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April 24, 2020

Future Care Bulletin Covid-19 Number 10

Dear Future Care Clients,

Please review prior bulletins.

As of April 23 there are **2,736,979** cases reported worldwide. I believe at least 10 times that many people have been infected. There have been **192,125** deaths.

As many of you know, I am clinically active working in the emergency department – at the front lines as they say. I thought I would give you a picture of what it is like. Miami is not as bad as New York, but we have over 150 Covid-19 patients admitted to the hospital and even patients who come in with other problems are turning out to be positive, even if they have no symptoms. Everyone is tested now before they are admitted and certainly before being taken to the operating room for any reason. The cases range from mild to quickly deteriorating and needing to be placed on ventilators. The best practice treatment keeps changing and the doctors and nurses try to keep up. Early on, we were intubating everyone very early, now we are trying not to – instead using high flow oxygen and placing the patients in a prone position for at least 50% of the time. Everyday recommendations are changing to implement the most current research or consensus.

You get to work early. You must make sure you have your mask, goggle and booties in place. You check to make sure there is enough PPE. Most of us now change into scrubs when we get to the hospital or use paper gowns we get at the hospital or have bought personally. We try to conserve our N-95 masks and figure out ways of re-sterilizing. Most of the rooms have negative airflow now with large plastic barriers over the doorways to private rooms. We try not to put suspected cases in the hallways. You hope you do not have any cardiac arrests or patients needing to go on ventilators that day as that is the highest risk procedure. You hope you do not accidentally break technique as you take of your PPE. You pray that you do not walk in to hear of any of your colleagues succumbing to the illness. We have had several residents, doctors and nurses become ill and one radiology technician has died. We are in better shape than many metropolitan facilities.

The humor is dark – very dark at times. Everyone works very well together – the is only one mission and there is only one gender, race and ethnicity under the PPE. Everything seems to take forever. The CT scanners are sanitized between every patient, delaying the turnaround for critical testing. It is hot inside the PPE all day and the masks can make you claustrophobic. The shifts seem longer than they are.
The community is amazingly supportive. Meals are sent in every day for lunch and breakfast. Some are from the best restaurants and chefs in Miami. I eat better at work than at home. We get discounts all over town at open businesses although I think they stay a few extra feet away. The best support we can have is for everyone to wear masks and practice social distancing and stay home when you can and decrease our workload just a bit. Fortunately, there does seem to be a light at the end of the tunnel.
I wanted to concentrate in this bulletin on testing as that has really become the topic of calls and conversation.
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PCR viral testing

This is still the gold standard. False negatives are an issue early in infection and with poor collection techniques (makes self-collection a bit more suspicious for false negatives). The best specimen is a good nasopharyngeal swab, although a good oral swab or swab from the turbinate area of the nasal passage should still be positive. Peak viral shedding is probably around day 5 and sicker patients appear to shed more virus.

The focus now is on making these tests available faster and closer to the bedside. New devices and technologies are being released and marketed daily. I will mention a few without endorsing any.

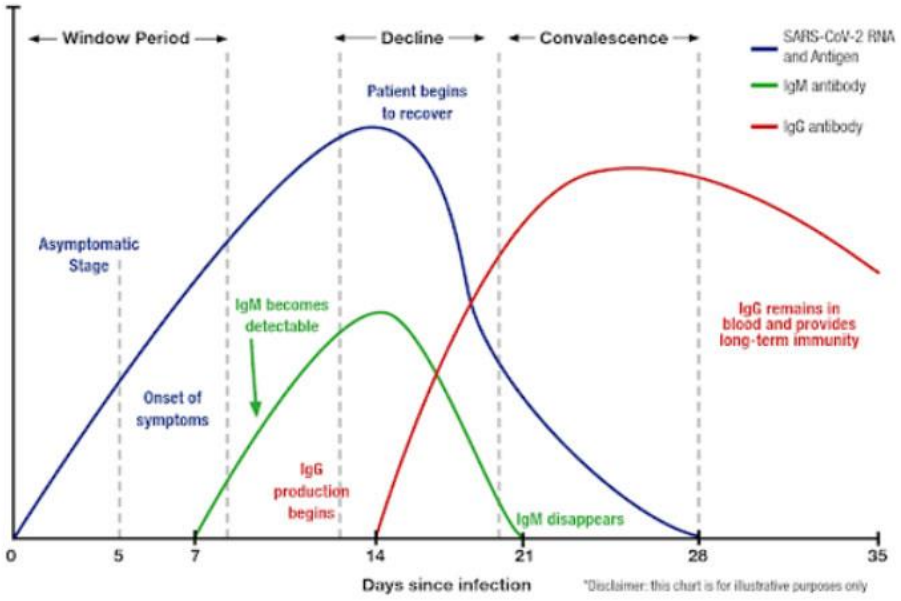
Cepheid - The Xpert Xpress SARS-CoV-2 test is a rapid, real-time RT-PCR test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in either nasopharyngeal, nasal, or mid-turbinate swab and/or nasal wash/ aspirate specimens collected from individuals suspected of COVID-19 by their healthcare provider. It is certified under EUA = Emergency Use Authorization – by FDA meaning it has not gone through the normal validation process. It requires shipment of a swab – preferentially to a CLIA-certified lab that has a GeneXpert Dx or GeneXpert Infinity Systems to run the test (23,000 worldwide placements claimed). Adequate sample collection is a requirement for a valid test. It comes 10 tests to a box.

Mesa Biotech Accula Point-of-Care Molecular System SARS-CoV-2 Test - 30 Minutes, very portable. Easy to use and to deploy – this is the best one I have seen for use on ships or at port if it can be accessed

Abbott has received emergency use authorization (EUA) from the U.S. Food and Drug Administration (FDA) for the molecular point-of-care test for the detection of novel coronavirus (COVID-19), delivering positive results in as little as five minutes and negative results in 13 minutes. The test runs on Abbott's ID NOWTM platform—a lightweight box (6.6 pounds and the size of a small toaster) which many emergency departments and doctor's offices already have in place.

All of these tests are based on the technology that a good swab is obtained and placed into viral medium in the tube collection kit and at the site of the test, the mixed solution is placed into a test cartridge and the cartridge placed into the machine.

Qualitative lateral flow IgM/IgG testing (immunoassay)



Recommendations for validating and product you may want to use.

I cannot really recommend any specific product. No product is FDA approved

Only Cellex and Mount Sinai lab have an EUA (Emergency Use Authorization) – maybe more by the time you read this

Over 90 products are for sale in US – some, in my opinion, are useless.

This is qualitative test with all of the concerns of false positives and negatives

False positives can occur cross reacting with other coronavirus and when there is very low frequency in a population – the better quality the test, the fewer the false positives. There is also some debate that some individuals may not mount a sustained antibody response to maintain positive IgG levels after the illness.

False negatives occur when the patient has not yet mounted an antibody response, usually early in the illness – by 7-10 days after symptoms onset, the IgM should be positive.

2) Go to the below web site to make sure the product is on the list to be sold in the US:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRL/rl.cfm

Put in QKO under product code

Again, these products have not been formally reviewed or vetted by the FDA and I offer no comment on their efficacy.

Look for manufacturer **NOT** located in China. Avoid re-packagers of Chinese products

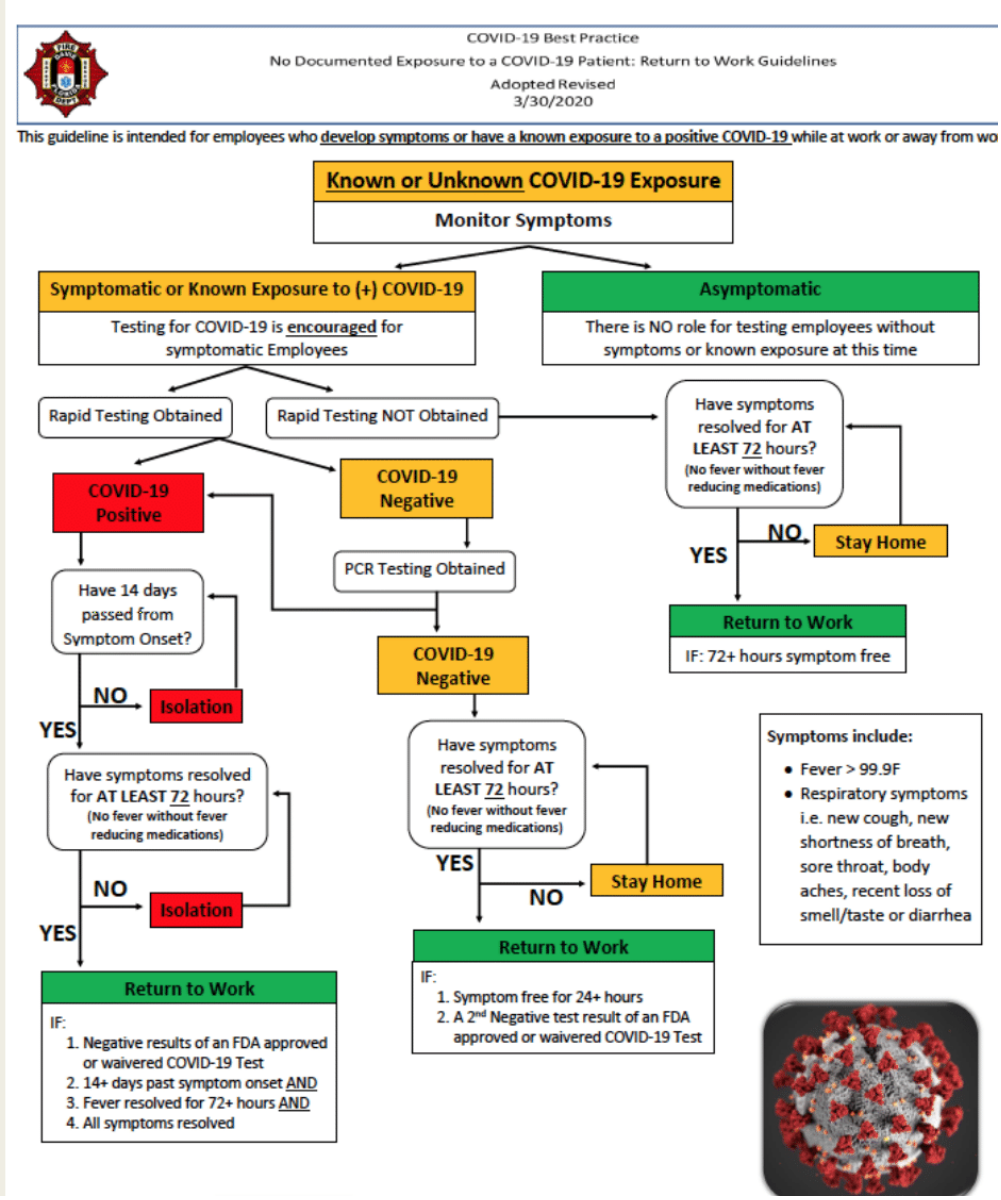
Ask whether product has at least a CE mark CE Mark. CE marking is a certification mark that indicates conformity with health, safety, and environmental protection standards for products sold within the European Economic Area. The CE marking is also found on products sold outside the EEA that have been manufactured to EEA standards.

Monocent would be an example:
US Manufactured / Registration number / no complaints filed / well established lab / CE certified

Determine if the test can be done with a finger stick or if it is only approved for whole blood/serum/plasma. Make sure it tests for both IgG and IgM. A few also test for other viruses – a plus but not needed for these purposes. Covid-19 can co-infect with other viruses.

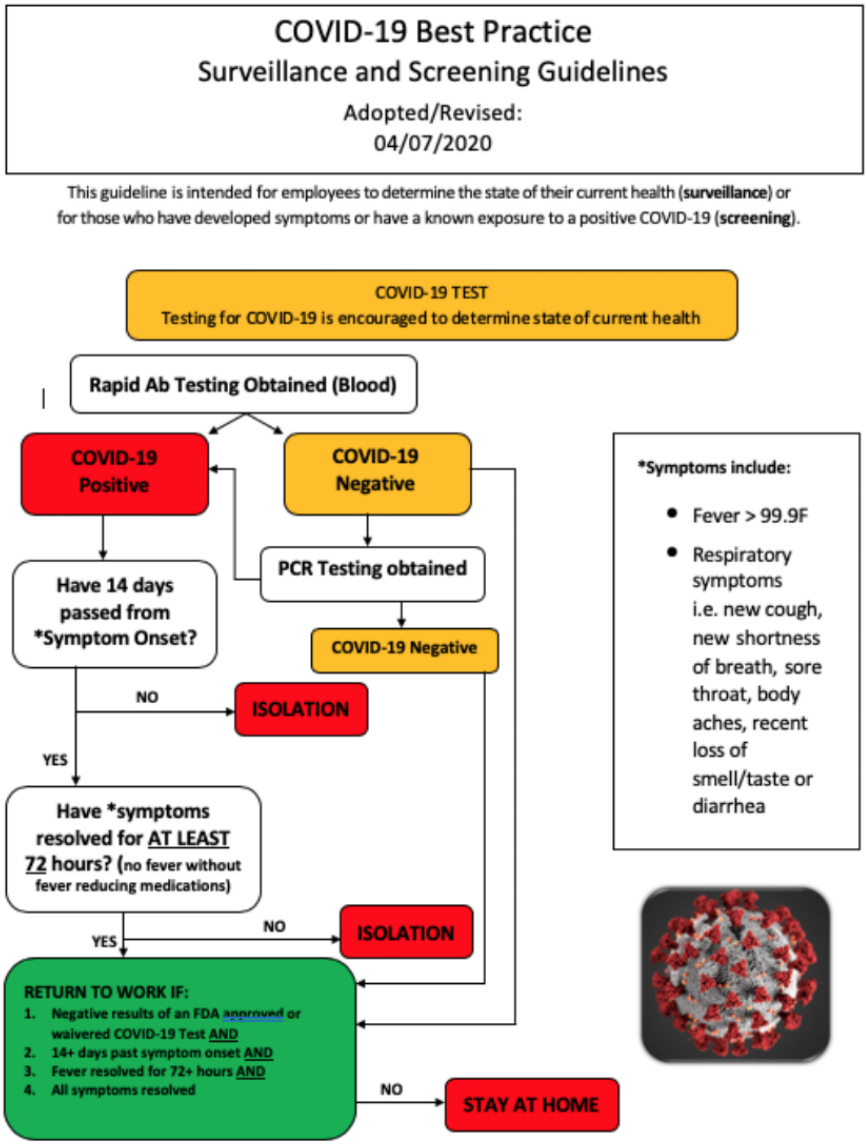
Immunoassays can also be done in a certified lab as qualitative and quantitative levels. Quantitative tells you the exact level of IgM and IgG and what is what will eventually be used as the gold test for whether someone has immunity and can return to the work force safely. Once we know how long immunity lasts, it will also help guide who needs vaccination.

The following is an example of a conservative algorithm that can be used in the management of crew. This would be the current approach to minimize risks. Any testing you elect to do on asymptomatic crew is outside current guidelines but can be instituted in addition to questionnaires, personal hygiene, masks for all crew on board, sanitation, pre-deployment isolation and temperature monitoring to further decrease risk. The addition of PCR nasopharyngeal swab testing, when available further decreases risk of introducing illness onto the ships. The availability of testing will drive the use of lateral flow rapid IgM/IgG and PCR testing into your algorithms.



The quality of the antibody test for a positive result relies upon its specificity for this particular coronavirus and not cross reacting to the presence of other coronaviruses (frequent causes of the common cold). Cross reaction will give a false positive and a false sense of infection and recovery. There are those that believe all positives should be confirmed by PCR.

We do not yet know if the presence of IgG infers only evidence of past infection or active immunity.



Immunity and Strategies

This is a very tricky virus and there is a huge amount we do not know. We have only been dealing with it for a few months. There is tremendous debate as to whether people are immune after infection. Could they still be infectious and shedding virus? How long? Is the shedding of virus clinically significant?

Researchers are not certain that people who have recovered from Covid-19 have immunity, though it would follow the usual pattern for viral infections. Does the presence of IgG just serve as a marker of prior infection or does it indicate immunity? Higher levels of antibodies generally mean a stronger physiological response, but it is unclear what levels are needed for immunity to the new coronavirus — or how long it might last.

Can people be re-infected – unlikely early after infection but we just don't know. If people are immune, will the IgG stay positive and confer long term immunity or just short-term immunity - we don't know. Is it for a few months, years, forever? Do we just need to obtain an IgG to see if it is present and you get a special pass or do we need to get quantitative titers of the IgG?

So, what strategies should be employed now? The more testing the better. Ideally, we would have 2 negative PCR tests 2 days apart, along with a positive measured titer of IgG. This testing would be repeated at some point in the future to determine length of immunity. Logistically, this is going to be difficult for at least a few months.

Because of this, different strategies are being proposed that range all the way form strategies involving no testing to those employing both PCR and some type of immunoassay.

As you know, my current recommendation for everyone to wear a mask or mask equivalent. However, whatever strategy you use, the crew member should wear a mask for 14 days after boarding minimum, when returning to the ships - or work – after a known or presumed Covid-19 infection. For example, if you have a crew member who is IgG positive and IgM negative - they can still wear a mask in public another 14 days - but that is also the crew member who should be sent off the ship in port and that is the crew member who should be offering to donate plasma with antibodies to critically ill COVID-19 patients.

Best practices for the work environment shoreside and at sea

Wear a face mask (bandanna or other face cloth covering if mask not available) at all times when in public
Refrain from shaking hands with co-workers.
Practice hand hygiene regularly. Soap and water works even better than hand sanitizer does.
Use your elbow instead of your hand to press elevator buttons.
Do not share food with co-workers.
Do not congregate in breakrooms or eat in large groups. Maintain 6 feet of social distancing whenever your mask comes down/off to eat or drink.
Keep your work area sanitized after others enter and leave.
Require anyone entering your work area or boarding your ship to abide by requirements for masks and hand washing.
Immediately report any illness to your supervisor

Thank you

Arthur L. Diskin, M.D., FACEP
Global Medical Director
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For additional information please contact physicians@futurecareinc.com. To refer a specific crewmember medical incident please continue to email our Contact Center at <firstresponse@futurecareinc.com> .