toxins, mainly enterotoxin A. Although enterotoxin A is the most common toxin in *Staphylococcus*-related food poisoning, the enterotoxin D we found is reported to be the second most common, supporting its role in this patient's enterocolitis (*6*). Enterotoxins G and I are not as well-studied but were associated with a food poisoning outbreak in Taiwan (*7*). Staphylococcal enterotoxins G and I induce enterocolitis by a combination of direct enterocyte cytopathy mediated by epidermal cell differentiation inhibitor toxins (disrupting the epithelial barrier) and enterotoxin superantigen-induced mucosal T-cell activation (*8*).

The risk factors for *S. aureus* enterocolitis include age, hospitalization, abdominal surgery, immunosuppression, gastric acid suppression, MRSA colonization, and previous antibiotic therapy. Fluoroquinolone use seems to be particularly associated with this complication (*1*). MRSA enterocolitis might be an underrecognized cause of AAC because stool culture in patients hospitalized for >72 hours has been discouraged (*9*). MRSA enterocolitis should be considered once *C. difficile* colitis and *Klebsiella oxytoca* colitis have been ruled out (*10*). Physicians should consider stool cultures for severe or prolonged AAC, and microbiology laboratories should report *S. aureus* overgrowth in stool. Oral vancomycin was effective in this case and seems to be the consensus choice for therapy based on previous reports.

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References

1. Avery LM, Zempel M, Weiss E. Case of antibiotic-associated diarrhea caused by *Staphylococcus aureus* enterocolitis. Am J Health Syst Pharm. 2015;72:943–51. http://dx.doi.org/10.2146/ajhp140672
2. Pressly KB, Hill E, Shah KJ. Pseudomembranous colitis secondary to methicillin-resistant *Staphylococcus aureus* (MRSA). BMJ Case Rep. 2016;pii: bcr2016215225. PubMed https://dx.doi.org/10.1136/bcr-2016-215225
3. Iwata K, Doi A, Fukuchi T, Ohji G, Shirota Y, Sakai T, et al. A systematic review for pursuing the presence of antibiotic associated enterocolitis caused by methicillin resistant *Staphylococcus aureus.* BMC Infect Dis. 2014;14:247. http://dx.doi.org/10.1186/1471-2334-14-247
4. Kalakonda A, Garg S, Tandon S, Vinayak R, Dutta S. A rare case of infectious colitis. Gastroenterol Rep (Oxf). 2015;4:328–30. http://dx.doi.org/10.1093/gastro/gov016
5. Watanabe H, Masaki H, Asoh N, Watanabe K, Oishi K, Kobayashi S, et al. Enterocolitis caused by methicillin-resistant *Staphylococcus aureus*: molecular characterization of respiratory and digestive tract isolates. Microbiol Immunol. 2001;45:629–34. http://dx.doi.org/10.1111/j.1348-0421.2001.tb01295.x
6. Pinchuk IV, Beswick EJ, Reyes VE. Staphylococcal enterotoxins. Toxins (Basel). 2010;2:2177–97. http://dx.doi.org/10.3390/toxins2082177
7. Chen T-R, Chiou C-S, Tsen H-Y. Use of novel PCR primers specific to the genes of staphylococcal enterotoxin G, H, I for the survey of *Staphylococcus aureus* strains isolated from food-poisoning cases and food samples in Taiwan. Int J Food Microbiol. 2004;92:189–97. http://dx.doi.org/10.1016/j.ijfoodmicro.2003.10.002
8. Edwards LA, O'Neill C, Furman MA, Hicks S, Torrente F, Pérez-Machado M, et al. Enterotoxin-producing staphylococci cause intestinal inflammation by a combination of direct epithelial cytopathy and superantigen-mediated T-cell activation. Inflamm Bowel Dis. 2012;18:624–40. http://dx.doi.org/10.1002/ibd.21852
9. Siegel DL, Edelstein PH, Nachamkin I. Inappropriate testing for diarrheal diseases in the hospital. JAMA. 1990;263:979–82. http://dx.doi.org/10.1001/jama.1990.03440070067034
10. Högenauer C, Langner C, Beubler E, Lippe IT, Schicho R, Gorkiewicz G, et al. *Klebsiella oxytoca* as a causative organism of antibiotic-associated hemorrhagic colitis. N Engl J Med. 2006;355:2418–26. http://dx.doi.org/10.1056/NEJMoa054765

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Serogroup B Meningococcal Disease Vaccine Recommendations at a University, New Jersey, USA, 2016

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In response to a university-based serogroup B meningococcal disease outbreak, the serogroup B meningococcal vaccine Trumenba was recommended for students, a rare

instance in which a specific vaccine brand was recommended. This outbreak highlights the challenges of using molecular and immunologic data to inform real-time response.

In 2016, two undergraduate students at a large state university in New Jersey were hospitalized for suspected meningitis. The New Jersey State Public Health Laboratory (Trenton, NJ, USA) identified serogroup B *Neisseria meningitidis* in cerebrospinal fluid specimens from both patients by culture and slide agglutination. Both patients recovered without sequelae.

The isolates were sent to the Centers for Disease Control and Prevention (CDC) Bacterial Meningitis Laboratory for species and serogroup confirmation and whole-genome sequencing. Isolates were confirmed by real-time PCR as serogroup B *N. meningitidis* and were classified by multilocus sequence typing as clonal complex 11, sequence type 11, which is typically associated with serogroups C and W. Whole-genome sequencing revealed that the isolates were genetically indistinguishable from one another but different from all previously characterized meningococcal isolates in the United States.

Two serogroup B meningococcal (MenB) vaccines are licensed in the United States: MenB-4C (Bexsero, GlaxoSmithKline Biologicals, Inc., Philadelphia, PA, USA [*1*]), licensed as a 2-dose series; and MenB-FHbp (Trumenba, Pfizer, Inc., New York, NY, USA [*2*]), licensed as a 2- or 3-dose series. Either Bexsero or the 3-dose series of Trumenba is preferred for outbreak response (*3*). Both MenB vaccines are expected to help protect against most circulating serogroup B meningococcal strains, and in general, no brand preference exists (*3*). However, because the vaccines target different antigens (Table), they are not interchangeable; the same brand must be used for all doses (*5*). The vaccines might also have different effectiveness against specific *N. meningitidis* strains (*5*).

Whole-genome sequencing identified a mismatch between the antigens in the outbreak strain and those targeted by Bexsero (Table), prompting concern that Bexsero might not provide optimal protection against the outbreak strain. Although the outbreak strain antigens also did not exactly match those included in Trumenba, cross-protection with Trumenba was expected based on prior testing by the manufacturer (Table) (*2*). The outbreak isolates were sent to an independent laboratory for flow cytometry to measure antigen expression and serum bactericidal activity testing using human complement (hSBA) to evaluate whether stored serum from healthy adults previously

Table. Molecular profile and flow cytometry analysis of the university outbreak strain with reference to MenB vaccine antigens, New Jersey, 2016*

Antigen	Outbreak strain	MenB-4C vaccine (Bexsero)	MenB-FHbp vaccine (Trumenba)	Interpretation
FHbp	A22†/2.19‡	B24†/1.1‡	A05†, B01†	The 2 FHbp subfamilies (A and B) are not expected to be cross-reactive. The outbreak strain has a subfamily A FHbp. MenB-FHbp contains FHbp from subfamilies A and B. Although the subfamily A FHbp contained in MenB-FHbp (A05) is not the same peptide allele as that in the outbreak strain (A22), some level of cross-reactivity is expected based on prior testing by the manufacturer (*2*). However, based on flow cytometry, the strain had relatively low expression of FHbp, which would be expected to decrease susceptibility to anti-FHbp bactericidal activity (*4*). MenB-4C contains a subfamily B FHbp, which is not expected to provide protection against the outbreak strain FHbp.
PorA	P1.5–1,10–1	P1.7–2.4	Not included	The PorA present in MenB-4C and in the outbreak strain are 2 different PorA variable region sequence types and are not expected to be cross-reactive; therefore, no protection based on PorA is expected for either vaccine.
NHba	p0020	p0002	Not included	The NHba present in MenB-4C and in the outbreak strain are 2 different peptide alleles. The extent of cross-reactivity is not known. By flow cytometry, low binding to the outbreak strain was observed by using antisera against NHba p0002, but it is unclear whether this low binding is attributable to the difference in sequence between p0020 and p0002, low NHba expression in the outbreak strain, or both. Low binding with NHba p0002 antisera is consistent with decreased susceptibility to anti-NHba bactericidal activity in persons vaccinated with MenB-4C, but the correlation between flow cytometric binding and hSBA response has not been established. No protection based on NHba is expected for MenB-FHbp.
NadA	Negative	2/3.8	Not included	The outbreak strain does not contain NadA; therefore, no protection based on NadA is expected for either vaccine.

*FHbp, factor H binding protein; hSBA, serum bactericidal activity testing using human complement; MenB, serogroup B meningococcal; NadA, Neisserial adhesion A; NHba, Neisserial heparin binding antigen.
†Pfizer classification scheme.
‡GlaxoSmithKline classification scheme.

vaccinated with Bexsero or Trumenba could kill the outbreak strain bacteria (*6*).

By flow cytometry, the outbreak strain had low expression of factor H binding protein and low binding with antisera to the Neisserial heparin binding antigen included in Bexsero (Table) (*7*). Nevertheless, preliminary hSBA results suggested that 2 doses of either Bexsero or Trumenba would provide some short-term protection against the outbreak strain. Among persons with preimmunization titers of <1:4, most had hSBA titers of ≥1:4 at 1 month after the second dose (13/13 for Bexsero [*7*] and 9/10 for Trumenba). However, by 4 months after the second dose, hSBA titers fell back to <1:4 for some persons vaccinated with Bexsero (4/8) and Trumenba (4/5). The third dose of Trumenba, administered at 6 months after the first dose and 4 months after the second, boosted hSBA titers against outbreak strain bacteria to ≥1:4 for 9/9 persons 1 month after completion of the 3-dose series. On the basis of consideration of the laboratory data, the best and longest-lasting protection against the outbreak strain was expected with the 3-dose series of Trumenba. Accordingly, the New Jersey Department of Health and the university, with support from CDC, recommended vaccination with 3 doses of Trumenba for ≈35,000 persons at the university.

Serum bactericidal antibodies are used as a serologic correlate of protection for meningococcal vaccines (*8*) and have been correlated with clinical efficacy for serogroup C (*9*). For the purposes of US licensure, the effectiveness of MenB vaccines was inferred by using hSBA. Although hSBA titers probably correlate with protection against serogroup B meningococcal disease, this link has yet to be directly demonstrated through postlicensure effectiveness data.

Although hSBA results informed the vaccination strategy in this outbreak response, this experience underlines the challenges in obtaining hSBA testing and interpreting molecular and immunologic data on meningococcal outbreak strains. The hSBA results for this outbreak strain show that, because of variable protein expression and unknown cross-protection, using the molecular profile of a serogroup B meningococcal strain to reliably predict hSBA response in vaccinated persons is difficult. Additionally, to what extent hSBA results from a limited number of test subjects correspond to real-life protection in a different population is not clear. Furthermore, hSBA testing is time-consuming, a limited amount of serum from immunized humans is available for hSBA testing, and few laboratories are able to routinely perform this testing. These challenges make it difficult to routinely use either molecular typing or hSBA results to guide real-time outbreak response.

This recommendation for a specific brand of MenB vaccine was a rare exception to the general recommendation that either brand of MenB vaccine can help protect persons at increased risk during a serogroup B meningococcal disease outbreak. The use of molecular and immunologic data as potential tools to inform meningococcal outbreak response requires further investigation before being routinely implemented.

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References

1. US Food and Drug Administration. Bexsero US package insert [cited 2016 Nov 18]. http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM431447.pdf
2. US Food and Drug Administration. Trumenba US package insert [cited 2016 Nov 18]. http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM421139.pdf
3. MacNeil JR. Considerations for use of 2- and 3-dose schedules of MenB-FHbp (Trumenba®). Presented at: meeting of the Advisory Committee on Immunization Practices; October 16, 2016; Atlanta, GA, USA [cited 2016 Nov 18]. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2016-10/meningococcal-05-macneil.pdf
4. Pajon R, Fergus AM, Koeberling O, Caugant DA, Granoff DM. Meningococcal factor H binding proteins in epidemic strains from Africa: implications for vaccine development. PLoS Negl Trop Dis. 2011;5:e1302. http://dx.doi.org/10.1371/journal.pntd.0001302
5. MacNeil JR, Rubin L, Folaranmi T, Ortega-Sanchez IR, Patel M, Martin SW. Use of serogroup B meningococcal vaccines in adolescents and young adults: recommendations of the Advisory Committee on Immunization Practices, 2015. MMWR Morb Mortal Wkly Rep. 2015;64:1171–6. http://dx.doi.org/10.15585/mmwr.mm6441a3
6. Beernink PT, Giuntini S, Costa I, Lucas AH, Granoff DM. Functional analysis of the human antibody response to meningococcal factor H binding protein. MBio. 2015;6:e00842–15. http://dx.doi.org/10.1128/mBio.00842-15
7. Giuntini S, Lujan E, Gibani MM, Dold C, Rollier CS, Pollard AJ, et al. Serum bactericidal antibody responses of adults immunized with the MenB-4C vaccine against genetically diverse serogroup B meningococci. Clin Vaccine Immunol. 2017;24:e00430–16. http://dx.doi.org/10.1128/CVI.00430-16
8. MacNeil JR, Rubin L, McNamara L, Briere EC, Clark TA, Cohn AC, et al. Use of MenACWY-CRM vaccine in children aged 2 through 23 months at increased risk for meningococcal disease: recommendations of the Advisory Committee on Immunization Practices, 2013. MMWR Morb Mortal Wkly Rep. 2014;63:527–30.
9. Borrow R, Balmer P, Miller E. Meningococcal surrogates of protection—serum bactericidal antibody activity. Vaccine. 2005;23:2222–7. http://dx.doi.org/10.1016/j.vaccine.2005.01.051

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