Compiled by Katherine Salciccioli MD

Contents include:

Brief summary:

ACC-CCA Webinar 3/18/2020 re: cardiovascular disease and COVID-19

C.S. MOTT CHILDREN'S HOSPITAL MICHIGAN MEDICINE CONGENITAL HEART CENTER

Articles reviewed:

- Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China (Pediatrics)
- COVID-19 in Children: Initial Characterization of the Pediatric Disease (editorial response, Pediatrics)

ACC-CCA Webinar:

To watch (~2 hours):

http://iv.docbook.com.cn/record/app-name/46018/2020-03-18-19-50-58_2020-03-18-20-45-58.mp4 http://iv.docbook.com.cn/record/app-name/46018/2020-03-18-20-45-58_2020-03-18-21-40-58.mp4 http://iv.docbook.com.cn/record/app-name/46018/2020-03-18-21-40-58_2020-03-18-22-01-22.mp4

General points:

- COVID genome: 79% in common with SARS, 51% with MERS
 - o 2.3% mortality vs 9.6% and 34%, respectively
- COVID is spherical with spikes which latch to cells and enter through ACE2
- COVID RNA found in sputum as well as blood and stool
- Respiratory viral particles ARE aerosolized
- Viral particles are found in alveolar cells themselves true viral PNA, not just ARDS
- Ro = 2.2-2.95 with median incubation 4-5 days (95th percentile 12 days); asymptomatic carriers are important vector for spread
- Chinese protocol: N95 around suspected/confirmed COVID, surgical mask in hospital at all times
- For now, RNA testing appears better than IgM/IgG (especially early in infection)

Cardiology-specific points:

- Given risks of transmission, virtual consults are likely best when at all possible
- Main cardiac complications: acute MI, myocarditis, heart failure
 - Have not been seen in isolation without PNA/sepsis
 - Recovery from
- Critically ill patients with COVID are coagulopathic microthrombi throughout on autopsy
 - Higher D-dimer independently associated with increased in-hospital mortality
 - o Systemic anticoagulation is recommended if no contraindication
- For acute MI, thrombolysis may be preferred over cath
 - Decreased transmission risk to cath lab team most labs can't do negative pressure
- For myocarditis, supportive care has led to recovery in some cases
 - o Steroids, IVIg, milrinone, diuretics
- Need to watch for long term CV effects in survivors SARS/MERS had metabolic syndrome issues (HLD, DM) after recovery

Medication issues:

- No solid data outside of WHO recommendations at this time
- Investigations into antiviral, immunomodulating medications ongoing
 - o Be wary of interactions with cardiac meds AND direct cardiotoxic effects
- ACE-I/ARB no data to support stopping chronic meds
- Ibuprofen no data to support avoidance

<u>Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China (prepublication release in Pediatrics)</u>

Authors: Yuanyuan Dong, Xi Mo, Yabin Hu, Xin Qi, Fang Jiang, Zhongyi Jiang, Shilu Tong

Key points:

- Study included 731 PCR-proven cases rest were suspected (fever + (cough or N/V/D or fatigue) + CXR)
- Children of all ages are susceptible to COVID-19, with time course and distribution of infections supporting person-to-person transmission
- Generally well-tolerated
 - o 4% asymptomatic, 51% mild, 39% moderate = supportive care at home
 - o 6% severe or critical
- Infants appear to have more severe manifestation, with severe/critical disease seen in:
 - o Age <1: 10.6 %
 - o Age 1-5: 7.3%
 - Age 6-10, 11-15, ≥16: 4.2%, 4.1% and 3.0% respectively
- No gender differences were seen
- One child had died at the time of publication 14y boy
- Overall, appears less likely to be severe/critical than adults: 5.9% vs 18.5%
 - Why? Speculated to be a combination of pathogen and host factors
 - Children have incompletely functioning ACE2 (lower binding capacity), thought to be the likely mode of cell entry for COVID
 - Children may have partial immunity due to being sick with multiple other viruses during winter respiratory season
 - Inflammatory/immune response once infected likely different than in adults
- Limitations:
 - Included suspected cases which could have been due to other pathogens
 - Didn't compare severity distribution between suspected and confirmed
 - o Exposure data not included, so can't determine incubation period, risk of infection with exposure

Table 1 Characteristics of Children' COVID-19 Cases in China

Characteristics All cases	A 11	Different Category			
	All cases	Confirmed	Suspected	P Value	
Median age (Interquartile range)	7.00 (11.0)	10.00(11.0)	6.00(10.0)	< 0.001	
Age group					
<1	379(17.7)	86(11.8)	293(20.8)		
1-5	493(23.0)	137(18.7)	356(25.2)		
6-10	523(24.4)	171(23.4)	352(24.9)	< 0.001	
11-15	413(19.3)	180(24.6)	233(16.5)		
>15	335(15.6)	157(21.5)	178(12.6)		
Gender					
Boy	1213(56.6)	420(57.5)	793(56.2)	0.567	
Girl	930(43.4)	311(42.5)	619(43.8)	0.367	
Severity of illness					
Asymptomatic	94(4.4)	94(12.9)	0(0.0)		
Mild	1091(50.9)	315(43.1)	776(54.9)		
Moderate	831(38.8)	300(41.0)	531(37.6)		
Severe	112(5.2)	18(2.5)	94(6.7)	< 0.001	
Critical	13(0.6)	3(0.4)	10(0.7)		
Missing	2(0.1)	1(0.1)	1(0.1)		
Days from symptom onset to diagnosis					
Median days (Interquartile range)	2(4.0)	3(4.0)	2(4.0)	< 0.001	
Range	0-42	0-42	0-36		
Province					
Hubei	984(45.9)	229(31.3)	755(53.5)		
Surrounding areas*	397(18.5)	155(21.2)	242(17.1)	< 0.001	
Others	762(35.6)	347(47.5)	415(29.4)		
Total	2143	731(34.1)	1412(65.9)		

Data are presented with median (Interquartile range) and n (%).

Table 2 Different Severity of Illness by Age Group

Age group*	Asymptomatic	Mild	Moderate	Severe	Critical	Total
<1	7(7.4)	205(18.8)	127(15.3)	33(29.5)	7(53.8)	379(17.7)
1-5	15(16.0)	245(22.5)	197(23.7)	34(30.4)	2(15.4)	493(23.0)
6-10	30(31.9)	278(25.5)	191(23.0)	22(19.6)	0(0)	521(24.3)
11-15	27(28.7)	199(18.2)	170(20.5)	14(12.5)	3(23.1)	413(19.3)
>15	15(16.0)	164(15.0)	146(17.5)	9(8.0)	1(7.7)	335(15.7)
Total	94	1091	831	112	13	2141(100)

Data were presented with number and percent (%);*Two cases had missing values.

<u>COVID-19 in Children: Initial Characterization of the Pediatric Disease</u> (response to above primary research article, prepublication release in *Pediatrics*)

Authors: Andrea T. Cruz, MD, MPH (Baylor) and Steven L. Zeichner, MD, PhD (UVA)

Key points:

- "suspected" COVID patients overall had more severe disease than PCR/sequencing proven
 - o Coinfection? Other viruses? Really hard to know
- Focusing on ONLY those with COVID-proven disease (not suspected):
 - o 13% were asymptomatic so likely even higher given that most asymptomatic kids not tested
 - Only 5% of those with symptoms had dyspnea or hypoxemia
 - Only 0.6% progressed to ARDS or organ failure
- Similar to other viruses and coronaviruses, higher risk populations exist:
 - o In this study, infants and younger children
 - o In other coronaviruses (and likely this one), underlying lung disease and immune compromise
 - **my input no comment on CHD, but this is likely true in higher risk CHD as well ie unrepaired, cyanotic, single V, abnormal pulmonary vasculature
- Children likely play a large role in community transmission
 - Higher percentage of upper respiratory involvement
 - Viral particles present in stool and likely shed for weeks
 - Asymptomatic patients make contact tracing and other epi measures much less effective
- Vertical transmission not yet documented
 - o **my input a few new case reports of infected newborns have come up in the last 2 days