The Complicated Task of Monitoring Vaccine Safety

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SYNOPSIS

Vaccination is an essential component of modern public health programs, and is among our most cost-effective medical interventions. Yet despite their clear effectiveness in reducing risks of diseases that previously attacked large proportions of the population, caused many deaths, and left many people with permanent disabilities, current vaccination policies are not without controversy. Vaccines, like all other pharmaceutical products, are not entirely risk-free; while most known side effects are minor and self-limited, some vaccines have been associated with very rare but serious adverse effects. Because such rare effects are often not evident until vaccines come into widespread use, the Federal government maintains ongoing surveillance programs to monitor vaccine safety. The interpretation of data from such programs is complex and is associated with substantial uncertainty. A continual effort to monitor these data effectively and to develop more precise ways of assessing risks of vaccines is necessary to ensure public confidence in immunization programs.

Text

At the beginning of the 20th century, the most serious threat to human life and well-being was infectious disease. Outbreaks of diseases such as diphtheria and pertussis were common, and mortality was significant; 160 of every 1000 children born at the turn of the century died of an infectious disease before the age of 5. Today parents in most developed countries no longer fear these diseases; a small group of parents, however, question whether the very vaccines that have prevented so much morbidity and mortality now cause more harm than the benefits they provide.

Vaccination is surely among the most significant public health interventions of all time. Nevertheless, the concept of vaccination--essentially, the introduction of foreign material into healthy individuals--has provoked controversy at times. Pasteur's first administration of rabies vaccines to humans was strongly protested by physicians and the public, and efforts to immunize British troops against typhoid at the turn of the century were bitterly opposed despite the encouraging results of earlier immunization efforts and the serious risk of typhoid faced by troops serving in the Boer War.

As the effectiveness of vaccines against diphtheria, pertussis, tetanus, typhoid, rabies, and other diseases became incontrovertible and vaccines came into more widespread use, the incidence of these diseases rapidly declined. In addition, advances in vaccine technology brought substantial reductions in the incidence and severity of side effects associated with rabies and typhoid vaccines, and reduced the risk of manufacturing problems such as contamination or incomplete inactivation of virus. With the clear evidence of both protection from disease and high levels of safety came increased acceptance of vaccination as a valuable safeguard of individual and public health. Support for routine vaccination was no longer controversial in the medical community by the mid 20th century.

Public concerns waned as well. By the mid-1950s, especially after the Salk polio vaccine became available, the benefit to any individual child of being vaccinated was clear: eliminating the possibility of contracting disease far outweighed the tiny risk of a serious adverse side effect from the vaccine itself. Today, in developed countries, diseases such as pertussis, diphtheria, measles and rubella are rare; polio has essentially been eradicated from the Western Hemisphere.

The success of vaccination in reducing the risk of disease has led in recent years to renewed public interest and concern about vaccine safety; in the context of minimal risks of contracting vaccine-preventable diseases, the risks of side effects, especially the very small chance of serious adverse effects, take on greater weight and need to be continually reevaluated.

A dramatic example of the need to balance adverse outcomes of vaccination against protection from disease is the case of polio. In 1996 it is almost a certainty that no child born in America will contract wild-virus polio, yet eight to ten people each year will develop paralytic polio as a result of vaccination with (or contact with someone vaccinated with) oral polio vaccine. This situation has led to recommendations for replacing some of the oral polio immunizations with inactivated vaccine, which will reduce the risk of vaccine-induced paralytic polio.

In the late 1970s and early 1980s substantial public attention in the United States as well as in other developed countries was given to the safety of whole-cell pertussis vaccines. A few parents who believed their children had been seriously injured as a result of vaccination brought their concerns to the public through the media. Vaccine coverage plummeted, with the consequent return of epidemic pertussis disease in Japan, the United Kingdom, and Sweden.'' In the United States, while public acceptance of pertussis vaccine generally remained high, numerous lawsuits were filed against vaccine manufacturers. This resulted in major increases in prices and decisions by several companies to discontinue manufacture of pertussis vaccines, resulting in temporary shortages. These events contributed to the passage of the National Childhood Vaccine Injury Act (NCVIA) in 1986. The NCVIA mandated important new initiatives relating to vaccine safety; it established the National Vaccine Injury Compensation Program, provided for an independent review of the available scientific evidence on adverse events attributable to vaccination,' and mandated physician reporting of certain vaccine-associated adverse events to the Secretary of the Department of Health and Human Services.

The Act also created a unified national system to help identify rare vaccine reactions. This system, initiated in 1990 and jointly managed by the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC), is called the Vaccine Adverse Event Reporting System (VAERS). VAERS receives reports of adverse events following vaccination from vaccine manufacturers, private practitioners, state and local public health clinics, and vaccinees themselves (or their parents or guardians). It is similar in intent and operation to surveillance systems for other types of pharmaceutical products, such as the MedWatch system maintained by the FDA, and to safety surveillance programs in other countries. Such systems are essential to the discovery of potential rare adverse consequences of pharmaceutical products that may not become evident until millions of people have been exposed to these products. But these surveillance systems have important limitations that complicate the interpretation of the data they accumulate.

The remainder of this paper will address the ways in which vaccine risks are assessed, some specific issues that have been raised by concerned members of the public, and the potential of

VAERS and other vaccine safety surveillance efforts to address these and other important issues relating to vaccine safety.

Safety Assessment during New Vaccine Development

Like other pharmaceuticals, vaccines must go through extensive clinical testing before they are marketed. Yet unlike other pharmaceutical products, vaccines are primarily targeted to healthy people, especially children; virtually every child will receive some vaccinations. Because healthy people are less willing to accept risk than people who need treatment for illness and because society is unwilling to impose unnecessary risks on healthy infants and children, vaccine developers must be particularly sensitive to the risks of adverse effects.

New vaccines are initially tested in small groups of adult volunteers following a series of laboratory and animal tests that establish, to the extent possible, the safety of delivery to humans. These adult studies are followed by larger but still preliminary studies in children. In all studies at the early stage of vaccine development, subjects are monitored intensively for any potential adverse effects. Rates of common expected reactions, such as swelling and fever, can begin to be estimated at this stage.

Manufacturing processes are also reviewed carefully by regulators to ensure appropriate conformance with good manufacturing practices designed to assure consistency, prevent errors, and avoid contamination with unwanted substances.

When preliminary studies indicate that the vaccine is both safe and producing the desired immune responses associated with disease protection, larger-scale clinical trials, usually randomized and placebo-controlled, are undertaken to provide definitive estimates of protective efficacy and more precise estimates of rates of the more common adverse effects. The control groups in these studies who do not receive the investigational vaccine are critical in distinguishing between vaccine-induced effects and those unrelated to the vaccine but occurring spontaneously in the population studied.

How Safe Is Safe?

The total number of people who have been exposed to a new vaccine by the time it is put on the market ranges from several hundred to tens of thousands, depending on the intended use of the vaccine. Even the largest of these pre-marketing studies, however, are inadequate to assess the vaccine's potential to induce infrequent but serious reactions. With approximately four million births a year in the United States, an adverse outcome occurring at a rate of one in 10,000 vaccinations--a rate far too low to be detected in conventionally sized clinical studies performed prior to marketing--would affect 400 babies each year.

Despite the difficulty of assessing these infrequent reactions, the virtually universal exposure of the population to vaccines makes it vitally important to understand even the very rare complications of vaccination. For this reason, it is essential to continue to collect information on vaccine-related adverse events even after the vaccine is approved for general use by the FDA.

Advent of a Unified Surveillance System

Prior to 1990, FDA and CDC each had their own reporting systems for vaccine-associated adverse events. The FDA system received reports primarily from vaccine manufacturers as they became aware of specific instances of adverse outcomes following vaccination with their products; the CDC system, known as MSAEFI (Monitoring System for Adverse Events Following Immunization), collected reports from state public health coordinators based on events observed at public clinics for which CDC provided vaccines.

As noted earlier, these systems were unified following passage of the NCVIA in 1986. The goal of a unified surveillance system was to increase the efficiency of the Public Health Service in collecting and assessing these reports and in monitoring the overall safety of vaccines.[18]

How VAERS Works

VAERS is a passive surveillance system, a repository for voluntarily submitted reports. (An active surveillance system, in contrast, would follow all individuals in a defined population to determine their responses to vaccination.) To encourage reporting of any possibly vaccine-induced adverse event, the criteria for reporting to VAERS are unrestrictive; the system accepts and includes any report submitted, no matter how tenuous the possible connection with vaccination might seem. As noted earlier, the NCVIA does require physicians to report (directly to VAERS, or the manufacturer) certain categories of serious outcomes occurring within a short period of time following specified childhood vaccinations, so one might expect a fairly complete reporting of such events; the lack of enforcement provisions or even any monitoring of reporting practices, however, precludes any assumptions about the extent to which such events are in fact reported. Thus, VAERS potentially suffers both from underreporting--not all vaccine-induced events are reported--and overreporting--coincidental events, not caused by vaccines, can be reported.

Approximately 10,000 reports per year are submitted to VAERS. About 15% of these describe a serious event, defined for regulatory purposes as an event resulting in a death, life-threatening illness, hospitalization, prolongation of existing hospitalization, or permanent disability. These reports are entered into the system by a Federal contractor and are reviewed by medical staff of the FDA's Center for Biologics Evaluation and Research and CDC. Most of the approximately 85% of reports not classified as serious describe events such as local reactions and fever occurring within a day or two of vaccination. Many of these events are clearly caused by the vaccine; they have been shown during placebo-controlled clinical trials to occur more frequently in vaccine recipients than in those receiving placebo. The serious events, unfortunately, are much more difficult to evaluate with regard to their causal association with vaccines. Such events are observed too infrequently, if at all, in clinical trials to assess their relation to vaccine. Most of these tend to be of a type known to occur in the absence of vaccines as well, so in an individual case it is almost never possible to assess definitively the role of the vaccine.

Temporal versus Causal Associations

Because of the large number of vaccine exposures, it is clear that temporal associations with adverse outcomes will occur even when there is no true causal association. With hepatitis B vaccine now recommended for all newborns, and other childhood vaccines (DTP, OPV, Hib) being administered to nearly all infants starting at two months of age, most health problems in infancy (of which there are many), whatever their cause, will occur in children who have been vaccinated. Some of these problems will by chance occur in recently vaccinated children.

An adverse event can be causally attributed to a vaccine if: (a) it conforms to a specific clinical syndrome (such as anaphylaxis immediately following vaccination); (b) a laboratory result confirms the association (for example, isolation of vaccine strain mumps vaccine virus from patient with aseptic meningitis); (c) the event recurs on re-administration of the vaccine (positive rechallenge); or (d) a controlled clinical trial or carefully designed epidemiologic study shows greater risk of adverse events among vaccinated than control groups. Because few of the adverse events reported to VAERS meet any of the first three criteria and because clinical trials are almost always too small to provide useful information on serious rare events, epidemiologic evidence is the basis for assessing causality for most serious adverse events that are investigated.

Strengths and Weaknesses of VAERS

As a data base for epidemiologic studies, VAERS has many weaknesses. One major problem is that, since unvaccinated people experiencing adverse events are not reported to VAERS, there is no control group to study. Thus, there is no way to assess whether the number of reported events is different from the number that would have been observed in the absence of vaccination.

The quality of the data is also less than optimal. Because reports are sent in by a wide variety of individuals, few of whom are experienced in completing data forms for medical studies, many reports omit important data and contain obvious errors. Given that VAERS receives over 10,000 reports annually, it is difficult to assure the accuracy and completeness of the database with current resources, although checks and follow-up are performed for a few key data items such as the type of vaccine administered and the severity of the event.

Finally, the administration of multiple vaccines at the same time, following currently recommended vaccine schedules, further complicates the assessment of adverse outcomes because there is usually no way to determine which of the vaccines (if any) was most likely to cause the outcome.

This is not to diminish the value of such a system. While VAERS data can rarely provide definitive evidence of causal associations between vaccines and particular reported outcomes, this type of national reporting system can rapidly document possible effects, generating early warning signals that can then be more rigorously investigated in focused studies. In a sense, VAERS is the front line of vaccine safety surveillance, so sensitivity takes precedence over specificity; reporting of all serious events following vaccination is encouraged, inevitably resulting in large numbers of reports that do not represent vaccine-induced problems.

VAERS data are especially valuable in assessing the safety of newly marketed vaccines. Careful review of reports coming in during the initial months of availability can provide additional reassurance about the safety of the vaccine or rapidly identify potential problems not observed during the investigational phase. For example, the recent review by Niu et al provided reassuring confirmation of the safety of hepatitis B vaccines in infants. FDA and CDC medical staff maintain ongoing intensive surveillance of the new varicella and hepatitis A vaccines.

The Case of Sudden Infant Death Syndrome (SIDS).

The case of SIDS exemplifies the problem with interpreting VAERS data. About 200 deaths a

year are reported to VAERS; most of these are of infants under one year of age; of these, most are diagnosed as SIDS. The reported time from vaccination until death varies from a few hours to many weeks or even months. In most cases multiple vaccines are involved, consistent with recommended immunization schedules. Because SIDS is a well documented (if not well understood) phenomenon that occurs both in the absence and presence of vaccination, one cannot presume a causal connection if SIDS follows shortly after vaccination; in fact, one can predict that such events would occur even in the absence of a causal connection because virtually all infants receive vaccines and because SIDS occurs at the relatively high rate of somewhat over one per thousand live births in the United States.

In response to public concerns arising in the early 1980s about the safety of DTP vaccines, the National Institute of Child Health and Development conducted a large case-control study directed specifically at the question of the association between SIDS and DTP vaccination. This study did not support the hypothesis that DTP vaccine caused SIDS; in fact, it demonstrated a lowered risk for SIDS in children receiving DTP vaccine. (The authors of the report suggested that this lowered risk estimate was more likely the result of differences in baseline health status between children who did and did not receive scheduled vaccinations than to any protective effect of the vaccine against SIDS.)

While this and other studies with similar results resolved the issue to the satisfaction of the scientific community, some members of the public have remained concerned about a possible connection between DTP vaccine and SIDS, citing the SIDS cases regularly reported to VAERS. In response to such concerns, FDA and CDC staff calculated the number of SIDS cases expected to occur by chance within a fixed number of days following immunization, accounting for the age-adjusted SIDS rate and the proportion of infants vaccinated at specific intervals, and determined that the number of cases reported for each time interval is far lower than would be expected to occur by chance alone. (Of course, these estimates may have been artificially lowered by underreporting of SIDS occurring shortly after vaccination.)

Advocacy groups raising concerns about vaccine safety regularly point out that the reasoning described above for SIDS is flawed; since nearly all children are vaccinated, how do we know that the background SIDS rate is not partially or even largely caused by vaccination? It is true that there is no satisfactory unvaccinated control group to turn to, since the small group of children in the United States who go unvaccinated through the first year of life would almost certainly differ in important ways from those who do receive vaccinations on schedule. Well-designed studies to date, including the study described above, have used an alternative approach based on the assumption that if immunization caused sudden infant deaths, it would do so within a few days of immunization. This approach allowed researchers to compare children who died of SIDS with age-matched controls with respect to time since vaccination.

Other risk factors for SIDS have been identified recently: these include prone sleep position; the thermal environment, including use of heavy and confining bedclothes; and maternal smoking.[,,] SIDS rates have decreased dramatically in several countries[,,,] in connection with back to sleep initiatives. These findings, while providing no additional direct evidence on the role of vaccines, do suggest a mechanism for SIDS that may be more related to the physical environment than to systemic factors in the child that might be affected by vaccination. Overall, the evidence continues to strongly negate any causal association between SIDS and vaccination.

The Safety of Vaccine Lots

Vaccine advocacy groups, organized and led primarily by parents who believe their children have died or suffered serious injury as a result of vaccination, have questioned whether particular vaccine lots may be more likely to induce such injuries. These groups have reviewed the publicly available VAERS database, which includes the vaccine lot number for most reports, and have raised questions about the safety of particular lots that appear to be associated with a higher number of reports.

Vaccines are manufactured in large lots from which vials for individual administration are derived. Procedures for the manufacture and release of vaccine lots are strictly regulated; prior to public release, each vaccine lot must undergo stringent testing to assure both the potency of the vaccine and the lack of contamination. Because of these procedures, the likelihood that there could be something wrong with any bulk lot is extremely low--but not zero.

VAERS can address the question of the safety of individual vaccine lots much more effectively than the question of causality in individual cases of adverse events. Since 1993, FDA medical officers have performed weekly reviews of lot-specific reporting. These reviews require much more information than simply the number of reports submitted for each vaccine lot, however; the numbers themselves are inadequate to support any conclusions about safety, for several reasons.

First, as noted earlier, there are errors in the database. The vaccine lot number may be miscopied by the reporter onto the VAERS form. This results in numerous lots in the database with a single report or a very few reports, providing a misleading contrast with the numbers of reports for valid lots.

Second, lot sizes can vary greatly. Clearly, the number of reports generated from a vaccine lot containing half a million doses cannot be sensibly compared with the number of reports generated from a lot only one-tenth as large. Data on lot size, although available to the FDA for monitoring purposes, do not appear in the VAERS database because these data are legally considered proprietary to the manufacturer and their release by FDA is prohibited.

Third, there is a time factor. Vaccine lots that have been on the market for only a few months will be associated with fewer reports than a lot released several years earlier.

Finally, there will always be chance variability in reporting rates. Even when the numbers of reports are standardized for lot size and length of time on the market (as they are for internal FDA review of the database), there will always be one lot associated with the highest rate of reports and one lot with the lowest. The more lots, the greater the difference between the highest and lowest rates will be; the difference may be quite large for old and widely used vaccines such as DTP even assuming all lots are equally safe.

When numbers of reports are compared between vaccines, there are further considerations. The database will contain more reports for a vaccine administered five times to each individual, such as DTP, than for a vaccine such as MMR that is administered only twice. There will be more reports for a vaccine that has been on the market for many years (such as DTP) than for a vaccine that has been available for only a few years (such as *Haemophilus influenzae* Type B vaccine). More death reports will be seen for vaccines given in infancy, when the background death rate is higher and SIDS is a factor, than for vaccines given later in childhood.

The FDA staff must take all of these factors into consideration when monitoring the database for unusual patterns of reporting from specific lots. Computerized methods are in place to identify lots with high reporting rates, accounting for lot size and time on the market. The threshold for identifying these lots is set deliberately low to ensure the earliest possible signal of a real problem.

Lots identified at this first screening stage are subject to additional scrutiny. The experience of related or sister lots (those made from the same large batch of product) is considered, since most problems should affect all lots from the same batch. The types of reports submitted are carefully reviewed; a series of similar events would be more suggestive than a scattering of events of different types with no unique syndrome evident. The results of the lot's initial safety testing is also reviewed. Additional information may be requested from the manufacturer, and in some cases the safety testing might be repeated.

Over the three years during which these monitoring procedures have been in place, no lot has been found to be unsafe. This result is not surprising given the stringency of the manufacturing and testing requirements to which vaccines are subject. Nevertheless, because of the possibility of such a problem arising, regular attention to lot-specific reporting will remain an important aspect of FDA's program of vaccine safety monitoring.

Using VAERS Data to Identify Possible New Reactions

Several investigations of VAERS data have uncovered previously unrecognized problems that may occur rarely in vaccine recipients. Beeler, Varricchio and Wise noted occasional instances of life-threatening thrombocytopenias following the administration of MMR vaccine, a previously unappreciated level of severity of a known side effect. Wise and Kiminyo documented a series of cases in which hair loss followed immunizations (primarily hepatitis B), a rare effect not previously reported. Braun and colleagues have identified a series of cases of severe injuries resulting from vaccination-induced fainting, or syncope.

Sometimes VAERS data may provide the useful and reassuring information that new problems have *not* been identified after additional experience with a vaccine, as in the previously noted report of Niu et al with regard to hepatitis B vaccine in infants.[27]

Using VAERS to Study Trends in Reporting of Adverse Events

VAERS data have also been used to compare reporting patterns over time and investigate changes in reporting rates that might be due to changes in vaccine practices. For example, CDC epidemiologists reviewed reports of fever, seizures, and hospitalizations following administration of a newly licensed combination of diphtheria, tetanus and acellular pertussis vaccine (DTaP). The rate of such reports was about one-third lower than the reporting rate following the standard DTP vaccine, consistent with--and confirming in the context of general practice--the safety findings of the prelicensure clinical trials[,].

Ecologic studies--that is, comparisons of outcomes during different time periods--using data from MSAEFI, the CDC surveillance that preceded VAERS, showed that a change from separate to simultaneous immunization with DTP and MMR vaccines at 15 months of age did not change the types of adverse events reported.[46] A combined analysis of MSAEFI and VAERS data indicated that the rates of reported hospitalizations and deaths following DTP

vaccine remained constant from 1985 to 1992, despite the addition of *Haemophilus influenzae* Type B vaccine to the routine infant immunization schedule. These studies provided some reassurance that by adding vaccines to the recommended immunization schedule gains in protection from disease were not offset by an increased burden of adverse events caused by the vaccines.

Reporting patterns have also been studied to estimate the extent of underreporting of adverse events. Researchers used the known rates of a variety of vaccine reactions, as reported in controlled studies, to estimate the reporting efficiency--the proportion of events actually occurring that are reported--of VAERS and predecessor passive surveillance systems. Reporting efficiencies were similar and, perhaps not surprisingly, were the highest for serious events such as vaccine-associated paralytic polio (about 70%) and lowest for minor events such as rashes following measles vaccination (less than 1%). This study provides suggestive evidence that for the events of greatest concern, VAERS reports represent substantially more than the tip of the iceberg.

Newer Approaches to Vaccine Safety Monitoring

While VAERS is the initial safety screen, potentially providing the earliest signal of any new vaccine reaction, a reporting system of this kind has major limitations, including underreporting, lack of specificity, and lack of a natural control group. To compensate for these limitations, other approaches to vaccine safety surveillance have been developed.

The increasing availability in recent years of computerized medical administrative data bases for defined populations such as health maintenance organization (HMO enrollees) has radically improved the ability to conduct pharmacoepidemiologic studies. In these databases, vaccination records can be linked to records of hospitalizations and diagnoses of serious conditions, minimizing the problem of underreporting of serious events encountered in VAERS. The enrollment in individual HMOs can number in the millions, permitting study of rare events. This capability can be further enhanced by collecting data prospectively from several HMOs under a well-defined research protocol and aggregating the data. In principle, all of the information necessary for rigorous epidemiologic analysis is available in such settings, including numbers of doses administered, comparison groups, and potential confounders.

Since 1990, the CDC has worked with four HMOs to organize a Large Linked Data Base (LLDB) for vaccine safety studies as part of the Vaccine Safety Datalink Project. In this project, automated vaccination records on half a million children under six years of age (representing about 2% of the U.S. population in this age group) are linked to their medical records; the project will soon be expanded to include older age groups. This resource is being used to examine particular associations identified by the Institute of Medicine in their study mentioned earlier as requiring further investigation[14,15] (for example, seizures following immunization) and is also regularly utilized to further evaluate potential associations identified through VAERS. One recent investigation confirmed an association between seizures and DTP and MMR vaccinations by comparing vaccine exposures within specified time periods (one day for DTP, one week for MMR).[48]

The Vaccine Safety Datalink Project also has its limitations, however. Because few nonimmunized controls are available within the HMOs, the project relies predominantly on comparison of incidence rates of adverse events between specified time periods following vaccination. These studies are therefore limited in their ability to investigate the association

between vaccination and events with delayed or insidious onset such as autism and learning disability. Adverse events that do not result in a health care visit (or, more generally, data not automated in the HMO) are also not easily studied. The geographical concentration of the project's HMOs on the West Coast of the United States may also limit the generalizability of results. Finally, even the large sample sizes available in this HMO consortium currently do not provide enough power to study extremely rare events such as Guillain-Barré syndrome (GBS) and encephalopathy in a timely manner; specialized studies are still required to address such issues. For example, to evaluate the occurrence of GBS following the 1993-1994 influenza vaccination season, a special study is being conducted by the CDC in which all cases of the syndrome in four states are being sought through the centralized statewide hospital discharge tapes.

Challenges for the Future

The continued development of new vaccines to prevent diseases such as chicken pox, rotavirus, pneumococcal pneumonia, and respiratory syncytial virus will intensify the challenges of vaccine safety monitoring. Concerns have been raised about reactions being exacerbated when vaccines are combined; while current experience does not suggest that there would be insurmountable safety problems with adding new vaccines to currently available combinations, the possibility of increased reactogenicity is well recognized.

The public concerns about the safety of vaccines that are frequently mandated prior to entry into public school, day care centers, universities, and workplaces are legitimate and important. We would all like such products to pose zero risk of adverse effects. Unfortunately, this goal is not achievable for any pharmacologically active product--if there is a beneficial effect, there will be some risk, however tiny, of an adverse effect.

It must be recognized that protection of individuals from serious diseases depends not only on their own immunization but on the immunization of others in their community; since vaccines are not 100% effective, people's chance of disease is lower if those around them remain healthy than if those around them carry the disease. This is why most communities require children to be vaccinated against certain diseases, assuming no contraindication, rather than leaving the choice to individual parents on the basis of their own risk-benefit assessments.

The overwhelming view of the medical/public health community is that the risks of vaccine reactions, both the common mild reactions and the rare, more serious reactions, are very much outweighed by the public health benefit conferred by current vaccination practices and policies. Epidemiologists, pediatricians, statisticians, and others involved in vaccine safety surveillance projects will continue to investigate new and improved methods to monitor vaccine safety. The goal of understanding what events might be caused or promoted by certain vaccines, and which individuals might be at high risk to experience such events, will remain a challenging but extremely important one for the public health community.

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