Even in good health, all ages are vulnerable

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Kara VanGuilder’s symptoms started one day in early March, with a cough and a vague feeling that she was coming down with something. By a week and a half later, she was running a high fever, soaked in sweat, barely able to tell night from day — shivering, coughing, weeping, praying.

“That’s the closest encounter I’ve had with death in my whole life. I really was convinced that weekend that I was going to die,” said VanGuilder, who received test results confirming COVID-19 on March 24, just as she was starting to feel better.

With cough and fever, VanGuilder had typical symptoms of COVID-19. But there’s one surprising aspect to her story: She is only 25 and was in excellent health, a runner training for a 10-kilometer race.

As COVID-19 spreads around the globe, data on those who fell ill have revealed clear patterns. Four out of five

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suffer only mild symptoms. Very few children get sick. Most of those who become severely ill are old or have an underlying health condition.

But as with any illness, there are outliers — such as young athletes who succumb or the Connecticut newborn who died of COVID-19 even though infections are exceedingly rare in young children.

Such experiences point to an enduring mystery: When a virus strikes, why do some healthy people get clobbered while others skate through?

“You can be perfectly healthy and this virus can kill you. I don’t think anyone has an explanation,” said Paul F. Bates, professor of microbiology at the University of Pennsylvania’s Perelman School of Medicine.

The novel coronavirus arrived only in December. Before then, no one had been infected with it, and the human immune system was not primed to act against it. But some people are able to mount a fast immune response, quickly producing proteins known as antibodies, tailored to block this virus from entering a cell.

“In some people, these antibodies develop faster than others,” Bates said. “We believe that will play into whether they can fight off the virus or not. For any virus, we really don’t know why some individuals develop better responses than others.”

Bates’s colleague at UPenn, microbiology professor Dr. Ronald G. Collman, is investigating an intriguing possibility that might explain the disparate responses to the virus: differences in the respiratory microbiome — the collection of bacteria and fungi that naturally inhabit the throats and noses of all people. The composition of this microbiome varies from person to person.

Collman has started examining samples from COVID-19 patients to see if there are any patterns in their microbiomes that might explain the variability in the virus’s severity.

“We’re interested in the question of whether the microbiome can influence whether people have mild disease or severe disease,” he said.

Collman is also looking at whether the microbes that get into the lungs when people are sick affect how severe their ill-
ness becomes.

Researchers also speculate that the quantity of virus particles that a person takes in all at once may also play a role in how sick that person becomes. This notion of “viral load” has been posited to explain the death of 31-year-old Li Wenliang, the Chinese doctor who first recognized that a new virus had emerged, and it’s why healthcare workers, faced with inadequate protective equipment, are especially worried.

But no firm data yet support this or other explanations, caution Dr. Kathryn Stephenson, who directs clinical trials at the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center in Boston. “Almost everything is speculation right now,” Stephenson said. “It’s just our best thinking with the data we have.”

Stephenson has a hunch that it will come down to genes: Some people may have a genetic predisposition to mount the overactive immune response that has been the hallmark of severe COVID-19 disease.

“At the end of the day we usually figure out that it’s genetic,” she said. “We’re born with little different variations.”

Such speculation, though, provides no help for someone like VanGuilder, an administrative assistant at Brigham and Women’s Hospital, who has no contact with patients.

VanGuilder said she first started feeling poorly March 9, before COVID-19 was dominating the news. Two days later, she visited an urgent care center, which diagnosed an upper respiratory infection. That same day, the World Health Organization declared COVID-19 a pandemic.

Her fever rose to 101 and her muscles ached, she said. She started to feel a little better for a few days but on March 17 found herself shaking with fever and racked with pain.

Another trip to urgent care yielded a diagnosis of pneumonia and an appointment for a COVID-19 test.

Driving to the Brigham for the test on March 20, VanGuilder could barely see through the sweat dripping from her forehead. For the next few days, she stayed alone in her Medford home, bed-bound, too weak to sit up, speaking frequently with her primary care doctor. She had no appetite and had lost her sense of smell — an occasional symptom of COVID-19.

“Water and prayer, that’s all I had,” she said. “On the night of the 22nd, that Sunday night, I literally got on my knees. I don’t consider myself a very religious person, but I got on my knees and I asked whoever was out there, God, would he just help me.”

VanGuilder did not advance to the most scary stage of the illness.

When COVID-19 progresses, the lungs start to give out, unable to take in enough oxygen. The patient will feel pain or pressure on the chest, and most worrisome, shortness of breath. That’s when it’s time to go to the hospital.

With the flu, a secondary bacterial pneumonia is often what leads to hospitalization and death. But COVID-19 is different from the flu. The lungs start to fail because the patient’s own immune system goes haywire, leading to acute respiratory distress syndrome.

Stephenson calls it “an enormous inflammatory response.” The body starts “sending red alert messages everywhere” — routing attack cells to the lungs, the muscles, the organs.

This phenomenon, known as a “cytokine storm,” can happen in response to other infections but seems to be a key feature in COVID-19’s lethality, including among the young.

Stephenson likens the condition to sending a thousand ambulances racing down a single highway. Each ambulance might be able to help on its own, but with so many at once “you’ve clogged the entire highway and no one can get there.”

At the same time, “ambulances” are headed to places where they’re not needed, like the liver and kidneys, “creating traffic jams everywhere.”

As their lungs weaken, about 10 percent of hospitalized people need a ventilator to breathe for them, Stephenson said. This buys time to build strength and fight off the infection. Many do recover, those who don’t usually die from multiple organ failure, she said.

The vast majority of people who die of COVID-19 are elderly or have serious underlying illnesses. Same goes for the majority of those hospitalized. The estimated rates of hospitalization ramp up with age, more steeply as you get older: 1 percent for people in their 20s, 8.1 percent for people in their 50s, 18.4 percent for those over 80.

The data so far show that about three-quarters of hospitalized people have an underlying condition. Coronavirus is especially dangerous for people with diabetes, chronic lung disease or asthma, serious heart conditions, conditions that weaken the immune system such as cancer treatment or smoking, severe obesity, and kidney disease. Even among those without such conditions, the risk of severe illness increases with age, because the immune system works less effectively as we get older.

But the news reports are re-
plete with stories of younger people falling victim. Most young people survive, but a significant proportion need hospital care, enough to potentially strain resources. A recent review of cases in the United States found that among 508 people hospitalized with COVID-19, one in five were between the ages of 20 to 44.

So younger people can get sick, sometimes severely, even though they are less likely to die. Data from Massachusetts show that COVID-19 strikes adults of all ages, but death comes primarily for the old.

At least 90 percent of Massachusetts COVID-19 deaths were in people age 60 or older. Only three who died were in their 30s, and all were known to have had pre-existing conditions. No COVID-19 patient younger than 30 has died in this state, as of Sunday.

But despite these stark age differences among those who die, adults of any age are clearly at risk of getting sick. The number of people in the state who have tested positive for COVID-19 is almost evenly distributed among age groups over 20. For example, as of Sunday, 14 percent of positive tests were in people in their 20s and 17 percent were in people over 70. (Only 2 percent of people younger than 20 have tested positive so far.)

Never admitted to the hospital, VanGuilder might be counted as a “mild” case. It didn’t feel mild to her, but she said Friday that she’s on the mend.

The fatigue lingered even after her fever broke. Recovery typically takes one to six weeks from onset of symptoms, depending on how sick the person was. But when she awoke on Thursday, nearly a month after her first symptoms, VanGuilder sensed a hint of vigor.

“I’m not feeling the most amazing I ever felt,” she said, “but I feel good enough to do my laundry.”

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PAUL F. BATES, professor of microbiology at the University of Pennsylvania’s Perelman School of Medicine

Kara VanGuilder looked outside while recovering.
A memorial for Dr. Li Wenliang, who first recognized the new virus threat and later died.