Editorial

Immunization Controversies

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Within the rapidly changing field of public health, vaccine-preventable diseases have become the subject of much controversy. Three articles in the current issue of the Journal illustrate practical problems that primary care clinicians face in complying with health promotion recommendations for immunizations.[1–3] These problems are likely to become even more complex as new vaccines and new immunization strategies are developed.

New Vaccines

Advances in biotechnology and genetic engineering are ushering in newer and safer vaccines. In the past 10 years, plasma-derived and yeast-derived vaccines against hepatitis B, an acellular vaccine against pertussis, and three vaccines against *Hemophilus influenzae* type b (Hib) have been introduced. The next 5 years will likely bring vaccines against varicella-zoster, hepatitis A, respiratory syncytial virus, and rotavirus. But along with this rapid development, technical production problems have occurred with vaccine potency, immunogenicity, and batch-to-batch consistency. These problems have involved at least one of the two available hepatitis B vaccines, at least one of the three available Hib vaccines, and the varicella-zoster vaccine.

Further research is necessary to investigate the combination of even more vaccines into single injections. Combinations currently in clinical testing include (1) whole cell-DPT (diphtheria-pertussis-tetanus) with Hib, (2) acellular-DPT with Hib, and (3) whole cell-DPT with recombinant hepatitis B. As indicated by Freed et al,[1] combination vaccines will be essential to gain physician, patient, parent, and nurse acceptance of the increasing number of vaccines and to avoid the "pin-cushion" effect.

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Vaccines are not highly profitable products for manufacturers, especially when compared with the development of new antihypertensives or new antibiotics. It therefore may be difficult to lure pharmaceutical manufacturers back into the vaccine development market unless profitability issues can be addressed.

New Immunization Strategies

Controversy with vaccine recommendations occurs when a change in immunization strategy is developed. In 1989, a second measles-containing vaccine was added to the schedule in order to increase the immunity of the general population.[4] Another example is the recent recommendation for universal infant immunization against hepatitis B.[1,5]

When immunization strategies change, practical problems arise, not only with how to implement the new strategy,[1] but how to determine which cohorts who were immunized by previous vaccination protocols should be covered by the newer strategy. Herold et al[2] clearly demonstrate the negative impact that poor prior documentation has when immunization strategies change, resulting in unnecessary use of health care dollars to revaccinate individuals who do not have proper documentation.

The logistical problem of whether and how to bring older cohorts into compliance with newer immunization strategies is further illustrated by Murata and Young.[3] Only 54% of surveyed physicians had been immunized against hepatitis B. The highest immunization rates were in the youngest physicians, who likely had the availability of medical school hepatitis B immunization programs. The lowest immunization rates occurred in physicians who had completed their residency training before the introduction of the first hepatitis B vaccine. A corollary to the documentation issue is also illustrated by this study. Even among physicians who had been immunized against hepatitis B within the past 10 years, 15.3% were uncertain about which vaccine they had received.

When immunization strategies are changed, manufacturers should be notified of the estimated increase in eligible individuals to ensure that the strategy does not outstrip the supply of vaccine. Insufficiency of vaccine supply has nearly occurred with hepatitis B vaccine, and has been a problem with influenza vaccine. The expansion of the influenza immunization strategy to include additional groups from the general population[6] has increased the total number of vaccine doses used, but without evidence that more individuals at highest risk for influenza are being immunized.

Public Sector–Private Sector Differences

The Advisory Committee on Immunization Practices (ACIP) serves as the vaccination advisory group for the Centers for Disease Control. The ACIP's membership includes public health officials, academicians, and liaison members from the federal, state, public, and private health care sectors. Before making recommendations concerning immunization practices, the ACIP interprets information and research presented by the Centers for Disease Control, the private health care sector, manufacturers, consumers, and other groups. The resulting ACIP recommendations are widely implemented in the public health sector and public health departments. Private sector recommendations are developed by specialty organizations such as the American Academy of Family Physicians (AAFP), American Academy of Pediatrics (AAP), and American College of Physicians (ACP). These usually concur with the recommendations of the ACIP. When differences in recommendations occur, however, clinicians are faced with confusion regarding the immunization needs for individual patients.

Such confusion has occurred with recommendations for the second dose of the measles vaccine. The ACIP and AAFP recommend that the second dose be given when every child enters kindergarten or the first grade, while the AAP has held to the recommendation that the second dose be given at entry into middle or junior high school, at age 11 to 12 years. What should the family physician recommend for the junior high school student? What should the pediatrician recommend for the kindergartener? The differences in recommendations, coupled with inconsistencies in state school immunization laws, have hampered the overall implementation of the revised measles immunization strategy.

With the rapid addition of newer vaccines to the recommended immunization schedule, the issue of cost has become extremely important. Vaccine costs differ widely between the public and private sectors. The AAFP has developed a position paper recommending that all childhood vaccines be available to all physicians at the public sector's cost to prevent the continuing shift of private patients into public health departments to receive their immunizations.[7,8]

With federally funded vaccine, however, comes the problem of the vaccine information pamphlets (VIPs). In the litigious environment of the mid-1980s, the number of vaccine manufacturers greatly decreased, causing vaccine prices to skyrocket. As a response, the National Childhood Vaccine Injury Act was enacted in 1986 to address liability issues, and also to ensure that parents were informed about the risks and benefits of immunizing their children. Distribution of VIPs, which became available in early 1992, is mandated when a federally funded vaccine is used. These brochures have been universally criticized as being too long, too complicated, and too negative in their presentation of risks of immunization. They need to be shortened, simplified, and rewritten to deemphasize possible adverse reactions to vaccines and better highlight their benefits. A congressional amendment has been drafted to permit these revisions.

Solutions

Problems exist with the implementation of our current immunizations program, and solutions must be developed to ensure that potential benefits are realized.

Immunization recommendations are currently developed using a disease-specific approach. This narrow focus can result in an amalgamation of recommendations that may or may not coordinate with the current immunization schedule.

The artificial dichotomy of viewing immunizations as either a childhood or an adult issue must be eliminated. Currently, federal funding is being directed at a specific age group (infants and children), perhaps at the expense of other groups such as adolescents and adults.

Immunizations against vaccine-preventable diseases must be seen as a lifelong preventive health measure. A more universal approach to the development of immunization recommendations may result in a more coherent set of guidelines and less disruption when the immunization strategy for one vaccine-preventable disease changes. This comprehensive approach is one that family physicians inherently use in approaching medical problems. The input of family physicians is increasingly needed on national committees and advisory groups empowered to make recommendations for immunization practices.

Research on effective immunization schedules and on multiple-antigen vaccines should be intensified. How

well will a 2-month-old child immunogenically respond to the combination vaccines against diphtheria, pertussis, tetanus, trivalent polio, Hib, hepatitis B, and others that may be recommended in the future, and by how few injections can these be administered? Current guidelines tend to force all new immunizations into a schedule of 2, 4, and 6 months of age. An alternative is to further expand the immunization visits at 15 to 18 months and 5 years of age. A new universal immunization visit at age 15 years, when the first diphtheria-tetanus booster is due, should be evaluated, which could be expanded to include other vaccines more appropriate to adolescents than infants.

Increased coordination, collaboration, and consensus development between groups that make immunization recommendations must occur. Resulting guidelines need to be disseminated in a timely, coordinated, and universal manner. The merging of public sector and private sector recommendations is becoming an increasing need. Implementation differences between the public health sector, physician specialty groups, and state laws will impede progress in increasing immunization rates.

Federal funding of all vaccines should be proposed. The continuing diversion of vaccine administration to public health departments creates an unnecessary stress on the system. Primary care physicians are willing to administer these vaccines in their offices if patients are not financially burdened.[8]

The role that has been imposed on our schools to be the primary enforcers of documentation of immunization status should be reconsidered. A more thoughtful approach to record-keeping is necessary. Immunization documentation should be viewed as not only a personal health record, but also as a public health record. Individually held documentation should be provided in addition to documentation in the medical record, as immunizations will likely be received at multiple locations over a lifetime. The quality of information recorded will become increasingly important as new vaccines and new strategies are implemented. Documents should include the full information on the type of vaccine given, the date given, and the signature of the health care provider, so that the record can be reinterpreted when immunization strategies change in the future. Mechanisms to centrally record immunizations in the public record,[2] such as a national registry, should be investigated.

Finally, it is important to recognize the existence of economic and noneconomic barriers,[1,3] including attitudes toward vaccines, accessibility, availability, and multiple injections; and to recognize that these barriers affect immunization compliance rates.[9]

It is essential that these controversies be dealt with immediately. Current policies have made immunization practices confusing, conflicting, cumbersome, and complicated. Immunizations are an extremely important and cost-effective public health measure. We cannot afford to lose further ground against vaccine-preventable diseases. We are already at risk of losing the protective benefit for which immunizations are intended.

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Editorial

Universal Neonatal Hepatitis B Immunization—Are We Jumping on the Bandwagon Too Early?

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Immunization recommendations have proliferated over the past few years, and family physicians now have a host of vaccines to prevent disease throughout the life cycle. The pediatric age group has been a special beneficiary of this explosion of biomedical technology. For example, by late 1991 our pediatric patients received 13 to 15 immunizations for polio, diphtheria, pertussis, tetanus, *Hemophilus influenzae*, measles, mumps, and rubella.

Are all these immunizations justified? The answer is a resounding *Yes!* These were common, devastating diseases, and immunizations have, in large part, brought them under control. Secular trends are an unlikely explanation. For example, in both England and Japan, a decline in the pertussis vaccine resulted in a prompt increase in this disease.[1]

We now have an immunization for the hepatitis B virus (HBV). The Centers for Disease Control (CDC) adopted a policy advocating the *routine use* of this immunization *at childbirth*. The American Academy of Pediatrics (AAP) followed. Recently the American Academy of Family Physicians (AAFP) concurred that all future newborns should receive three immunizations against this disease. Now that three wise and powerful organizations agree, should clinicians follow this recommendation? Simply put, is the routine immunization of *all* newborns for HBV justified?

In favor of universal immunization, Shapiro and Margolis of the National Center for Infectious Diseases, Centers for Disease Control, wrote:

> . . . childhood HBV infections are widespread in certain ethnically defined populations in low endemic areas, further emphasizing the potential benefits of hepatitis B vaccination of infants. Consequently, immunization advisory groups in the United States have recently endorsed a strategy to eliminate HBV transmission among adults and children through universal infant immunization.[2]

This logic seems frail. They state that because *certain* populations are at high risk, the CDC endorses a strategy to eliminate HBV transmission among *adults* by immunizing *all infants*. They propose to vaccinate newborns to prevent a primarily adult illness. This premise requires closer scrutiny.

There are many organizations that create practice guidelines, and often these guidelines conflict.[3–6] It is therefore up to each individual physician to determine what is best for his or her patients. There are criteria or tests that any preventive measure must meet in order to be justified.[7] It is important that the measure *satisfy all criteria before it receives our support*. Instead of taking the CDC, AAP, and AAFP evaluation of the topic, each physician should apply these five criteria to routine neonatal HBV immunization before deciding how to manage the newborn.

1. Does the condition have a significant impact on health? HBV has a significant potential to cause major health problems. The disease is highly contagious,[8] and after contracting it, an adult has a 5% to 10% chance of developing chronic hepatitis. In children under the age of 5 years this rate increases to 25% to 50%.[9,10] Finally, chronic carriers of HBV carry a 100-fold increased risk of developing hepatocellular carcinoma.[11]

The lifetime risk of hepatitis B, however, is at most 5%,[8,12] and 60% to 70% of the disease occurs in high-risk populations.[9] In addition, the disease is uncommon in children, with only 2400 of the 300,000 annual cases of hepatitis B occurring before age 10 years.[13] Most of these children are high-risk infants who would be immunized under a selective rather than universal immunization program. The disease is serious, but because of its low incidence in the young, we must have more infor-

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mation before determining whether it has a "significant impact on health" in this age group.

2. Are there any hazards associated with the immunization? There is no evidence of the lifelong safety of the hepatitis B immunization, though there are no known significant adverse effects in adults or children after 10 years. In children, however, there may be serious short-term effects, but this is purely conjecture at this point. Young children receiving the Hib vaccine may develop lower antibody titers to the other childhood immunizations, thus potentially rendering all childhood immunizations less effective.[14] Presumably, adding yet another immunization to the already crowded immunization schedule in the first 6 months of life may overwhelm the child's ability to mount an appropriate immune response. Although adverse effects of larger-scale administration of hepatitis B vaccine along with the polio, diphtheria, tetanus, pertussis, and *H influenzae* vaccines are unknown, there is evidence of a decrease in the immune response to HBV when the vaccine is given too early.[12,15]

Thus, newborn immunization may not be as effective as later immunization, and it carries the potential of a decreased immune response to the primary pathogens of childhood. These two concerns, coupled with the exceedingly low incidence of hepatitis B in children, raises the question whether the immunization offers more harm than benefits. Even the CDC emphasizes the need for continued monitoring of the immunization's safety.[12] In our opinion the immunization fails to pass this second test.

3. Will immunization make it possible to change the prognosis of the disease? The immunization is at least 90% effective in the short term.[12] However, titers fall in up to 60% of people after 9 years, though immunologic memory persists.[12] There is no evidence of the immunization's effectiveness after 10 years.[16] For this reason the need for a booster is likely, as with all other immunizations given in the first 18 months of life. So, while the immunization is effective, the program of universal newborn immunization *does not* pass the third test. There is insufficient data that such a childhood immunization program will offer immunity as an adult, when it is most needed.

4. Is the immunization acceptable to the patient and the physician? Not all parents agree that immunizations are justified.[17] Nevertheless, both patients and physicians generally regard immunizations as acceptable, and the hepatitis B vaccine has fewer side effects than most. On the other hand, a significant number of physicians anticipate negative parental reactions and nurse resistance to giving three injections (DPT, Hib, and HBV) at a single well-child visit. It is not clear whether the immunization passes the fourth test.[18]

5. Is the immunization cost-effective? In this context, *cost-effectice* means that the benefits of the immunization justify the costs. Assume the three-dose schedule costs $50, has no side effects, and is 90% successful at preventing the disease. Given a 5% lifetime risk of the disease, the immunization program costs only $1100 per case of hepatitis B prevented. This cost seems reasonable.

Does this mean that routine immunization of newborns for hepatitis B is cost-effective? Hardly. The most cost-effective method is to immunize "endemic" populations, and hepatitis B is primarily a disease of adolescence and adulthood; it is essentially unknown in children before age 10 years. Given that 4 million infants are born in this country each year, a universal immunization program costing only $50 per infant will cost $200 million each year. Since the majority of the program's effect will not be seen for 15 to 20 years, the nation will spend $3 to $4 billion before a significant effect on hepatitis B is seen. If the emphasis were placed instead on high-risk newborns or mandatory immunizations of teenagers, the costs would be much less and the effects more immediate.

The important question, however, is not hepatitis B but the carrier state. Using the data given above, between 6173 and 12,346 immunization series (ie, up to 37,000 vaccinations) are needed to prevent one case of HBV carrier state. For those who believe that hepatocellular carcinoma is a valid rationale for the newborn immunization program, similar calculations demonstrate that approximately 2 million immunization series (6 million vaccinations for $100 million) are necessary to prevent one case of hepatocellular carcinoma. In short, universal newborn immunization is not cost-effective.

What about the CDC's argument that teenagers are too hard to immunize? Would you really implement a childhood immunization program that may not work when needed just because the program is convenient? Are there better mechanisms of assuring the compliance of teenagers? Two examples are proof of immunization before entering high school (similar to the requirement that children be immunized before starting kindergarten) and proof of immunization before getting a driver's license. Immunization programs based in the school would be less expensive than office-based programs and would also improve compliance in teenagers. Such a program could be tied to tetanus and rubella boosters, thus increasing the compliance and decreasing the costs associated with these immunizations as well.

First and foremost, our efforts should be concentrated on preventing the spread of hepatitis B. Universal newborn hepatitis B immunization may eventually prove to be justified, but in 1993 it is a premature policy. The program fails at least four of the five criteria, and we should abandon the practice outside of carefully designed

clinical trials. Instead, we should focus our resources on the immunization of teenagers and high-risk children.

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