Good morning and TGIF.

First the results of my informal poll: is testing once per month going to have an impact of transmission in schools that participate in the Texas initiative? You all overwhelmingly said NO. In follow-up to the discussion on testing the FDA put out an alert on false-positive results using the rapid antigen test. [see below] In my discussion last Monday, I outlined the unintended consequences of false positive tests. In my effort to review across age and subjects, the next review is on screening of potential cardiac involvement in competitive athletes recovering from COVID-19. The next selection of the updated AAP/CHA updates on cases in pediatrics. There were more new cases of COVID-19 reported in children during the week ending Oct. 29 than any other week during the pandemic. Fortunately, severe illness and deaths remain very low. The last article is a fascinating report on prolonged infectious SARS-CoV-2 shedding from an asymptomatic immunocompromised cancer patient.

Have a relaxing weekend-have several articles in the queue to share Monday. If any of you have articles to share, please feel free to share with me so I can share with our larger audience.

Ed

FDA Alert: Potential for False Positive Results with Antigen Tests for Rapid Detection of SARS-CoV-2 - Letter to Clinical Laboratory Staff and Health Care Providers Summary
November 5,2020
https://www.fda.gov/medical-devices/letters-health-care-providers/potential-false-positive-results-antigen-tests-rapid-detection-sars-cov-2-letter-clinical-laboratory
The U.S. Food and Drug Administration (FDA) is alerting clinical laboratory staff and health care providers that false positive results can occur with antigen tests, including when users do not follow the instructions for use of antigen tests for the rapid detection of SARS-CoV-2. Generally, antigen tests are indicated for the qualitative detection of SARS-CoV-2 antigens in authorized specimen types collected from individuals who are suspected of COVID-19 by their healthcare provider within a certain number of days of symptom onset. The FDA is aware of reports of false positive results associated with antigen tests used in nursing homes and other settings and continues to monitor and evaluate these reports and other available information about device safety and performance.

The FDA reminds clinical laboratory staff and health care providers about the risk of false positive results with all laboratory tests. Laboratories should expect some false positive results to occur even when very accurate tests are used for screening large populations with a low prevalence of infection. Health care providers and clinical laboratory staff can help ensure accurate reporting of test results by following the authorized instructions for use of a test and key steps in the testing process as recommended by the Centers for Disease Control and Prevention (CDC), including routine follow-up testing (reflex testing) with a molecular assay when appropriate, and by considering the expected occurrence of false positive results when interpreting test results in their patient populations. Remember that positive predictive value (PPV) varies with disease prevalence when interpreting results from diagnostic tests. PPV is the percent of positive test results that are true positives. As disease prevalence decreases, the percent of test results that are false positives increase. [For example, a test with 98% specificity would have a PPV of just over 80% in a population with 10% prevalence, meaning 20 out of 100 positive results would be false positives]

In general, antigen tests are not as sensitive as molecular tests. Due to the potential for decreased sensitivity compared to molecular assays, negative results from an antigen test may need to be confirmed with a molecular test prior to making treatment decisions. Negative results from an antigen test should be considered in the context of clinical presentation, patient history and epidemiological information.

Screening of Potential Cardiac Involvement in Competitive Athletes Recovering from COVID-19: An Expert Consensus Statement

J Am Coll Cardiol Cardiovasc Imaging. Published online October 30, 2020
DOI: 10.1016/j.jcmg.2020.10.005 Highlights

The authors review our current understanding of the complications COVID-19 including sub-clinical cardiac pathology such as myocarditis, pericarditis and right ventricular dysfunction in the absence of significant clinical symptoms which pose a challenge. The potential implications of these findings in athletes can be significant given the concern that exercise, during the acute phase of viral myocarditis, may exacerbate myocardial injury and precipitate malignant ventricular arrhythmias which can cause sudden death. These concerns have led to the development and publication of expert consensus documents aimed at providing guidance for the evaluation of athletes after contracting COVID-19 in order to permit safe return-to-play. Cardiac imaging is at the center of these evaluations.

This review seeks to evaluate the current evidence regarding COVID-19 associated cardiovascular disease and how multi-modality imaging may be useful in the screening and clinical evaluation of athletes with suspected cardiovascular complications of infection. Guidance is provided with diagnostic "red flags" that raise the suspicion of pathology. Exercise induced cardiac remodeling may be misinterpreted as COVID-19 related cardiac injury. They discuss the strengths and limitations of relevant imaging modalities and an approach to return to play decision making.

ECG is a useful adjunct in the RTP algorithm, but in isolation it lacks sensitivity for myocarditis.
· Troponin assays lack standardization in athletes but are recommended as part of the RTP risk stratification algorithm.
· Echocardiographic techniques are currently considered first-line in the imaging of an athlete post–COVID-19.
· Remain cautious of unnecessary testing and appreciate that screening protocols may vary according to athletic discipline and setting.

Recent studies employing CMR have identified a high prevalence of cardiac abnormalities in patients recovering from COVID-19. The long-term prognosis associated with these abnormalities is unknown.
● The presence of LGE is associated with an adverse cardiac prognosis in patients with non–COVID-19 myocarditis.
● Steady-state free precession cine imaging, parametric mapping (native T1, T2 and ECV), and LGE imaging should be performed at experienced CMR centers for all athletes undergoing a CMR study in cases of suspected COVID-19 myocarditis.
● Local consistency and proficiency in T1 and T2 mapping pulse sequence/parameters employed, data analysis and reporting with normal reference ranges are important.
● A CMR abnormality of native T1 or T2 (> 2 SD above local normal reference mean), ECV (>30%) or any LGE can support a clinical diagnosis of myocarditis.
● The CMR study should be obtained >10 days from the time of initial diagnosis.

Athletic Remodeling*	'Red Flags' that Increase Suspicion for Pathology
Left Ventricle	
Symmetric dilation of all four cardiac chambers	Disproportionate or severe LV dilation (LVeDD >70 mm in men and >60 mm in women)
No regional structural or functional wall motion abnormalities	Segmental wall motion abnormality
Symmetric wall thickening <12mm (<15mm in black male athletes)	Asymmetric regional wall thickening
Normal or low-normal ejection fraction	LV ejection fraction <50%
Normal or supra-normal tissue-Doppler myocardial velocities	Low (AGE) tissue-Doppler E´ myocardial velocities for age or raised E/e'
Augmentation of low-normal LV Ejection Fraction ≥10% with exercise	Failure to augment low-normal LV Ejection Fraction with exercise
Global longitudinal strain ranges from -16 to -22%.	Abnormal global longitudinal strain#
Compliant LA with normal reservoir function	Increased atrial stiffness
Right Ventricle	
Similar degree of RV dilation to that of the LV	RV:LV basal end-diastolic diameter ratio (apical view) >1.0
Usually no more than moderate dilation	RV end-diastolic area > 15 cm^2/m^2 or RV end-diastolic volumes >260ml
Co-ordinated and consistent regional wall motion and deformation	Segmental wall motion abnormalities
Normal or low-normal systolic function	Fractional area change <35% or 3D RV ejection fraction <44%
Good augmentation of RV function with exercise	Reduced RV augmentation with exercise (RVFAC or strain)
Co-ordinated RV contraction	RV mechanical dysynchrony >40ms

Comment: This article provides guidance with diagnostic "red flags" that raise the suspicion of pathology. Specific emphasis is placed on the unique challenges posed in distinguishing athletic cardiac remodeling from sub-clinical cardiac disease. (see above) The strengths and limitations of different imaging modalities are discussed and an approach to return-to-play decision making for athletes' post COVID-19, as informed by multi-modality imaging.

American Academy of Pediatrics and the Children's Hospital Association Weekly Report
November 2, 2020
https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/
For the week ending October 29th, over 61,000 cases were reported in children, bringing the number of COVID-19 cases for the month of October to nearly 200,000 and the total since the start of the pandemic to over 853,000, per the AAP the Children's Hospital Association (CHA) weekly report. There were more new cases of COVID-19 reported in children during the week ending Oct. 29 than any other week during the pandemic. For the week ending Oct. 29, children represented 13.3% of all cases. For the full length of the pandemic, 11.1% of all COVID-19 cases have occurred in children, although severe illness is much less common: 1.7% of all hospitalizations (data from 24 states and New York City) and 0.06% of all deaths (data from 42 states and New York City) per the AAP and CHA report on November 2, 2020.

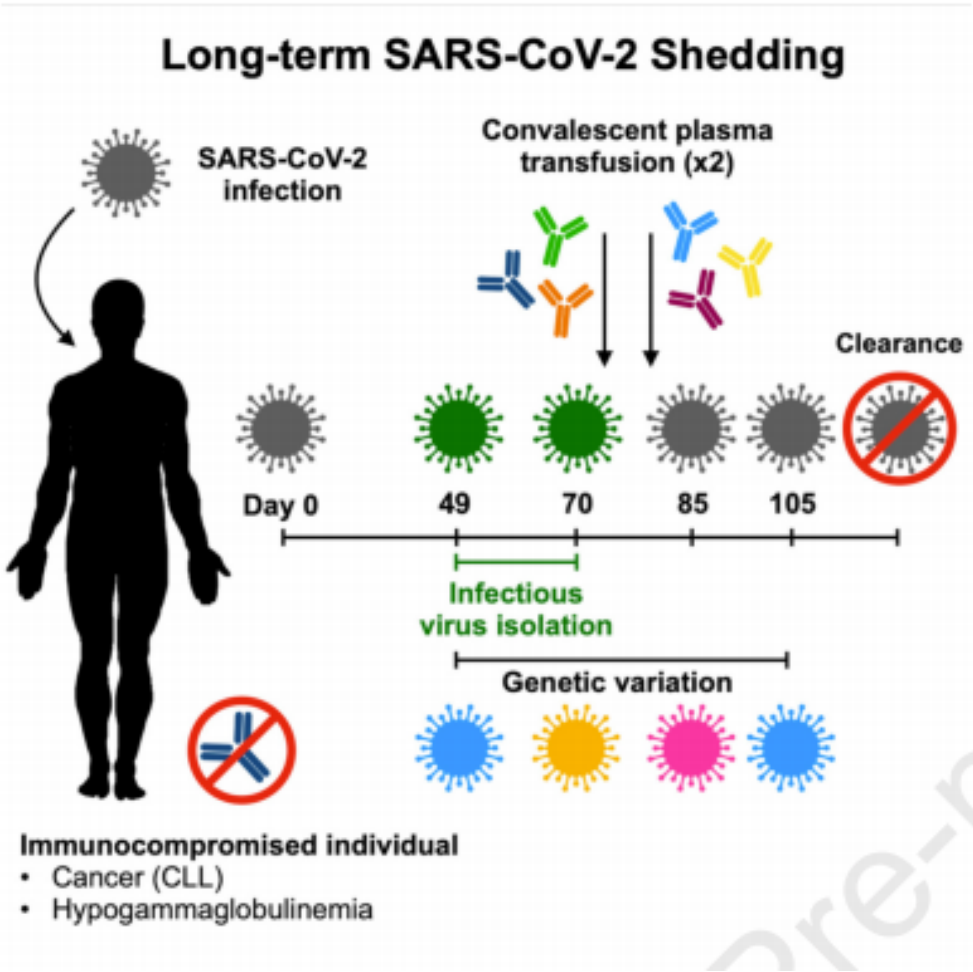
Other data show that 1,134 per 100,000 children in the United States have been infected by SARS-CoV-2, up from 1,053 the previous week, with state rates ranging from 221 per 100,000 in Vermont to 3,321 in North Dakota. In Wyoming, 25.5% of all COVID-19 cases have occurred in children [amazing], the highest of any state, while New Jersey has the lowest rate at 4.9%, the AAP/CHA report showed.

Comment: The number of reported COVID-19 cases in children is likely an undercount because children's symptoms are often mild, and they may not be tested for every illness or tested at all.

Case Study: Prolonged Infectious SARS-CoV-2 Shedding from an Asymptomatic Immunocompromised Cancer Patient

Cell published online November 4, 2020
doi.org/10.1016/i.cell.2020.10.049

Researchers report a case of a Washington state woman with chronic lymphocytic leukemia and hypogammaglobulinemia who was admitted to a Seattle-area hospital for severe anemia, tested positive for SARS-CoV-2, for the first time on March 2nd by PCR, and continued to test positive through Jun 15 while remaining asymptomatic. Due to acquired hypogammaglobulinemia caused by her CLL, the patient received intravenous immunoglobulin (IVIG) every 4 to 6 weeks as part of her treatment regimen. In addition, the patient was given convalescent plasma on May 12 and 23 but continued to have positive PCR. Despite two transfusions of convalescent plasma, nasopharyngeal swabs at day 85 and 105 remained positive for both gRNA and sgRNA, suggesting that the convalescent plasma therapy was not successful in rapidly clearing the infection from the upper respiratory tract in this patient. Although the presence of sgRNA at these timepoints suggests active viral replication, infectious SARS-CoV-2 could not be cultured after day 70. Live SARS-CoV-2 was successfully isolated from nasopharyngeal swabs 49 days and 70 days past the initial positive PCR test. Throughout the course of infection there was marked within-host genomic evolution of SARS CoV-2. Deep sequencing revealed a continuously changing virus population structure with turnover in relative frequency of the observed genotypes over the course of infection. Despite genetic changes in the SARS-CoV-2 isolated from the patient, replication kinetics did not significantly change.



Comment: The information available to date on SARS-CoV-2 infection in immunocompromised patients, including those with cancers such as CLL, is limited. CDC recommends consultation with public health and infectious diseases in terms of length of isolation in severely immunosuppressed patients. The major limitation of this study is that it comprises only a single case, making it difficult to draw general conclusions.