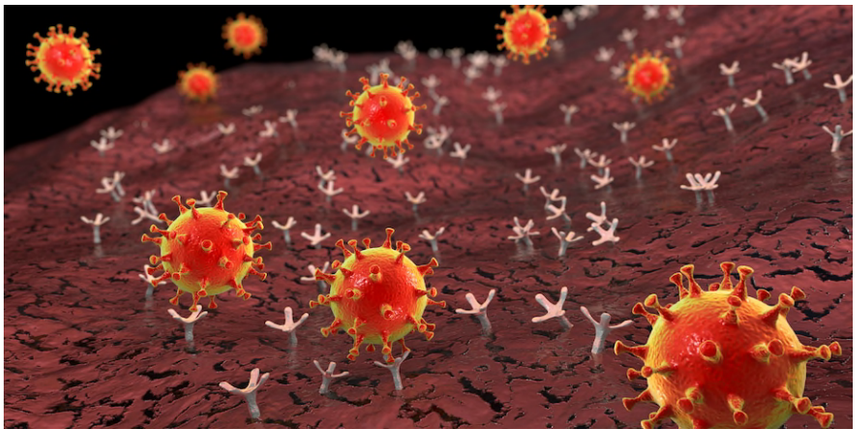
This week, Sette and others from the team reported new research in Science providing evidence the T cell responses may derive in part from memory of “common cold” coronaviruses.

“The immune system is basically a memory machine,” he said. “It remembers and fights back stronger.”

Interestingly, the researchers noted in their paper, the strongest reaction they saw was against the spike proteins that the virus uses to gain access to cells — suggesting that fewer viral copies get past these defenses.

“The current model assumes you are either protected or you are not — that it’s a yes or no thing,” Sette added. “But if some people have some level of preexisting immunity, that may suggest it’s not a switch but more continuous.”

Childhood vaccines



A scientific illustration of the SARS-CoV-2 coronavirus binding to a receptor on a human cell. This attachment is the initial step in the development of a coronavirus infection. (Kateryna Kon/Science Photo/Getty Images)

Nearly 2,000 miles away, at the Mayo Clinic in Rochester, Minn., Andrew Badley was zeroing in the possible protective effects of vaccines.

Teaming up with data experts from nference, a company that manages their clinical data, he and other scientists looked at records from 137,037 patients treated at the health system to look for relationships between vaccinations and coronavirus infection.

They knew that the vaccine for smallpox, for example, had been shown to protect against measles and whooping cough. Today, a number of existing vaccines are being studied to see if any might offer cross-protection against SARS-CoV-2.

The results were intriguing: Seven types of vaccines given one, two or five years in the past were associated with having a lower rate of infection with the new coronavirus. Two vaccines in particular seemed to show stronger links: People who got a pneumonia vaccine in the recent past appeared to have a 28 percent reduction in coronavirus risk. Those who got polio vaccines had a 43 percent reduction in risk.

Venky Soundararajan, chief scientific officer of nference, remembers when he first saw how large the reduction appeared to be, he immediately picked up his phone and called Badley: “I said, ‘Is this even possible?’”

The team looked at dozens of other possible explanations for the difference. They adjusted for geographic incidence of the coronavirus, demographics, comorbidities, even whether people had had mammograms or colonoscopies under the assumption that people who got preventive care might be more apt to social distance. But the risk reduction still remained large.

“This surprised us completely,” Soundararajan recalled. “Going in we didn’t expect anything or maybe one or two vaccines showing modest levels of protection.”