



Health-care workers in New York protest against compulsory swine flu vaccination.

PUBLIC HEALTH

An injection of trust

Faced with outbreaks of preventable diseases, public-health experts need to win over parents who refuse vaccinations.

BY MICHAEL EISENSTEIN

In July 2013, public-health officials in Wales finally began to breathe a sigh of relief. The measles epidemic that had raged through the country for eight months and infected more than 1,200 patients — hospitalizing 88 and killing one — was finally coming under control. The respite was brief, however, as just months later a second outbreak emerged in the same region, with 36 new cases by mid-November (see “Exposed and unvaccinated” page S18).

The outbreaks primarily afflicted children whose parents had opted not to let them have the measles–mumps–rubella (MMR) vaccine. Their refusal was broadly attributed to lingering fears related to a now discredited link between the MMR vaccine and autism. Parents remained hesitant even after the first outbreak, and a strong vaccination push reached fewer than half of the eligible children.

The re-emergence of vaccine-preventable diseases has become increasingly common worldwide. For example, in 2012 the US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, reported the largest number of US cases of pertussis (whooping cough) for nearly 60 years. In Japan, rubella cases leapt from 87 in 2010 to

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5,442 in just the first 4 months of 2013. And in France, the World Health Organization (WHO) reported 14,000 cases of measles in 2011. “There are lots of examples in wealthy, developed countries,” says Seth Berkley, chief executive of the Global Alliance for Vaccination and Immunization (GAVI) in Geneva, Switzerland. Given the narrow margins of ensuring protection against such outbreaks, even a few parents who refuse paediatric vaccination can jeopardize the control and elimination of diseases that are prominent killers of infants and children elsewhere in the world.

Vaccine refusal dates back to the nineteenth century, when the UK Government permitted ‘conscientious exemption’ for those opposed to smallpox vaccination. But today’s reasons for refusal are very different. “We ask citizens to get vaccines to prevent 14 different diseases, which can mean as many as 26 inoculations in the first few years of life, to prevent diseases that people mostly don’t see, using biological fluids that most people don’t understand,” says Paul Offit, head of the infectious-diseases division at the Children’s Hospital of Philadelphia in Pennsylvania. “It’s not surprising that people are hesitant.”

PERSONAL REASONS

Most public-health experts view vaccination programmes as unalloyed successes. One analysis estimates that immunization has prevented 75–106 million cases of disease

in the United States alone¹. Since the 1980s, every US state has required a standard battery of vaccines for school enrolment. There is strong participation too in much of Western Europe, where these vaccines are merely ‘recommended’. “The vast majority of children are immunized, with coverage of over 90% across Europe,” says Pier Luigi Lopalco, head of the vaccine-preventable diseases programme at the European Centre for Disease Prevention and Control (ECDC) in Stockholm. When Australia faced falling vaccination rates in the 1990s it introduced incentives that rewarded both clinics and parents. “Our immunization rates rose by at least 10%, which was a major increase,” says Julie Leask, a social scientist specializing in immunization policy at the University of Sydney.

But some vaccination programmes allow people to refuse for personal reasons. In much of Europe, no medical consultation is required. In the United States, parents must actively register their refusal; 48 states recognize religious exemptions and 18 allow ‘personal belief exemptions’. The refusal numbers are low — just 2% for 2010–2011, according to the CDC — but epidemiologist Saad Omer of Emory University in Atlanta, Georgia, has observed a disconcerting rise. “The rate of refusal has gone up, and even the rate of change compared to previous years has accelerated,” he says. Indeed, CDC data indicate that the percentage of non-medical exemptions essentially doubled between 2006 and 2011. Different states require different levels of effort: some require medical consultation, others simply a signature. Omer found that non-medical exemption rates were 2.3 times higher in states with easy requirements than in those with steeper administrative barriers². “If you make it easier for a parent who is hesitant and on the fence to claim an exemption, it looks like they will,” he says.

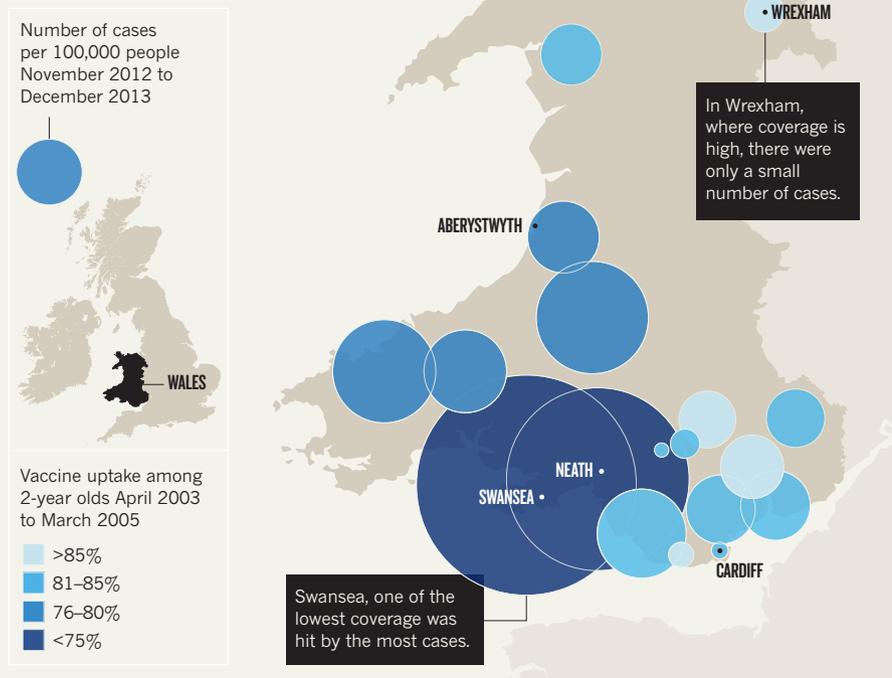
Unvaccinated families also tend to cluster. Leask notes that in Australia “the refusal rate is 1.7% nationally, but in some regions that can climb to around 20%.” Some clustering also occurs in self-contained religious groups. The ‘Bible Belt’ region of the Netherlands, which is home to several communities of Orthodox Protestants that have rejected vaccination, has been the site of a large ongoing measles outbreak, and in October 2013 an unvaccinated 17-year-old girl died from measles. More recently, international travellers have enabled this epidemic to make the leap to Canada.

SCARE STORIES

Instead of religious dogma, many clusters of vaccine refusals result from shared concerns about whether children may be harmed by the inoculations. “Refusal is multifaceted, but perceptions of vaccine safety contribute more than other factors,” says Omer. These worries can result in delayed vaccination, outright refusal or selective inoculation of children, where the

EXPOSED AND UNVACCINATED

A drop in coverage of MMR vaccine in Welsh children led to a rise in vulnerability to a measles outbreak.



decision is a product of both risk calculation and emotional response.

A single scare can cast a long shadow. The story of Andrew Wakefield, a gastroenterologist at the Royal Free Hospital in London whose work led to a widespread belief in a link between the MMR vaccination and autism, is well known. As parents panicked, MMR vaccination rates in England and Wales fell from over 90% in 1997 to less than 80% in 2004, with similar drops in the United States and across Western Europe. Although thoroughly discredited, Wakefield's ideas are kept in circulation by vocal networks of anti-vaccine activists. "In southern Europe, especially Italy, this alleged link between autism and MMR is re-emerging in the newspapers and on a lot of websites," says Lopalco. Activist organizations also promote unfounded fears that vaccines trigger medical conditions such as multiple sclerosis or contain toxic levels of chemicals such as aluminium, or that infants' immune systems are overwhelmed by the number of vaccinations³.

In fact, vaccines undergo extensive and continuous surveillance to identify adverse events overlooked during clinical trials. For example, the CDC operates the Vaccine Safety Datalink (VSD) with nine large US 'managed care organizations', tracking data from more than 9 million individuals. "We can update these databases weekly, and thus virtually conduct real-time monitoring when a new vaccine is introduced," says Frank DeStefano, director of the CDC's Immunization Safety Office. Data

from the VSD helped disprove the connection between MMR and autism, but have also identified real adverse events, such as when 197 children in a cohort of 1.8 million who had received the MMR vaccination developed immune thrombocytopenic purpura⁴. "It's a relatively benign blood disorder where there's easy bruising and bleeding, but it can be scary," says Jason Glanz, an epidemiologist affiliated with the VSD at the Kaiser Permanente Institute for Health Research in Denver, Colorado.

The CDC continues to fight the myth of a vaccine-autism link and recently demonstrated that there was no link between exposure to numerous vaccine antigens and autism⁵. "A substantial proportion of parents still have concerns along these lines," says DeStefano. Leask notes that the MMR story draws strength from the lack of a robust biological explanation for autism. "This causal hunger drives people to look around for a culprit," she says, adding that vaccines were once linked to sudden infant death syndrome (SIDS) until the medical community got a better understanding of the risk factors.

FORGOTTEN FOES

Studies suggest that parents who delay or refuse vaccines tend to be well educated and seek out information that gives them active control of their child's health. Some consult practitioners of complementary and alternative medicine, who may eschew vaccines in favour of non-pharmaceutical approaches to preventing diseases, or promote alternative vaccine

schedules that leave children underprotected. Based on a large study of undervaccination in eight managed care organizations, Glanz concluded that at least 12–13% of parents "are deliberately not giving vaccines on time"

Many parents also visit anti-vaccination websites that use anecdotal evidence to promote an agenda of parental choice that builds on an underlying mistrust of the government and the pharmaceutical industry³. "They use narratives and tell stories," says Neal Halsey, director of the Institute for Vaccine Safety at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. "We present numbers and risk levels, and those things don't resonate with hesitant parents."

For such parents, emotional descriptions of children who have allegedly been injured by vaccines may prove more persuasive than tales of half-forgotten diseases. "My wife ran the intensive care unit at a major teaching hospital in America, and she's never seen a case of measles or tetanus," says Berkley. "I think that's a big factor." He points out that vaccines are generally embraced in the developing world, where these diseases remain all too real — the WHO estimates that 158,000 people died from measles in 2011. "In general, people there desperately want vaccines and will walk for a day to get them," he says. But in nations with long-standing vaccination programmes, such as the United States or United Kingdom, it's easy to dismiss these diseases as harmless unless you've experienced the potential complications, which include pneumonia and encephalitis. "When I've talked with parents of unvaccinated children who have been admitted to hospital with complications from pertussis or measles, they inevitably say, 'I never knew it could be this serious,'" says Halsey.

If large numbers of parents continue to opt out of vaccination programmes, these may well become more familiar experiences. In a well-vaccinated community, even unvaccinated individuals benefit from herd immunity. The threshold for this benefit depends on both the disease and the vaccine; for measles, the CDC estimates that herd immunity requires 92–94% vaccine coverage. But herd immunity breaks down when coverage drops even in small pockets of otherwise well-vaccinated regions. Omer and colleagues found that this effect may have contributed to a 2010 pertussis outbreak in California that infected more than 9,000 individuals⁶. "The clustering of refusals was associated with the clustering of pertussis," says Omer. Pertussis is particularly problematic because the vaccine is less protective than others and its effectiveness wanes over time. Loss of herd immunity could also help more serious diseases to return: the detection of poliovirus in Israel and outbreaks in war-torn Syria led the ECDC to announce⁷ that such countries "should urgently consider implementing targeted action and improving vaccine coverage".

Wary parents are only part of the problem. “It’s also people who haven’t gotten up to date, either unwittingly or because they have fallen through the cracks,” says Leask. But those who sit on the fence represent a potentially serious gap in a nation’s immunity, and the MMR panic has shown how quickly this gap can widen.

OFF THE FENCE

The trick is to address worries while preserving public confidence — often a difficult balancing act. Controversy lingers over a 1999 recommendation from the CDC and the American Academy of Pediatrics to remove the ethyl mercury-containing preservative thiomersal from single-dose vaccines. This precaution was based on concerns over cumulative environmental mercury exposure in children, although subsequent research showed that ethyl mercury is eliminated from the body much faster than predicted. Offit believes this decision fuelled misconceptions that thiomersal contributes to autism. “We branded it with a scarlet letter, and today people are still scared of getting flu vaccines in the multidose preparations that contain thiomersal,” he says. However, Halsey defends the decision as necessary to protect public trust. “None of us had any concerns about autism,” he says. “But if we had not done it, I think that more people would be rejecting those vaccines.” In other cases, the negative impact is clearer. For example, France still has poor uptake of the hepatitis B vaccine following the government’s 1998 suspension of vaccination, a decision based on false reports of a link with multiple sclerosis.

When the press spotlights potential adverse events, especially with backing from celebrities such as actress Jenny McCarthy or high-profile scientists such as Wakefield, it can even shake the faith of medical professionals. “If you have a provider who is less confident in a vaccine’s safety and less motivated, that will have a lot of carry-over effects,” says Leask.

Heidi Larson of the London School of Hygiene and Tropical Medicine helps public-health experts respond rapidly to avoid creating a lingering atmosphere of doubt by identifying pockets of concern early (see “Adverse reactions”). “Publics have long memories,” says Larson. “We need to be vigilant and never for a minute take for granted any individual’s acceptance of any health technology.” Larson directs the Vaccine Confidence Project (VCP), which scans news and social media for signs of concern⁸. “We’re trying to use a systematic approach to characterize what breeds confidence and lack of confidence, and identify things that tip it one way or another,” she says. Networks of pro-immunization parents are also helping to counter anti-vaccine propaganda. For example, epidemiologist Edgar Marcuse of the University of Washington in Seattle is recruiting such parents as peer-educators through the Vax Northwest programme to lower his state’s exemption

CASE STUDY

Adverse reactions

Vaccination initiatives are generally welcomed in the developing world, where disease mortality and morbidity remain clearly visible threats, but even there they are vulnerable to misinformation and miscommunication. In the mid-1990s, a Catholic organization disseminated misinformation that the tetanus vaccine had contraceptive effects. Vaccination rates plummeted in Catholic communities until public-health professionals reached out to the Vatican to help resolve the crisis.

The handling of such conflicts can make or break a vaccination programme. In 2003, northern Nigeria boycotted the polio vaccine, fuelled by political issues and mistrust of the Western pharmaceutical industry and by rumours that the vaccine was a plot to sterilize Muslims. The public-health community overcame this boycott (and a similar movement in India) by working with local Islamic clergy and community leaders. In contrast, two demonstration projects for the human papillomavirus vaccine in India were derailed in 2010 by campaigners from women’s groups. After early attempts to engage the national government over the programme were rebuffed, the activists mounted an aggressive campaign calling for an investigation of the deaths of four vaccine recipients. The deaths proved unrelated to the vaccine, but the projects were halted amid public opposition. “[The protesters] started talking about things related to it being too expensive, not giving cervical screening, and the need to have a public forum,” says Heidi Larson of the London School of Hygiene and Tropical Medicine. “They didn’t

initially focus on the vaccine safety issue, but when they weren’t being listened to, they searched for adverse events because that gets more of a reaction.”

Larson believes that more attentive monitoring of online expressions of public concern — through her Vaccine Confidence Project (VCP), for example — could bring attention to these issues sooner. Local protests are often fuelled by online activists in the United States and Europe. By keeping tabs on rumours and reports of possible adverse events, governments and public-health officials can adapt engagement strategies accordingly. This won’t solve every problem — Larson notes that recent attacks against vaccination workers in Pakistan and Nigeria are the acts of militants, rather than expressions of public refusal. More generally, however, the VCP could help to engage disenfranchised communities early, before boycotts or protests become necessary. “We’re trying,” says Larson, “to be anticipatory, rather than in crisis management.” **M. E.**



Polio vaccination in Nigeria.

rate. The final decision on whether to vaccinate, however, happens in the clinic. “Even among vaccine refusers, we found that primary health-care providers were the most frequently used and trusted source of vaccine information,” says Omer. Honesty is the best policy. Like any medicine, vaccines carry real risks, ranging from minor swelling to rare but serious events such as seizures or anaphylaxis, and doctors can build trust by candidly framing these facts alongside the dangers of disease.

“If you put boundaries around the risk and you say what it is, it becomes much less mysterious,” says Leask. Her team has devised a decision-support framework that helps clinicians to deliver targeted information for parents who are cautious supporters, hesitant or ardent refusers. The emphasis is on winning over the parents through listening and empathy, rather than challenging contrary beliefs. Ideally, she says, this intervention will be delivered before

the baby is, reaching mothers ahead of any decisions about vaccination.

Offit notes that in his experience, the trump card of medical authority also helps. “Both parents and doctors want to do what’s best for the child,” he says. “But they’re coming for your expertise — it’s okay to be an expert.” ■

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