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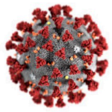
California Association of Long Term Care Medicine



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Webinar Series
COVID-19: CALTCM Weekly Rounds

May 11, 2020

1

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To request a copy of our 501(c)(3) status letter or current Form W-9, please contact the CALTCM Executive Office at (888) 332-3299 or e-mail: info@caltcm.org

2

Thank you to our Planning Committee!

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Michelle Eslami, MD, FACP, CMD
Janice Hoffman-Simen , Pharm.D., EdD, APh, BCGP, FASCP
Ashkan Javaheri, MD
Albert Lam, MD
Jay Luxenberg, MD
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Michael Wasserman, MD, CMD

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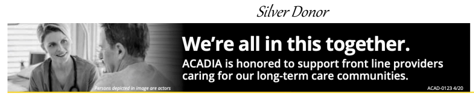

ACADIA Pharmaceuticals

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Webinar Moderator

Janice Hoffman-Simen, Pharm.D., EdD, APh, BCGP, FASCP
Director, Postgraduate Residency Program, Jewish Home for the Aging; Associate Professor of Pharmacy Practice and Administration; Western University of Health Sciences

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5

Webinar Faculty

Ashkan Javaheri, MD, CMD
Geriatrician, Mercy Medical Group–Dignity Health Medical Foundation; Head of the Geriatric Division, Associate Clinical Professor, UC Davis School of Medicine

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Webinar Faculty

Heather D'Adamo, MD

Staff Attending Physician, Community Living Center, VA Greater Los Angeles; Assistant Professor, UCLA Geriatrics; Director of SNF and LTC Curriculum of the VA UCLA Geriatrics Fellowship

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Webinar Faculty

Dana Saffel, PharmD

President, CEO; PharmaCare Strategies, Inc.; Board Member; American Society of Consultant Pharmacists

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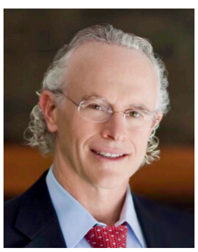

Webinar Faculty

Michael Wasserman, MD, CMD

Geriatrician, President, CALTCM,
Medical Director, Eisenberg Village,
Los Angeles Jewish Home

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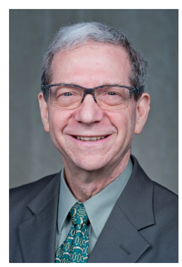

Webinar Faculty

Jay Luxenberg, MD

Chief Medical Officer, On Lok
CALTCM, Wave Editor-in-Chief

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10

Hot off the Press:

What We Know <u>Now</u>

Ashkan Javaheri, MD, CMD
Mercy Medical Group, Sacramento, CA

11

Quote of the Day

- "The situation is very fluid, and it changes hour to hour and day to day. No one knows how long this pandemic will last and what its ultimate toll on the health of the world's population and economy will be."
  - Dr. Heather D'Adamo's article in JAGS

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12

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Epidemiology of Covid-19 in a Long-Term Care Facility in King County, Washington

- From Feb 28 (first case)- March 18, 2020
- total of 167 confirmed cases of Covid-19 affecting 101 residents, 50 health care personnel, and 16 visitors
- Hospitalization rates for facility residents, visitors, and staff were 54.5%, 50.0%, and 6.0%, respectively
- As of March 18, the preliminary case fatality rate was 33.7% for residents and 6.2% for visitors; no staff members had died.
- .

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13

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Epidemiology of Covid-19 in a Long-Term Care Facility in King County, Washington

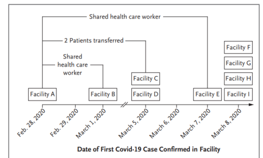

Figure 2. Timeline Showing Long-Term Care Facilities in King County with One or More Confirmed Cases of COVID-19.
The first nine long-term care facilities (e.g., nursing homes or assisted living facilities) in King County with one or more confirmed cases of Covid-19 are shown according to the date of the first confirmed case. Facilities are those identified as of March 9, 2020. The direction of potential introduction of Covid-19 from one facility to another is unknown.

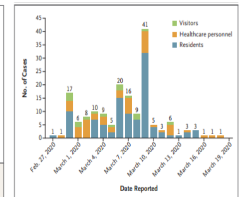

Figure 1. Confirmed Cases of Covid-19 Linked to Facility A.
Shown are cases of Covid-19 in Washington that had been epidemiologically linked to Facility A as of March 18, 2020.

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14

Take Home Message

- Long-term care facilities are vulnerable to respiratory disease outbreak
- Staff should expect much better outcome
- Staff working in multiple facilities and transferring patients can transmit the disease
- Early detection and preparedness can help preventing the unwanted spread

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15

1

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16

JAMA | Original Investigation

Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area

Safiya Richardson, MD, MPH; Jamie S. Hirsch, MD, MA, MSB; Mangala Narasimhan, DO; James M. Crawford, MD, PhD; Thomas McGinn, MD, MPH; Karina W. Davidson, PhD, MASc; and the Northwell COVID-19 Research Consortium

- 5700 patients (median age, 63 years).
- The most common comorbidities were hypertension (3026; 56.6%), obesity (1737; 41.7%), and diabetes (1808; 33.8%).
- At triage, 30.7% of patients were febrile, 17.3% had a respiratory rate greater than 24 breaths/minute, and 27.8% received supplemental oxygen.
- The rate of respiratory virus co-infection was 2.1%.
- 14.2% were treated ICU
- 12.2% received invasive mechanical ventilation,
- 3.2% needed dialysis
- 21% died
- **As of April 4, 2020, for patients requiring mechanical ventilation 3.3% were discharged alive** and 24.5% died

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17

Take Home Message

- Older patients with more comorbidities are at risk for worse outcome
- Co-infection with other viral diseases are not common
- ONLY 3.3% of patients who required mechanical ventilation leave the hospital alive

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18

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Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020

Table 1

Results of testing for SARS-CoV-2 in intensive care unit, Huoshenshan Hospital, Wuhan, China, 2020*

Area, sample	Intense positive/weak positive/negative†	Rate of positivity, %
Contaminated area		
Isolation wards		
Floor	6/1/3	70
Computer mouse	4/2/2	75
Trash can	0/3/2	60
Sickbed handrail	2/4/8	42.9
Patient mask	1/1/3	40
Air outlet filter	4/4/4	66.7
Indoor air near the air outlet (sampling site 1 in Figure 2, panel A)	2/3/9	35.7
Indoor air near the patients (sampling site 2 in Figure 2, panel A)	2/6/10	44.4
Indoor air near the doctors' office area (sampling site 3 in Figure 2, panel A)	0/1/7	12.5

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19

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Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020

Table 2

Results of testing for SARS-CoV-2 in general ward, Huoshenshan Hospital, Wuhan, China, 2020*

Area, sample	Intense positive/weak positive/negative†	Rate of positivity, %	Av
Contaminated area			
Isolation ward	1/1/11	15.4	
Floor	0/1/11	8.3	
Doorknob	0/1/11	8.3	
Air outlet	0/0/12	0	
Sickbed handrail	1/1/8	20	
Patient mask	0/2/9	18.2	
Indoor air (sampling site 1 in Figure 2, panel C)	0/0/5	0	
Indoor air (sampling site 2 in Figure 2, panel C)	1/1/11	15.4	

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20

Take Home Message

- Floors are heavily contaminated
- The soles of medical staff shoes might function as carriers
- SARS-CoV-2 was widely distributed in the air and on object surfaces in both the ICU and GW, implying a potentially high infection risk for medical staff and other close contacts.
- ICU is worse than general ward
- SARS-CoV-2 aerosol distribution characteristics in the GW indicate that the transmission distance of SARS-CoV-2 might be 4 m.

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21

2

- https://wwwnc.cdc.gov/eid/article/26/7/20-0764_article#comment

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22

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COVID-19 Outbreak Associated with Air Conditioning in Restaurant, Guangzhou, China, 2020

Table 2

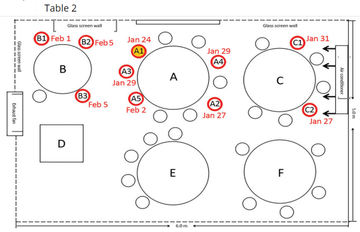

Figure. Sketch showing arrangement of restaurant tables and air conditioning airflow at site of outbreak of 2019 novel coronavirus disease, Guangzhou, China, 2020. Red circles indicate seating of future case-patients; yellow-filled red circle indicates index case-patient.

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23

Take Home Message

- Droplet transmission can be prompted by air-conditioned ventilation and the direction of the airflow.
- To prevent spread of COVID-19 in restaurants increasing the distance between tables and improving ventilation may help.
- Maybe safer to eat outside and keep your distance.

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24

nature medicine

Brief Communication | Published: 29 April 2020

Antibody responses to SARS-CoV-2 in patients with COVID-19

- Antibody responses to SARS-CoV-2 in 285 patients with COVID-19.
- Within 19 days after symptom onset, 100% of patients tested positive for antiviral immunoglobulin-G (IgG).
- Both IgG and IgM titers plateaued within 6 days after seroconversion.
- Serological testing may be helpful for the diagnosis of suspected patients with negative RT–PCR results and for the identification of asymptomatic infections.

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25

Take Home Message

- Serological testing can identify asymptomatic patients or symptomatic patients with negative PCR
- Specificity >99% and sensitivity 96% identify past SARS-CoV-2 infection in people who were infected at least 1 to 3 weeks previously.
- Antibody test results should not be used to diagnose someone with an active SARS-CoV-2 infection

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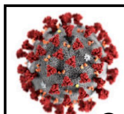
26



COVID-19 in Geriatrics and LTC: ABCD's of COVID-19

Original Article by Heather D'Adamo, Thomas Yoshikawa, and Joe Ouslander

Lessons Learned: An Update

Heather D'Adamo, MD

27

ABCD's of COVID-19, then

- Awareness: symptoms
- Behavior: screening; absence of SARS-Cov2 testing;
- Containment: practices to disrupt the spread, PPE
- Decisions: open communication with local, state and federal entities, advance care planning; create a clinical decision tree

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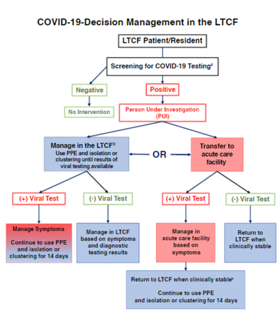
28

ABCD's of COVID-19, then



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29

ABCD's of COVID-19, then

- Testing limited:

Screening to test for COVID-19 in the LTCF

CDC Recommendations on Who to Test for COVID-19

1. Hospitalized patients who have signs and symptoms compatible with COVID-19 in order to inform decisions related to infection control.
2. Other symptomatic individuals such as, older adults and individuals with chronic medical conditions and/or an immunocompromised state that may put them at higher risk for poor outcomes (e.g., diabetes, heart disease, receiving immunosuppressive medications, chronic lung disease, chronic kidney disease).
3. Any persons including healthcare personnel, who within 14 days of symptom onset had close contact with a suspect or laboratory-confirmed[4] COVID-19 patient, or who have a history of travel from restricted areas within 14 days of their symptom onset.

For details, see https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html

Los Angeles Department of Public Health Testing Criteria

LAC DPH Public Health Lab (PHL) COVID-19 Testing Criteria

Clinical Features	and	Epidemiologic Risk
Fever **or** signs/symptoms of lower respiratory illness (eg, cough, shortness of breath)	AND	Any healthcare worker (defined as a person providing direct clinical care to patients) who worked while symptomatic in an acute or long-term care facility[1] -or- A resident of a long-term care facility -or- Paramedic personnel and Emergency Medicine Technicians (EMTs)
Part of a cluster of 2 or more cases of a presumed infectious acute respiratory illness within a 72-hour period	AND	Any congregate living setting (eg, assisted living facility for older adults, homeless shelters

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30

New Framework

- CONTAINMENT
- Awareness
- Behavior
- Decisions

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31

New Framework - ISOLATION

- CONTAINMENT IS CENTER
- In the absence of a treatment, when the stakes are high:
  - ISOLATION is the name of the game and we should ISOLATE AGGRESSIVELY

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32

Awareness

- Don't wait for the fever:
  - Prodrome
  - Asymptomatic spread
- Isolate for any change of condition

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33

Behavior

- Continue with no visitors, no in-person meetings, no communal dining or activities; institute telehealth alternatives
- Continue with screening residents and staff, but imagine that all are infected. DO NOT BE REASSURED BY LACK OF SYMPTOMS
- Educate staff on PPE:
  - N95 masks for those who might be exposed
  - Surgical masks for those that might expose
- ISOLATE your staff from the residents
  - invest in surgical masks for everyone.
  - If known COVID unit: N95 are necessary
- Algorithm for testing constantly changing (CDC was behind)

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34

ISOLATE AGGRESSIVELY

- PPE and testing should be put toward this goal
  - If you have little access to testing:
    - physically isolate for very little change;
    - Everyone wears masks – maybe including the residents?
  - If you have limited access to testing:
    - Consider pooled testing, in consultation with your lab
    - Staff testing may be more important than resident testing
  - If you have unlimited testing:
    - Test every 5-7 days
    - Consider creating a COVID only unit

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35

DECISIONS

- **Admission/Readmission criteria**
  - Department of Health is often involved
  - Isolating/Testing new admissions?
- **COVID facilities**
- **Partner** with local hospitals and health departments for PPE and testing
- Be aware of all staff living arrangements. Help them avoid infection!

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36

SUMMARY: Take Home Message

- ISOLATION is the key
- Imagine everyone in your staff is infected
- Testing and PPE should be used strategically, based on availability
- Partner with staff, local hospitals, local, state, federal health departments
- **Support CALTCM**

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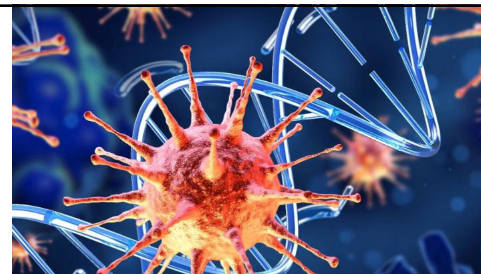
37



Dana Saffel, PharmD
CPh, BCGP, FASCP
President, CEO
PHARMACARE STRATEGIES

COVID Treatment Update

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38

3

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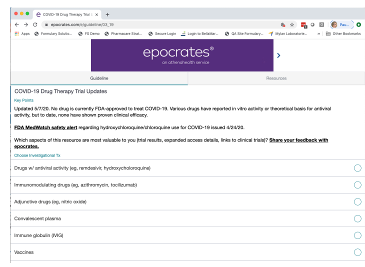
39

- Much of the following information is available at Epocrates COVID drug therapy trial updates https://www.epocrates.com/e/guideline/03_19



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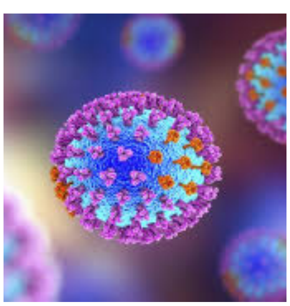
40

Antivirals



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41

Antivirals

No drug is currently FDA-approved to treat COVID-19

Drug	Proposed MOA	Drug	Proposed MOA
ACEIs/ARBs (eg, losartan, telmisartan, ramipril)	Blocks viral entry by inhibiting ACE2 receptors	Ivermectin	In vitro activity against SARS-CoV-2
Atovaquone *(Mepron)*	Activity against RNA-dependent RNA polymerases; in vitro activity against arboviruses (eg, Zika)	Lopinavir/ritonavir *(Kaletra)*	Interferes w/ maturation of viral particles by inhibiting protease enzymes
DPP-4 inhibitors (eg, linagliptin)	Blocks viral entry; reportedly blocks MERS-CoV entry receptor (DPP-4)	Nitazoxanide *(Alinia)*	*Interferes w/ host-regulated pathways involved in viral replication rather than a virus-targeted mechanism; broad-spectrum in vitro activity against various viruses, including coronaviruses*
Famotidine	*Binds to protease implicated in viral replication*	Sirolimus *(Rapamune)*	*Targets mTOR complex involved in replication of various viruses, including coronaviruses*
Favipiravir China & Japan	*Terminates viral replication by binding to RNA-dependent RNA polymerase*	Tranexamic acid *(Lysteda, Cyklokapron)*	Reduces infectivity and virulence by inhibiting conversion of plasminogen to plasmin (plasmin interacts w/ viral surface proteins to increase binding to cellular receptors)
Remdesivir (EAU)	Terminates viral replication by binding to RNA-dependent RNA polymerase; circumvents proofreading activity by exonucleases	Umifenovir China & Russia	*Inhibits fusion of viral and cellular membranes by intercalating into membrane lipids*
Hydroxychloroquine Chloroquine	Inhibits viral entry and replication via intracellular alkalinization, interferes w/ maturation of viral particles through impaired glycosylation; indirect immunomodulatory effects		

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42

No drug is currently FDA-approved to treat COVID-19

Remdesivir

- **Proposed MOA**: terminates viral replication by binding to RNA-dependent RNA polymerase; circumvents proofreading activity by exonucleases
- **FDA approved use**: Investigational - EUA issued May 1, 2020
- **Adult Dose[1]:**
  - For adults not requiring invasive mechanical ventilation and/or ECMO - single loading dose of 200 mg IV over 30 to 120 minutes on Day 1 followed by once-daily maintenance doses of 100 mg IV over 30 to 120 minutes for 4 days (days 2 through 5). If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).
- **Important AEs[1]**:
  - Increased liver transaminases
- **Studies[2]:**
  - 11 in progress
  - 2 suspended/terminated
  - 1 completed

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1. Fact Sheet for Health Care Providers. Emergency Use Authorization (EUA) for Remdesivir (GS-5734™). https://www.fda.gov/media/137566/download
2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/results?cond=COVID&term=remdesivir&cntry=&state=&city=&dist=

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43

No drug is currently FDA-approved to treat COVID-19

Remdesivir … *what we know*

- Remdesivir in Adults With Severe COVID-19: A Randomised, Double-blind, Placebo-controlled, Multicentre Trial[1]
  - Terminated early due to low enrollment and control of epidemic in China; no difference in time to clinical improvement or 28-day mortality in pts w/ ≤10 days from sx, non-significant difference in time to clinical improvement and 28-day mortality
  - Viral loads decreased at similar rates in both groups; ADRs similar btwn groups (RDV 66%, placebo 64%); higher D/C rates in RDV (12%) vs placebo (5%)
  - **Study considerations:** underpowered due to low enrollment; imbalanced baseline characteristics despite randomization; possible delay in tx start; questionable utility of subgroup analyses
- Compassionate Use of Remdesivir for Patients With Severe COVID-19[2]
  - Prospective, observational study: 53 hospitalized pts (median age, 64y) w/ O_2 sat <94% on RA or receiving O_2 support received RDV 200 mg IV x1 dose on day 1, then 100 mg daily x9 days (median time btwn sx and tx start, 12 days); 64% pts w/ invasive ventilation, 24% w/ minimal to no O_2 support
  - 68% of pts had improved O_2 support category, 57% of pts w/ mech vent extubated, 13% of pts died; 60% experienced ADRs (23% serious); 23% of pts had elevated LFTs
  - **Study considerations:** non-comparative; selection and sampling bias; no prespecified endpoints; duration of f/u shorter than planned; significant proportion had mild dz; delayed tx initiation from sx onset
- Adaptive COVID-19 Treatment Trial[3]
  - Placebo controlled: hospitalized patients
  - Patients who received remdesivir had a 31% (11 days) faster time to recovery than placebo (15 days) (p<0.0001). Results also suggested a survival benefit with mortality rate of 8% for remdesivir versus 11.6% for placebo

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1. Wang y. et al., The Lancet. April 29, 2020. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31022-9/fulltext
2. Grein J, et al. NEJM. April 10, 2020. https://www.nejm.org/doi/full/10.1056/NEJMoa2007016
3. NIAID trial results - unpublished

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44

No drug is currently FDA-approved to treat COVID-19

Hydroxychloroquine / Chloroquine

- **Proposed MOA**: inhibits viral entry and replication via intracellular alkalinization, interferes w/ maturation of viral particles through impaired glycosylation; indirect immunomodulatory effects
- **FDA approved use**: Investigational - EUA Issued March 30, 2020
- **Adult Dose[1]:**
  - Adults > 50kg - 800 milligrams of hydroxychloroquine sulfate on the first day of treatment and then 400 milligrams daily for four to seven days of total treatment based on clinical evaluation
- **Important AEs[1]**:
  - QT interval prolongation. Use with caution in patients with cardiac disease, QT prolongation, a history of ventricular arrhythmias, bradycardia, uncorrected potassium or magnesium imbalance, and during concomitant administration with QT interval prolonging drugs such as azithromycin and some other antibacterial drugs. Monitor the electrocardiogram during treatment.
  - Myocarditis, pericarditis, and cardiomyopathy may increase risk for arrythmia. Monitor for cardiac injury. Severe hypoglycemia: Hydroxychloroquine sulfate has been reported to decrease insulin clearance and resistance. Loss of consciousness in patients with or without the use of antidiabetic medications has been reported.
  - FDA Cautions Against Use Outside of the Hospital Setting or a Clinical Trial Due to Risk of Heart Rhythm
- **Studies[2]:**
  - 167 in process for hydroxychloroquine
  - 6 in process for chloroquine
  - 3 completed for hydroxychloroquine

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1. Fact Sheet for Health Care Providers. Emergency Use Authorization (EUA) for Hydroxychlroquine. https://www.fda.gov/media/136537/download
   EAU for Chloroquine. https://www.fda.gov/media/136535/download
2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/results?cond=COVID&term=hydroxychloroquine&cntry=&state=&city=&dist=

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45

No drug is currently FDA-approved to treat COVID-19

Hydroxychloroquine … *some of what we know*

- Hydroxychloroquine in Patients With COVID-19: An Open-label Randomized, Controlled Trial[1]
  - Multicenter, open-label, RCT; 150 hospitalized pts (mean age, 46y, 99% mild or moderate dz, 76% received other antivirals) randomized 1:1 to SOC, or SOC plus HCQ 1,200 daily x3 days, then 800 mg daily for total of 2-3wk based on dz severity; 17 days mean time btwn sx onset and randomization; study D/C early based on results from pre-planned interim analysis
  - No difference in primary endpoint of viral clearance (85% HCQ vs 81% SOC) or secondary endpoint of sx improvement rate (67% HCQ vs 60% SOC); higher rate of ADRs in HCQ group (30% vs 9%)
  - **Study considerations:** not peer reviewed; randomized but open-label; most pts received other potential antivirals; delayed tx initiation from sx onset; almost all pts had mild-moderate dz; higher HCQ dose and duration than other studies
- Outcomes of Hydroxychloroquine Usage in United States Veterans Hospitalized With Covid-19[2]
  - Retrospective cohort study; 368 hospitalized pts (median age 69y) treated w/ HCQ (n=97), HCQ and AZ (n=113), or supportive care only (n=158); 32% of supportive care pts received AZ w/o HCQ; sicker pts more likely to receive HCQ or HCQ + AZ
  - Unadjusted analysis: Death occurred in 28% of HCQ pts, 22% of HCQ + AZ pts, 11% of no-HCQ pts; mech vent occurred in 13% of HCQ pts, 7% of HCQ + AZ pts, 14% of no HCQ pts
  - Analysis adjusted for baseline imbalances: higher risk of death in HCQ group vs no-HCQ (adjusted HR 2.61) but no difference in HCQ + AZ vs no-HCQ; no difference in mech vent in HCQ vs no-HCQ and HCQ + AZ vs no-HCQ
  - **Study considerations:** non-randomized, retrospective w/ propensity score adjusted analysis; tx bias; cohort characteristics impact external validity; dosing and duration not provided; drug exposure based on dispensing records

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1. https://www.nejm.org/doi/full/10.1056/NEJMoa2012410
2. https://www.medrxiv.org/content/10.1101/2020.04.10.20060558v2

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46

No drug is currently FDA-approved to treat COVID-19

Hydroxychloroquine … *more of what we know*

- No Evidence of Clinical Efficacy of Hydroxychloroquine in Patients Hospitalized for COVID-19 Infection and Requiring Oxygen: Results of a Study Using Routinely Collected Data to Emulate a Target Trial[1]
  - Observational cohort study: 181 hospitalized pts (median age 60y, 84 treated w/in 48h after admission w/ HCQ 600 mg/day; 97 not treated) requiring O_2 by mask or NC; excl use of other drugs (TCZ, LPV/r, RDV) to treat COVID-19, ICU care, non-invasive vent w/ positive airway pressure, or mech vent
  - 7-day median time btwn sx and admission; HCQ group had lower rates of comorbidities and received add'l abx incl AZ (20%); no-HCQ group had higher rates of confusion at admission; 8 pts in no-HCQ group received HCQ >48h after admission
  - No difference in primary outcome (ICU transfer or death by day 7): 21% in HCQ vs 22% in no-HCQ; similar rates of death (HCQ 3%, no-HCQ 5%) and progression to ARDS (HCQ 28%, no-HCQ 24%); 8 HCQ pts had ECG changes requiring D/C, 1 pt had heart block
  - **Study considerations:** not peer reviewed; non-randomized; weighted propensity score model; only incl pts w/ mild dz; different protocols at study sites; possible selection bias
- The QT Interval in Patients With COVID-19 Treated With Hydroxychloroquine and Azithromycin[2]
  - Retrospective, observational study; 84 hospitalized pts (mean age, 63y) w/ confirmed SARS-CoV-2 treated w/ HCQ plus AZ; comorbidities incl CAD (11%), HTN (65%), CKD (7%), DM (20%), COPD (8%), CHF (2%); 7% on amiodarone tx
  - Mean QTc interval increased from 435 msec at baseline to 463 msec; 30% pts had QTc prolonged by >40 msec; 11% pts developed QTc interval of >500 msec; no cases of torsade de pointes; acute renal failure only predictor of maximal QTc >500 msec on multivariate analysis
  - **Study considerations:** non-comparative; small sample size; pts had other risk factors for QT prolongation besides HCQ plus AZ tx; HCQ and AZ dosing not provided

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1. https://www.medrxiv.org/content/10.1101/2020.04.10.20060699v1
2. https://www.nature.com/articles/s41591-020-0888-2

May 11, 2020

47

No drug is currently FDA-approved to treat COVID-19

Hydroxychloroquine … *even more*

- + Hydroxychloroquine and Azithromycin as a Treatment of COVID-19: Results of an Open-Label Non-randomized Clinical Trial; **full-text *Int J Antimicrob Agents* article**
- + Clinical and Microbiological Effect of a Combination or Hydroxychloroquine and Azithromycin in 80 COVID-19 Patients With at Least a Six-Day Follow-up: An Observational Study; **fu+ll-text *Travel Med Infect Dis* article**
- − No Evidence of Rapid Antiviral Clearance or Clinical Benefit With the Combination of Hydroxychloroquine and Azithromycin in Patients with Severe COVID-19 Infection; **full-text article**
- − A Pilot Study of Hydroxychloroquine in Treatment of Patients With Common Coronavirus Disease-19 (COVID-19); **full-text *J Zhejiang Univ* article**
- + Efficacy of Hydroxychloroquine in Patients With COVID-19: Results of a Randomized Clinical Trial; **pre-print *medRxiv* article**
- − Risk of QT Interval Prolongation Associated With Use of Hydroxychloroquine With or Without Concomitant Azithromycin Among Hospitalized Patients Testing Positive for Coronavirus Disease 2019 (COVID-19); **access *JAMA Cardiol* article**
- − Assessment of QT Intervals in a Case Series of Patients With Coronavirus Disease 2019 (COVID-19) Infection Treated With Hydroxychloroquine Alone or in Combination With Azithromycin in an Intensive Care Unit; **access *JAMA Cardiol* article**
- − Hydroxychloroquine Versus COVID-19: A Rapid Systematic Review and Meta-Analysis; **pre-print *medRxiv* article**
- + Early Hydroxychloroquine Is Associated with an Increase of Survival in COVID-19 Patients: An Observational Study. https://www.preprints.org/manuscript/202005.0057/v1

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May 11, 2020

48

Immunomodulators

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May 11, 2020

49

Immunomodulators

No drug is currently FDA-approved to treat COVID-19

Drug	Proposed MOA	Drug	Proposed MOA
Acalabrutinib *(Calquence)*	*Reduces inflammatory response by inhibiting malignant B-cell proliferation via inhibition of Bruton tyrosine kinase (BTK)*	Ibrutinib *(Imbruvica)*	*Reduces inflammatory response by inhibiting malignant B-cell proliferation via inhibition of Bruton tyrosine kinase (BTK)*
Anakinra *(Kinerret)*	*Reduces inflammatory response by inhibiting IL-1 receptors*	Leflunomide *(Arava)*	*Reduces inflammatory response by inhibiting dihydroorotate dehydrogenase; in vitro effects against SARS-CoV-2*
Azithromycin	*No direct antiviral activity; indirect immunomodulatory effects*	Prazosin	*Reduces inflammatory response by blunting catecholamine effects on cytokine production*
Baricitinib *(Olumiant)*	*Reduces inflammatory response by disrupting cytokine pathways via inhibition of janus-associated kinases (JAK)*	Ravulizumab *(Ultomiris)*	*Reduces inflammatory response by modulating activity of complement pathways*
Canakinumab *(Ilaris)*	*Reduces inflammatory response by inhibiting IL-1 receptors*	Ruxolitinib (Jakafi)	*Reduces inflammatory response by disrupting cytokine pathways via inhibition of janus-associated kinases (JAK)*
Colchicine	*Reduces inflammatory response by inhibiting interleukin pathways via interference w/ inflammasome complex assembly; reduces cell infectivity by interrupting endocytosis via inhibition of microtubule polymerization*	Sarilumab *(Kefzara)*	*Reduces inflammatory response by inhibiting IL-6 receptors*
Corticosteroids	*Reduces inflammatory response via inhibition of multiple cytokines*	Selinexor *(Xpovio)*	*Reduces inflammatory response by disrupting cytokine pathways via inhibition of exportin 1 (XPO1); XPO1 inhibitors have activity against many viruses, incl RNA viruses, and expected to have activity against SARS-CoV*
Duvelisib *(Copiktra)*	*Reduces inflammatory response by disrupting cytokine pathways via inhibition of phosphatidylinositol 3-kinase (PI3K)*	Situximab *(Sylvant)*	*Reduces inflammatory response by inhibiting IL-6 receptors*
Eculizumab *(Soliris)*	*Reduces inflammatory response by modulating activity of complement pathways*	SSRIs (fluoxetine, fluvoxamine)	*Reduces inflammatory response by modulating activity of complement pathways*
Etoposide	*Reduces inflammatory response; has been effective for cytokine storm caused by other diseases; topoisomerase II inhibitors suppress RNA virus replication in vitro*	Statins *(Atorvasttin)*	*Reduces inflammatory response by mitigating cytokine activation pathways; attenuates CV component or complications assoc w/ COVID-19; epidemiological data suggest protective effects in influenza pneumonia*
		Tocilizumab *(Actemra)*	*Reduces inflammatory response by inhibiting IL-6 receptors*

50

50

Herbs
Supplements
Vitamins

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51

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Herbs

Drug	Speculated Benefit
Astragalus	*Has been suggested for COVID-19 tx/prevention based on immunostimulatory effects & ↓inflammatory cytokines, though others raise theoretical concerns about cytokine storm potential* *Traditionally used in Chinese medicine for immune boosting against cold/flu, now suggested w/ or w/o other herbs for COVID-19, but standardization of regimens lacking*
Echinacea	*Has been suggested for COVID-19 prevention based on historical use in cold/flu sx relief* ***Cytokine storm debate.** Some suggest OK for prevention, but should d/c @ COVID-19 sx onset, due to possible immune inflammatory up-regulation; theory based on in vitro E purpurea study on ↑inflammatory cytokine production in human macrophages and other limited data*
Elderberry	*Has been suggested for COVID-19 tx/prevention based on historical use in cold/flu sx relief* ***Cytokine storm debate.** Some suggest OK for prevention, but should d/c @ COVID-19 sx onset, due to possible immune inflammatory up-regulation; theory based on in vitro S nigra (Sambucol) study on ↑inflammatory cytokine production in human monocytes[3]*

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52

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Supplements

Drug	Speculated Benefit
Acetylcysteine	***Antiviral hypothesis**. Purported to ↓ epithelial cell SARS-CoV-2 entry based on in vitro data. Nebulized heparin + NAC ("H-NAC") proposed as COVID tx.* ***Immune hypothesis**. Proposed as immune booster & detoxifier (antioxidant, free-radical fighter); anti-inflammatory (eg, for excessive immune response assoc w/ severe COVID dz); resp tract remedy*
Melatonin	**Antiviral hypothesis:** Melatonin could indirectly affect ACE2 expression, which is involved in SARS-CoV-2 cell entry **Cytokine storm hypothesis:** Observed ↓TNF-α, IL-6 in melatonin supplement users, anti-oxidant effects proposed to ↓excessive immune up-regulation "cytokine storm" linked to severe COVID-19 **Sleep-immunity hypothesis:** Sleep <6 h/night linked to ↑susceptibility to experiment-induced rhinovirus infxn. Though marketed as sleep aid, AASM doesn't support for sleep onset/maintenance insomnia, based on studies (melatonin 2 mg, pts >55 yo)
Quinine	*Since quinine is a natural form of the compound in synthetic chloroquine and hydroxychloroquine, some media influencers hypothesize it may be as valuable as these drugs against COVID-19* *CAUTION: Dosing challenges and adverse effects likely limit use.*
Quercetin	***Antiviral hypotheses**. Theorized to interfere w/ ACE2 receptors that could ↓COVID-19 entry into cells, & as ionophore to ↑zinc's general antiviral action. In vitro studies suggest ↓viral load for other viruses. COVID-19 human clinical trial announced, but role/dose unknown* ***Immune boosting hypothesis**. Has been suggested for COVID-19 tx/prevention based on immunostimulatory effects*

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53

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Vitamins & Minerals

Drug	Speculated Benefit
Silver (colloidal)	*Colloidal silver (silver particles in liquid) isn't safe or effective for tx of any dz/condition, per FDA NCCIH*
Vitamin C	*Reduces inflammatory response and production of reactive oxygen species via anti-inflammatory and antioxidant properties; supports host defenses and protects host cells against oxidative stress*
Vitamin D	*↑D deficiency prevalence in pts w/ factors assoc w/ ↑COVID risk—older, obesity, smoker, lung dz—as well as winter, ↓sun, dark skin, certain latitudes, poor diet;[5] vit D's role in immunity; non-COVID resp infxn studies* ***Megadoses** (eg, 150,000 IU D3 qd x3 days) to prevent/tx COVID-19 promoted by some media influencers, based on vit D use as immune-booster, anti-inflammatory for ↓"inflamm-aging"[4]* ***Cytokine storm debate.** Some suggest vit D may ↓cytokine storm immune up-regulation linked to severe COVID-19; others suggest vit D could exacerbate it, if taken after sx onset[8]*
Zinc	*impairs replication of various viruses, incl coronaviruses, by inhibiting RNA-dependent RNA polymerase; intracellular concentrations increased by HCQ and CQ*

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54

Other Medication Management Strategies

- **Evaluate medication regimen to reduce the number and length of medication administration times**
  - **Discontinue medications that are no longer providing a beneficial effect**
  - **Change medications to options that can be given once or twice daily**
    - **Extended release**
    - **Longer half-life**
- **ACE/ARB** – Keep using in current patients
  - 4 new observational studies indicate no increase in contracting COVID-19 or difference in disease process
- **STEROIDS** – Avoid systemic use if possible.
  - If continued use is required, recognize increased risk of infection with COVID and potential worsening disease progression
  - Late stage COVID infections may require systemic steroids
- **NSAIDS** – Keep using in current patients
  - Per EMA and WHO no scientific evidence establishing a link between ibuprofen and worsening of COVID-19

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55

Nebulizers

- Nebulizer use in COVID patients is controversial[1,2]
  - No way to separate virus particles generated from patient versus nebulizer[3]
- Switch from nebulizer is only necessary when:
  - Patient is positive for COVID-19 or at high suspicion of COVID-19
  - MDI with spacer (holding chamber) is available
  - Patient is cognitively and physically able to comply with MDI dosing requirements
- If nebulizer must be continued:
  - Full PPE must be worn during nebulization treatments
  - Consider switching to long-acting bronchodilators (once or twice daily) to reduce exposure time and frequency

1. Yu IT, Li Y, Wong TW, Tam W, Chan AT, Lee JH, *et al.* Evidence of airborne transmission of severe acute respiratory syndrome virus. *N Engl J Med* 2004;**350**:1731–9.
2. Hugonnet S, Pittet D. Transmission of severe acute respiratory syndrome in critical care: do we need a change? *Am J Resp Crit Care Med* 2004;**169**:1177–8.
3. Simonds AK, et al. Evaluation of droplet dispersion during non-invasive ventilation, oxygen therapy, nebuliser treatment and chest physiotherapy in clinical pr e infections. Health Technology Assessment 2010; Vol. 14: No. 46, 131–172.

CALTCM May 11, 2020

56

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57

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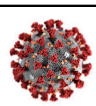
58



Upcoming Events:

May 18th: Mental Health Awareness

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59

Save the Date for the following CALTCM events:

Leadership & Management in Geriatrics: July 31 & August 1

46th Annual Meeting: 2020 CALTCM Summit for Excellence: October 8-10

CALTCM May 11, 2020

60