Return to Sports after COVID
A Practical Guide to Safe Play
(with conversation about post vaccine myopericarditis)

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Objectives

Identify cardiovascular complications following COVID infections in children to include acute manifestations and those related to multi inflammatory syndrome in children (MIS-C)

Advocate for safe return to play for children after a COVID infection through the use of guidelines detailed by the American Academy of Pediatrics and American Heart Association

Communicate the most Up-To-Date information from the CDC and Seattle Children’s Heart Center regarding post COVID vaccine myopericarditis to include the Children’s algorithm for the evaluation and treatment of affected patients.
Interrupt at Any Time
# COVID’S Broad Impact on Kids and Young Adults

<table>
<thead>
<tr>
<th>Since pandemic’s start 7.7 million people age 12-29 years in the United States have been diagnosed with COVID-19</th>
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<tbody>
<tr>
<td>2,767 deaths</td>
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<td>Almost 500 children age 0-17 have died from COVID</td>
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<td>Long-term adverse health effects even after mild infection in children is well recognized.</td>
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<td>4,000 cases of MISC</td>
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SARS-CoV-2 and Angiotensin Converting Enzyme 2 Receptor

ACE2 receptor locations: Nasopharynx, lung, heart, kidney, gut smooth muscle, liver, neurons, immune cells.

**Favorable** enzymatic action of ACE2 downregulates Angiotensin II converting it to Angiogenesis 1-7 (counters the RAS).

Viral internalization, **downregulates efficacy** of ACE2. Leads to rising Angiotensin II.
8-28% of adult patients with COVID-19 show evidence of cardiac injury.

+ hsTroponin (cardiac biomarker)

+ NTpro/BNP

5x the risk of ventilation, heart failure, coagulopathy, rhythm disturbances, and mortality.

Complex interplay of inappropriate immune-mediated inflammatory response.

Cardiomyopathy/myocarditis
Pericarditis/Heart Failure
Arrhythmias
Endothelial disruption-vasculitis, thrombosis
COVID in Kids

• <18 years—Children less susceptible, less effected
  • 40% risk of acquiring disease after exposure (>80% over 18yrs)
  • 20-30% with symptoms who acquire disease (>60% if over 60 yrs)
  • Less likely to have severe disease
    • AAP definition: ICU admission/Ventilation or MIS-C
    • AHA definition: Any child hospitalized with COVID-19 infection or complication
Multisystem Inflammatory Syndrome in Children (CDC definition)

Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C)

- An individual aged <21 years presenting with fever\(^i\), laboratory evidence of inflammation\(^i\), and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); AND
- No alternative plausible diagnoses; AND
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms

\(^i\)Fever >38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours

\(^i\)Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin
MIS-C CDC information (updated 28 June 21)

4196 cases (48 states, Puerto Rico, Washington D.C.)

37 deaths

Summary

• Most cases were in children and adolescents between the ages of 1 and 14 years, with a median age of 9 years.
• Cases have occurred in children and adolescents from <1 year old to 20 years old.
• 62% of reported cases have occurred in children who are Hispanic or Latino or Black, Non-Hispanic
• 99% of cases (2,591) tested positive for SARS CoV-2, the virus that causes COVID-19. The remaining 1% were around someone with COVID-19.
• More than half (60%) of reported cases were male.

https://www.cdc.gov/mis-c/cases/index.html
Cardiac Manifestations with MIS-C

Table 2: Prevalence of Different Cardiac Signs and Symptoms in Patients With Multisystem Inflammatory Syndrome in Children (MIS-C)

<table>
<thead>
<tr>
<th>Clinical, laboratory, and imaging findings</th>
<th>Reported frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock (cardiogenic or vasodilatory)</td>
<td>50% to 80%</td>
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<tr>
<td>Criteria of complete or incomplete KD</td>
<td>22% to 64%</td>
</tr>
<tr>
<td>Left ventricular dysfunction (by echocardiogram or elevated BNP)</td>
<td>51% to 76%*</td>
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<tr>
<td>Elevated troponin</td>
<td>68% to 95%</td>
</tr>
<tr>
<td>Elevated BNP or NT-proBNP</td>
<td>78% to 100%</td>
</tr>
<tr>
<td>ECG findings (arrhythmia, nonspecific ST, T wave changes, prolonged PR and QT intervals)</td>
<td>Unknown</td>
</tr>
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Echocardiogram findings

1. Left ventricular dysfunction                                                | 31% to 58%         |
2. Coronary artery dilation and aneurism formation (dilation z score 2 to 2.5, small aneurism z score 2.5 to 5, medium z score 5 to 10, and giant z score >10 or diameter >8 mm) | 14% to 48%         |
3. Pericardial effusion and mitral regurgitation                               | Unknown            |
4. Chest X-ray (small pleural effusions, atelectasis, consolidation)          | Unknown            |
5. Cardiac CT (similar to chest X-ray and few have ground-glass appearance)   | Unknown            |
6. Cardiac MRI (left ventricular dysfunction, myocardial edema, and tissue injury without evidence of scarring in the acute phase of MIS-C) | Unknown            |
Pathophysiology

- Virus can harbor within myocytes (autopsy results)
- Unclear regarding replication
- Increase risk of myocardial inflammation/injury
- Vasculitis
- Unclear if end result is directly related to virus vs host immune response
Echocardiographic Findings in MIS-C*

- LV systolic and diastolic dysfunction
  - Most common in setting of shock
  - Defined as an EF <52-54%
  - Myocarditis
- Pericardial/Pleural effusions
- Abnormal deformational indices
  - Strain and Strain Rate
- Mitral regurgitation

- Most children recover echocardiographic function 2-5 days (up to two weeks)!!
- CMR results are evolving. (MUSIC Trial)

* As compared to KD and age-matched controls. Matsubara et al. JACC Oct 2020
Coronary Artery Anomalies

- Highly variable among case series
- Range 8-24%
- Most aneurysms are small (z score +2.5 to 5)
- Some reports of large/Giant CA
- May occur during convalescent period
- Time course to normalization is presently unclear.

Valverde et al. Circulation 2021
ECG abnormalities

• 1/3rd of patients

• Repolarization abnormalities (ST or T wave abnormalities)

• Spectrum of reported rhythm disturbances
  • First Degree AVB (pr prolongation) most common
  • Rare progression to advanced AVB
  • VF/VT case reports

• 75% normalized at time of discharge

What is the Worry?

Law et al. Circulation. 2021
Circulation

AHA SCIENTIFIC STATEMENT

Diagnosis and Management of Myocarditis in Children

A Scientific Statement From the American Heart Association

Endorsed by the Myocarditis Foundation

Yuk M. Law, MD, FAHA, Chair; Ashwin K. Lal, MD, Vice Chair; Sharon Chen, MD, MPH; Daniela Čiháková, MD, PhD; Leslie T. Cooper Jr, MD, FAHA; Shriprasad Deshpande, MBBS, MS; Justin Godown, MD; Lars Grosse-Wortmann, MD; Joshua D. Robinson, MD; Jeffrey A. Towbin, MD, FAHA; on behalf of the American Heart Association Pediatric Heart Failure and Transplantation Committee of the Council on Lifelong Congenital Heart Disease and Heart Health in the Young and Stroke Council
Myocarditis

Associated with sudden cardiac death, especially with exercise

Risk may not correlate with degree of inflammation

Has been observed even with normal systolic function
COVID-19 Interim Guidance: Return to Sports and Physical Activity

Divided into Categories of Severity following COVID-19 Infection
1. Asymptomatic/Mild Symptoms (<4 days fever, <1 week mild symptoms)
2. Moderate Symptoms (>= 4 days of fever, >= 1 week of symptoms, non ICU hospital stay and NOT MIS-C)
3. Severe Symptoms (ICU stay, MIS-C diagnosis)

AAP recommends “clearance” by a physician in all settings**

AHA 14-element screening evaluation tool—emphasis on cardiac symptoms: chest pain, SOB, palpitations, syncope

Physical Exam

Mild COVID Symptoms: New OR positive findings: ECG and referral to Cardiology

Moderate COVID Symptoms: Add ECG. Abnormal EKG or Symptoms, referral to Cardiology

Severe COVID Symptoms: Referral to Cardiology
Coronavirus Disease 2019 and the Athletic Heart
Emerging Perspectives on Pathology, Risks, and Return to Play

Jonathan H. Kim, MD, MSc; Benjamin D. Levine, MD; Dermot Phelan, MD, PhD; Michael S. Emery, MD, MS; Mathew W. Martinez, MD; Eugene H. Chung, MD, MSc; Paul D. Thompson, MD; Aaron L. Baggish, MD
Conflicting Guidelines
Conflicting Guidelines

American Academy of Pediatrics
Dedicated to the Health of All Children

COVID-19 Interim Guidance: Return to Sports and Physical Activity

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Moderate COVID Symptoms: Add ECG. Abnormal EKG or Symptoms, referral to Cardiology
Severe COVID Symptoms: Referral to Cardiology

Updated June 10, 2021
Conflicting Guidelines
Proposed Pediatric COVID-19 Return to Sports Guidelines

Dr. Matt Studer, Dr. Josiah Peñalver and Dr. Cory Noel
Seattle Children’s Regional Cardiology

Pediatric patient with h/o COVID-19 infection and asymptomatic for > 10 days

Asymptomatic or mild symptoms (no fever, < 4 days of symptoms), > 10 days from positive test and afebrile > 24 hours

Severe symptoms: (Abnormal cardiac testing, MIS-C, ICU stay)

Moderate symptoms (fever >/= 4 days, prolonged bedrest or non-ICU hospital stay and no abnormal cardiac testing)

Age < 12 years

Normal preparticipation screening evaluation and exam

No evidence of myocarditis

YES

Cleared for sports participation without further testing

Concern for myocarditis

Myocarditis guidelines:
- Recommend testing including EKG, echo, Holter, exercise stress test, +/- cMRI
- Exercise restrictions for 3-6 months

Age >/= 12 years

High intensity competitive sports or physical activity

EKG prior to participation

Normal EKG

REFER TO CARDIOLOGY Evaluation and testing as dictated by cardiologist

Abnormal EKG or positive symptoms

References
1. CDC guidelines: COVID-19: Quarantine vs. Isolation (cdc.gov)
3. Bethesda 36 guidelines
The following progression was adapted from Elliott N, et al, infographic, British Journal of Sports Medicine, 2020:

**Stage 1:** Day 1 and Day 2 - (2 Days Minimum) - 15 minutes or less: Light activity (walking, jogging, stationary bike), intensity no greater than 70% of maximum heart rate. NO resistance training.

**Stage 2:** Day 3 - (1 Day Minimum) - 30 minutes or less: Add simple movement activities (e.g. running drills) - intensity no greater than 80% of maximum heart rate.

**Stage 3:** Day 4 - (1 Day Minimum) - 45 minutes or less: Progress to more complex training - intensity no greater than 80% maximum heart rate. May add light resistance training.

**Stage 4:** Day 5 and Day 6 - (2 Days Minimum) - 60 minutes - Normal training activity - intensity no greater than 80% maximum heart rate.

**Stage 5:** Day 7 - Return to full activity/participation (i.e., contests/competitions).
What are the Broader Implications of Reduced Physical Activity on Children’s CV Health in the COVID-19 Era?

Study: Virtual education linked with decreased physical activity, worsening emotional health

Melissa Jenco, News Content Editor
March 18, 2021

Researchers analyzed data from a survey of 1,290 parents of children ages 5-12 years conducted in the fall of 2020. Their findings were published today in the Centers for Disease Control and Prevention’s (CDC’s) Morbidity and Mortality Weekly Report.

About 46% reported their child was receiving virtual education. 31% In-person and 23% combined. Hispanic, Black and non-Hispanic other/multiracial parents reported virtual instruction more often than White parents.

Among parents of virtual learners:

- 63% reported a decrease in their child’s physical activity vs. 30% of in-person families.
- 58% reported a decrease in time spent outside vs. 27% of in-person families.
- 86% reported a decrease in in-person time with friends vs. 70% of in-person families and
- 25% reported worsened mental or emotional health vs. 16% of in-person families.
COVID-19 Vaccine Associated Myopericarditis
Vaccine associated myopericarditis

- As of July 12th 2021, 1047 reports of myocarditis and pericarditis have been reported in vaccinated people under age 30 years
  - Pfizer/BioNTech or Moderna vaccines
- Male teen and young adult predominance.
- Most common symptoms chest pain, elevated cardiac enzymes, ST or T wave changes, dyspnea, and abnormal echocardiography/imaging.
  - Variable rates of decreased ventricular function on echocardiography
  - Very high prevalence of abnormal CMR in those tested
    - Late gadolinium enhancement and myocardial edema
- Average 2-3 days after second dose of mRNA vaccine
- CDC Advisory Committee on Immunization Practices (ACIP) has said available data, “suggest likely association of myocarditis with mRNA vaccination in adolescents and young adults.”
Pediatric Heart Network (unpublished)

- 140 cases post vaccine peri/myocarditis
- 17% decrease function by echo
- 85% of those with cMR were abnormal
- 1 patient with > trivial PCE
Myopericarditis after the Pfizer mRNA COVID-19 Vaccine in Adolescents

J Peds 2021

• SCH report on 13 patients age 12-17 years with chest pain 1 week post second dose of Pfizer vaccine
  • 12/13 male
• All had myocardial inflammation and edema on CMR
• Reported incidence
  • 0.008% in adolescents 16-17 years
  • 0.01% in children 12-15 years

• Following AHA/ACC acute myocarditis recommendations for exercise restrictions of up to 6 months and long-term cardiac surveillance
Evaluation and Treatment

• Symptoms 2-3 days up to 30 days post 1st or 2nd Vaccination
• Evaluation with ECG* and laboratory data
  • Troponin testing*
  • CRP/ESR
  • COVID pcr swab and antibody testing
• If abnormal*, echocardiogram and admission for treatment/serial testing
• Treatment protocols vary
  • NSAID for preserved ventricular function
  • IVIG, steroids for decreased ventricular function
• Discharge when troponin testing has normalized (or at least down trending)
• CMR around time of diagnosis (+/-)
• CMR testing at 3 months post event
Though the clinical course appears mild with likely resolution of symptoms and signs, it is reasonable to restrict or defer strenuous physical activity and competitive sports until after complete resolution of symptoms, signs, hemodynamic, rhythm, diagnostic and biomarker abnormalities. If a person develops myocarditis or pericarditis after the first dose of an mRNA
VACCINATE!!!!!!

Potential Risk of Myocarditis with COVID-19 Vaccination

<table>
<thead>
<tr>
<th>Females</th>
<th>Males</th>
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<tbody>
<tr>
<td>8-10 myocarditis cases</td>
<td>56-69 myocarditis cases</td>
</tr>
<tr>
<td>4-5 myocarditis cases</td>
<td>45-56 myocarditis cases</td>
</tr>
<tr>
<td>2 myocarditis cases</td>
<td>15-18 myocarditis cases</td>
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Risks

Potential Prevention of COVID-19, Hospitalizations, ICU admissions and Death with COVID-19 Vaccination

<table>
<thead>
<tr>
<th>Females</th>
<th>Males</th>
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<tbody>
<tr>
<td>8500 Covid-19 cases</td>
<td>8500 Covid-19 cases</td>
</tr>
<tr>
<td>183 Hospitalizations</td>
<td>183 Hospitalizations</td>
</tr>
<tr>
<td>38 ICU admissions</td>
<td>38 ICU admissions</td>
</tr>
<tr>
<td>1 Death</td>
<td>1 Death</td>
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<table>
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<tr>
<th>12-17 Years</th>
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<tbody>
<tr>
<td>14,000 Covid-19 cases</td>
</tr>
<tr>
<td>1127 Hospitalizations</td>
</tr>
<tr>
<td>93 ICU admissions</td>
</tr>
<tr>
<td>13 Deaths</td>
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<th>18-24 Years</th>
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<tbody>
<tr>
<td>15,000 Covid-19 cases</td>
</tr>
<tr>
<td>1459 Hospitalizations</td>
</tr>
<tr>
<td>87 ICU admissions</td>
</tr>
<tr>
<td>4 Deaths</td>
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Benefits

Potential prevention of COVID-19 related myocardial injury, MIS-C, post-acute sequelae SARS-CoV-2 infection

for every million second dose COVID-19 mRNA vaccinations

Cautionary Tales – A Tsunami of Misery

19th June, 2020
Summary

• We have a proposed model of the pathophysiology of COVID-19 on the ACE2/angiotensin pathway and its impact on the cardiovascular system

• We have become better at identifying and treating MIS-C, but long-term risks are still being elucidated

• In those patients with severe COVID or MIS-C – or those patients demonstrating symptoms with sports participation – following myocarditis guidelines likely reduces the risk of sudden cardiac death

• The overwhelming majority of children follow a COVID infection can be safely and easily returned to full activity, play, competition

• Post-vaccine myopericarditis is rare and the benefits of vaccination still outweigh the risk

• For now, post-vaccine myopericarditis patients are being treated in a similar category as myocarditis