

Today's Agenda

Time (MT)	Presentation	Presenter(s)
Noon – 12:05 pm	Welcome, Announcements, Introductions	Lachelle Smith, Director, ECHO Idaho
12:05 – 12:10 pm	Idaho Epidemiology Curves and Public Health Updates	Carolyn Buxton Bridges, MD, FACP
12:10 – 12:15 pm	Treatment Updates	Cathy Oliphant, PharmD
12:15 – 12:35 pm	COVID-19 Critical Care	Paula Carvalho, MD
12:35 – 12:55 pm	Critically Ill COVID Patient Case and Q&A	ECHO Panel Sky Blue, MD Paula Carvalho, MD
12:55 – 1 pm	Closing Pearls, Announcements, Call to Action	Megan Dunay, MD, MPH Lachelle Smith, Director, ECHO Idaho

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Idaho Epidemiology Curves and Public Health Updates

Carolyn Buxton Bridges, MD, FACP

Governor's Coronavirus Working Group, Former CDC Public Health Physician and Researcher

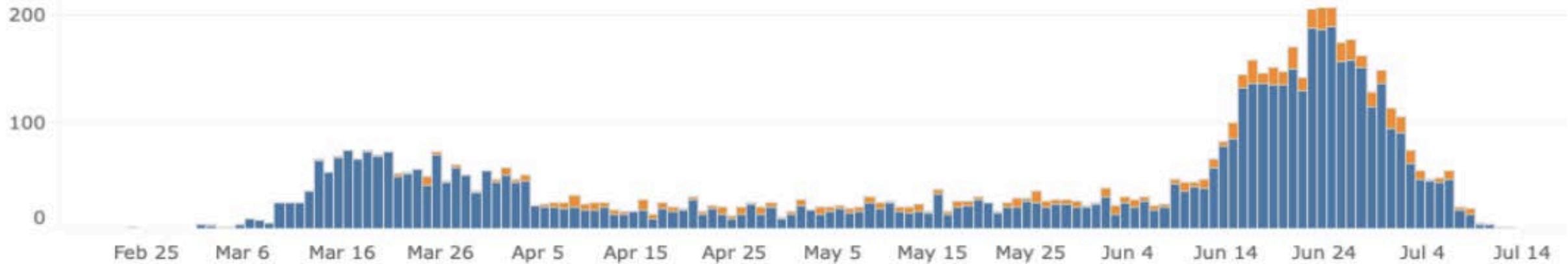
Case Counts and SARS-CoV-2 PCR Testing in Idaho

	5/19/2020	6/15/2020	7/6/2020	7/13/2020
Total lab-confirmed and probable	2,455	3,462 ($\Delta 556$)	8,052 ($\Delta 4,590$)	11,402 ($\Delta 3,350$)
Deaths	74	88 CFR $88/3462=2.5$	94 ($\Delta 6$) CFR $6/4590=0.1$	102 ($\Delta 8$) CFR $8/3350=0.2$
Hospitalizations	213	270	387 ($\Delta 117$)	500 ($\Delta 113$)
ICU admissions	89	100	130 ($\Delta 30$)	144 ($\Delta 14$)
Healthcare personnel	295	366 ($\Delta 57$)	596 ($\Delta 230$)	760 ($\Delta 164$)
Total tests	37,847	65,306 ($\Delta 17,436$)	107,925 ($\Delta 42,619$)	129,540 ($\Delta 12,615$)

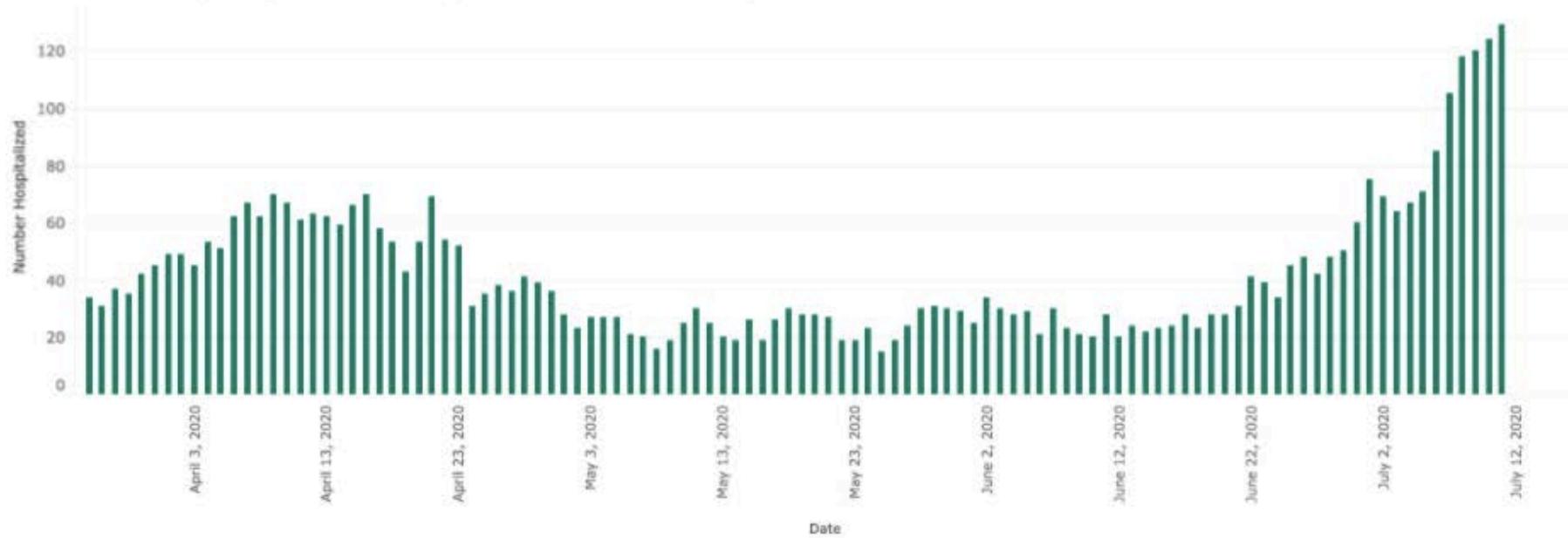
Case Classi...
 ● Probable...
 ○ Confirme..



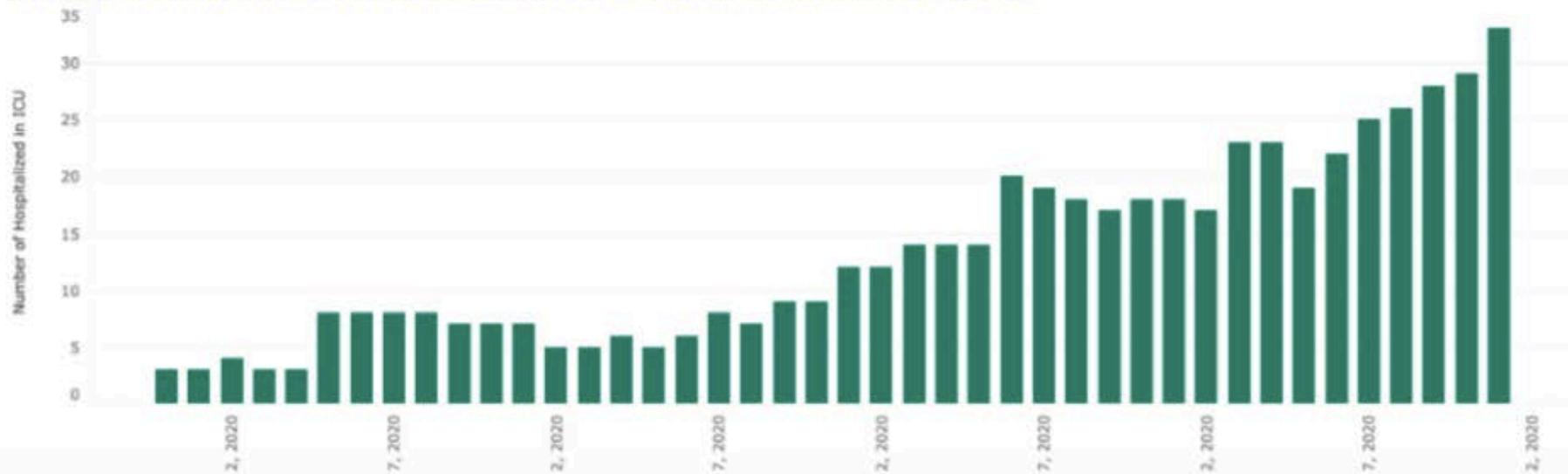
COVID-19 by Date of Onset



Patients currently hospitalized in an inpatient bed who have suspected or confirmed COVID-19



Patients currently hospitalized in the Intensive Care Unit (ICU) with confirmed COVID-19



Community Mask Wearing

- CDC recommends wearing cloth facial coverings as source control, when in public and social distancing may not be maintained
- Limited data on cloth facial covering effectiveness
 - Some studies estimating filtering capacity suggest likely impactful in preventing especially large droplet spread from source patient
- Hong Kong study (VC-C Cheng) estimating possible impact of public mask use which might also include mix of surgical masks and cloth facial coverings
- Recent review article by Chou, et al. Annals Intern Med on community and healthcare-setting mask vs N95 use
 - Overall in HC settings, limited differences sometimes for N95 vs surgical mask
 - In community settings, less effective likely due to compliance

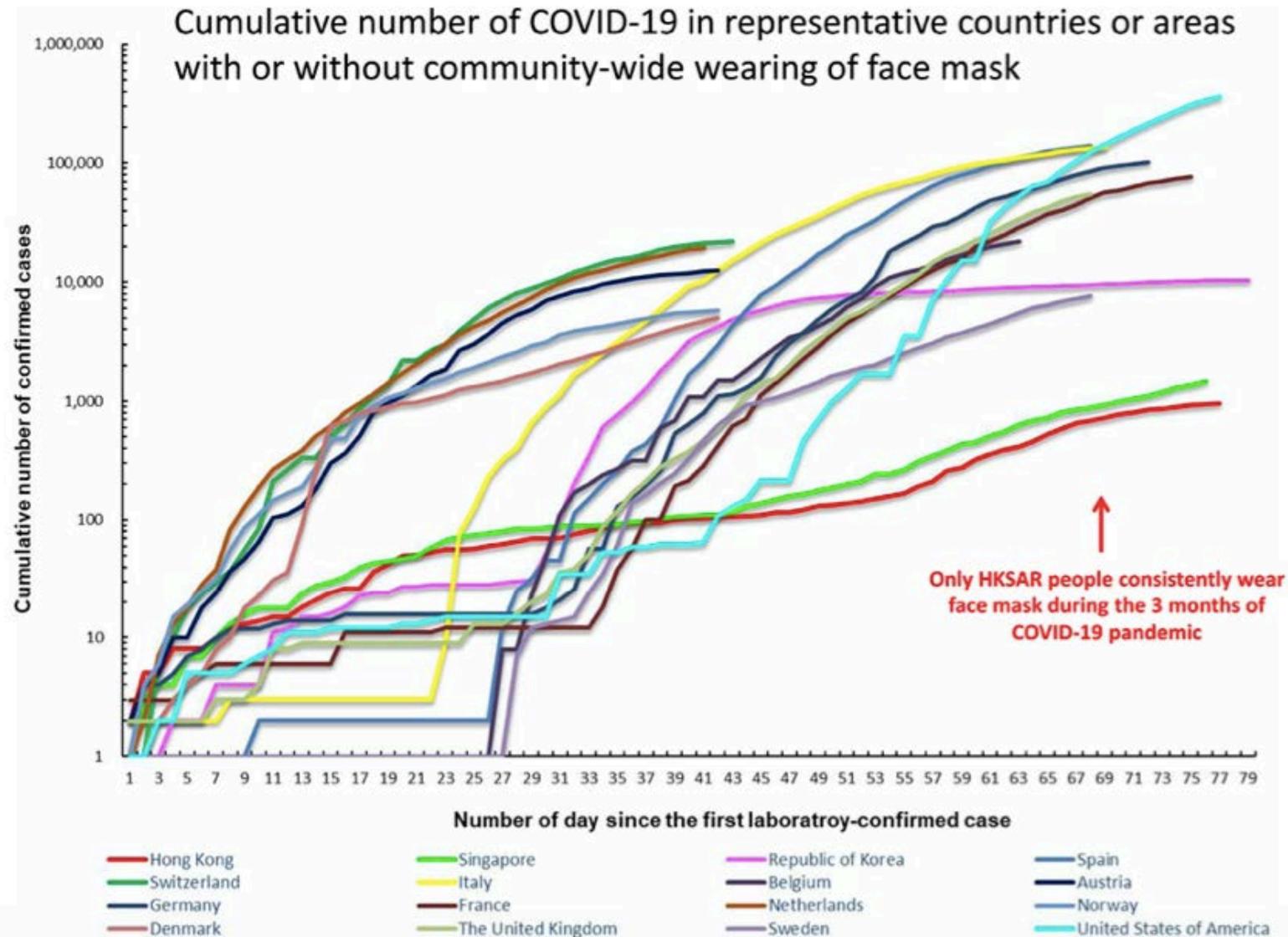
<https://annals.org/aim/fullarticle/2764367/effectiveness-surgical-cotton-masks-blocking-sars-cov-2-controlled-comparison>.
<https://www.acpjournals.org/doi/pdf/10.7326/M20-3213>.
<https://doi.org/10.1016/j.jinf.2020.04.024>.

VC-C Cheng, et al. The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2, J Infect 2020

- Examined mask use among public in HK-SAR
 - >95% compliance
 - Among the 961 confirmed cases (and excluding household clusters)
 - 11 clusters of 113 persons directly engaged in mask-off activities such as dining, bars, karaoke, and exercise in fitness clubs.
 - 3 clusters involving 11 persons engaged in mask-on settings at the workplace.
- Compared cases in HK-SAR with other countries with less mask use and controlling for population density
 - Concluded high compliance with mask use in public likely contributes to reducing community spread

VC-C Cheng, et al. The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2, J Infect 2020

V.C.-C. Cheng, S.-C. Wong and V.W.-M. Chuang et al./Journal of Infection 81 (2020) 107–114



VC-C Cheng, et al. The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2, J Infect 2020

Table 1

Incidence of coronavirus disease 2019 (COVID-19) infection in Hong Kong Special Administrative Region (HKSAR) as compared with that of selected countries as of 8 April 2020 (at day 100 after official announcement of pneumonia outbreak in Wuhan, Hubei Province, China)^a.

Countries or city	Population (million) ^b	Cumulative number of confirmed case ^c	Number (percentage) of death	Incidence per million population ^d	P value (incidence compared with HKSAR)	Population density: population per km ² (rank in the world) ^e
Hong Kong SAR ^f	7.45	961	4 (0.4%)	129.0	Not applicable	6782 (3 rd)
Western Pacific Region						
Singapore	5.70	1,481	6 (0.4%)	259.8	P<0.001	7894 (2 nd)
South Korea	51.78	10,384	200 (1.9%)	200.5	P<0.001	517 (13 th)
European Region						
Spain	47.10	140,510	13,798 (9.8%)	2,983.2	P<0.001	93 (89 th)
Switzerland	8.59	22,164	641 (2.9%)	2,580.2	P<0.001	208 (48 th)
Italy	60.24	135,586	17,129 (12.6%)	2,250.8	P<0.001	200 (51 st)
Belgium	11.52	22,194	2,035 (9.2%)	1,926.6	P<0.001	376 (22 nd)
Austria	8.90	12,640	243 (1.9%)	1,420.2	P<0.001	106 (76 th)
Germany	83.15	103,228	1,861 (1.8%)	1,241.5	P<0.001	233 (41 st)
France	67.06	77,226	10,313 (13.4%)	1,151.6	P<0.001	123 (68 th)
Netherlands	17.44	19,580	2,101 (10.7%)	1,122.7	P<0.001	420 (16 th)
Norway	5.37	5,863	69 (1.7%)	1,091.8	P<0.001	17 (171 st)
Denmark	5.82	5,071	203 (4.0%)	871.3	P<0.001	135 (64 th)
The United Kingdom	66.44	55,246	6,159 (11.1%)	831.5	P<0.001	274 (32 nd)
Sweden	10.33	7,693	591 (7.7%)	744.7	P<0.001	23 (159 th)
Region of Americas						
United States of America	329.45	363,321	10,845 (3.0%)	1,102.8	P<0.001	34 (145 th)

Treatment Updates

Cathy Oliphant, PharmD

Infectious Disease, Professor and Interim Chair, ISU College of Pharmacy

COVID Pharmacologic Treatments

- Tocilizumab
- Remdesivir
- Corticosteroids
- Anticoagulation

Tocilizumab

- Interleukin-6 receptor antagonist
 - IL-6 is part of the cytokine storm
 - The cytokine release is marked by elevation of coagulation markers, multi-organ dysfunction, respiratory failure and death.
- Two studies have recently demonstrated lower death rates in mechanically ventilated patients

Tocilizumab: University of Michigan

(Clinical Infectious Diseases - <https://doi.org/10.1093/cid/ciaa954> - published 7/11/2020)

- Single center observational study
- 78 COVID mechanically ventilated patients received tocilizumab (vs 76 patients w/std care) from 3/9-4/20/20
 - Groups similar but tocilizumab group was younger (55 vs 60 yo), less likely to have CKD/lung dz
 - Most patients intubated w/in 24 hr admission or 48 hr of transfer
- Tocilizumab was associated with improved survival:
 - 45% reduction in hazard of death and improved status
- Reduced case fatality rate at 28 days (18% vs 36%, $p=0.01$)
- Increase in patients discharged from hospital during study period (56% vs 40%, $p=0.04$)
- Tocilizumab treated had increased frequency of super-infections (no difference in 28 day death rate)
 - 54% vs. 26%

Tocilizumab: Milan, Italy

(Journal of Infectious Diseases -

<https://doi.org/10.1016/j.jinf.2020.07.008>)

- Single-center retrospective study
- 74 tocilizumab treated patients were matched with 148 matched controls from 3/13-4/3/2020
 - 70% critically ill
 - Median age 59
- Critically ill experienced benefit whereas less severe did not benefit
- Tocilizumab patients had improved survival ($p=0.035$) but longer hospital stays ($p=0.019$)
- At the end of follow-up:
 - 65% of tocilizumab treated patients were improved or stable
 - 35% of tocilizumab treated patients had clinical deterioration (death or worsened mechanical ventilation requirements)
- Significant AEs in tocilizumab treated patients
 - Increased infections (32%)
 - Worsening respiratory status

Remdesivir

- Hospitalized, severe patients
 - SpO₂ ≤ 94% on room air or
 - Requiring supplemental oxygen, mechanical ventilation, ECMO
- Data have demonstrated:
 - Shorter time to recovery (11d vs 15 d p<0.001) in patients with a median time from onset s/s to remdesivir initiation < 10 d)
 - Improved discharge rates in patients with s/s < 10 days
- Dosing
 - Day 1: 200 mg x 1
 - Days 2-5: 100 mg daily for patients not requiring mechanical ventilation (if no clinical improvement, may extend to 10 days)
 - Days 6-10: 100 mg daily for mechanically ventilated patients

Corticosteroids

- RECOVERY Trial
- Dexamethasone use was associated with a reduction in overall 28 day mortality
 - 21.6% vs 24.6%
 - 35% reduction in mechanically ventilated vs 20% in those receiving supplemental oxygen (no mechanical ventilation)
- Reduction in 28 day mortality greatest in those with s/s > 7 d vs those with recent onset
- Also associated with reduced duration of hospitalization and increased probability of D/C within 28 days
- Dosing:
- IDSA and NIH Guidelines recommend dexamethasone 6 mg daily (IV or PO) for up to 10 days in patients receiving mechanical ventilation or supplemental oxygen
 - 10 days or until hospital discharge (which occurs first)
 - Equivalent dosing if dexamethasone not available:
 - 32 mg methylprednisolone
 - 40 mg prednisone

COVID & Thrombosis

- Severe COVID can result in cytokine storm, systemic inflammatory response and coagulopathy (that is prothrombotic)
- The enhanced prothrombotic state induced by severe COVID is associated with venous and arterial microthrombi
- Data demonstrates incidence of VTE of up to 27% with mortality rates up to 40-60%
- VTE prophylaxis is essential in these patients

COVID & Anticoagulation

- CDC estimates that ~90% of hospitalized COVID patients have at least one increased risk of thrombosis
- Tang et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost.* 2020;18:1094-99
 - 449 COVID patients
 - 99 received heparin (primarily LMWH)
 - DVT prophylaxis reduced 28 day mortality by 20% in patients with an SIC score ≥ 4 or D-dimer $\geq 3,000$ ng/ml (or 6x ULN)
 - 28-day mortality 40% vs 64.2%, $p=.029$ for SIC Score ≥ 4
 - 28-day mortality 32.8% vs 52.4%, $p=.017$ for elevated D-dimer
 - No increase in major bleeding

COVID & Anticoagulation

- Bikdeli et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up. JACC 2020;75(23). DOI: 10.1016/j.jacc.2020.04.031
- Barnes et al. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. J of Thrombosis and Thrombolysis 2020;50:72-81
- Spyropoulos et al. Scientific and Standardization Committee Communication: Clinical Guidance on the Diagnosis, Prevention and Treatment of Venous Thromboembolism in Hospitalized Patients with COVID-19. 27 May 2020. <https://doi.org/10.1111/jth.14929>
- Treatment Guidelines:
 - NIH
 - WHO
 - International Society for Thrombosis and Haemostatis
 - American Society of Hematology

COVID & Anticoagulation: VTE Prophylaxis in non-ICU Patients

- All hospitalized patients with COVID should be considered for VTE prophylaxis
- Standard dose VTE prophylaxis
 - Enoxaparin 40 mg daily if BMI < 40 kg
 - *Preferred over UFH – due to dosing schedule (once or twice daily)
 - BMI \geq 40 kg: Enoxaparin 40 mg Q12
 - If CrCl < 30 ml/min, enoxaparin 30 mg daily
 - UFH – standard dose

COVID & Anticoagulation: VTE Prophylaxis in ICU Patients

- All hospitalized patients with COVID should be considered for VTE prophylaxis
- VTE prophylaxis Dosing
 - Enoxaparin 30 mg Q12 if BMI < 40 kg
 - *Preferred over UFH – due to dosing schedule
 - BMI \geq 40 kg: 50% increase for obese
 - If CrCl < 30 ml/min, enoxaparin 30 mg daily
 - UFH – standard dose
 - Data demonstrate that patients with D-dimer > 2,000 or SIC score \geq 4 benefit from BID dosing of enoxaparin
 - Data do not support treatment dose heparin for prophylaxis

COVID & Anticoagulation: Duration of VTE Prophylaxis

- Extended post-discharge thromboprophylaxis should be considered for all hospitalized patients with COVID-19 that meet high VTE risk criteria
 - VTE prophylaxis post-discharge
 - Up to 45 days
- *Non-COVID trials have evaluated VTE prophylaxis post-discharge using the following durations
- Enoxaparin 6-14 days
 - Rivaroxaban (Xarelto) 31-39 days
 - Betrixaban (Bevyxxa) 35-42 days

COVID-19 Critical Care

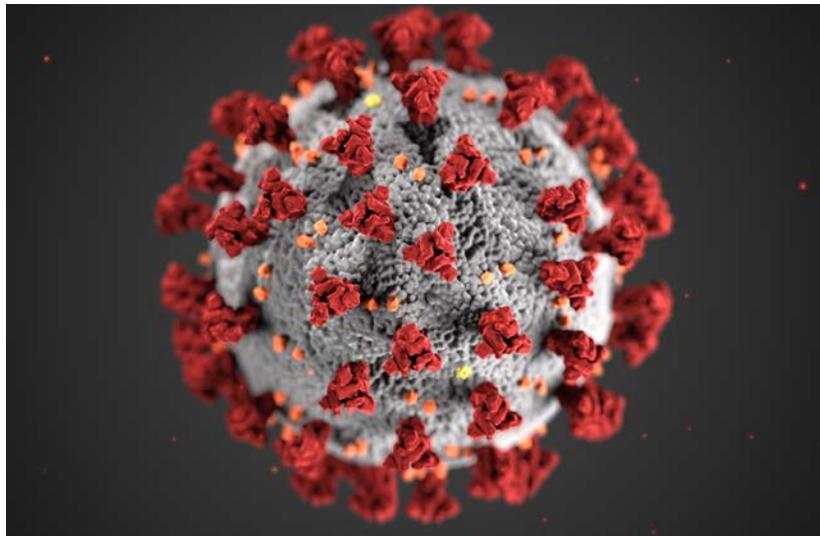
Paula Carvalho, MD

Boise VA Medical Center

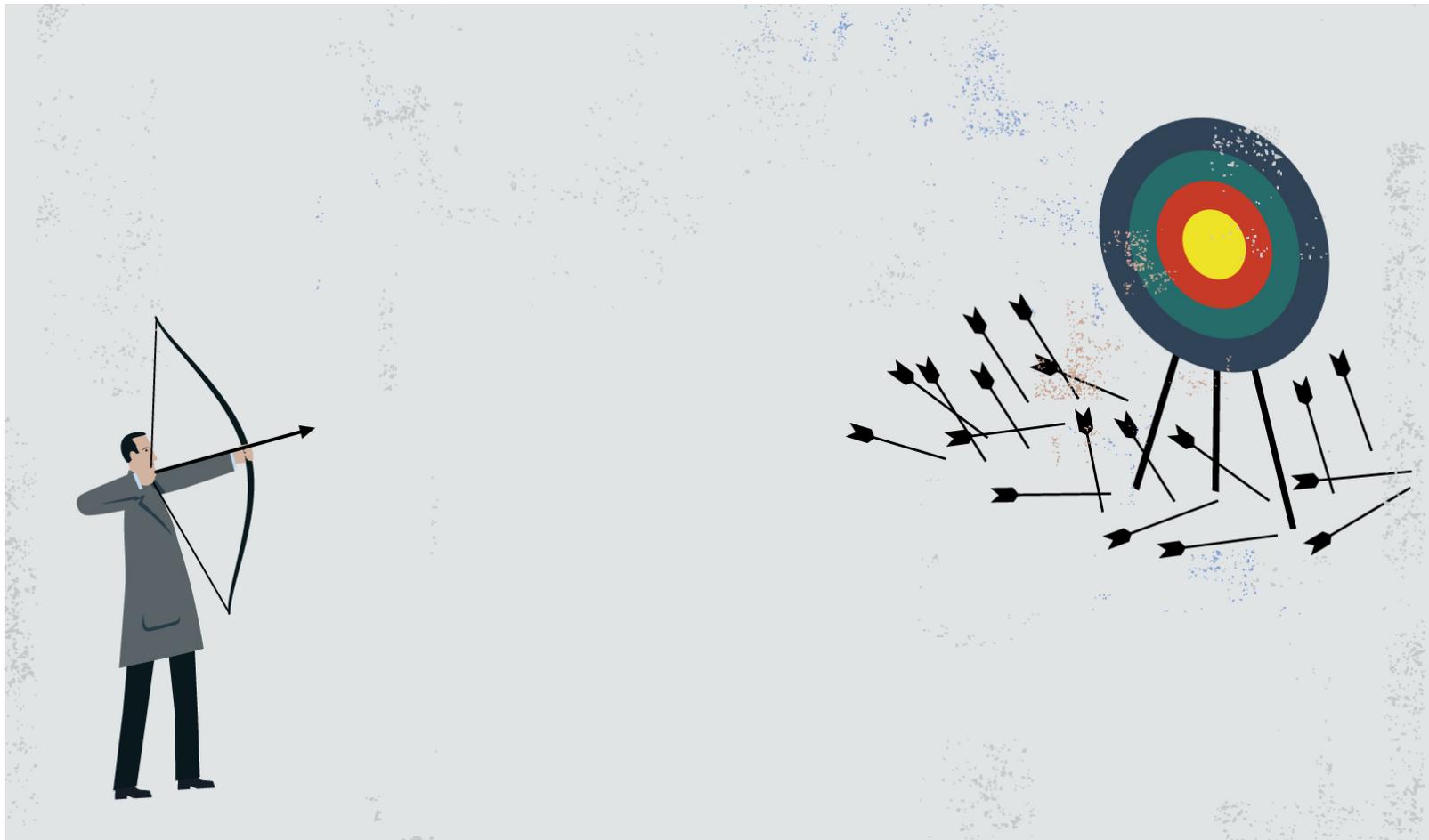
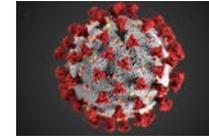
Learning Objectives

To develop an understanding of:

- Viral duration and aerosol science
- How to oxygenate a patient with COVID-19
- The role of corticosteroids in COVID-19



The science of coronavirus



A word about aerosols and viral duration: What do we know?

Aerosol and surface stability of SARS-CoV-2

Conditions:

- 21-23°C
- 40% humidity
- 7 day observation period

Hours

Aerosol:	3
Plastic:	72 (rapid decrease in stability at 72h)
Stainless steel:	72 (rapid decrease in stability at 48h)
Cardboard:	24
Copper:	4

N Engl J Med 2020;382:1564

Glass: 9 days

J Hosp Inf 2020;104:246

Aerosols:

Aerosol-generating procedures*:

- Bronchoscopy
- Intubation
- Suctioning
- Nebulizer treatments

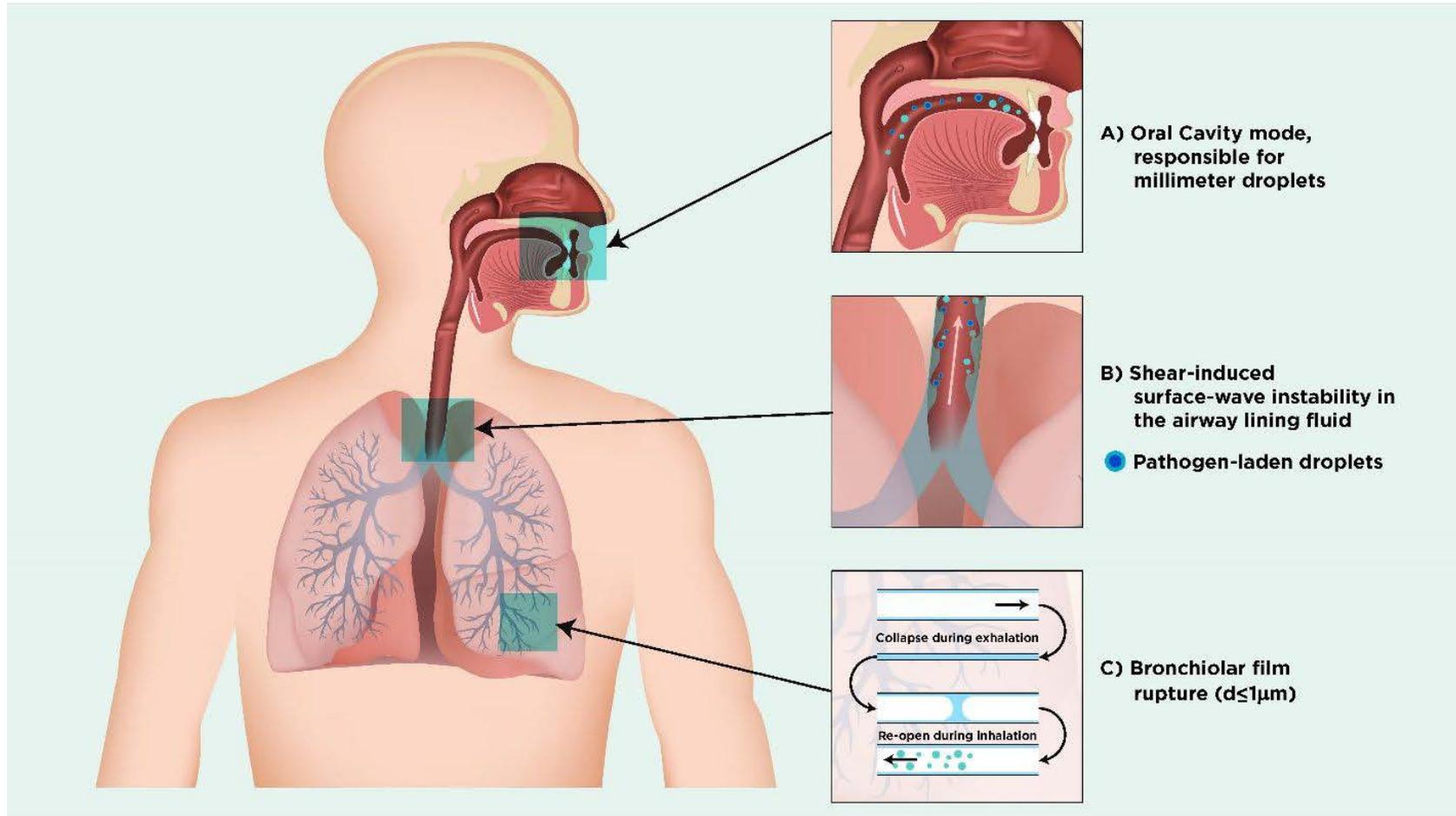
* *Generate potentially infectious bioaerosols*

Aerosol-dispersing procedures*:

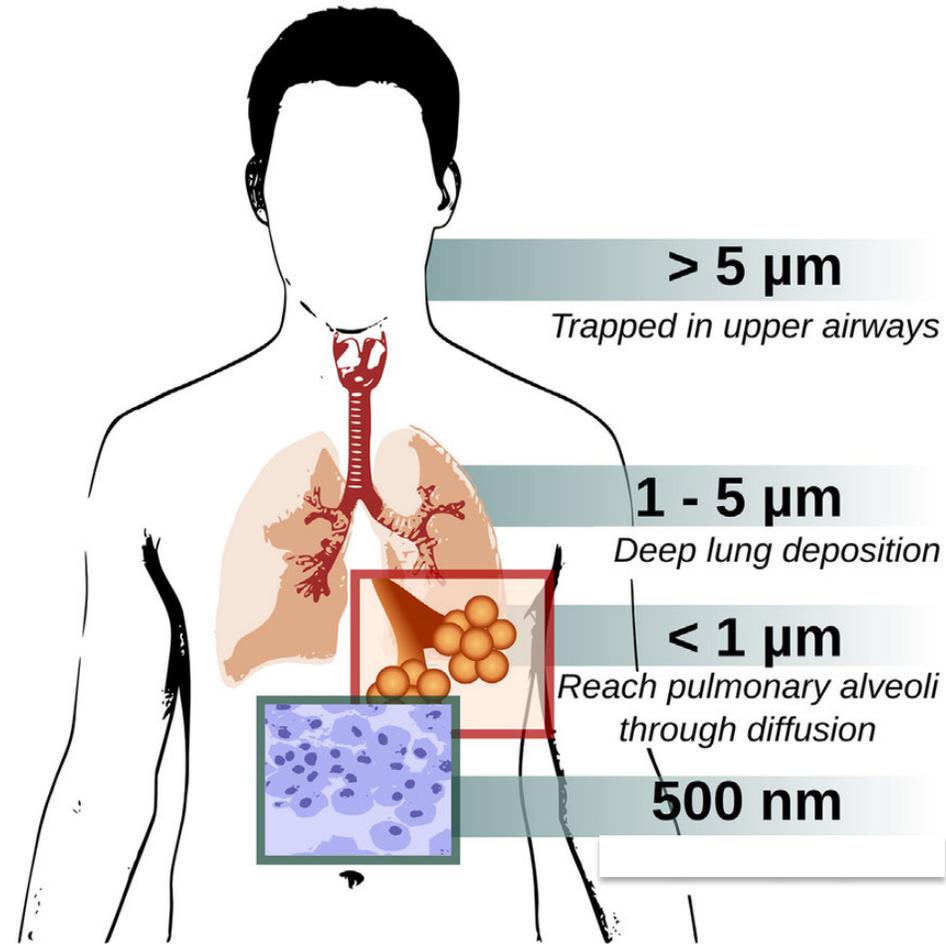
- Oxygen therapy
- Humidified high-flow nasal cannula (HFNC)
- Non-invasive ventilation (NIV)
- Manual ventilation

* *These devices do not contain pathogens unless the device is contaminated*

Aerosol production



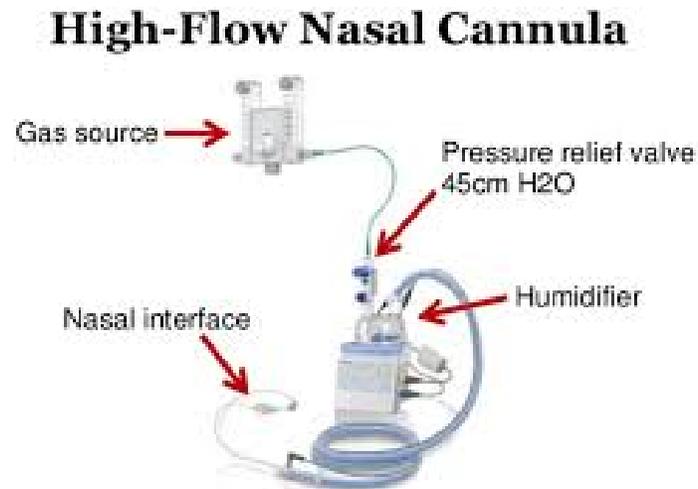
Aerosol deposition



The patient with COVID-19 and hypoxemia:

- Start with supplemental oxygen to target an SpO₂ of 90-96%
- If low-flow oxygen (≤ 6 L/minute) is not sufficient, use non-invasive methods of oxygenation

First choice: High-flow nasal cannula



The patient with COVID-19 and hypoxemia:

- If low-flow oxygen (≤ 6 L/minute) is not sufficient, use non-invasive methods of oxygenation

Second choice:

Non-invasive ventilation with positive airway pressure

* good mask seal

* negative-pressure room



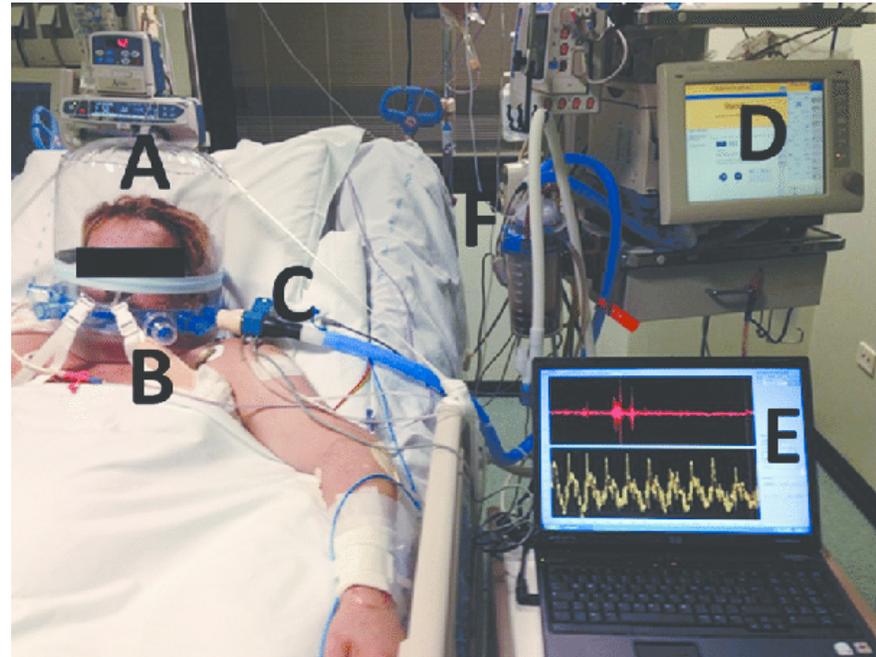
The patient with COVID-19 and hypoxemia:

- Consider proning therapy:



The patient with COVID-19 and hypoxemia:

- Non-invasive ventilation with positive airway pressure
- Helmet ventilation



The patient with COVID-19 and hypoxemia:

Mechanical ventilation:

- Rapid progression
- No improvement on HFNC > 50L/minute + FIO₂ 60%
- Increased PaCO₂
- Hemodynamic instability

Management:

ARDSnet low-tidal volume, PEEP, targeting plateau pressure \leq 30 cm H₂O

An overview of corticosteroids in COVID-19

- Initial recommendation: NEVER
- Surviving Sepsis Campaign:

Use in mechanically ventilated patients with ARDS (consensus based on weak data)

Kolleikas et al.

6 patients with COVID-19 and hyperinflammatory syndrome + ARDS:
Methylprednisolone 125 mg IV daily at least 8 days into symptoms:
100% clinical improvement, no intubations

An overview of corticosteroids in COVID-19

So et al.

- 7 patients with COVID-19 on mechanical ventilation
- Methylprednisolone 500 mg or 1000 mg upon intubation, daily x 3, then 1 mg/kg with downward taper
- 100% survival

Yuan et al.

- 132 patients with non-severe COVID-19 (retrospectively analyzed, 74 received steroids, 58 did not)
- Methylprednisolone 40-60 mg daily for ~ 11 days
- No difference in outcome, with suggested morbidity for patients who received steroids

An overview of corticosteroids in COVID-19

The RECOVERY trial:

- Randomized hospitalized patients to usual care (n=4321) versus dexamethasone 6 mg daily x 10 days (n=2104)
- Primary outcome was mortality at 28 days

Results:

Dexamethasone = 21.6% mortality

Usual care = 24.6% mortality (p<0.001)

Subgroups pre-specified by degree of respiratory support:

Mechanical ventilation: 29% vs 40% (NNT = 8 patients)

Oxygen requirement (SpO₂<92%): 21.5% vs 25% (NNT = 25 patients)

No oxygen requirement: 17% vs 13.2% (No benefit)

An overview of corticosteroids in COVID-19

Comments and concerns:

- In RECOVERY trial, baseline mortality in UK ICU was much higher than expected
- Patients on steroids, diabetics, were not studied
- Timeline of treatment not always standardized
- Steroids delay viral clearance
- Peer review not yet done on this study
- Should steroids with low mineralocorticoid activity be used?
- If viral replication peaks in week 2 of illness, what is optimal timing of steroid administration?

Summary:

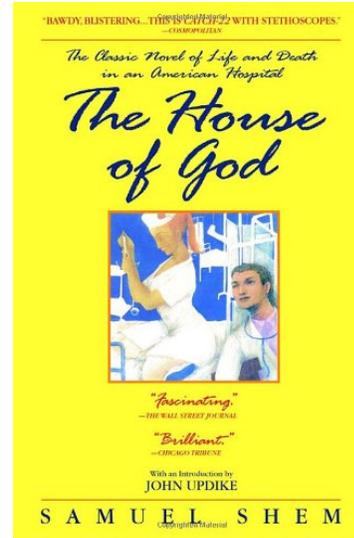
1. Respiratory infection with COVID-19 can be reduced or eliminated by interrupting bio-aerosol transmission in 3 phases:
 - Reducing the release of virus at the source
 - Impending pathogen transportation
 - Protecting susceptible persons

Summary:

2. The common agreement on treatment of respiratory failure is:
 - Oxygen to provide SpO₂ target of 90-96%
 - If low-flow oxygen ($\leq 6\text{L/minute}$) is not sufficient, non-invasive methods should be tried first rather than immediate intubation
 - HFNC delivery is preferable to NIV

Summary:

3. Steroids might help...



Patients with COVID-19 and hypoxemic respiratory failure are most likely to respond favorably to corticosteroids. Extensive literature review for determination of appropriate timing and patient selection is needed

References

- Koliekas L et al.: ORCID iD:0000-0002-4420-609X, 2020
- So et al.: Respir Case Rep 8(6):2020 e00596
- Yuan M et al.: Shock 2020 (June 2)
- Dhand et al.: Am J Respir Crit Care Med 10.1164, June 16 2020
- RECOVERY Collaborative Group:
<https://doi.org> June 22, 2020

Patient Case Presentation

Megan Dunay, MD, MPH

Geriatrician, Boise VA and Medical Director for Geriatrics and Extended Care for VA Pacific Northwest Region

Patient Case, Ms. Ada

- 44yo F with hx of mild intermittent asthma (using albuterol MDI once every couple of weeks at baseline) and GERD (taking famotidine PRN) admitted to acute care hospital with COVID after attending a wedding last weekend.
- On admit:
 - SpO2 85% on RA, up to 92% on 3L O2 via NC. All other VS stable.
 - CV: RRR no murmur, no edema, normal distal pulses
 - Lungs: Crackles throughout bilateral bases, occasional wheeze
 - Abd: benign
 - Neuro: non-focal

Ms. Ada

- Admit Imaging: CXR with groundglass opacities B and hazy retrocardiac opacity
- Admit Labs:
 - WBC 3.2, Hgb/HCT: 14/56
 - BUN 32/Cr 1.21
 - CRP: 2.1, ESR 42
 - Lactate 2.9
 - Blood cultures ordered; Urine antigens ordered
 - *COVID swab + 48 hours prior to admission – obtained by PCP*

Ms. Ada

- Admitted to stepdown unit, negative pressure room
 - Started on Remdesivir
 - Able to use albuterol MDI q 2hrs
 - Overnight does ok, sats hold at 94% on 5L NC
- Hospital Day 1:
 - SpO2 progressively worsens: requiring 10L NC to maintain sats
 - Temp increases to 100.4
 - HR increases to low 100's
 - Rapid Response Called:
 - Exam notable for tachycardia, respiratory distress, pronounce wheezes and coarse crackles
 - ABG: pH 7.55/PCO₂ 30/PO₂ 63/HCO₃⁻ 22
 - CXR: groundglass opacities persist, diffuse patchy opacities present now too, mostly at periphery

Ms. Ada

- How do we adequately oxygenate this patient?
 - Is there a role for non-invasive ventilation?
 - How do we know when to intubate?
 - How should ventilator settings be managed?
- What pharmacologic agents should we consider in treating this patient?
 - Steroids?
 - Antimicrobials?
 - Albuterol, ipratropium? By what means? Nebulizers?
- What is the natural history of this patient's condition?
 - What should we be counseling family to expect?
 - What complications should we watch for?
 - What is the real mortality risk in someone like this?

JOIN US FOR OUR NEXT SESSION!

For information, please visit uidaho.edu/echo

- Tuesday, July 21 at noon MT

Ongoing Resource List

RESOURCES FROM TODAY'S SESSION AND PAST SESSIONS CAN BE FOUND IN OUR ONGOING RESOURCE LIST.

<https://iecho.unm.edu/sites/uidaho/download.hns?i=440>