Are Vaccines Safe? Risk Communication Applied to Vaccination

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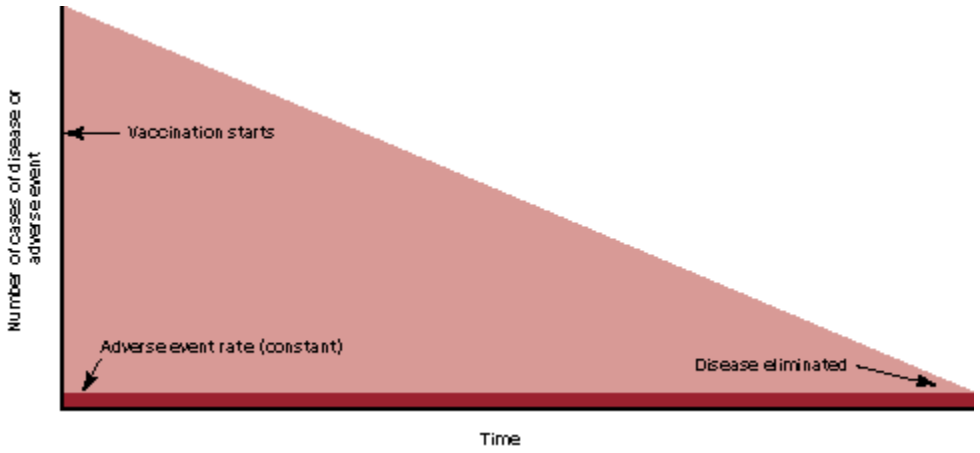
Hazard, risk, likelihood, chance, odds, probability. Health risks seem to make the news more often than ever, even though many risks are at their lowest levels in history.1-3 It is, after all, a recent development that parents can expect all their children to live to adulthood. Vaccines can take considerable credit for allowing parents to watch their children grow up. Vaccines are also part of the reason children can watch their grandparents grow old. The only health intervention that has saved more lives and averted more misery than vaccines is clean water.4 Vaccines have saved more lives than any surgical technique or any class of medication, including antibiotics. Even so, no vaccine is perfectly safe, nor perfectly effective. In the last few years, a wide variety of accusations have been leveled at some routinely used vaccines: alleged associations with diabetes, Crohn's disease, autism, multiple sclerosis, and other serious disorders, often with little supporting factual basis.5-6 How do we assess vaccine risks, help people put risks into perspective, and recommend whether or not to get vaccinated? In the 1970s, controversies over environmental issues such as nuclear power and industrial wastes were common. To help resolve these controversies, to the mutual benefit of citizens, commerce, and the community, the field of risk communication arose.7-8 Risk communication is an interactive process to exchange information and opinions among individuals, groups, and institutions. This method has been used in communities across the country to make decisions about power plants, radon, waste sites, and other community issues. To be effective, risk communication must address the experiences, beliefs, and values of both message recipients and message providers. The goal of all parties in a risk-communication process should be informed decision-making, individually and collectively. Vaccines are unusual among prescription drugs, in that they are given to healthy people to keep them healthy. As a result, we tolerate far less risk in vaccines than we tolerate in drugs used to treat cancer, for example.6,8 This article reviews the concept of risk, especially risks from vaccines. Special emphasis is given to ways of explaining risk to people seen by clinicians in day-to-day practice. Issues related to consumer-focused mass communications on health are discussed elsewhere.9,10



VACCINE RISKS IN PERSPECTIVE

Decades ago, when hundreds of thousands of Americans contracted diphtheria, poliomyelitis, or measles each year, few people stopped to ask about vaccine side effects. Now that vaccines have succeeded so well that these vaccine-preventable diseases are virtually unheard of, people injured by vaccine side effects can sometimes outnumber the cases of disease that do occur. This phenomenon has caused some people to scrutinize the side effects, forgetting about the diseases that the vaccines have successfully vanquished.11-12 Figure 1 illustrates

one way of viewing the correlation of a vaccine's benefits and its risks. The left-hand part of the triangle represents the situation when a new vaccine is first introduced. The disease's full burden of morbidity and mortality is evident. Over time, as more people use the vaccine, the incidence of disease diminishes, represented by the top line falling from left to right. Meanwhile, adverse events from the vaccine are taking place at a relatively constant rate, as a fixed percentage of the number of people vaccinated. This is represented by the small, horizontal rectangle at the bottom of the figure. At first, on the left, the number of people harmed by the vaccine is small in relation to the number of cases of disease. Later, on the right, when the full benefit of the vaccine is realized, the side effects are more readily apparent, outnumbering cases of disease. Nonetheless, continued vaccination is important, even on the right side of this figure. Continued vaccination avoids regressing back up the curve, from right to left, with the return of the disease's dreaded morbidity and mortality. Rotavirus vaccine or Lyme disease vaccine would be located along the left-hand margin of Figure 1, each vaccine having been licensed just a few months ago. Pneumococcal vaccine would be located a little further along the graph, having reached only about 35% of the people for whom it is recommended, even though licensed 20 years ago. Haemophilus influenzae type b (Hib) vaccine and tetanus toxoid would be positioned near the right margin, with near universal vaccine coverage and with disease at all-time low levels. For each of these vaccines, expected side effects are mild and temporary. The case is different for poliovirus vaccines in the United States today. Poliomyelitis would be located at the farthest right tip of the triangle in Figure 1. Zero domestic cases of poliomyelitis in the United States are outnumbered by the handful of cases of vaccine-associated paralytic poliomyelitis (VAPP) each year. This situation favors use of injectable poliovirus vaccine (IPV) for a child's first two doses, rather than oral poliovirus (OPV).13 The statistics of VAPP are not in dispute, although the relative merits of several policy options have been debated at length.

VACCINE-PHOBIA

Concerns about vaccine safety began with the first vaccine, Jenner's smallpox vaccine. In Leicester, England, opposition to compulsory vaccination in the 1880s led to an antivaccination political party and public demonstrations.14 Pertussis vaccine has been the center of controversy since the mid-1970s, with disputed claims about the ability of whole-cell pertussis vaccine to cause encephalopathy. When allegations of serious side effects peaked, immunization rates in England, Sweden, Japan, and elsewhere fell off sharply. Predictably, cases of pertussis disease skyrocketed, killing hundreds of unvaccinated children.11,15-16 Later, more detailed analyses showed that whole-cell pertussis vaccine is temporally associated with acute encephalopathy, but there is no evidence of an association with lasting neurologic damage.8,12,17-18 More recently, measles-mumps-rubella (MMR) vaccine was portrayed as associated with inflammatory bowel disease, Crohn's disease, and autism in news reports, triggered by articles in British journals in 1997 and early 1998.19-21 Multiple subsequent analyses pointed out the logical and biological flaws in these assertions and failed to find any such association.5-6,16,22-26 Unfortunately, these responses came much later than the headlines warning of vaccine-associated harm. Scientists frequently complain that the media tells stories about adverse vaccine events quicker and louder, regardless of the evidence for the adverse association, than stories about vaccine safety or value are told.12,21,27-28 A fleeting accusation on a television news program that childhood vaccines might increase the risk of insulin-dependent diabetes also suffered from flaws in logic and biology.26 Also in the recent news have been allegations that hepatitis B vaccine predisposes people to develop multiple sclerosis (MS). French regulators recently stopped some hepatitis B immunization programs, despite scientific evidence that found no link between MS and vaccination. Indeed, the medical advisory panel of the National Multiple Sclerosis Society concurs that there is no evidence of a link, as do the Centers for Disease Control and Prevention (CDC) and the World Health Organization.26,29-30 Other complaints over the years have attempted to link vaccination with sudden infant death syndrome or other maladies.5-6,31 Many of these allegations arose when temporal coincidences were confused with a true cause-effect relationship. In other cases, researchers reached conclusions that were not justified on the basis of the people studied. A common thread seems to be links between vaccines and disorders for which there is no readily apparent precipitating factor. There seems to be little reason to expect allegations of vaccine-induced harm to abate, as fear of disease fades even further and public expectations of safety rise. At present, about 50 serious vaccine-associated injuries occur each year in the United States, in the course of protecting a population of 275 million into which 3.9 million children are born annually.32

VACCINE EUPHORIA

To be fair, the opposite scenario-irrational seeking of vaccines or scientifically debatable use of vaccines-also occurs. In the case of rabies vaccine, for example, the national goal is to reduce usage.33-35 This situation results, in large part, because public fear of death from rabies overshadows the vaccine's relatively benign adverse-effect profile. Pressure to use meningococcal vaccine in community outbreaks arises periodically, where demand for the vaccine may exceed an objective assessment of the vaccine's utility.36 For example, public

clamoring for meningococcal vaccine during an early 1998 outbreak in Rhode Island exceeded the health department's capacity to vaccinate. The health department had planned to offer meningococcal vaccine to all state residents between 2 and 22 years of age over the course of 6 to 12 months. Long lines and media attention caused that plan to be condensed into 6 to 8 weeks.37 Health departments of neighboring states, which had the luxury of greater physical and psychological distance from the clamoring, saw no reason to offer vaccine in this way. Here again, the relative harmlessness of the vaccine permitted health departments to give the people what they wanted. The explanation may lie in health officials seeing only marginal value in a vaccination campaign from the perspective of the community as a whole, whereas individuals may prefer to reduce their personal risk as much as possible. Another example of an overuse scenario occurred in Canada during a 1991-92 outbreak of group C meningococcal disease.38-39 Several clusters of group C meningitis cases were identified by public-health authorities. Most clusters consisted of fewer than 10 people each. Media attention on the cases and deaths led to public hysteria. About 145,000 young people were vaccinated in the Ottawa region alone, even though the disease rates were essentially the same as in previous years, before the publicity. Some have speculated that intense media coverage of funerals and victims' grieving families led political leaders to order mass immunization campaigns. One public-health official said "the media would have been better served if it had been given more uniform information [from health experts] and if it had not published a lot of inflammatory, anecdotal comments that could not be substantiated."39

GENERAL RISK PERCEPTIONS

What is risk? Risk is the probability of a hazard causing harm.40-41 A hazard is a set of circumstances that may have harmful consequences. The opposite of a hazard is a benefit. The judgment that benefits outweigh risks (or hazards) is sometimes implicit, sometimes explicit. Risk is composed of several major elements, including likelihood, severity, and duration.41-42 The probability that a vaccination will cause pain at an injection site is substantial. But injection-site reactions are typically minor and transient. Protection from a deadly disease easily overshadows this negative effect. All risks are not equal. People accept a higher level of risk if that risk is taken on voluntarily (eg, driving, skiing, smoking cigarettes) than if this risk is imposed by others (eg, asbestos, radon, pesticide residues). People also fear and focus on dramatic risks (eg, rabies, snakebites, "flesh-eating" bacteria) more than mundane risks (eg, influenza, cigarettes) that actually may be a greater threat. For example, the news media may devote a disproportionate amount of time to stories of people who need organ transplants, compared to the larger number of people harmed by cardiovascular disease. Less than one person dies of rabies, on average, each year in the United States. Each year, meanwhile, 10,000 to 40,000 people die from the effects of influenza and 40,000 from pneumococcal disease. The conventional example is the media's focus on individual airline crashes compared to the aggregate risk of many automobile accidents. On average, a few hundred people die in airplane crashes each year, whereas 40,000 people die annually on U.S. highways.12,43-47 Experts tend to equate risk with mortality levels. In contrast, lay people seem to assess risk in terms of characteristics such as voluntariness of exposure, familiarity, control, potential for catastrophe, equity, and level of knowledge.1 Dreaded risks tend to involve a lack of control, catastrophic potential, fatal consequences, or inequitable distribution of risks and benefits. Unknown risks are typically characterized as unobservable, new, or delayed hazards. Risks perceived to be associated with clear benefits (eg, avoiding influenza) may be more acceptable than risks that are perceived as providing little direct benefit (eg, avoiding poliomyelitis). Risks fairly distributed are more acceptable than risks unfairly distributed. Natural risks (eg, solar or cosmic rays) are more acceptable than manmade risks (eg, nuclear power plants). Familiar risks (eg, automobile travel) are more acceptable than exotic risks (eg, air travel). Risks threatening adults are more acceptable to adults than risks affecting children.7,46,48-49 People are more willing to accept a risk that involves a gain than a loss, even if the potential loss is of the same magnitude and probability as the potential gain.43 When it comes to gains, most people are risk-averse, preferring a sure thing over a gamble. For potential losses, people are risk-seeking, preferring gambles to certain losses (although buying insurance is a common exception to this tendency).7,43 Furthermore, many people assess risks of illness with an optimistic bias, perceiving themselves to be less at risk than may be the actual case.46,50-51 We live in an uncertain world. Our lives are considerably less uncertain than when our ancestors wondered if they would have sufficient food and water to survive the winter. Nonetheless, the human mind uses mental rules or strategies, called heuristics, to guide decision-making and deal with uncertainty. Heuristics help simplify decisions about complex subjects. These rules may sometimes be biased away from recognizing true or actual risks. These biases may lead to either overestimates or underestimates of an objective probabilistic estimate of risk.1,43,52 Some commonly recognized heuristics are known by these labels: compression, availability, framing, anchoring, common definitions, exposure, comparisons, omission bias, and status quo. Each is discussed below. Compression: Many people compress risks, overestimating the frequency of rare risks (eg, vaccine-associated paralytic poliomyelitis) and underestimating the frequency of more common risks (eg, traffic accidents, influenza deaths).8,12,46 Availability: People often overestimate risks of infrequent or dramatic events (eg, airplane crashes, cancer) and underestimate risks of familiar causes of disease and death (eg, heart disease, auto

accidents).1,8,44,46,49,51 Availability increases the importance of news media reports of events that are new or dramatic. Media coverage may cause people to overestimate the frequency of events reported out of proportion to their true magnitude. Anecdotes of this kind can be very powerful in shaping opinion. Framing: How choices are presented, called framing, influences decisions.7,53-54 For example, a particular choice might be described as either a 95% chance of success or a 5% chance of failure. Both descriptions are equally correct, by definition. But when given a choice, people will more often select a 95% chance of success over a 5% chance of failure. For vaccines, it may be more important to describe how many lives vaccines can save, rather than how many lives are lost from uncontrolled diseases. It is also important to frame issues according to the audience. For example, you may want to explain the benefits of vaccination to people who view vaccines as generally safe. With those who question vaccine safety, it may be more effective to frame the decision in terms of the risks of illnesses prevented by vaccination.8,12,46 Facts do not necessarily change initial opinions or decisions, presumably because strong views influence the way subsequent information is interpreted.1,8 This suggests that influencing initial opinions may require different information or formatting than efforts to change opinions. Anchoring: People may estimate the probability of an event based on probabilities for other events discussed recently. For example, if people are asked to estimate how many people are harmed by something, they will select a higher number if told that 40,000 people die in auto accidents than if told that 1,000 die from electrocution. As a result, one should give probability estimates that will help people perceive actual risks.8,46 Common Definitions: The meaning of words such as likely, unlikely, rare, and common vary according to context and among speakers and audience.55-56 Experts have proposed standardized definitions for levels of risk, equating terms such as low, very low, minimal, and negligible with specific probabilities of decreasing magnitude.40,44,57 These proposals are internally rational, but no one has yet figured out a way to get the general public to use these schemes.8,46 Exposure: People tend to underestimate the cumulative probability of multiple exposures to a risk. This is important for exposures such as cigarettes and somewhat applicable to the risks of VAPP.8,46 Comparisons: People may infer that a level of risk in one dimension applies in other dimensions as well. This is a problem if average risks are low, but risks in some subgroups are substantially higher. For example, the risk of breaking a bone is generally low, but higher among children and downhill skiers. For vaccines recommended universally for a population, adverse events should be distributed fairly throughout the population. The opposite situation arises if large numbers of people decline vaccines, because the burden of any adverse events is shifted on a different segment of the community.8,46 Omission Bias: Some people would prefer to make an error of omission, rather than an error of commission. For example, they would prefer to take a chance that their child would be infected with a vaccine-preventable disease, rather than suffer harm from intentional vaccination, regardless of the relative probabilities of each event. This factor appears to operate in only a subset of people.8,46 Status Quo: Many people prefer to avoid disrupting the status quo. These people may be vaccinated or not vaccinated because others in their community are doing the same.8,46 Many people have a difficult time understanding numbers and probability. Many Americans can be described as innumerate, a term for the numerical equivalent to illiteracy.3,45,58-59 For many, one-in-a-million is a colloquial saying, rather than a mathematical probability. This poses problems if you try to convey risks in numerical terms. Nonetheless, it may be helpful to summarize the choices as a 1-in-500 risk of infection, a 1-in-2,000 risk of death from disease, and a 1-in-500,000 risk of an adverse event due to the vaccine. People may be motivated differently, depending on whether risk is presented as a percentage risk reduction (a relative measure) or the same mathematical values converted to an absolute risk reduction.7,54,60 For example, reducing risk from 20 per 100 to 10 per 100 and reducing risk from 2 per 1,000 to 1 per 1,000 are both relative risk reductions of 50%. In the first case, however, this is an absolute risk reduction of 10% (20% - 10% = 10%), whereas the second case is an absolute risk reduction of 0.01% (0.02% 0.01% = 0.01%).

VACCINE RISK PERCEPTIONS

Vaccine decisions are known to be influenced by perceptions of disease susceptibility, disease severity, vaccine benefits, barriers to vaccination, and the influence of respected people.8,61-64 Other factors that may affect decisions among people who consciously choose to decline vaccines include a reluctance to make a decision when the likelihood of an event is unknown ("ambiguity aversion"), a preference for errors of omission over errors of commission ("omission bias"), and doubts about the veracity of medical claims of vaccine efficacy and safety. Some people are willing to take advantage of herd immunity, allowing their children to go unvaccinated if most other children are vaccinated ("free-loading"). Others seek vaccines in order to contribute to herd immunity and help others in the community ("altruism").65 Another heuristic that works in favor of vaccination is "bandwagonning" (similar to status quo), in which people accept vaccines principally because others are being vaccinated.8,12,64 An analysis of antivaccine attitudes in industrialized countries suggests that there are three common themes: fear of vaccine side effects, philosophic objections to vaccination, and antigovernment or personal freedom sentiments.66 Six common misconceptions about vaccination were discussed in a previous column in this series.67 A vaccine side effect might have little impact in terms of number of people harmed. But if

the technology of vaccines is poorly understood or unfamiliar, the social disturbance can be greater than a far larger number of people harmed in some other way, such as by automobile accidents.1 For vaccines, the relevant concerns might be the rarity of adverse events (making it difficult to determine risk groups and risk probabilities precisely), scientific disagreements on how to interpret existing data, lack of defined clinical syndromes for some alleged adverse events, and lack of pathophysiological understanding of how a vaccine might mediate an adverse event (eg, whole-cell pertussis vaccine and temporal links to neuropathies).8,12,18 Are risk perceptions different for pediatric immunizations, where a parent makes decisions for a child, than for adult immunizations, where the person is making his or her own decisions? The differential characteristics of risk communications for pediatric and adult infectious diseases have not been contrasted in any article we identified. But we speculate that dread of disease or dread of adverse vaccine reactions may be stronger, on average, in a parent's desire to protect children than in adults' desire to protect themselves. Conversely, optimistic bias may be stronger, on average, in an adult believing that he or she is not vulnerable to influenza or pneumococcal disease, the infectious risks of which have been incompletely communicated to the public.

DISCUSSING VACCINE RISKS

People are different. One size does not fit all when it comes to explaining risk. Some prefer short, simple messages about a vaccine's benefits and risks.8,12,68 These people, presumably a majority of the population, will be satisfied with the summary information comprising the Vaccine Information Sheets (VISs) published by the Centers for Disease Control and Prevention. Others want more detailed information. Some will scour the literature to explore every fact they can find. The goal of risk communication involving vaccines should be informed consent.68 True consent to vaccination is only possible if the individual has received all the information he or she wants and understands that information. Then an informed vaccine decision can be made. Providing this information demonstrates respect for the individual. From the clinician's perspective, the consent process can be part of the efforts to identify contraindications to vaccination (eg, severe hypersensitivity, immunodeficiency). Consent is a challenge when implementing state mandates for immunization to attend schools, widely credited with achieving high levels of immunization delivery to children and near elimination of many vaccine-preventable diseases. Reconciling individual consent and community benefit can be problematic.8,12 Fortunately, the net effect of vaccines is beneficial to individuals, as well as to communities. Glanz and Yang reviewed many elements of risk communication, explaining the chance of harm to the public.51 They discuss the many interactions between a message, its source, the communication channel, and the intended audience. They point out how hard it is to balance clarity and simplicity with completeness and accuracy. Another difficult balancing act is the tension between the duty to warn and avoiding undue alarm. Credibility, a combination of both expertise and trustworthiness, is essential to stimulate individual or community action. For people who mistrust government and corporate enterprises, the credibility of health agencies and vaccine manufacturers is diminished.8 Calman proposes that risks be described along three axes: avoidable-unavoidable, justifiable-unjustifiable, and serious-nonserious.40 Considering these classification dichotomies, people can reach personal or community decisions about whether risks are acceptable or unacceptable. Thus, the risk of anaphylaxis after a vaccine might be described as avoidable, justifiable, and serious, with a subsequent determination that vaccination is acceptable. Society is moving VAPP after OPV from justifiable to unjustifiable, as the use of inactivated poliovirus vaccine increases.13 Given that many people do not have a firm grasp of the numerical meaning of probability, and given issues of framing and anchoring, it may be prudent to provide both absolute changes in risk and relative changes in risk. For example, when explaining the value of Lyme disease vaccine, one should provide the vaccine's relative efficacy: reduction of disease incidence by 76% after three doses. But one should also give perspective for this reduction by explaining that disease incidence (the attack rate) fell from 12 cases per 1,000 people in the placebo group to 2 cases per 1,000 vaccine recipients.69-70 Several authors have suggested ways of demonstrating to patients that you appreciate their concerns and have sought responsible answers to their questions.43,49,52,71 These recommendations appear in Table 1. One way to overcome omission bias in a parent is to reframe the question from the child's perspective: would the child prefer a greater or lesser chance of disease (or death) and would it matter if the outcome occurred as a result of someone's act or omission. The limits of free-loading can be illustrated in describing the people who have no choice but to avoid vaccination (eg, those with allergies or mmunodeficiencies). Some people make decisions based on stories of people with whom they can identify.12,33 The Immunization Action Coalition publishes stories of people who contracted vaccine-preventable diseases, in contrast to anecdotes about people allegedly harmed by vaccines. Internet links to this and other sources of information to refute misinformation espoused by anti-vaccination movement appear in Table 3.

IMPLICATIONS FOR PHARMACISTS

People will ask you questions about vaccine side effects for which we have reliable, scientific observation.

Understanding the principles of risk communication will help you describe benefits and risks, as well as assist them with personal decision making.12 Using these principles, you can remind people of how devastating the diseases can be. Another approach is to put risks in perspective. When a questioning patient or parent expresses a worry about a vaccine side effect, the pharmacist can offer a more balanced assessment, by asking, "Compared with what?" If the situation involves something like a 1-in-500 risk of infection, a 1-in-2,000 risk of death from disease, and a 1-in-a-million risk of a serious vaccine-associated effect, patients and parents can be more fully educated about vaccines and their value, personal and societal. Pharmacists can use the tools that people respond to, such as case reports. It may be difficult to explain the cost-effectiveness analyses for the new varicella vaccine and the morbidity and mortality of the disease if the listener does not take a community perspective. The personal value of prevention is more easily explained to some people by focusing on individual cases of hospitalization for varicella pneumonia, flesh-eating bacterial superinfections, or death. Both approaches are scientifically valid. It is a question of matching the argument to the audience. At other times, people will raise new questions about vaccine side effects, including new accusations of harm. At these times, it is important to remain open to the possibility of previously undetected adverse associations. Healthy skepticism is appropriate for assessing new complaints. Each complaint should be balanced against the vaccine's track record. We have a public responsibility to fully investigate any accusation of harm from a vaccine. It is important to report suspected problems to national vaccine monitoring programs, such as the Vaccine Adverse Event Reporting System (VAERS, 800-822-7967) or the Canadian Vaccine Associated Adverse Events Surveillance System (VAAESS). Remind people that anecdotal case reports need to be independently confirmed by other researchers. Remind them that coincidences are not grounds for a cause-and-effect relationship. Be wary of alleged side-effects where the side effect naturally peaks in the age group being vaccinated (eg, hepatitis B vaccine and multiple sclerosis, pertussis vaccine and eurologic anomalies). Why has the effect not been seen before, given millions of prior doses? The Canadian Division of Immunization offers five questions to ask about the credibility of anti-vaccine information (see Table 3).71-72 In addition, we would add: What are potential sources of bias in case selection or conclusions? Were evaluators blinded to exposure status? Vaccines have had unparalleled success in reducing the incidence of death and disease. Paradoxically, this success may result in an undue emphasis on vaccine side effects. Risk communication offers a set of tools for explaining risks in proportion to benefits. After all, when we refer to the safety of any drug, we are talking about relative safety: safety relative to the alternative of not using the drug.