On November 17, 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 an update on the recent rise in COVID-19 cases and hospitalizations, booster shots, pediatric vaccination and information on new COVID-19 oral therapeutics. DPH officials also responded to member questions asked in advance and during the call.

COVID-19 Case and Hospitalization Update

Dr. Brown:

- COVID-19 cases are increasing again in Massachusetts. Although this is not completely unexpected with the weather getting colder and people spend more time indoors, it is disheartening. Looking at this current increase in cases in the context of the whole pandemic, Massachusetts is still way below what we were experiencing, back in the winter of late 2020 into 2021, but it's also only November, and DPH is concerned about where this latest case increase may lead. Massachusetts is also in a very different place than a year ago, with one of the highest vaccination rates in the country. Hopefully, the high rate of vaccination will continue to act in our favor as we move into the winter.

- Massachusetts has one of the highest testing rates in the country. One of the questions asked frequently is if case rates are going up just because more testing is being conducted. Unfortunately, that does not appear to be the answer. Massachusetts percent positivity has also increased. If what we were actually seeing was an increase in cases that was only due to increased testing, that should have resulted in a decrease in our percent positivity and that is not the case.

- Hospitals are continuing to feel very strained. This has been the situation for about six weeks now. During this time period, DPH was told by hospitals that there was a baseline of just over 500 COVID-19 cases (across the Commonwealth) requiring hospitalization, but the constraints were not just from COVID-19 hospitalizations, but also a result of an increase in high acuity cases of different illnesses in addition to staff shortages and other issues. Unfortunately, with the recent increase in COVID-19 cases, we are now also seeing an increase in COVID-19 hospitalizations, which is continuing to stress the hospital system. DPH continues to talk with hospitals to discuss the best ways to try to load balance and share resources among the hospitals.

- DPH is seeing the first evidence of influenza cases. Massachusetts influenza vaccination rates are lower than usual at this point in the year. This adds to the concerns around hospital capacity constraints.
COVID-19 Vaccination Update

Mr. Cranston:

- Massachusetts has very encouraging numbers on the vaccination front with close to 10.9 million total doses administered and 4.8 million individuals are fully vaccinated. Even using a revised denominator, including the over 500,000 people in the 5 to 11-year-old age group, that still represents 73% of Massachusetts residents fully vaccinated.
- As of yesterday (November 16th) there were 88,635 doses of COVID-19 pediatric vaccine administered to kids between the ages of 5 and 11. That represents about 17% of that age group, which is really tremendous in the short period of time since vaccinations were authorized for that age group.
- Massachusetts is approaching 800,000 COVID-19 vaccine booster doses administered.

COVID-19 Therapeutics Update

Dr. Madoff:

- The Commonwealth continues to roll out monoclonal antibodies. Several hundred doses are given out on a weekly basis. All three products are available and can be requested from DPH.
- There are now about 20 facilities that are infusing monoclonals around the State and we are poised to open three new infusion sites through a contractor geographically spread around the State. DPH expects at least two of those sites to be open early next week and another site probably the following week. Each site will have about four infusion chairs and be able to infuse 25 or 30 patients per day.
- Monoclonals are effective in preventing progression to serious illness. The window is within 10 days of diagnosis or symptom onset and in mild to moderate COVID-19 not requiring hospitalization for those at risk for progression to severe disease. That includes a number of categories including elderly, BMI greater than 25, and a number of other comorbidities that put somebody into a high risk of progression.
- There are two oral COVID-19 therapeutics currently in the pipeline.
  - The first, molnupiravir is pretty far along in the process. We have heard that we may see this therapeutic available in the State as early as the end of this month, possibly the first week in December. It is pending U.S. Food and Drug Administration (FDA) emergency use authorization (EUA). What we know about it is what the company has released from their trials. This therapeutic was given for similar indications to the monoclonal antibody (mild to moderate COVID-19) administered within five days of symptom onset. It showed approximately a 50% reduction in severe COVID-19 hospitalization and no deaths occurring in the several hundred treated patients versus 10 deaths in the placebo group. It appears to offer substantial protection against death, which is, of course, a very strong and convincing endpoint. The data and the details of the trials that are not yet available and nothing has been peer reviewed at this point. DPH is just learning about how it will be distributed. It sounds like quantities initially will be limited, and we don't know really the time frame over which that will be replenished. We also don't know for whom this therapeutic will be authorized. The studies were done in unvaccinated patients, and that could conceivably be one of the criteria for administration. It is also likely molnupiravir is a nucleoside analog that is incorporated into mammalian DNA, and so a potential mutagen carcinogen, and early indications are that pregnancy testing would be required for women of childbearing age before administration.
  - The second is Paxlovid from Pfizer. It is an inhibitor of the coronavirus protease, which is required to process the protein products that are produced by the coronavirus genome and
make the virus work effective. Protease inhibitors, similar to the protease inhibitors that are used in HIV, appear to be very highly effective in vitro. This drug is co-administered with ritonavir in order to boost its effectiveness. Based on relatively small clinical trials of several hundred participants, Paxlovid given within three days of onset of symptoms of COVID-19 was found to reduce the risk of hospitalization compared to placebo in non-hospitalized high-risk adults with COVID-19, and also showed, similarly, 100% efficacy in preventing death in recipients. The trial was also performed in unvaccinated individuals. Paxlovid has just been submitted to FDA. We do not know the timeline for approval or availability of this drug as yet, but it does certainly sound promising. It does not appear to carry the risks of a nucleoside analog. In both clinical trials, adverse events were not seen, essentially and were similar between the placebo and treatment arms for both drugs.

Responses to questions provided in advance of the call:

**Question:** _Does DPH have any guidance for the upcoming holiday season?_  
**Dr. Brown:** DPH’s holiday guidance is similar to what the [CDC holiday guidance](https://www.cdc.gov/coronavirus/2019-ncov/index.html) states which is to think about who you are celebrating with and whether or not they are vaccinated, make sure you are protecting particularly vulnerable individuals meaning people who are at higher risk for severe disease from COVID. The primary message continues to be that if you are not vaccinated, you should get vaccinated and if you're eligible for a COVID-19 vaccine booster, then you should get that as well.

**Question:** _The Curley School in Boston closed recently due to a recent increase in COVID-19 cases. There appears to be a difference between state and city officials position regarding closing schools. Can DPH add any insight into why the decision was made to close the Curley School and if COVID-19 cases are now being seen in more schools?_  
**Dr. Brown:** They had a significant number of cases in a short period of time in multiple different grades. There were quite a few agencies weighing in on what was the best approach. I'm not sure that there is a single right answer to the situation. The Boston Public Health Commission has the authority to help make decisions for schools that are in their jurisdiction. The Department of Elementary and Secondary Education definitely had a role to play in those conversations, and their primary goal is to keep students in class as much as possible. I think Boston Public Health Commission had the same goal, but they also want to make sure that they are preventing spread of disease, and in the end, they made the decision that they thought was best for the school. We are seeing an increase in COVID-19 cases in schools. I am not saying that means that we are necessarily seeing more transmission in schools. That is a very difficult question to answer and difficult to parse out. The school testing surveillance program has indicated that there's been about a 40% increase over a period of a couple of weeks in the number of cases that are being identified in school. That is significant, but the percentage is still low. The increase is relatively consistent with, and tends to mirror, community levels, which is not unexpected.

**Question:** _Is the Test and Stay program for schools working as intended?_  
**Dr. Brown:** I would say that the Test and Stay program is working very much as intended. The program allows students who are close contacts to attend in-person classes and partake in extracurricular activities provided they test negative every day. I don't have the numbers right in front of me, but the Test and Stay program has preserved a large number of school days for students who are close contacts that otherwise would have missed school at home in quarantine.
**Question:** We have heard the FDA is considering making booster shots more widely available to those 18+. Can DPH discuss what is being considered and why?

**Mr. Cranston:** This week the FDA will be taking up a consideration of expanding booster shot indication for everybody age 18 and up. I’d like to highlight that other large jurisdictions, like California and New York, have already made policy decisions around expanding their recommendations for booster doses. I would say we're looking at their experiences and their policies with great interest. More to come on that, and maybe very soon.

**Question:** Please update us on the rollout of the Pfizer pediatric vaccines for children between the ages of 5-11 years old. Is there anything pediatric practices should know and how has the uptake of 5-11 vaccine been so far?

**Mr. Cranston:** DPH went into the 5 to 11 vaccination roll out with a great expectation that pediatricians in particular and pediatric practices in general would play a major role in this uptake. We recognize that it's a lot of additional work for pediatric practices. We're pleased that smaller dose trays have facilitated ordering throughput and storage considerations. It appears to us, from everything we're hearing, not only from the pediatric providers, but the pharmacy pediatric vaccinators, that appointments are going as fast as they're being posted and that the demand and the willingness of parents, guardians, and other caregivers to arrange for their young children to be vaccinated is vigorous in Massachusetts. While we will continue to urge that younger children receive their vaccine, it doesn’t seem like we have to do a great deal of arm twisting. It seems the only limitation right now is about capacity.

**Question:** The 15 minute observation period after vaccination for 5-11 years impacts pediatric practice’s ability to immunize large numbers of children in a short period of time due to space issues. (e.g., the 15 minute wait times have made it hard to give more than 100 in a 3-hour clinic as compared to 500-900 in a flu clinic). Is there data to support the 15 wait time, and is there any flexibility with the recommendation now that we have more experience with this vaccine?

**Mr. Cranston:** The 15-minute observation period after vaccination is not specific to the 5 to 11 age group, but it's actually across the board for COVID-19 vaccination. I know this may be a weak argument, but basically, all vaccinations have a recommended observation period. The occurrence of adverse events is hard to predict. Some people may have had historic experience with an allergic reaction they can point to, but it's not always clear when a reaction, such as syncope, will occur in a given individual and an adverse reaction may not be predictable from their clinical history. For that reason, there has always been a good argument in the interest of patient protection for a wait period. The 5 to 11 indication of COVID-19 vaccine is still under EUA, and the experience in this age group is far less than with other pediatric vaccines. That may be a good, not from a specific data-driven perspective of data on adverse events, but an appropriate clinical caution when we have new experience with a new population and vaccine under an EUA to observe more rigorously the 15-minute wait time with full understanding that creates patient flow, space, and patient inconvenience. We are not able to provide more flexibility in that area. It is tied to the EUA, and it is part of the packaging accompanying this vaccine.

**Question:** With regard to vaccine mandates in the healthcare setting and people losing their job by not being vaccinated, why does masking with N95 in the healthcare setting not allow for those unvaccinated to continue to work in the healthcare setting?
Mr. Cranston: While I cannot second-guess institutional policies and decisions, I have to say I'm the wrong person to ask on this question. I actually really do want to reverse the question, which is, why is there continuing resistance on the part of health care workers to be vaccinated when we know the clear benefits of COVID-19 vaccination in terms of symptomatic disease and, particularly, serious illness and risk of death. This is a time when we need every health care worker we can get to be attending to the very crisis in hospitalization that Dr. Brown spoke to. I'm not going to be a good respondent to the benefits of N95 masks (which are clear) relative to vaccination when I'm a strong advocate for health care workers to be fully vaccinated.

**DPH responses to questions asked during the call:**

**Question:** If somebody received monoclonal antibody, does that in the long term impair their immune response to vaccine, and would it change what’s recommended regarding further booster shots?  
**Dr. Madoff:** The CDC has recently updated their guidance on that topic. The thought is that, yes, high levels of antibody that would be from the monoclonal antibodies might impair the immune response because it's passively administered antibody that might essentially neutralize the vaccine and the antigen that's produced in response to the vaccine. This is strictly theoretical, but CDC has recommended against immunization in a window of time after administration of monoclonal antibodies. There's a three-month window where vaccine shouldn't be given following administration of monoclonal antibody when it's given for therapeutic purposes—in other words for someone who has had COVID-19. The window for post-exposure prophylaxis, when a monoclonal antibody is given strictly for post-exposure prophylaxis not for treatment of COVID-19, is one month.

**Question:** For people who have been vaccinated and are planning to get their booster but get COVID-19 in between, the CDC site says wait at least 10 days (the isolation period) but I'm wondering if there is information about the likelihood of side effects or the likelihood of benefit or the likelihood of really necessity of getting the booster 10 days after. Would it be better to wait longer in terms of not having dramatically untoward side effects? Do we know that yet or is it too new in the booster cycle to really know?  
**Dr. Madoff:** I don't think we really know the answer to that. I think there's extensive evidence of safety of boosting or vaccination of any sort following COVID-19 infection. The reason for the 10-day wait is, as you mentioned, because that's the isolation period, and we don't want people who are infectious being around vaccinators or other people who are getting immunized, but there does not appear to be any risk to it. There is evidence that vaccination does enhance immunity, even in patients who have recovered from COVID-19. Beyond that, I think there are a lot of unanswered questions.