On October 27, 2021, the Massachusetts Medical Society (MMS) held its informational call for members with the Massachusetts Department of Public Health (DPH). Kevin Cranston, MDiv, Assistant Commissioner and Director, Bureau of Infectious Disease and Laboratory Sciences, Larry Madoff, MD, Medical Director, Bureau of Infectious Disease and Laboratory Sciences, and Catherine Brown, DVM, MSc, MPH, State Epidemiologist and State Public Health Veterinarian participated. DPH officials provided clarity on the new recommendations for COVID-19 vaccine booster shots, the latest on Pfizer-BioNTech’s COVID-19 vaccine for children ages 5 to 11, and their perspective on current COVID-19 case rates. DPH officials also responded to member questions asked during the call.

**COVID-19 Cases, Variants and Hospitalizations**

**Dr. Brown:**

- Massachusetts seems to have come down off of the latest peak from the Delta Variant surge. Case numbers have stabilized, but cases are not actively declining. Daily case numbers are coming in between 1,200 and 1,400 a day. There is concern that as the weather gets colder, and people are indoors more, that cases could start to rise again.

- DPH is seeing a lot of breakthrough infections. Breakthrough infections are those cases of COVID that are occurring in people who have been fully vaccinated (received either two doses of Moderna or Pfizer-BioNTech or one dose of Johnson & Johnson/Janssen and are diagnosed with COVID two weeks after that primary vaccination series). The reason there are a lot of breakthrough infections is because Massachusetts has a high vaccination rate. To illustrate, if you have 100% of your population vaccinated, then 100% of your cases are going to be breakthrough cases. Basically, the more people you have vaccinated, the more people are going to have breakthrough infections. Unvaccinated people are still at much higher risk for developing COVID, and they are at substantially higher risk of developing severe disease from COVID. This is an important nuance that is hard for some to understand. People see the breakthrough numbers and worry about it, but it really is just a factor of our really excellent vaccination rates in combination with a highly transmissible variant, the Delta Variant.

- Recently, a variant called Delta Plus has been in the news. To put the Delta Plus in perspective, back to January of this year, people were concerned about the Alpha Variant. At the time, it was called B.1.617. Subsequently, there was concern about the P.1 Variant. While there were certainly clusters related to those variants, it wasn’t until the Delta Variant came along that we had a variant with significant epidemiologic difference, meaning it was much more highly transmissible. Since the middle of July, 98% of the COVID cases in the United States (U.S.) have been due to that Delta Variant. The fact
that there have been so many COVID cases has allowed opportunity for the virus to continue to evolve. The more cases you have, the faster the virus evolves. If you actually examine the Delta Variant, it turns out that there are over 100 different sub-variants of Delta, but they’re all slightly different. One of those is this Delta Plus. Delta Plus has been associated with a recent increase in cases in the United Kingdom (U.K.). At this point, there is not enough known about this Delta Plus Variant to know whether it has either a clinical or epidemiologic characteristic that would make it concerning. It is not known yet whether Delta Plus carries increased vaccine resistance or is more transmissible than original Delta. The fact that we don’t know can be scary, but the U.S. has gotten to a point where a significant amount of genomic sequencing is being done on viruses that are found in the U.S. and we are tracking the occurrence and emergence of variants in a much better way than earlier in the pandemic. At this point in Massachusetts, there have been five known cases of Delta Plus. DPH continues to monitor the situation with Delta Plus as well as other variants. We should not be focused on a single variant until we have evidence that there’s an emerging variant that is concerning.

- Hospital capacity remains limited. Compared to earlier in the pandemic, hospitals are not capacity constrained because of COVID patients rather there are a lot of other high acuity cases in the hospital. This likely reflects the fact that many people delayed care during the pandemic and now they’re more comfortable seeking health care. These patients may have chronic diseases that were not managed adequately during the pandemic and therefore are now requiring hospitalization. DPH is continuing to monitor hospital needs and constraints.

**COVID-19 Therapeutics Update**

**Dr. Madoff:**

- Molnupiravir, an investigational oral antiviral medicine, has been submitted to U.S. Food and Drug Administration (FDA) for emergency use authorization (EUA). DPH is hearing from federal partners that it might be available in Massachusetts soon. So far, clinical data are only available from the manufacturer’s press release, but it does seem to show promise. Molnupiravir is a nucleoside analog drug similar to other antiviral agents. When administered orally within five days of onset of mild to moderate COVID in an outpatient setting, it has been shown to reduce the risk of hospitalization and serious illness by about 50% in high risk individuals. This effectiveness is probably less effective than the monoclonal antibodies that are currently approved by EUA, but it is much easier to administer and can be given quickly. Molnupiravir acts as a mutagen to the virus and causes incorporation of faulty RNA in the virus. However, it is also, at least theoretically, a mammalian cell mutagenic, that can be incorporated into human DNA. This is something to know and that gives us a little bit of pause about the use of this agent in people with COVID. The treatment is short, it’s a five day course, so clinicians will need to balance the risks and benefits. Considering the amount of press regarding people being concerned about the mRNA vaccines and incorporation into their DNA, which does not happen. This therapeutic, in fact, might be incorporated into mammalian DNA. This it’s just something to note.

- DPH continues to see less uptake of monoclonal antibody therapeutics than expected and encourages clinicians to consider monoclonal antibodies for their eligible patients. There are now three: the Lilly product, bamlanivimab plus etesevimab; the Regeneron product, casirivimab plus imdevimab; and a third product, sotrovimab. They are all authorized under EUA for treatment of mild to moderate COVID within 10 days of a test in outpatients. Find locations that have received monoclonal antibodies [here](#).

**Vaccine Update**

**Dr. Madoff:**
• The Pfizer-BioNTech COVID-19 vaccine has full FDA approval for adults. All of the other vaccines and indications are still under EUA. Pfizer-BioNTech’s COVID-19 vaccine for 12 to 17-year-olds is under EUA, Moderna’s COVID-19 vaccine and the Johnson & Johnson/Janssen vaccine are under EUA for all recipients.

• The current state of FDA approval and Advisory Committee on Immunization Practices (ACIP) recommendation includes an additional dose of mRNA vaccine for immunocompromised individuals who have received a primary series of the mRNA vaccines. That recommendation is for the same vaccine at the same dose that they initially received for individuals who are at least moderately immunocompromised.

• The FDA has approved, and Centers for Disease Control and Prevention (CDC) has released booster recommendations for all three available COVID-19 vaccines, both of the mRNA vaccines as well as the Johnson and Johnson/Janssen vaccine.
  o Everyone who received the Johnson & Johnson/Janssen vaccine at least two months ago.
  o Those individuals and who are at least six months after their primary series of the mRNA vaccines (Pfizer-BioNTech or Moderna) and who fall into one of the following categories:
    ▪ 65 years and older
    ▪ Age 18+ who live in long-term care settings
    ▪ Age 18+ who have underlying medical conditions
    ▪ Age 18+ who work or live in high-risk settings
  o The FDA has authorized, and CDC has also given permission to boost with a heterologous vaccine. While the same vaccine is preferred and recommended, heterologous vaccines can be given based on availability or clinical considerations. Someone who received a primary series of the Pfizer-BioNTech vaccine who is eligible for a booster dose can receive the Moderna vaccine and vice versa. Any of the three vaccines can be given to recipients of the Johnson & Johnson/Janssen vaccine. There is now sufficient evidence in the literature in terms of increased antibody response, this is now deviating from official recommendations, to say that recipients of the Johnson & Johnson/Janssen vaccine may benefit from receipt of the mRNA vaccines as their booster dose so this is something to consider.
  o Booster doses are also recommended for those who are immunocompromised. Those individuals can receive a booster dose after their third/additional dose of the mRNA vaccine. The intricacy of the vaccine recommendations is that those people are actually recommended for what would be a fourth dose of vaccine after six months after their receipt of the additional dose. For almost everyone, that would not be until February of next year.
  o There is a lengthy and worthwhile document on the CDC COVID-19 Vaccine web page called Clinical Considerations for COVID-19 Vaccinations which goes into detail about vaccination against COVID and how to use the different vaccines in different settings, in immunocompromised individuals, and people who've received a different vaccine.

• There is no longer any prescription against co-administration of any vaccine. People are encouraged to get a flu vaccine this year, and it can be co-administered or administered any time before or after a COVID vaccine without any precautions or contraindications.

• Information on pediatric vaccine is rapidly evolving. The FDA’s Vaccines and Related Biological Products Advisory Committee (VRBPAC) recommended to FDA Pfizer-BioNTech’s vaccine at a reduced dose of 10 micrograms for children ages 5 to 11 and, basically, to all children in that age group. There was a lot of discussion at the VRBPAC meeting. The FDA still has to formally approve the pediatric
vaccine based on VRBPAC's recommendation, which is expected to happen. The ACIP is planning to meet next week to discuss that recommendation.

- The Pfizer-BioNTech’s 5-11 vaccine will be a different formulation and presentation from the adult vaccine. It will also be packaged and distributed differently. The pediatric formulation will come in a different colored vial, an orange cap vial in the 10 microgram dose. It does require diluents.
- Moderna has submitted its pediatric COVID-19 vaccine for approval for EUA to FDA. It appears to have similar efficacy and safety data to the Pfizer-BioNTech vaccine, but that has not yet been acted on by any regulatory authority.

Mr. Cranston:

- The CDC is pre-positioning the Pfizer-BioNTech pediatric doses in the states. Massachusetts has done extensive surveying of the various sectors and DPH continues to be encourage practices that serve pediatric patients to consider being a site for vaccination. DPH wants as many opportunities, locations, appointments available and clinics available for families to vaccinate their younger children as possible.
- Over 180,000 doses are slated for Massachusetts. Shipping will occur fairly soon and in time so that if the ACIP does recommend the 5 to 11 indication for Pfizer-BioNTech those doses may be available to begin administration as early as late next week.
- DPH had 299 providers who requested doses. The CDC has indicated that they have a preference for pediatric formulation for Pfizer-BioNTech to be administered by pediatric practices.
- There is an additional 87,000 doses that were slated for retail pharmacies separate from that state allocation. Over 280 retail pharmacy stores have indicated their availability to vaccinate. CVS and Walgreens are by far the largest volume vaccinators followed by other well-known entities like Walmart, Topco, Rite Aid, Costco, Albertsons, et cetera. Not all stores in the federal retail pharmacy partnership are going to be administering doses to 5 to 11-year-olds because of the more limited supply.
- There's at least one vaccine site location in 255 of our 351 cities and towns in Massachusetts.
- The population of the 5 to 11-year-olds in Massachusetts is 515,000 individuals. DPH anticipates that there will be at least 267,000 doses available to the Commonwealth in the initial allocation. That includes those first shipments and then subsequent shipments. The initial shipment will come in 300 dose allocations, followed by 100 dose allocations. The 100 dose increments will enable a much wider array of pediatric providers and other providers serving pediatric populations to be able to participate in the vaccination effort.
- DPH has extended the time frame by which we expect pediatric doses to be administered. For most other providers all ship doses need to be administered within 30 days or expected to be administered within 30 days. For pediatric providers that expectation is extended to 45 days due to expected challenges around numbers of appointments, space, and staffing considerations and to make sure that as many pediatric providers as possible are participating in this effort.
- DPH’s Vaccine Equity Initiative is fully ramping up to address the pediatric formulation availability. This will include continuing their linguistically and culturally focused outreach to our 20 Vaccine Equity Initiative communities and continuing to partner with community based organizations, faith based organizations, and community health centers.
- DPH will be sponsoring five high throughput sites. These will not be the same kind of volume as the mass vaccination sites that were set up. but we'll be able to move hundreds of individuals through vaccination lines where they're set up. DPH will be positioning those five sites in areas where we continue to see relative deserts of participating private providers, hospital systems, or pharmacies. The
Responses to questions provided in advance of the call:

**Question:** Can you direct us to where we can find information for parents of young children who may be concerned about the safety of the vaccine?

**Mr. Cranston:** We have already set up on the mass.gov website, a 5 to 11 age group webpage. We recognize it's still preliminary information and will be continuing to update it as more information comes, particularly from the ACIP. That will be one of the sources for information for parents and others interested in safety and efficacy of the Pfizer-BioNTech indication. As in the past, we expect the CDC to develop some targeted materials that we will make available as well. It is likely that our communications department will take those materials and the information coming out of ACIP and develop a targeted campaign directed towards the pediatric population, but we have to wait for the full ACIP recommendation before we can legitimately do any of that promotional work.

**Question:** Will the state set up school based clinics or weekend clinics? Does the state have any plans to help pediatric and family practices partner with schools or even with each other to run clinics?

**Mr. Cranston:** We have conducted outreach to school systems regarding their plans to participate in the overall effort. Most school based clinics are operating at the high school level predominantly and will not be serving younger individuals. Schools certainly can partner with our mobile vaccination vendors, with community health centers, with local boards of health in their community, and with local private providers as well. I can affirm that at least six school districts have made requests to receive vaccines for this age group, including several of our larger vaccine equity communities.

**Question:** The mask mandate for schools was extended yesterday, can DPH provide insight on what data drove the extension and are there any incentives for school districts to reach 80-90% vaccination levels?

**Dr. Madoff:** The Department of Early and Secondary Education released guidance that they will continue to impose a mask mandate on school children at least through the beginning of next year. Part of that mask mandate includes a provision that schools that reach an 80% vaccination rate of students and staff will be permitted to not mask vaccinated individuals. So that itself is an incentive for kids and for parents and schools to encourage vaccination among their students. Certainly, we know from long experience that a providers recommendation is a strong impetus to getting kids vaccinated so that's going to be an important component.

DPH responses to questions asked during the call:

**Question:** I was wondering if there's a child who is going to turn 12 within the next two or three weeks, should they get the half dose first or should they wait for the full dose?

**Dr. Madoff:** I'm not sure how to answer that. There may be more detailed information or a recommendation that may come from ACIP. There are some gray areas and things that fall between the cracks. I would say clinically it's probably not very important, one way or the other, but we wouldn't recommend giving a dose of anything outside of the recommended age range.

**Question:** You mentioned a CDC website that has particularly good information about details around each vaccine, can you verify that site? Could you repeat the three categories of monoclonal antibodies that have plan is for these to fill in some of the geographic gaps in availability of the pediatric vaccine once it begins flowing.
been approved for treatment? Lastly, which agents did you say may have some pause around causing side effects? Was that the oral agent that might be mutational or was that one of the IV antibodies?

**Dr. Madoff:** The page that I’m talking about from the CDC website, called [Clinical Considerations for COVID Vaccination](https://www.cdc.gov/vaccines/covid-19/professionals/considerations/index.html), which answers many vaccine related questions. I look at it all the time because there is detailed guidance. The pause was about the potential mutagenicity of the not yet authorized Molnupiravir, the oral agent. I do want to stress this is just a theoretical concern, but I wanted to mention it. There’s a lot of enthusiasm for use of this drug, so I just wanted to point out that there are, as with any drugs, some potential downsides. There are three monoclonal antibodies: the Lilly product, the Regeneron product and the most recently authorized is called sotrovimab and I can’t recall the manufacturer. The first two incidentally are also authorized for post-exposure prophylaxis in addition to treatment of early COVID in high risk individuals. Post-exposure prophylaxis indication is for individuals who have been exposed or in congregate settings where there’s an outbreak. It can be given in those congregate settings as well even to those who don’t have a positive COVID test to prevent development of COVID. Again, that’s the Lilly product and the Regeneron product. One other just minor note is that Regeneron product can be given subcutaneously as well as intravenously and for the post-exposure prophylaxis there’s no preference given to one route over the other. All three are provided free by the government and distributed by the state. There are a number of sites that are available throughout the state where patients can be referred for infusion. They are all authorized under EUA for [treatment of mild to moderate COVID](https://www.cdc.gov/coronavirus/2019-ncov/treatment-monoclonal-antibodies.html) within 10 days of a test in outpatients. Find locations that have received monoclonal antibodies [here](https).

**Question:** I’m asked quite frequently by my patients which booster I recommend, given that there’s now crossover. Is there any true evidence base for recommending one mRNA vaccine booster or the other or is either one ok?

**Dr. Madoff:** Our recommendation and CDC’S recommendation is to use the same mRNA vaccine that they received in the initial vaccination series. There’s some evidence that the heterologous booster elicits a slightly higher antibody response. I think the differences are not great or likely to be clinically relevant, so I don’t have a strong recommendation. Honestly, I’ve been asked this by my friends and colleagues as well. I don’t think there’s strong evidence to support using a heterologous vaccine. I think if it’s what’s available the person should get it, but I don’t think that I would recommend it. In contrast to that, I think there’s reasonable evidence that an mRNA vaccine given to people who were immunized with the Johnson & Johnson vaccine does elicit a substantially higher antibody response. I think it would be reasonable to recommend in that setting.

**Question:** Where I live, churches and charities are sponsoring outdoor events and not requiring masks. The virus is transmissible outside. One of the groups is preparing to have a sale with vendors with tables outside and customers and will not require masks. Of course, my opinion is they should have masks, but I’m wanting to prevent any possible transmission. What is your opinion about outdoor events being unmasked?

**Dr. Brown:** I think you actually answered the question. Are we trying to prevent every single transmission or are we trying to balance the cost and benefit? The potential benefit being people getting out, being involved in social activities and starting to feel as if life will get back to some semblance of normal at some point. Transmission can happen outdoors. I would say that is true. It would be much more likely between people who are having really close contact for a prolonged period of time. Being outdoors is not 100% preventative, but it reduces the risk substantially. Again, I think it comes back to what is the goal. Is the goal actually trying to prevent every single infection, in which case, you’re right, it shouldn't be held at all or are we trying to balance risks and benefits?
Follow-up: The question is, if these outdoor events are held, should they require masks?
Dr. Brown: My opinion is that there are benefits to more normal social interactions. It's outdoors, which lowers the risk. Maybe there could be messaging around people being vaccinated, but the Commonwealth does not require masking outdoors for specifically because transmission is significantly less under most outdoor situations. These are decisions that are often made at the community level or at the institution level and it really is a cost benefit decision.