The 60-Year-Old Scientific Screwup That Helped Covid Kill

Megan Molteni May 13, 2021 6:00 AM

All pandemic long, scientists brawled over how the virus spreads. *Droplets! No, aerosols!* At the heart of the fight was a teensy error with huge consequences.

Photograph: Naila Ruechel

Early one morning, Linsey Marr tiptoed to her dining room table, slipped on a headset, and fired up Zoom. On her computer screen, dozens of familiar faces began to appear. She also saw a few people she didn't know, including Maria Van Kerkhove, the World Health Organization's technical lead for Covid-19, and other expert advisers to the WHO. It was just past 1 pm Geneva time on April 3, 2020, but in Blacksburg, Virginia, where Marr lives with her husband and two children, dawn was just beginning to break.

Marr is an aerosol scientist at Virginia Tech and one of the few in the world who also studies infectious diseases. To her, the new coronavirus looked as if it could <u>hang in the air</u>, infecting anyone who breathed in enough of it. For people indoors, that posed a considerable risk. But the WHO didn't seem to have caught on. Just days before, the organization had tweeted "FACT: #COVID19 is NOT airborne." That's why Marr was skipping her usual morning workout to join 35 other aerosol scientists. They were trying to warn the WHO it was making a big mistake.

Over Zoom, they laid out the case. They ticked through a growing list of superspreading events in restaurants, call centers, cruise ships, and a <u>choir rehearsal</u>, instances where people got sick even when they were across the room from a contagious person. The incidents contradicted the WHO's main safety guidelines of keeping 3 to 6 feet of distance between people and frequent handwashing. If SARS-CoV-2 traveled only in large droplets that immediately fell to the ground, as the WHO was saying, then wouldn't the distancing and the handwashing have prevented such outbreaks? Infectious air was the more likely culprit, they argued. But the WHO's experts appeared to be unmoved. If they were going to call Covid-19 airborne, they wanted more direct evidence —proof, which could take months to gather, that the virus was abundant in the air. Meanwhile, thousands of people were falling ill every day.

On the video call, tensions rose. At one point, Lidia Morawska, a revered atmospheric physicist who had arranged the meeting, tried to explain how far infectious particles of different sizes could potentially travel. One of the WHO experts abruptly cut her off, telling her she was wrong, Marr recalls. His rudeness shocked her. "You just don't argue with Lidia about physics," she says.

Morawska had spent more than two decades advising a different branch of the WHO on the impacts of air pollution. When it came to flecks of soot and ash belched out by smokestacks and tailpipes, the organization readily accepted the physics she was describing that particles of many sizes can hang aloft, travel far, and be inhaled. Now, though, the WHO's advisers seemed to be saying those same laws didn't apply to virus-laced respiratory particles. To them, the word *airborne* only applied to particles smaller than 5 microns. Trapped in their group-specific jargon, the two camps on Zoom literally couldn't understand one another.

When the call ended, Marr sat back heavily, feeling an old frustration coiling tighter in her body. She itched to go for a run, to pound it out footfall by footfall into the pavement. "It felt like they had already made up their minds and they were just entertaining us," she recalls. Marr was no stranger to being ignored by members of the medical establishment. Often seen as an epistemic trespasser, she was used to persevering through skepticism and outright rejection. This time, however, so much more than her ego was at stake. The beginning of a global pandemic was a terrible time to get into a fight over words. But she had an inkling that the verbal sparring was a symptom of a bigger problem—that outdated science was underpinning public health policy. She had to get through to them. But first, she had to crack the mystery of why their communication was failing so badly.

Marr spent the first many years of her career studying air pollution, just as Morawska had. But her priorities began to change in the late 2000s, when Marr sent her oldest child off to day care. That winter, she noticed how waves of runny noses, chest colds, and flu swept through the classrooms, despite the staff's rigorous disinfection routines. "Could these common infections actually be in the air?" she wondered. Marr picked up a few introductory medical textbooks to satisfy her curiosity.

According to the medical canon, nearly all respiratory infections transmit through coughs or sneezes: Whenever a sick person hacks, bacteria and viruses spray out like bullets from a gun, quickly falling and sticking to any surface within a blast radius of 3 to 6 feet. If these droplets alight on a nose or mouth (or on a hand that then touches the face), they can cause an infection. Only a few diseases were thought to break this droplet rule. Measles and tuberculosis transmit a different way; they're described as "airborne." Those pathogens travel inside aerosols, microscopic particles that can stay suspended for hours and travel longer distances. They can spread when contagious people simply breathe.

The distinction between droplet and airborne transmission has enormous consequences. To combat droplets, a leading precaution is to wash hands frequently with soap and water. To fight infectious aerosols, the air itself is the enemy. In hospitals, that means expensive isolation wards and N95 masks for all medical staff. The books Marr flipped through drew the line between droplets and aerosols at 5 microns. A micron is a unit of measurement equal to one-millionth of a meter. By this definition, any infectious particle smaller than 5 microns in diameter is an aerosol; anything bigger is a droplet. The more she looked, the more she found that number. The WHO and the US Centers for Disease Control and Prevention also listed 5 microns as the fulcrum on which the droplet-aerosol dichotomy toggled.

There was just one literally tiny problem: "The physics of it is all wrong," Marr says. That much seemed obvious to her from everything she knew about how things move through air. Reality is far messier, with particles much larger than 5 microns staying afloat and behaving like aerosols, depending on heat, humidity, and airspeed. "I'd see the wrong number over and over again, and I just found that disturbing," she says. The error meant that the medical community had a distorted picture of how people might get sick.

Linsey Marr stands in front of a smog chamber in her laboratory at Virginia Tech. For years, she says, the medical establishment treated her as an outsider.

Photograph: Matt Eich

Epidemiologists have long observed that most respiratory bugs require close contact to spread. Yet in that small space, a lot can happen. A sick person might cough droplets onto your face, emit small aerosols that you inhale, or shake your hand, which you then use to rub your nose. Any one of those mechanisms might transmit the virus. "Technically, it's very hard to separate them and see which one is causing the infection," Marr says. For long-distance infections, only the smallest particles could be to blame. Up close, though, particles of all sizes were in play. Yet, for decades, droplets were seen as the main culprit.

Marr decided to collect some data of her own. Installing air samplers in places such as day cares and airplanes, she frequently found the flu virus where the textbooks said it shouldn't be—hiding in the air, most often in particles small enough to stay aloft for hours. And there was enough of it to make people sick. In 2011, this should have been major news. Instead, the major medical journals rejected her manuscript. Even as she ran new experiments that added evidence to the idea that influenza was infecting people via aerosols, only one niche publisher, *The Journal of the Royal Society Interface*, was consistently receptive to her work. In the siloed world of academia, aerosols had always been the domain of engineers and physicists, and pathogens purely a medical concern; Marr was one of the rare people who tried to straddle the divide. "I was definitely fringe," she says.

Thinking it might help her overcome this resistance, she'd try from time to time to figure out where the flawed 5-micron figure had come from. But she always got stuck. The medical textbooks simply stated it as fact, without a citation, as if it were pulled from the air itself. Eventually she got tired of trying, her research and life moved on, and the 5-micron mystery faded into the background. Until, that is, December 2019, when a paper crossed her desk from the lab of Yuguo Li.

An indoor-air researcher at the University of Hong Kong, Li had made a name for himself during the first SARS outbreak, in 2003. His investigation of an outbreak at the Amoy Gardens apartment complex provided the strongest evidence that a coronavirus could be airborne. But in the intervening decades, he'd also struggled to convince the public health community that their risk calculus was off. Eventually, he decided to work out the math. Li's elegant simulations showed that when a person coughed or sneezed, the heavy droplets were too few and the targets—an open mouth, nostrils, eyes—too small to account for much infection. Li's team had concluded, therefore, that the public health establishment had it backward and that most colds, flu, and other respiratory illnesses must spread through aerosols instead.

Their findings, they argued, exposed the fallacy of the 5-micron boundary. And they'd gone a step further, tracing the number back to a decades-old document the CDC had published for hospitals. Marr couldn't help but feel a surge of excitement. A journal had asked her to review Li's paper, and she didn't mask her feelings as she sketched out her reply. On January 22, 2020, she wrote, "This work is hugely important in challenging the existing dogma about how infectious disease is transmitted in droplets and aerosols." Even as she composed her note, the implications of Li's work were far from theoretical. Hours later, Chinese government officials cut off any travel in and out of the city of Wuhan, in a desperate attempt to contain an as-yet-unnamed respiratory disease burning through the 11-million-person megalopolis. As the pandemic shut down country after country, the WHO and the CDC told people to wash their hands, scrub surfaces, and maintain social distance. They didn't say anything about masks or the dangers of being indoors.

A few days after the April Zoom meeting with the WHO, Marr got an email from another aerosol scientist who had been on the call, an atmospheric chemist at the University of Colorado Boulder named Jose-Luis Jimenez. He'd become fixated on the WHO recommendation that people stay 3 to 6 feet apart from one another. As far as he could tell, that social distancing guideline seemed to be based on a few studies from the 1930s and '40s. But the authors of those experiments actually argued for the possibility of airborne transmission, which by definition would involve distances over 6 feet. None of it seemed to add up. Scientists use a rotating drum to aerosolize viruses and study how well they survive under different conditions.

Photograph: Matt Eich

Marr told him about her concerns with the 5-micron boundary and suggested that their two issues might be linked. If the 6-foot guideline was built off of an incorrect definition of droplets, the 5micron error wasn't just some arcane detail. It seemed to sit at the heart of the WHO's and the CDC's flawed guidance. Finding its origin suddenly became a priority. But to hunt it down, Marr, Jimenez, and their collaborators needed help. They needed a historian.

Luckily, Marr knew one, a Virginia Tech scholar named Tom Ewing who specialized in the history of tuberculosis and influenza. They talked. He suggested they bring on board a graduate student he happened to know who was good at this particular form of forensics. The team agreed. "This will be very interesting," Marr wrote in an email to Jimenez on April 13. "I think we're going to find a house of cards." The graduate student in question was Katie Randall. Covid had just dealt her dissertation a big blow—she could no longer conduct inperson research, so she'd promised her adviser she would devote the spring to sorting out her dissertation and nothing else. But then an email from Ewing arrived in her inbox describing Marr's quest and the clues her team had so far unearthed, which were "layered like an archaeology site, with shards that might make up a pot," he wrote. That did it. She was in.

Randall had studied citation tracking, a type of scholastic detective work where the clues aren't blood sprays and stray fibers but buried references to long-ago studies, reports, and other records. She started digging where Li and the others had left off—with various WHO and CDC papers. But she didn't find any more clues than they had. Dead end.

She tried another tack. Everyone agreed that tuberculosis was airborne. So she plugged "5 microns" and "tuberculosis" into a search of the CDC's archives. She scrolled and scrolled until she reached the earliest document on tuberculosis prevention that mentioned aerosol size. It cited an out-of-print book written by a Harvard engineer named William Firth Wells. Published in 1955, it was called *Airborne Contagion and Air Hygiene*. A lead!

In the Before Times, she would have acquired the book through interlibrary loan. With the pandemic shutting down universities, that was no longer an option. On the wilds of the open internet, Randall tracked down a first edition from a rare book seller for \$500—a hefty expense for a side project with essentially no funding. But then one of the university's librarians came through and located a digital copy in Michigan. Randall began to dig in.

In the words of Wells' manuscript, she found a man at the end of his career, rushing to contextualize more than 23 years of research. She started reading his early work, including one of the studies Jimenez had mentioned. In 1934, Wells and his wife, Mildred Weeks Wells, a physician, analyzed air samples and plotted a curve showing how the opposing forces of gravity and evaporation acted on respiratory particles. The couple's calculations made it possible to predict the time it would take a particle of a given size to travel from someone's mouth to the ground. According to them, particles bigger than 100 microns sank within seconds. Smaller particles stayed in the air. Randall paused at the curve they'd drawn. To her, it seemed to foreshadow the idea of a droplet-aerosol dichotomy, but one that should have pivoted around 100 microns, not 5.

The book was long, more than 400 pages, and Randall was still on the hook for her dissertation. She was also helping her restless 6year-old daughter navigate remote kindergarten, now that Covid had closed her school. So it was often not until late at night, after everyone had gone to bed, that she could return to it, taking detailed notes about each day's progress.

One night she read about experiments Wells did in the 1940s in which he installed air-disinfecting ultraviolet lights inside schools. In the classrooms with UV lamps installed, fewer kids came down with the measles. He concluded that the measles virus must have been in the air. Randall was struck by this. She knew that measles didn't get recognized as an airborne disease until decades later. What had happened?

Part of medical rhetoric is understanding why certain ideas take hold and others don't. So as spring turned to summer, Randall started to investigate how Wells' contemporaries perceived him. That's how she found the writings of Alexander Langmuir, the influential chief epidemiologist of the newly established CDC. Like his peers, Langmuir had been brought up in the Gospel of Personal Cleanliness, an obsession that made handwashing the bedrock of US public health policy. He seemed to view Wells' ideas about airborne transmission as retrograde, seeing in them a slide back toward an ancient, irrational terror of bad air—the "miasma theory" that had prevailed for centuries. Langmuir dismissed them as little more than "interesting theoretical points."

But at the same time, Langmuir was growing increasingly preoccupied by the threat of biological warfare. He worried about enemies carpeting US cities in airborne pathogens. In March 1951, just months after the start of the Korean War, Langmuir published a report in which he simultaneously disparaged Wells' belief in airborne infection and credited his work as being foundational to understanding the physics of airborne infection.

How curious, Randall thought. She kept reading.

In the report, Langmuir cited a few studies from the 1940s looking at the health hazards of working in mines and factories, which showed the mucus of the nose and throat to be exceptionally good at filtering out particles bigger than 5 microns. The smaller ones, however, could slip deep into the lungs and cause irreversible damage. If someone wanted to turn a rare and nasty pathogen into a potent agent of mass infection, Langmuir wrote, the thing to do would be to formulate it into a liquid that could be aerosolized into particles smaller than 5 microns, small enough to bypass the body's main defenses. Curious indeed. Randall made a note.

When she returned to Wells' book a few days later, she noticed he too had written about those industrial hygiene studies. They had inspired Wells to investigate what role particle size played in the likelihood of natural respiratory infections. He designed a study using tuberculosis-causing bacteria. The bug was hardy and could be aerosolized, and if it landed in the lungs, it grew into a small lesion. He exposed rabbits to similar doses of the bacteria, pumped into their chambers either as a fine (smaller than 5 microns) or coarse (bigger than 5 microns) mist. The animals that got the fine treatment fell ill, and upon autopsy it was clear their lungs bulged with lesions. The bunnies that received the coarse blast appeared no worse for the wear.

For days, Randall worked like this—going back and forth between Wells and Langmuir, moving forward and backward in time. As she got into Langmuir's later writings, she observed a shift in his tone. In articles he wrote up until the 1980s, toward the end of his career, he admitted he had been wrong about airborne infection. It was possible.

A big part of what changed Langmuir's mind was one of Wells' final studies. Working at a VA hospital in Baltimore, Wells and his collaborators had pumped exhaust air from a tuberculosis ward into the cages of about 150 guinea pigs on the building's top floor. Month after month, a few guinea pigs came down with tuberculosis. Still, public health authorities were skeptical. They complained that the experiment lacked controls. So Wells' team added another 150 animals, but this time they included UV lights to kill any germs in the air. Those guinea pigs stayed healthy. That was it, the first incontrovertible evidence that a human diseasetuberculosis—could be airborne, and not even the public health big hats could ignore it.

The groundbreaking results were published in 1962. Wells died in September of the following year. A month later, Langmuir mentioned the late engineer in a speech to public health workers. It was Wells, he said, that they had to thank for illuminating their inadequate response to a growing epidemic of tuberculosis. He emphasized that the problematic particles—the ones they had to worry about—were smaller than 5 microns.

Inside Randall's head, something snapped into place. She shot forward in time, to that first tuberculosis guidance document where she had started her investigation. She had learned from it that tuberculosis is a curious critter; it can only invade a subset of human cells in the deepest reaches of the lungs. Most bugs are more promiscuous. They can embed in particles of any size and infect cells all along the respiratory tract.

What must have happened, she thought, was that after Wells died, scientists inside the CDC conflated his observations. They plucked

the size of the particle that transmits tuberculosis out of context, making 5 microns stand in for a general definition of airborne spread. Wells' 100-micron threshold got left behind. "You can see that the idea of what is respirable, what stays airborne, and what is infectious are all being flattened into this 5-micron phenomenon," Randall says. Over time, through blind repetition, the error sank deeper into the medical canon. The CDC did not respond to multiple requests for comment.

In June, she Zoomed into a meeting with the rest of the team to share what she had found. Marr almost couldn't believe someone had cracked it. "It was like, 'Oh my gosh, this is where the 5 microns came from?!" After all these years, she finally had an answer. But getting to the bottom of the 5-micron myth was only the first step. Dislodging it from decades of public health doctrine would mean convincing two of the world's most powerful health authorities not only that they were wrong but that the error was incredibly—and urgently—consequential.

While Randall was digging through the past, her collaborators were planning a campaign. In July, Marr and Jimenez went public, signing their names to an open letter addressed to public health authorities, including the WHO. Along with 237 other scientists and physicians, they warned that without stronger recommendations for masking and ventilation, airborne spread of SARS-CoV-2 would undermine even the most vigorous testing, tracing, and social distancing efforts.

The news made headlines. And it provoked a strong backlash. Prominent public health personalities rushed to defend the WHO. Twitter fights ensued. Saskia Popescu, an infection-prevention epidemiologist who is now a biodefense professor at George Mason University, was willing to buy the idea that people were getting Covid by breathing in aerosols, but only at close range. That's not airborne in the way public health people use the word. "It's a very weighted term that changes how we approach things," she says. "It's not something you can toss around haphazardly."

The mannequins in this chamber were used to test the efficacy of masks.

Photograph: Matt Eich

Days later, the WHO released an updated scientific brief, acknowledging that aerosols couldn't be ruled out, especially in poorly ventilated places. But it stuck to the 3- to 6-foot rule, advising people to wear masks indoors only if they couldn't keep that distance. Jimenez was incensed. "It is misinformation, and it is making it difficult for ppl to protect themselves," he tweeted about the update. "E.g. 50+ reports of schools, offices forbidding portable HEPA units because of @CDCgov and @WHO downplaying aerosols."

While Jimenez and others sparred on social media, Marr worked behind the scenes to raise awareness of the misunderstandings around aerosols. She started talking to Kimberly Prather, an atmospheric chemist at UC San Diego, who had the ear of prominent public health leaders within the CDC and on the White House Covid Task Force. In July, the two women sent slides to Anthony Fauci, director of the National Institutes of Allergy and Infectious Diseases. One of them showed the trajectory of a 5micron particle released from the height of the average person's mouth. It went farther than 6 feet—hundreds of feet farther. A few weeks later, speaking to an audience at Harvard Medical School, Fauci admitted that the 5-micron distinction was wrong—and had been for years. "Bottom line is, there is much more aerosol than we thought," he said. (Fauci declined to be interviewed for this story.)

Still, the droplet dogma reigned. In early October, Marr and a group of scientists and doctors published a letter in *Science* urging everyone to get on the same page about how infectious particles move, starting with ditching the 5-micron threshold. Only then could they provide clear and effective advice to the public. That same day, the CDC updated its guidance to acknowledge that SARS-CoV-2 can spread through long-lingering aerosols. But it didn't emphasize them.

That winter, the WHO also began to talk more publicly about aerosols. On December 1, the organization finally recommended that everyone always wear a mask indoors wherever Covid-19 is spreading. In an interview, the WHO's Maria Van Kerkhove said that the change reflects the organization's commitment to evolving its guidance when the scientific evidence compels a change. She maintains that the WHO has paid attention to airborne transmission from the beginning—first in hospitals, then at places such as bars and restaurants. "The reason we're promoting ventilation is that this virus can be airborne," Van Kerkhove says. But because that term has a specific meaning in the medical community, she admits to avoiding it—and emphasizing instead the types of settings that pose the biggest risks. Does she think that decision has harmed the public health response, or cost lives? No, she says. "People know what they need to do to protect themselves."

Yet she admits it may be time to rethink the old droplet-airborne dichotomy. According to Van Kerkhove, the WHO plans to formally review its definitions for describing disease transmission in 2021.

For Yuguo Li, whose work had so inspired Marr, these moves have given him a sliver of hope. "Tragedy always teaches us something," he says. The lesson he thinks people are finally starting to learn is that airborne transmission is both more complicated and less scary than once believed. SARS-CoV-2, like many respiratory diseases, is airborne, but not wildly so. It isn't like measles, which is so contagious it infects 90 percent of susceptible people exposed to someone with the virus. And the evidence hasn't shown that the coronavirus often infects people over long distances. Or in well-ventilated spaces. The virus spreads most effectively in the immediate vicinity of a contagious person, which is to say that most of the time it looks an awful lot like a textbook droplet-based pathogen.

For most respiratory diseases, not knowing which route caused an infection has not been catastrophic. But the cost has not been zero. Influenza infects millions each year, killing between 300,000 and 650,000 globally. And epidemiologists are predicting the next few years will bring particularly deadly flu seasons. Li hopes that acknowledging this history—and how it hindered an effective global response to Covid-19—will allow good ventilation to emerge as a central pillar of public health policy, a development that would not just hasten the end of this pandemic but <u>beat back future ones</u>.

To get a glimpse into that future, you need only peek into the classrooms where Li teaches or the Crossfit gym where Marr jumps boxes and slams medicine balls. In the earliest days of the pandemic, Li convinced the administrators at the University of Hong Kong to spend most of its Covid-19 budget on upgrading the ventilation in buildings and buses rather than on things such as mass Covid testing of students. Marr reviewed blueprints and HVAC schematics with the owner of her gym, calculating the ventilation rates and consulting on a redesign that moved workout stations outside and near doors that were kept permanently open. To date, no one has caught Covid at the gym. Li's university, a school of 30,000 students, has recorded a total of 23 Covid-19 cases. Of course Marr's gym is small, and the university benefited from the fact that Asian countries, scarred by the 2003 SARS epidemic, were quick to recognize aerosol transmission. But Marr's and Li's swift actions could well have improved their odds. Ultimately, that's what public health guidelines do: They tilt people and places closer to safety.

On Friday, April 30, the WHO quietly updated a page on its website. In a section on how the coronavirus gets transmitted, the text now states that the virus can spread via aerosols as well as larger droplets. As Zeynep Tufekci <u>noted</u> in *The New York Times*, perhaps the biggest news of the pandemic passed with no news conference, no big declaration. If you weren't paying attention, it was easy to miss.

But Marr was paying attention. She couldn't help but note the timing. She, Li, and two other aerosol scientists had just published an editorial in *The BMJ*, a top medical journal, entitled "Covid-19 Has Redefined Airborne Transmission." For once, she hadn't had to beg; the journal's editors came to her. And her team had finally posted their paper on the origins of the 5-micron error to a public preprint server.

In early May, the CDC made similar changes to its Covid-19 guidance, now placing the inhalation of aerosols at the top of its list of how the disease spreads. Again though, no news conference, no press release. But Marr, of course, noticed. That evening, she got in her car to pick up her daughter from gymnastics. She was alone with her thoughts for the first time all day. As she waited at a red light, she suddenly burst into tears. Not sobbing, but unable to stop the hot stream of tears pouring down her face. Tears of exhaustion, and relief, but also triumph. *Finally*, she thought, *they're getting it* right, because of what we've done.

The light turned. She wiped the tears away. Someday it would all sink in, but not today. Now, there were kids to pick up and dinner to eat. Something approaching normal life awaited.

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