

# An injection of confidence

Scientists explore new and old methods to counter anti-vaccine propaganda and overcome vaccine hesitancy so as to increase vaccination rates

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Vaccination is widely regarded as one of the most successful achievements of medicine and public health. It has helped to drastically reduce the threat of the most devastating childhood diseases, such as measles, polio, diphtheria, tetanus, pertussis, as well as *Haemophilus influenzae* and rotavirus infections. Thanks to vaccines, smallpox has been declared eradicated from the world in 1980 and polio is on the brink of being eradicated as well. According to the WHO, vaccination prevents an estimated 2.5 million deaths each year—in other words, it saves five lives every minute.

“When there is a serious infection, people look to vaccines as the answer because prevention is always better than treatment. With Ebola or Zika, everyone was very eager to have a vaccine”, said Kathryn Edwards, Director of Vanderbilt University’s Vaccine Research Program, who also serves on the American Academy of Pediatrics’ committee on infectious disease. But once vaccines are available and successful, they become victims of their own success. Many vaccine preventable childhood diseases have lost their threat, at least in the developed world. “Young doctors and parents don’t fear these diseases like we used to do. The better our vaccines are, the more difficult it is for parents to appreciate their importance”, Edwards said.

## A persistent problem

Many people instead focus their attention on adverse reactions, perceived or real. Although only few people are radically opposed to vaccines *per se*, anti-vaccine groups are very vocal and they have an impact on people’s perceptions. A much larger group is “hesitant”: somewhere between complete acceptance and complete rejection and vulnerable to the

propaganda put forth by anti-vaccine groups. In a recent study, 13.5% of the respondents from the USA stated that they disagree that vaccines are safe—and the situation is worse in Europe, where the number gets as high as 41% in France [1]. Many opponents also see mandatory vaccination programs as an infringement of their freedom of choice.

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This is problematic for public health, because high vaccination rates are required to establish and maintain herd immunity, to disrupt infection chains, and to contain disease outbreaks. As no vaccine is 100% effective and as some people cannot be vaccinated for medical reasons, there are always a small number of people in a population who are vulnerable to infection. Deliberately unvaccinated people are therefore not only a risk to themselves but also to others, and they have played a central role in disease outbreaks in the past. Over the past decade, vaccine preventable diseases, such as measles, poliomyelitis, and pertussis, have periodically re-emerged in parts of the developed world where vaccination rates were low. Vaccine preventable diseases are rare, but they are only rare because most people get vaccinated. “It’s like 4-way stop. If one person does not stop, we are still doing fine. But if 2, 3 or 4 do not, we will have an accident”, said Edwards. Not getting vaccinated—hoping not to contract a disease because everyone else is vaccinated—is somewhat selfish. Vaccine preventable

diseases can be back in no time when vaccination rates drop.

In the USA, vaccination is mandatory for school entry and the more difficult it is to get an exemption, the higher the vaccination rates. “I think it is quite clear in the US that compulsory vaccination has been very helpful”, commented Daniel Salmon, deputy director of the Institute for Vaccine Safety at Johns Hopkins University’s Bloomberg School of Public Health. Although such laws and regulation may help, the more efficient strategy is to convince people that vaccines are efficient at preventing disease, do no harm, and help to protect society. Initiatives such as the WHO Strategic Advisory Group of Experts (SAGE) Vaccine Hesitancy Working Group have been investigating the reasons for vaccine hesitancy and try to find ways to improve confidence in vaccines. Vaccine hesitancy is a complicated issue, it has many facets and there is no single solution. A look at the history may help understand the issue.

## A history of opposition

In 1796, Edward Jenner introduced smallpox vaccination by exposing a young boy to the related but harmless cowpox virus. The new method spread quickly, and, after a few years, smallpox vaccination was routinely performed in many European countries and in the Americas. But there were many skeptics who found it counterintuitive that deliberately infecting a person with a disease would do him any good. In 1853, the British government made it mandatory to vaccinate all children. Many people saw these laws as violation of civil rights and, as opposition increased, the British Parliament gave in and introduced a conscience clause in 1898,

which allowed individuals to opt out of compulsory vaccination.

Fears were also fueled whenever vaccines were linked to major risks and, indeed, there have been cases when vaccination did considerable harm. One of the worst pharmacologic disasters in US history occurred in 1955 when, shortly after the development of the polio vaccine, the US government launched a mass vaccination campaign. The program was abandoned within a month after cases of atypical polio were reported. Thousands of children had received a vaccine in which the poliovirus, manufactured by the California-based Cutter Laboratories, was not fully inactivated. The incident killed 10 children and left 200 paralyzed.

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Another incident that shook confidence in vaccines occurred in 1976, when an influenza virus related to the stain that set off the 1918 flu pandemic, caused the death of a recruit at Fort Dix, New Jersey. Health officials were alarmed, and a mass immunization program was launched, but was quickly suspended after cases of Guillain-Barré syndrome appeared among vaccinated persons. The suspected flu pandemic never arrived—no one outside Fort Dix ever fell ill—but more than 400 million people were vaccinated, which probably caused several hundred cases of Guillain-Barré syndrome.

As tragic as these historical incidences of production errors and mismanagement are, they are nonetheless rare. However, people's anxieties are also fueled by rumors, and these rumors often have their origin in science. In 1974, researchers from the Hospital for Sick Children in London, UK, suggested that pertussis inoculation as part of a triple vaccine (DPT) may cause neurological complications. Although the study was small and the evidence was vague, the story was widely covered by the UK media. The “Association of Parents of Vaccine-Damaged Children” formed, supported by Gordon Stewart, a medical professor at the University of Glasgow. As a result, vaccination rates dropped from about 80 to 30% between 1974 and 1978, followed by three

major epidemics of pertussis in the UK. In the USA, DPT caused a controversy after a one-hour television documentary, featuring children who were allegedly harmed by DPT vaccination. Again, it triggered the formation of an outspoken anti-vaccine group and much publicity. However, overall vaccination rates were affected less than in the UK.

#### False studies and rumors

Nearly 25 years after the DPT debate, Andrew Wakefield published a study in *Lancet*, in which he suggested that the MMR vaccine was linked to autism. The study was later discovered to be fraudulent and *Lancet* formally retracted the paper in 2010. In addition, Wakefield had a serious conflict of interest: He had been hired by a lawyer to find scientific evidence that could be used in a class action lawsuit against drug companies. Wakefield's discredit took the wind out of the sceptics' sails—but the damage had been done. Again, anti-vaccine groups had formed, the media had their role in spreading fear, immunization rates dropped considerably, and measles outbreaks subsequently occurred throughout the UK. Today, the belief that MMR vaccination causes autism is still widespread, despite solid scientific evidence against it.

Once the rumor mill starts spinning, it is almost impossible to stop it. Both the DPT and the MMR vaccine controversies began with a small scientific study and then went viral. In both cases, anti-vaccine groups, the media and a medical advocate—Gordon Stewart and Andrew Wakefield, respectively—played their part. However, there is another theme: In both cases, the debate originated in the UK and then crossed the Atlantic to the USA, where its impact was much smaller. One explanation for this difference is the “more fertile UK ground”, as some scholars have called it [2]. In Britain, the rejection of vaccines has a long history going back to the times of Jenner, which has left its traces. Centuries later, the public and the medical profession are still particularly skeptical toward vaccines. In addition, the MMR anxiety in England came on the heels of the mad cow disease, when the government had downplayed the risk for humans and withheld information. “Publics have memories, and the crisis over the risks of mad cow disease had created a lot of distrust in the government”, explained Heidi Larson of

the London School of Hygiene and Tropical Medicine, who has previously headed the Global Communication for Immunization at UNICEF and chaired the Advocacy Task Force for the Global Alliance for Vaccines and Immunization (GAVI).

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Distrust does not necessarily start with the vaccine, but it has a lot to do with a general confidence in health authorities. There are other examples to illustrate this point. France suffered a major health scandal in the early 1990s, after it surfaced that the *Centre National de Transfusion Sanguine* knowingly had distributed HIV-contaminated blood products. Shortly thereafter, fears spread in France that hepatitis B vaccine causes multiple sclerosis and the French Ministry of Health decided to temporarily suspend the school-based hepatitis B vaccination program in 1998. According to a recent review of vaccine hesitancy in 67 countries, France is top on the list [1]. In 2003, five northern Nigerian states boycotted the polio vaccine after rumors had spread that it was an American conspiracy to spread HIV and to sterilize Muslim girls. Again, the underlying reasons are outside the field of vaccination. One such factor was a deep historical distrust of Western powers by some Muslim populations. Another was political interests and tension between the northern Islamic regions of the country and the central government [3].

#### Injecting confidence

What can be done to counter vaccine hesitancy? There have been many suggestions, but the magic bullet has not yet been discovered. Yet, it seems clear that simply telling people that vaccines are safe is not enough. “Many public health interventions to promote vaccination have been based on a ‘knowledge-deficit’ approach, assuming that vaccine hesitant individuals would change their mind if given the proper information”, writes Eve Dubé of the Quebec National Institute of Public Health in a review on strategies to address vaccine hesitancy [4].

A number of studies have investigated different communication strategies, but so far the results say more about what does not work than what does. The impact of educational information such as brochures, pamphlets, or posters on parents' intention to vaccinate their children has been limited [4,5]. Moreover, current communication strategies may even backfire. For example, one study showed that information material refuting the link between MMR vaccine and autism actually increased vaccine hesitancy among parents who had the least favorable attitudes; and images of sick children or a dramatic narrative about an infant who almost died of measles increased fears of the vaccine's side effects [6]. "Scaring people into vaccination does not help", Salmon concluded. "There are many ways in which people perceive information. Decision making is a complicated process and we haven't figured it out yet. Maybe it is about who you talk to and how you talk to them".

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Larson argues along the same lines. "The public health community gives the information that *they* think is important. This is not necessarily sensitive to the kinds of concerns people have", she said. But communication is a two-way process—giving information and listening. "I don't think we can ever underestimate the importance of listening", Larson argued. Listening helps understand some of the causes for people's worries that might not be evident at first sight. Larson gave an example: In the early 2000s, just like in Nigeria, people in under-served, dominantly Muslim populations in India refused polio vaccines suspecting them to be unsafe. "But when we talked to them, some of the mothers said: We don't want our children being vaccinated by men, but rather by women. We don't want them vaccinated by people coming from Delhi, we would rather have someone from our local communities vaccinating our children so we know who to talk to if there is a problem", Larson recalled. Understanding people's concerns may guide the way toward improvements. Do they have a problem with the delivery process, like in the Indian case? Are people concerned because they think vaccines are

not effective or is it because they think they are not safe? Do they think their religion is compatible with vaccination? "Sometimes people are simply unhappy with the vaccination program, they don't feel they are treated well at the clinic", Larson said.

Indeed, health providers play an important role in building confidence since they have a strong influence on their patients. "I think the first thing pediatricians need to do to help parents overcome their anxieties is listen to the questions that they have and to provide informative answers to the questions", Edwards said. This may require some time—but it is time that is well invested from a public health point of view. As Larson put it, "just the act of listening is important and it is definitely the first step of trust-building". Building confidence requires several levels. The public needs to trust the health authorities as well as the health providers. And, of course, the health providers themselves need to trust that vaccines are safe.

#### Building trust

"Vaccines are held to a higher safety standard than most drugs and biologics because they are being given to healthy populations and you don't really know who is going to become infected and who is not", Salmon said. Indeed, existing vaccines have been gradually improved to make them safer. For example, in industrialized countries, acellular pertussis vaccines have gradually replaced the use of whole cell vaccines, which are made from killed bacteria and often come with adverse reactions such as arm swelling at the site of injection or fever. Similarly, many countries have recently switched to using inactivated polio vaccine that is given as an injection, as opposed to the oral vaccine that contains attenuated viruses that can revert to virulence and become transmissible vaccine-derived polioviruses. In addition, many new vaccines have been developed and science does a lot to make vaccines safe.

"Introducing new vaccines takes numerous years of very careful assessment of the vaccine's safety, with many successively larger trials. And even after the vaccines are licensed, safety assessments continue to occur", Edwards said. Adverse events may have escaped detection in a trial if they are rare, or if there is a delay between exposure to the vaccine and the onset of symptoms. When the H1N1 vaccine was introduced,

Salmon served as the Director of Vaccine Safety in the National Vaccine Program Office at the US Department of Health and Human Services and ran the US safety monitoring program. "We had 35 million people anonymously under active surveillance for that vaccine program", Salmon said. The researchers improved old systems for safety monitoring and developed new ones to meet the challenge of detecting rare events while distinguishing false positives from real adverse events caused by the vaccine. "We looked really hard, we did so in a very public and transparent way", Salmon explained. In the end, they found vaccination came with a very small risk of Guillain-Barré syndrome, affecting 1–3 people per one million—and the public did not freak out", according to Salmon. Apparently, the public can handle a small risk pretty well when they know they can trust that health officials are open about anything else they may find. "We like to think that what we did help build confidence", Salmon said but added that "[c]onfidence is a really elusive thing, it is hard to nail we are just starting to characterize what it is. And to know how to improve confidence is much more complex".

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The challenge of building confidence in vaccines is today as relevant as never before. There are more vaccines available, and children receive up to 25 shots in the first 6 months of their lives, depending on the country. In addition, society has changed. The Internet gives people a voice, it makes them feel empowered and they have the communication tools to express that. People are embracing their rights, they want to make their own choices. "They have no tolerance for patronizing and being told what to do. I call it the Arab spring of vaccination", Larson said. "I am all for rights, but I do not think the public health community was prepared for public's embracing their right to health, their right to information, their right to voice and choice. The health community is now paying back for years and years of telling the public 'take this, it's good for you'".

On the positive side—history tells us that building confidence is indeed possible.

There has always been opposition to vaccination, and there have always been crises that have put vaccination programs at risk. But crises have been overcome; MMR vaccination rates are back to normal in the UK, and polio vaccination has returned to India and Nigeria [3]. There is still a lot to be done, but the health community can learn from these experiences—about the importance of transparency, about the central role of health providers in building confidence, and the importance of listening and responding to the need of specific societal groups. They can learn how to deal with a public that think and decide for themselves.

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