Frequently Asked Questions: Meningococcal B Vaccine

In June, 2015 the U. S. Advisory Committee on Immunizations Practices (ACIP) gave Men B vaccines a Category B recommendation, making the vaccine optional:

A serogroup B meningococcal (Men B) vaccine series may be administered to adolescents and young adults 16 through 23 years of age to provide short term protection against most strains of serogroup B meningococcal disease. The preferred age for Men B vaccination is 16 through 18 years of age (1).

This is an unusual recommendation, and, as a result, many physicians have questions about the vaccine. Below is a list of frequently asked questions:

Should low risk patients age 16 to 23 be advised to get one of the new Men B vaccines?

There is no clear answer to that question. Persons age 16 to 23 are at an increased rick of contracting meningococcal infections. On the other hand, the incidence of the disease is low and seems to be getting lower. There is limited information about the efficacy and safety of the vaccines. This is why the US Advisory Council on Immunizations Practices gave this recommendation a B rather than an A rating(1,2).

Why did the ACIP give the recommendation for routine Men B vaccination of persons 16 to 23 years of age a category "B" recommendation instead of a category A recommendation like most vaccines?

Category B recommendations are not common and call for personalized clinical decision making between clinician and patient (3). In a report to the ACIP the Meningococcal Work Group noted, "key data on Men B vaccines are not yet available". (2)

What about patients that are at greater risk of Meningococcal B infections?

The ACIP recommends use of Men B vaccines among certain individuals aged ≥10 years at increased risk for serogroup B meningococcal disease. This includes: those with complement component deficiencies, anatomic or functional asplenia, microbiologists routinely exposed to isolates of Neisseria meningitides, and those at increased risk because of a serogroup B meningococcal disease outbreak. This was a **category A** recommendation. (4)

How common are Meningococcal B infections?

All serotypes of Meningococcal disease are rare, and the incidence seems to be decreasing. The incidence of all Meningococcal B serotype infections in the United States is estimated to be about 200 cases per year among persons of all ages. The incidence of Men B is highest in children age 5 or younger with an estimated 75-100 cases per year, but the Men B vaccines are not licensed in the United States for this age group. The estimated average number of cases in 11-24-year-olds in the US is 54-67 cases per year. Cases tend to occur in clusters; since 2009, seven outbreaks of serogroup B meningococcal disease have occurred on college campuses. Cases have occurred in settings outside of college campuses as well (2).

What is the difference between the meningococcal vaccines we have been using and the new Men B vaccines?

The first meningococcal vaccine developed was a polysaccharide vaccine (5). The use of the vaccine has been limited by its short duration of action.

The next vaccines developed were the quadrivalent meningococcal conjugate vaccines, composed of capsular polysaccharide conjugated to a protein, cover meningococcal strains ACWY (Men ACYW). The Men ACYW are recommended for routine use in adolescents aged 11 or 12 years, with a booster dose at age 16 years (6).

The polysaccharide in the B strains of meningococcus is similar to a polysaccharide found in humans making Men B vaccines more challenging to develop (7). The development of these vaccines required sequencing of the bacterial genome to find proteins unique to the Neisseria bacterial wall that could be used as antigens to stimulate immunity in humans. Using this innovative process, two Men B vaccines, MenB-FHbP (Trumenba®) and MenB-4C (Bexsero®), were developed. Each vaccine is composed of novel protein or lipoprotein antigens. Therefore, the vaccines are not interchangeable.

How effective are the Men B vaccines in preventing Meningococcal B infections?

Because the incidence of disease is low, clinical trials of vaccine effectiveness are not practical. Instead vaccine efficacy was based on "complement mediated antibody killing" detected in serum of individuals who received the vaccines, a surrogate measure of protection (1,2, 8, 9). In separate studies vaccines were given to different adolescent populations ranging in age from 11-65 years. Eighty-four percent of subjects who received 3 doses of Men B FHpB and 63-94% who received two doses of MenB4C were considered immune, based on immunogenicity studies to 4 strains of Meningococcus B that occur in the US (1,2). Other strains will be tested in the future. There was evidence of waning immunity in both vaccines over time (1,2,8,9).

Will immunizing populations decrease carriage of the Meningococcal B bacteria?

So far limited studies have not shown a decrease of asymptomatic carriage in immunized populations. More studies are planned (2).

What are the risks and side effect of the Men B vaccines?

Both vaccines have a tendency to cause minor, self- limiting reactions such as pain at the injections site, fever, headache, fatigue, myalgia and arthralgia. The incidence of these reactions does not seem to be higher than similar reactions with other vaccines (8,9).

There is a theoretic risk that Men B vaccines could cause autoimmune disease. Both vaccines contain factor H binding protein which in animal models was noted to be cross-reactive with human factor H. It is not known if auto-antibodies are generated in humans, and the clinical significance of any antibodies is unknown (1).

So far each vaccine has reported one case of non-fatal anaphylaxis (2). Given the current low incidence of meningococcal B disease, it is theoretically possible that the risk of death from vaccine anaphylaxis is greater than the risk of death from the disease.

Initial licensing was based on three to four thousand cases. This is low compared to numbers reported in the licensing of most new vaccines because FDA approval for the Men B vaccines was granted via an accelerated process. Additional data on more cases was collected when the vaccines were used during outbreaks on college campuses.

For the **MenB-FHbP vacci** 13 cases of autoimmune conditions in the 4,576 persons who received the MenB-FHbP vaccine and none in the 1,028 controls (8). On closer examination the reported conditions were felt to predate the vaccine, have other explanations for causation or did not have a higher rate than expected in the population. Additional information was presented at the June, 2015 ACIP including 7 creditable serious adverse events (pyrexia, vomiting, vertigo, chills, headache, anaphylaxis, and neutropenia in 4 out of 9,808 persons who received at least one dose of this vaccine. All adverse effects resolved without long-term consequences (1,2).

For the MenB no serious adverse events in 3,139 persons who received at least one dose of MenB 4C in clinical trials reviewed by the FDA. In addition, 15,351 persons received MenB 4C when it was administered during outbreaks on college campuses. Serious adverse events included two reports of juvenile arthritis, but one case had symptoms that predated the vaccine. One case of thyroiditis was also felt to have symptoms predating the vaccine. There was one case of anaphylaxis that was felt to be related to the vaccine (9). The ACIP also reported an additional 59,091 people received the Men 4C vaccine during outbreaks on college campuses. Only three serious adverse events occurred: rhabdomyolysis, anaphylaxis and fever (2).

What is the price of the Men B vaccines?

MenB-FHbp is a 3-dose series with a Centers for Disease Control and Prevention (CDC) private sector price of $115.75 per does or $347 for the series. MenB-4C is a 2-dose series with a CDC price of $160.75 per doses or $322 for the series (10). Both vaccines will be covered by third-party payers in accordance with the Affordable Care Act. Assuming a birth cohort of 4,000,000 the cost of vaccinating all 16 to 23-year-olds would be over a billion dollars. The ACIP estimates the cost per Quality Adjusted Life Year (QALY) to be in excess of 4 million dollars (1,2).

Are the vaccines covered by insurance?

Under provisions of the Affordable Care Act, the vaccine should be covered by insurance. The Vaccines for Children Program should cover qualified children under the age of 18.

When will there be more information about the men b vaccines?

In the United Kingdom (UK) Men B vaccines are approved for children age 8 weeks to two years. As in the US, this age group has higher incidence of disease than the adolescent/young adult age group (11). As a result of experience with the vaccines in the US and UK, more information will emerge in the next

few years. Until then physicians and patients need to understand the potential risks as well as benefits on these new vaccines.

Where can I get more information?

More information is available at the ACIP Web site.

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