A Look to the Future

As another new year is upon us, it seems relevant to review a few of the vaccines that are in the later phases of clinical trials and the FDA licensure process. These vaccines include a product that attempts to fill the vacancy left by the withdrawal of Rotashield from the market in 1999, a vaccine that will be targeted at older individuals to prevent herpes zoster, two products that are touted as anti-cancer vaccines, and a combination vaccine that protects against MMR and Varicella.

Merck & Co., Inc. has created Rotateq®, an oral, liquid pentavalent vaccine that is designed to protect against rotavirus gastroenteritis. Rotavirus infection causes an estimated one-half million deaths in children under five years of age worldwide each year. In the United States, Rotavirus is responsible for significant morbidity (including primary care office visits, lost wages, ED visits/hospitalizations, etc.) and approximately 20-40 deaths each year. Clinical trials have not shown an increased risk of intussusception which was the inciting factor for the withdrawal of Rotashield’s predecessor, the Wyeth product Rotashev, in 1999. The FDA was scheduled to review Rotateq at a December 2005 meeting.

The FDA was also set to review Zostavax™, another Merck product, in December 2005. This vaccine is targeted at an older population to prevent the development of herpes zoster (shingles), to prevent postherpetic neuralgia, and to reduce shingles-associated pain. The results of the clinical trial were published in a June 2, 2005 issue of the New England Journal of Medicine and indicate a favorable response to the vaccine compared to placebo.

Two vaccines, Gardasil® (a Merck product) and Cervarix™ (a GlaxoSmithKline product) are in different stages of the review and licensure process. These vaccines are aimed at reducing infection with several types of the human papillomavirus (HPV) which can lead to cervical cancer. Several interesting issues surround the potential use of these vaccines including whether to vaccinate just women or both men and women and the recommended age to institute the series.

Finally, with the September 2005 licensure of Merck’s Proquad®, the question again surfaces as to whether or not a routine second dose of varicella will be recommended. Proquad is a combination vaccine for both MMR and Varicella. The vaccine was approved for children ages 12 months to 12 years and might open an avenue for the recommendation of a varicella vaccine booster without adding an additional injection to the schedule. The Advisory Committee on Immunization Practices (ACIP) will need to decide if a varicella booster will be immunologically beneficial and economically feasible.

For the most up to date information on new vaccines’ status, go to the Red Book® Online Table-Status of Licensure and Recommendations for New Vaccines at www.aapredbook.aappublications.org/news/vaccstatus.shtml.

Hepatitis A Revisited

On October 28, 2005 the Advisory Committee on Immunization Practices (ACIP) recommended that all children in the United States receive vaccination against the virus that causes Hepatitis A. Once approved by the director of the CDC and the Secretary of Health and Human Services, these recommendations will be officially published in the Morbidity and Mortality Weekly Report. Universal vaccination of all children is an expansion of a previous 1999 ACIP recommendation to vaccinate only children in those states where the incidence of Hepatitis A is greater than 20 cases per 100,000 people and to consider vaccination in those states that have between 10-20 cases per 100,000 people per year. Pennsylvania was considered a low risk state and thus, vaccination with Hepatitis A has not previously been a part of the routine childhood immunization schedule.

As a review, infection with the virus that causes Hepatitis A can lead to a myriad of symptoms including fever, malaise, anorexia, jaundice, and nausea. Young children (those less than 6 years of age) often have asymptomatic infection and those with symptoms are often without the telltale jaundice. Older children and adults are typically symptomatic for several weeks with some infections lasting up to 6 months. While chronic infection does not occur, fulminant liver failure is a rare but serious complication of Hepatitis A infection. Up to 100 fatal infections are reported each year in the U.S.

Transmission of the virus causing Hepatitis A infection is classically by the fecal-oral route although other modes of transmission (e.g., vertical, transfusion) have been documented. In up to 50% of cases, the source cannot be determined, probably owing in part to transmission from persons with asymptomatic infection. In addition, common-source food borne outbreaks can occur as was seen at a restaurant outside Pittsburgh, Pennsylvania in 2003. This epidemic resulted in 4 deaths and over 600 known cases of infection and was traced back to tainted green onions from Mexico.

In addition to the new universal recommendation to vaccinate all children, the ACIP and the CDC continue to recommend that other “high risk” individuals receive the Hepatitis A vaccine. These individuals would include travelers to areas Hepatitis A is endemic, males who engage in homosexual/bisexual activity, injection drug users, those with other chronic liver diseases, and patients with clotting-factor diseases (owing to the use of pooled Factor concentrates).

With the recent licensure of both brands of the inactivated Hepatitis A vaccines for administration to patients 12 months and older, the path for universal childhood immunization for the virus that causes Hepatitis A infection has been paved. The ACIP recommends a two dose series to commence between 1 to 3 years of age with catch up immunization to be done for preschoolers. Look for specific and official recommendations in an upcoming MMWR publication following the necessary reviews.