Credit: Eric Collins

Rethinking herd immunity

The global rise of 'vaccine hesitancy' is changing the landscape of disease transmission.

Lynne Peeples

On January 13, 2008, an unvaccinated seven-year-old boy returned home to San Diego from a family vacation in Switzerland. He and his family were unaware at the time that he had been infected with measles during their trip[1,2]. He became sick within a week of arriving home, and only received a diagnosis of measles the following week. Public health officials scrambled to assess the situation and ultimately determined that, by unintentionally importing the virus causing measles, he had exposed 839 people in the San Diego area to it, of whom 11 also developed the disease, including a hospitalized infant who was too young to be vaccinated.

This all happened despite the fact that some 95% of children in San Diego County had been vaccinated against the disease. That proportion, according to the concept of herd immunity, should be enough to keep measles at bay and protect those left unvaccinated. So, why did the outbreak still occur? That question has become increasingly common as outbreaks of preventable disease increasingly crop up in areas thought to have good population-level protection.

Public health researchers note two critical factors that continue to drive epidemics of measles, polio, whooping cough (pertussis) and other vaccine-preventable diseases — even when broad vaccination rates are high: growing numbers of domestic and international travelers, and proliferating pockets of parents who choose not to vaccinate their children.

"The risk of transmission for some of these diseases in a globally connected world is higher," says Orin Levine, director of vaccine delivery at the Bill & Melinda Gates Foundation in Seattle. "Infectious disease threats don't recognize and are not bound by borders; the best line of defense we have is to create virtual walls of immunity by increasing vaccination coverage everywhere in the world so that viruses can't make anybody anywhere sick."

Levine and others talk about a need to consider population immunity at both

a global and hyperlocal level. Take the case of the seven-year-old boy who returned to San Diego with measles. His parents had chosen not to vaccinate him or his siblings. And he attended a San Diego charter school in which parents of 17% of the students had signed personal beliefs exemption forms to opt their children out of required vaccinations. So while the average vaccination rate may have been high across the county, it varied locally; rates in some neighborhoods like his fell far below the necessary threshold to achieve herd immunity.

In effect, a cluster of unvaccinated children acts as piled-up kindling. When the infected boy returned home, he was the match that lit the pile. And the fuel kept the virus sustained long enough that it could jump to other vulnerable piles. "If you've got disease popping up in a community, that herd immunity in essence goes away," says Seth Berkley, CEO of Gavi, the Vaccine Alliance, a public–private health partnership that aims to increase access to immunizations.

Recent headlines describe similar stories: an unvaccinated five-year-old French boy reintroduced measles to Costa Rica in February, and ongoing measles outbreaks in the US have resulted from infected travelers transporting the virus from under-vaccinated areas of Eastern Europe and Israel to close-knit under-vaccinated communities in Washington State and New York. A man traveling in March from the affected ultra-Orthodox Jewish community in New York unknowingly sparked another outbreak in Southeast Michigan.

In January, the World Health Organization (WHO) listed 'vaccine hesitancy'[3], which describes the reluctance or refusal to vaccinate despite the availability of vaccines, among the top ten global health threats in 2019. Irrational concerns about vaccine safety, such as the now-debunked theory that the vaccine against measles, mumps and rubella causes autism, continue to circulate globally, expedited by the widening availability of mobile phones and the Internet.

"This social contagion is so important, and can't be disentangled from the disease itself," says Alessandro Vespignani, a computational epidemiologist at Northeastern University in Boston. Hesitancy among parents in Houston or Hong Kong could well put parents in Caracas or Cologne at greater risk of misinformation, and all of their children at greater risk of infection. "We live in a globally interconnected world, and there is no way that what we do locally is not having an impact on the global scale."

Sussing out susceptibility clusters

Measles is among the most contagious of all infectious diseases. Some nine out of every ten unvaccinated people who come into contact with the virus will contract it. And someone can be contagious for days before they know they are infected, providing plenty of time for a ride on a plane or train, or at least a solid social schedule. Although the virus may not recognize borders, the toll it takes varies widely around the world. Measles fatality rates are below 0.1% in developed countries[4], yet rates exceed 10% in some poor countries where people may be undernourished or lack access to care. Between 2000 and 2017, measles vaccination prevented an estimated 21.1 million deaths[5] around the world, according to the WHO.

It was during a mid-2000s measles epidemic in Marcel Salathé's home country of Switzerland[6] — the epidemic that spread to San Diego, as well as to Austria, Norway and other nearby counties — when he began to contemplate the role of beliefs in the spread of vaccine-preventable disease. Word was out that many Swiss parents had deliberately avoided getting their children vaccinated.

Salathé, a digital epidemiologist at the Swiss Federal Institute of Technology Lausanne, had always incorporated the behavior of viruses, but not that of humans, in his models of infectious disease dynamics. But soon he began to see that belief systems, too, were a powerful predictor. In a 2008 paper[7], he described how opinion-generated 'susceptibility clusters' — pockets of vaccine-hesitant parents and their children, for example — allow a virus to persist and to jump to other clusters. The phenomenon, he suggested in the paper, "effectively reduces herd immunity."

In a survey after the San Diego outbreak, local parents who chose not to vaccinate their children said they believed that getting these immunizations against vaccine-preventable diseases was unnecessary because of the low risk of catching these diseases. After all, measles was declared eliminated in the US in 2000. In countries like the US, "hesitancy exists because of the success of vaccines," says Gavi's Berkley. In contrast, he says, in many developing countries today, "you see children dying and becoming disabled all around you [from vaccine-preventable disease]. When that happens, of course, parents — at least parents who understand science — want their children to be protected."

"The vast majority of people around the world want access to immunization," adds Kate Dodson, vice president for global health strategy with the United Nations Foundation. Yet one in five people who want the measles vaccine, she adds, are not able to get it. Often, those one in five people also cluster together as they face common political, economic or cultural challenges. In the Democratic Republic of the Congo, 1.8 million children miss out on a full course of vaccines every year[8] due largely to difficulties in reaching clinics or clinics running out of vaccines. Ongoing conflict in parts of Pakistan and Syria impedes access to vaccines for many people[9].

The end result of poor access to vaccines parallels that of vaccine hesitancy. Both barriers need to be addressed, according to public health researchers, as either can create a geographic cluster of unvaccinated people that becomes fertile ground for a virus to proliferate. "Are they refusing to be vaccinated or failing to be vaccinated? From the standpoint of the measles virus, it doesn't care why they aren't vaccinated," says Matthew Ferrari, a statistical disease modeler at The Pennsylvania State University in University Park. To measles, he adds, a cluster arising from a lack of access "looks just like a kindergarten full of kids whose parents are actively refusing vaccination."

Viral spread

Misinformation, says Berkley, "really is spreading at the speed of light." And the implications go beyond measles to other diseases. Berkley refers to measles as the "canary in the coal mine." Because of its high rate of infectiousness, it is usually the first vaccine-preventable disease to show up when overall vaccination rates start slipping. Should trends continue, outbreaks of pertussis, tetanus and other diseases that require lower levels of coverage to achieve herd immunity, could be close behind.

For this reason, measles is "the perfect disease to study," adds Bruce Lee, an international health professor at the Johns Hopkins School of Public Health. Its rise can also raise a warning that further vaccine-preventable diseases such as hepatitis B, for which symptoms tend to be less obvious and more delayed, "may be spreading more quietly and insidiously."

Social-media-fueled anti-vaccination campaigns are thwarting measles vaccination efforts around the world, including in India, Israel, Madagascar, Venezuela and the Ukraine, among other countries. In northern Nigeria, work to eradicate polio is being derailed by dangerously false rumors that the vaccine is contaminated with anti-fertility agents and that vaccine deployment is a ploy to infect children with the monkeypox virus. And it is not only conflict and poverty that stop some parents in Pakistan from vaccinating

their children. Distrust in vaccination campaigns grew — and reverberated online — after the US conducted a sham hepatitis B vaccination project in its targeting of Osama bin Laden[10]. The Central Intelligence Agency attempted to obtain DNA from Osama's relatives to confirm his whereabouts before storming the Abbottabad compound.

Ulterior motives are at play as well. The Russian Twitter bots responsible for spreading fake news during the 2016 US election have also been pushing anti-vaccine misinformation to further promote political polarization[11]. Meanwhile, some websites appear to be cashing in on parents' fears by selling anti-vaccine books, supplements and online seminars.

All that online vaccine hesitancy chatter may at least have one silver lining: the creation of valuable data. Salathé has found that tracking tweets on Twitter[12], for example, can help identify local clusters of vaccine hesitancy. Data from Internet search engines and other social media sites, too, offer volumes of useful data.

Combining that behavioral data with streams of information from medical records, flight logs and mobile phones may enable models to more powerfully predict the spread of vaccine-preventable diseases and better target vaccination and education campaigns. According to Vespignani, "This is a way to simulate disease much closer to what we do with the weather forecast."

In addition to long incubation time, another difficulty in modeling a disease like measles is relative scarcity in recent decades. "Now, unfortunately, we have enough cases and outbreaks where modeling can become a kind of good intelligence," Vespignani says.

To account for the geographical variability in vaccine coverage, which has also been a hurdle for modelers, researchers are now rapidly increasing their resolution. In a paper[13] published in April, Jonathan Mosser and colleagues estimated vaccine coverage at a resolution of 5 km by 5 km in 52 African countries. They found that while diphtheria–pertussis–tetanus (DPT) vaccine coverage had increased across Africa, "substantial geographic inequalities" persisted within and across countries. Better localization of clusters of unvaccinated people could improve simulations of disease spread, says Mosser, a clinical fellow at the Institute for Health Metrics and Evaluation at the University of Washington in Seattle. "All the ingredients are there," adds Salathé, noting the recent availability of big data, computational power and complex algorithms. "The challenge is really to put everything together."

Good policy

Policy approaches may aid in tackling vaccine hesitancy, too. On May 10, in response to a measles outbreak that had sickened 74 kids, Washington State Governor Jay Inslee (D) signed a bill to remove the ability of parents to exempt their children from measles, mumps and rubella vaccination for personal or philosophical reasons. Every US state allows exemptions when medically necessary. And all but three states allow religious exemptions. Washington had been among the more than a dozen remaining states that also allow exemptions for 'personal, moral or other beliefs'.

In a 2018 paper[14], Peter Hotez, dean of the National School of Tropical Medicine at Baylor College of Medicine in Houston, and his colleagues identified 15 counties in the US with populations at risk for measles and other vaccine-preventable diseases because of high rates of non-medical exemptions. About half of those counties are reporting outbreaks of measles in 2019.

Even a 2015 state ban on all non-medical exemptions seems to have fallen short in California, where another bill has now been proposed that would prevent parents from doctor-shopping for medical exemptions to bypass the law[15].

Vaccination has always been the province of either local or state governments. In 1905, the US Supreme Court upheld the authority of Cambridge, Massachusetts, to require vaccination against smallpox after a minister refused over safety concerns. But more action is needed at the national and international levels, says Lawrence Gostin, a professor of global health law at Georgetown University. He laid out a detailed three-pronged strategy in a paper published in April[16].

"The federal government, as a matter of constitutional law, is not permitted to directly tell states what to do," he says. "But it can condition federal dollars based on the states' conformance with federal standards which, in this case, would be to eliminate or significantly tighten all non-medical exemptions."

He is also recommending that the feds work with social media companies to "filter out unscientific, unsubstantiated information about vaccines," as well as fund state and local advocacy campaigns to restore faith among the public in the safety and importance of vaccines. "The campaign wouldn't accuse parents of being ill-willed," says Gostin. "It would assume, as I assume, that if most mothers and fathers had access to reliable, trusted sources of scientific information then they would do right thing and vaccinate their children."

Hotez highlights the same three strategies — and underscores their urgency. He has spent most of his career developing vaccines for globally neglected diseases, and says he worries that the spreading vaccine hesitancy will "compound the problem" of introducing new vaccines for malaria, dengue and the like.

"All countries that are experiencing significant vaccine hesitancy should have a similar kind of plan," Gostin adds. "Vaccines were the greatest public health achievement of the 20th century, and we want it to continue into the 21st century." ❐

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