ACG Virtual Grand Rounds
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Week 5: Refractory GERD: New Options for Treatment 2020
Philip O. Katz, MD, MACG
April 29, 2020 at Noon EDT

Week 6: Celiac Disease: 10 Things Every Clinician Should Know
Amy S. Oxentenko, MD, FACG
April 30, 2020 at Noon EDT

Visit gi.org/ACGVGR to Register

Participating in the Webinar
Listen using your computer audio.
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All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

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ACG will send a link to a CME & ABIM MOC evaluation to all attendees on the live webinar.

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Disclosures:

Moderators:
Mark B. Pochapin, MD, FACG
David A. Greenwald, MD, FACG

Speakers:
Brian P. Bosworth, MD, FACG
Vivek Murthy, MD, FCCP
Katherine Hochman, MD, FHM
Ritu Agarwal, MD
Ira M. Jacobson, MD, FACG
Mark B. Pochapin, MD, FACG
David A. Greenwald, MD, FACG

According to ACCME guidance, because there are no current preventive or specific treatments for coronavirus infection, there are no relevant conflicts of interest for any speakers or moderators.
Our Panel of Experts

- Brian P. Bosworth, MD, FACG
  NYU Langone Medical Center
  Gastroenterologist
  Hospital Systems Gearing up for a Surge

- Vivek Murthy, MD, FCCP
  Montefiore Medical Center
  Pulmonologist
  Pulmonary Manifestations of COVID-19
  and Treatment Considerations

- Katherine Hochman, MD, FHM
  NYU Langone Health
  Internist
  Being an Internist and a Hospitalist for Patients with COVID-19

- Ritu Agarwal, MD
  Mount Sinai
  Hepatologist
  Liver Manifestations of COVID-19
  for the Gastroenterologist

- Ira M. Jacobson, MD, FACG
  NYU Langone Medical Center
  Hepatologist
  Clinical Trials for Managing COVID-19—In Use Now!

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The Tsunami Has Arrived
It Could Have Been Much Worse
Projected Needs for Hospital and ICU Beds in New York State - March 2020

Projected Needs for Hospital and ICU Beds in New York State - March 2020

It Could Have Been Much Worse

Social Distancing Appears to be Effective...

New York City COVID-19 Gearing Up for the Surge

Brian P. Bosworth, MD, FACP
ACG Governor, Manhattan
Chief of Medicine, NYU Langone Health Tisch Hospital
Professor of Medicine, NYU Grossman School of Medicine
Brian.Bosworth@nyulangone.org
Timeline of the current international outbreak

Mid-January, 2020: First case outside China (Thailand); family clusters reported. Airport screenings in U.S.

Late January, 2020: First cases in S. Korea, US. Reports of HCW infections in China. WHO decides against emergency declaration. Multiple cases in U.S, France, Canada.


January 31, 2020: CDC quarantines flight from China, declares public health emergency.


Early February, 2020: China with >20,000 cases.


Mid-February, 2020: Retrospective case finding -> total cases >60,000 in China. Cruise ship quarantines in place.

Late February, 2020: Marked increase in infections in S. Korea, Iran, Italy. Estimated case-fatality rate 2-3%. Additional countries affected. Shortage of testing capacity in U.S. Social distancing encouraged.


March 10, 2020: >10,000 in Italy. New Rochelle, NY “containment zone”.


March 14, 2020: France classifies most businesses. Travel restrictions in Germany, Spain. South Africa declares national state of disaster.

COVID-19 in NYC

US data: 629,264
New York State: 213,779
Guideline-Directed Management of Pulmonary Complications of COVID-19

Vivek Murthy, MD, FCCP
Assistant Professor of Medicine
Associate Director of Interventional Pulmonology and Bronchoscopy
Montefiore Medical Center, Albert Einstein College of Medicine
Respiratory Pathogenesis of SARS-CoV2 Infection

• The respiratory tract is a primary target of coronaviruses with type II pneumocytes as a focus
• ACE2 receptor, highly expressed on type II pneumocytes, site of viral entry
• Close proximity to rich capillary bed may enable rapid transmission
• Normal functions of type II pneumocytes are generation of surfactant and alveolar repair

Pathologic findings reported with SARS-CoV2 and MERS
• Diffuse alveolar damage
• Denuded bronchiolar epithelium
• Extensive hyaline membrane formation
• Type 2 pneumocyte hyperplasia
• Edematous alveolar septa with lymphocytic infiltrate
• ARDS

Risk factors for hypoxic respiratory failure (19%)
• Age >60 years
• Male gender
• +DM, malignancy, immunocompromised status
• Progression may be rapid, within 12-24 hours of onset
• Median time to developing ARDS 8-12 days
• Median time to mechanical ventilation 10.5-14.5 days
• Median time to VAP after intubation was 8 days
Support of Oxygenation/Ventilation in the Setting of SARS-CoV2 Infection

- Titrate SpO2 to a range between 92-96%.
  - Chu et al in a 2018 meta-analysis of 25 RCTs in 16,000 critically ill pts requiring supplemental O2, higher target SpO2 >96% associated with increased mortality without improvement in other outcomes.
  - In the DCO2 trial ARDS pts randomized to conservative (88-92%) vs liberal (96%) O2 arms—stopped early due to deaths in the conservative arm.

Support of Oxygenation/Ventilation in the Setting of SARS-CoV2 Infection

- Oxygen Therapy in ARDS
  - Death from any cause at 28 days: 34.3% conservative vs 26.5% liberal.
  - Difference: 7.8 percentage points, 95% CI -4.8 to 15.5.

Semple et al. 2020

Alhazzani, Møller, Arabi, Loeb, Gong, et al. CCM. 2020

American College of Gastroenterology
Support of Oxygenation/Ventilation in the Setting of SARS-CoV2 Infection

Adjusted for age, BMI, sex, SOFA score.


28,723 patients
8,564 patients

The Role of High Flow Nasal Cannula

HFNC: May reduce # of intubations, probably doesn’t reduce mortality or hospital LOS, probably doesn’t increase risk of transmitting SARS-CoV2 significantly.

Rochwerg et al, in a meta-analysis of 9 RCTs (2093 pts) found in patients randomized to HFNC vs NC:

- RR for intubation was 0.85 (95% CI 0.74–0.99)
- RR for mortality was 0.94 (95% CI 0.67–1.31)

In an analysis of HCW transmission in the 2003 Toronto SARS-CoV outbreak, HFNC was noted to be associated with increased risk of transmission, however NIPPV and other activities were.

The Role of Non-Invasive Positive Pressure Ventilation ("CPAP" or "BiPap")

NIPPV: Avoid BiPap as much as possible unless the patient’s underlying comorbidities (e.g. COPD) strongly favor its use.

Extrapolating from data on 302 critically ill MERS pts, 92% of patients initiated on NIPPV ultimately required endotracheal intubation with no difference in mortality or ICU LOS.

In a meta-analysis of 1384 patients in 8 RCTs looking at HFNC vs NC or NIPPV prior to consideration of mechanical ventilation, both were inferior to HFNC.

- OR for requiring intubation 0.48 for HFNC vs NIPPV (CI 0.31–0.73, p<0.0006)
- OR for ICU mortality 0.35 for HFNC vs NIPPV (CI 0.21–0.59, p<0.0001)
The Role of Non-Invasive Positive Pressure Ventilation ("CPAP" or "BiPap")

- Significant concern regarding the risk of aerosolization of SARS-CoV2 with NIPPV compared to other modalities
- Odds ratio for "super-spreading" nosocomial infection events in the 2003 SARS-CoV outbreak (case-control study of 86 SARS wards at 21 hospitals in China):
  - NIPPV, OR 11.8 (95% CI 1.92-70.8, p=0.007)
  - Minimum distance between beds <1 meter, OR 6.38 (95% CI 1.68-28.75, p=0.006)
  - Performing CPR, OR 3.81 (95% CI 1.04-13.87, p=0.04)

Management Schematic for Respiratory Failure in COVID-19 Infection

- NIPPV – Non-invasive positive pressure ventilation (CPAP/BiPAP)
- HFNC – High flow nasal cannula
- NMBA – Neuromuscular blockade (e.g. cisatracurium)
Modalities of Oxygen Therapy

• Nasal cannula: 24-44% \(\text{FiO}_2\)
• Each "liter" is ~4% above 20% (1L is 24%, 2L 28%, 3L 32%, 4L 36%, 5L 40%)
• Use cautiously in patients with hypercapnia as it can mask/worsen hyperventilation
• Wean aggressively as long as \(\text{SpO}_2 > 92\%\)

• Venturi mask: 10-50% \(\text{FiO}_2\)
• Non-rebreather: 100% \(\text{FiO}_2\)
• High flow nasal cannula: 30-100% \(\text{FiO}_2\)
• Continuous positive airway pressure (CPAP)
• Bi-level positive airway pressure (BiPap)
• Mechanical ventilation

• A face mask step-up from NC, may be helpful in patients with hypoxia and mouth-breathing
• Similar caution in patients with hypercapnia
• The louder it is, the lower the \(\text{FiO}_2\) because it’s entraining more room air
• Non-rebreather: 100% \(\text{FiO}_2\)
• High flow nasal cannula: 30-100% \(\text{FiO}_2\)
• Continuous positive airway pressure (CPAP)
• Bi-level positive airway pressure (BiPap)
• Mechanical ventilation

• Mask of last resort; many patients with SARS-CoV-2 tolerate this and can be weaned prior to requiring intubation, but usually use of a non-rebreather as a ward patient a sign they are failing
• Set the wall flow rate to >12LPM; if the reservoir is empty, can’t guarantee \(\text{FiO}_2\) is 100%
• High flow nasal cannula: 30-100% \(\text{FiO}_2\)
• Continuous positive airway pressure (CPAP)
• Bi-level positive airway pressure (BiPap)
• Mechanical ventilation

American College of Gastroenterology
Modalities of Oxygen Therapy

- Nasal cannula: 24-44% FiO₂
- Venturi mask: 35-50% FiO₂
- Non-rebreather: 100% FiO₂
- High flow nasal cannula: 30-100% FiO₂
  - You set a flow rate (20-40 L/min) and an FiO₂ (30-100%)
  - Delivers warmed, humidified air (try to avoid humidification in SARS-CoV2, but in IPC is okay without)
  - Provides a small but helpful amount of PEEP
  - Supports ventilation to a very limited degree (↓ CO₂ in the anatomic dead space)
- Continuous positive airway pressure (CPAP)
- Bi-level positive airway pressure (BiPap)
- Mechanical ventilation

- Continuous positive airway pressure (CPAP)
- Bi-level positive airway pressure (BiPap or “S/T Mode”)
  - You set a PEEP (inspiratory pressure), FiO₂, and can be given by nasal or full face masks
  - Ideal for hypercapnic patients (not acute or chronic)
  - For acute indications requires close titration by blood gas (if not very hypoxic, VBG is fine)
  - The difference between iPAP and ePAP is the gradient for ventilatory support; a bigger gradient means more support to offload CO₂
  - iPAP should range 5-30, ePAP 5-15, 10/5 and 30% is a good place to start
  - Be cautious using CPAP or BiPap in a patient with very impaired mental status as the risk of aspiration is high
Medical Therapies for COVID-19 Infection

There are no definite effective therapies for SARS-CoV2 infection, but several classes of medication are being investigated:

- **Antiviral agents** (remdesivir, lopinavir+ritonavir)
- **Hydroxychloroquine/chloroquine**
- **Immunomodulators**
- **Anti-Il-6** (sarilumab, tocilizumab)
- **Anti-Il-1** (anakinra)
- **Corticosteroids**
- **Anticoagulation**
- **Antibiotics** (secondary bacterial infection)
- **Convalescent plasma**

Basic Approach to the Hypoxic SARS-CoV2 Patient

- On arrival, check a chest x-ray, EKG, ABG; avoid CT Chest if possible unless another dx is suspected
- Consider secondary bacterial pneumonia if worsening and start empiric antibiotics
- Maintain on minimum supplemental O2 to maintain SpO2 92-96%
- Escalate to HPNC if possible before using a non-rebreather (reasonable to touch base with Pulm/CC at this point); avoid CPAP/BiPAP unless there is a very specific indication
- If underlying COPD/Asthma, use metered dose inhalers rather than nebulizer therapy
- If on mechanical ventilation, consider daily ABG to aid in titration, though if tidal volume/rate are stable and the patient is overall improving, could also just wean FiO2/PEEP by 1%
- If in distress on oxygen therapy (lethargic/tachypneic), check an ABG and consider PE

To access a PDF of the SCCM Guidelines Statement for managing COVID-19, please use the QR code above.
A HOSPITALIST'S APPROACH TO A COVID-19 PATIENT

Katherine Hochman, MD
April 17, 2020

Getting Started

- Practice donning and doffing your PPE
- Get FIT tested (shave your beard!)
- Know how to mine your EMR
- Eat a big breakfast
- Your phone is contaminated! Use a plastic bag.
- Put N95 on tight but not too tight (avoid a HAPI)
- Get to know your team, especially the respiratory therapists (as proring in now standard), physical therapists
- Practice self-kindness ... it's going to be tough
Getting Started: Know How to Mine Your EMR

INFLAMMATORY MARKERS

COVID-directed therapy

A Snapshot of the NYC Experience

Who gets hospitalized? Who gets intubated?

**STRONGEST HOSPITALIZATION RISKS:**
- Age
  - >75 years (OR = 66.8)
  - 65-74 years (OR = 10.8)
- Obesity
  - BMI > 40 (OR = 6.2)

**STRONGEST CRITICAL ILLNESS RISKS:**
- Admission O2 sat < 88% (OR = 6.9)
- First d-dimer > 1500 (OR = 6.9)
- First Ferritin > 2500 (OR = 6.9)
- First CRP > 200 (OR = 5.78)
Who gets hospitalized? Who gets intubated?

**DECISION TREE ANALYSIS FOR HOSPITALIZATION:**
- Age >65 years
- Obesity

**DECISION TREE ANALYSIS FOR CRITICAL ILLNESS:**
- Admission O2 sat ≤88%
- Procalcitonin > 0.5
- Troponin <0.1 (protective)
- Age > 65 years
- CRP > 200

Follow ACE2

- SARS-CoV2 gains entry via ACE2
- ACE2 present in:
  - Lung
  - Kidneys
  - Heart
  - Vascular epithelium
  - Brain
  - Gut/ Iber


COVID-19 COURSE OF INFECTION

Course of COVID-19 Infection

[Diagram showing the course of COVID-19 infection with stages: asymptomatic, mild, non-severe, severe, critical, and hospital/ICU admission.]

https://www.acep.org/content/covid-19-update/consult
COVID and the Kidneys

NORMAL

Angiotensinogen

Renin

Angiotensin I

ACE

Angiotensin II

ACE2

Aldosterone

COVID

Angiotensinogen

Renin

Angiotensin I

ACE

Angiotensin II (vasoconstriction)

ACE2

Aldosterone (K+ wasting)

COVID and the Kidneys

PREVALENCE

- AKI: 15-27% (independent RF in mortality)
- PROTEINURIA: 44%
- HEMATURIA: 27%
- HYPOKALEMIA: 62%

CLINICAL PEARLS

- AGGRESSIVE POTASSIUM REPLACEMENT (up to 3 grams/day for severe hypokalemia)
- END OF URINARY K+ LOSS PORTENDS GOOD PROGNOSIS
- CRRT is a supportive measure

COVID and the Heart

PREVALENCE

- 7-28% troponinemia
- 22% of ICU patients showed cardiac injury
- Mortality = 51% cardiac injury vs 4.5% without cardiac injury

CLINICAL PEARLS

- 2 patterns of cardiac injury:
  - Non-cardiac symptoms: troponin tracks with inflammatory markers in cytokine storm
  - Cardiac symptoms (palpitations/chest pain): viral myocarditis/arrhythmias, ST elevations, low EF
  - EKG on admission (useful for QTC interval)
  - Mild troponin elevation – no cardiac imaging
  - Standard heart failure, arrhythmia therapy
  - No change in ACEi/ARB management
COVID and the Blood

**PRESENTATION**
- WBC 4.7
- ALB < 1.5 (83% of patients lymphopenic)
- ALB < 700 patients in ICU
- NLR (neutrophil-lymphocyte ratio)
  - < 3.13 = 10% severe
  - > 3.13 = 5% severe disease

**CLINICAL PEARLS**
- Patients are very hypercoaguable and should be anticoagulated
- Not classic DIC picture (high d-dimers and fibrinogen but mild thrombocytopenia).

COVID and the Nervous System

**PREVALENCE**
- 36.4% neurological symptoms
  - CNS (dizziness - 17%, headache - 13%, AMS - 7%, stroke - 6%)
  - PNS (taste impairment - 6%, smell impairment - 5%)
- Skeletal muscle injury/ muscle pain and CPK >200 - 10%
- Severe COVID patients are more likely to have neurologic symptoms (45.5% vs. 32.5%)

**CLINICAL PEARLS**
- Covid patients with neurologic symptoms often lack typical cough and fever
- Many patients come in with syncope as a presenting symptom + autonomic instability

*Note:* This page contains images of presentations or slides, not natural text. The content is transcribed as text for readability.
SUMMARY RECOMMENDATIONS

- THE CARE OF THE COVID PATIENT IS LARGELY SUPPORTIVE
- SILENT HYPOXIA IS REAL (patients don’t realize that they are hypoxic)
- PATIENTS CAN DECLINE VERY RAPIDLY WITH NO WARNING
- Get a health care proxy signed on admission/ involve palliative care early
- Prone whenever possible
- Don’t forget about patient’s diet order (or your diet!)
- Patients are terrified and lonely
- Make sure to speak with families

Evaluation of Abnormal Liver Enzymes in COVID-19 Patients

Ritu Agarwal, MD
Assistant Professor of Medicine
Director, Liver Fellows’ Practice
Division of Liver Diseases
Icahn School of Medicine at Mount Sinai

Background

- ACE-2 is a molecular target for SARS-COV-2
- ACE-2 receptors occur on liver and biliary epithelial cells
- Elevated liver enzymes are fairly common in hospitalized COVID-19 patients: 14-53%
- Liver injury in mild COVID-19 patients is typically transient and resolves with supportive care
- Seldom have liver failure
- Liver injury is more common in severe than in mild COVID-19 patients
Explanation of Liver Injury

Remains Unclear

- Indication of underlying pre-existing liver disease
- Direct Virus Induced Effect
- Immune Inflammatory Response to the Virus
- Could DILI be present as well

Evaluation of Elevated Liver Enzymes in COVID-19

Mostly Hepatocellular Injury
- Mild-moderate elevated AST, ALT, elevated LDH, ferritin
- Mildly elevated or normal bilirubin
- Elevated AST>ALT common sources outside liver (e.g. myositis)
- Low serum albumin is a marker of COVID severity

Might be reflective of:
- Drug Induced Liver Injury
- Cytokine Release
- Ischemia and Congestion
- Myositis

Liver Pathology

- Limited Reports
- Nonspecific
- Microvesicular steatosis
- Mixed mild lobular and portal activity
Evaluation of Elevated Liver Enzymes in COVID-19

History
• Alcohol: How many drinks per day and last drink? History of withdrawal?
• Medications
  - Home medications
  - Specific to COVID:
    - Acetaminophen use at home (Dose and Duration)
    - Herbal medications at home
    - Antibiotics (Azithromycin, Augmentin, Cephalosphorins)
    - Vitamins

Speak to family and household members

Workup Recommendation

Follow Daily:
Hepatic Function Panel including Total and Direct Bilirubin
PT

Limit Ultrasound and MRI:
Unless high suspicion of biliary obstruction OR thrombus

COVID-19 patient with elevated liver enzymes

AST and ALT < x5ULN (200 IU/L)

Viral Hepatitis Screening:
HAV IgM
Hep B sAg
Hep B core IgM
Hep B surface Ab
Hep C Ab

Acetaminophen
CK, BNP
INR,
Fibrinogen

Quantitative IgG

AST and ALT > x5ULN (200 IU/L)

Viral Hepatitis Screening:
HAV IgM
Hep B sAg
Hep B core IgM
Hep B core IgG
Hep B surface Ab
Hep C Ab

AMS
Phosphatidylethanol (Phet)
Acetaminophen
CK, BNP
INR,
Fibrinogen

Quantitative IgG

Treatment-Drug Induced Liver Injury

Medication Function Liver Injury TotalInclusion
Hydroxychloroquine Aminoglycoside Anti-malarial Low likelihood of cause Non-steroidal (rare)
Azithromycin Macrolide Anti-malarial Well known cause of liver injury
Cephalosphorins Bactericidal Antibiotic Cholestatic
Remdesivir Nucleotide Analogue Hepatocellular
Tocilizumab IL-6 Inhibitor Mild hepatocellular
Sarilumab IL-6 Inhibitor Mild hepatocellular
Statins HMG-CoA reductase inhibitor Mild - Moderate hepatocellular

Livertox https://www.ncbi.nlm.nih.gov/books/NBK547852/
COVID-19 in Patients with Chronic Liver Disease

- No evidence that patients with stable chronic HBV, HCV, PBC, PSC, NAFLD have increased susceptibility to SARS-CoV-2
- NAFLD/NASH patients have comorbidities (DM, HTN, Obesity) increased risk of severe COVID-19
- Continue treatment for hepatitis B or C
- Continue surveillance for HCC (cirrhosis and HBV) as close to intervals as possible.
  - Arbitrary 2 month delay reasonable. Review reason for delay with patient.
  - Emphasize immunization for Streptococcus pneumoniae and Influenza

HCV-Medication Interactions

- Interactions with Experimental COVID-19 Therapies

COVID-19 Immunosuppression

- Effects of immunosuppression remain unclear
- Immunosuppression possibly protective from the reactive immune response
- Age and metabolic comorbidities (Obesity, HTN, DM) in post transplant patients might be associated with increased risk of severe COVID-19 disease
Patients with Chronic Liver Disease and COVID-19

Immunosuppression

- In immunosuppressed patients without COVID-19
  - Do not make anticipatory adjustments to immunosuppression
- In immunosuppressed liver patients with COVID-19
  - Consider minimizing high dose prednisone
  - Consider reducing azathioprine or mycophenolate or calcineurin inhibitor doses
  - Individual decision based on severity of COVID-19, graft history, timing post transplant
  - Consult transplant hepatology colleagues
- Initiate immunosuppression in patients with or without COVID-19 who have strong indications for treatment (autoimmune hepatitis, graft rejection)
- In patients with COVID-19 use prednisone or immunosuppression cautiously when benefit might be outweighed by risks (alcohol hepatitis)

Immunosuppressants- COVID-19 Therapies

Management Conclusion

- Limit acetaminophen < 2 grams daily
- Careful history from patient and family for alcohol and home medications
- COVID-19 liver injury is typically hepatocellular, transient and mild
- Mechanism of injury unclear
- Consider Drug Induced Liver Injury and extra hepatic sources of injury
- Continue immunosuppression when appropriate but consider dose reduction in patients with severe COVID-19
SARS-CoV-2 Life Cycle

- Spike protein on the virus binds to ACE2, a cell-surface protein, to enter the cell.
- Mpro, also known as 3CL protease, cleaves the S protein.
- Cleaved S protein binds to ACE2.
- New SARS-CoV-2 replicates itself in the cells of those infected.

Potential Therapeutic Targets in COVID-19

- Remdesivir: An adenosine analog that inhibits viral RNA-dependent RNA polymerase (RdRp).
- Single phosphate group
- Addition of two phosphate groups
- Remdesivir
- ATP
- RDV/TP

Remdesivir: A Nucleotide Prodrug

- Adenosine analog
- Single phosphate group
- Cleavage and addition of two phosphate groups
- Remdesivir
- ATP
- RDV/TP

Background on Remdesivir

• Inhibits RNA-dependent RNA polymerase activity among a diverse group of RNA viruses including filoviruses (e.g. Ebola, Sudan, Marburg), paramyxoviruses (e.g. RSV, Nipah, Hendra) and pathogenic coronaviruses

• Nonhuman primates: therapeutic efficacy of remdesivir against Ebola virus but survival inferior to monoclonal antibodies in PALM study (NEJM 2019)

• Activity against SARS-CoV and/or MERS-CoV in mouse infection models, non-human primates, and human airway epithelial cell assays

• Cell culture studies show potent SARS-CoV-2 suppression at micromolar level

Antiviral activities of Test Drugs Against 2019-nCoV in Vitro

Compassionate Use of Remdesivir for COVID-19

• 61 patients, 53 with analyzable data
• 30/53 (57%) on mechanical ventilation
• 4/53 (8%) receiving ECMO
• Median follow-up 18 days
  • 36/53 (68%) had improvement in oxygen-support class
  • 17/53 (32%) receiving mechanical ventilation were extubated
  • 25/53 (47%) were discharged
  • 7/53 (13%) deaths
  • 6/34 (18%) receiving invasive ventilation died vs 1/19 (5%)
Compassionate Use of Remdesivir for COVID-19

Authors pointed out:
- 28 day mortality 22% in lopinavir/ritonavir trial: only 1/189 were on ventilation
- 66% mortality in 44/67 on mechanical ventilation in Wuhan, China
- Need randomized trials acknowledged: large studies in progress

An “Early Peek” at Remdesivir Data From a Compassionate Use (Uncontrolled) Study From a US University Center

- 113 “severe” patients given remdesivir
  - “Most discharged”
  - “2 deaths”
  - Patient quoted: “It was a miracle”

Critical to get data from ongoing randomized trials
- If effective: Optimal timing of drug remains to be defined, as does potential drug supply, to determine range of patients who should be treated

Clinical Trials With Hydroxychloroquine

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of Study</th>
<th>n</th>
<th>Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xu et al.</td>
<td>Consecutive series</td>
<td>26</td>
<td>• 50% of patients were discharged at day 13 with remdesivir therapy.</td>
</tr>
<tr>
<td>Chen et al.</td>
<td>Randomized</td>
<td>43</td>
<td>• Remdesivir therapy significantly decreased time to viral clearance (2.3 vs. 3.5 days).</td>
</tr>
<tr>
<td>Chen et al.</td>
<td>Randomized</td>
<td>43</td>
<td>• Remdesivir therapy significantly decreased time to viral clearance (2.3 vs. 3.5 days).</td>
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<tr>
<td>Molina et al.</td>
<td>Randomized series</td>
<td>22</td>
<td>• Remdesivir therapy significantly decreased time to viral clearance (2.3 vs. 3.5 days).</td>
</tr>
<tr>
<td>Malherbe et al.</td>
<td>Randomized international</td>
<td>80</td>
<td>• Remdesivir therapy significantly decreased time to viral clearance (2.3 vs. 3.5 days).</td>
</tr>
</tbody>
</table>

A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19


N=199 randomized patients

IL‐6R or IL‐6 Monoclonal Antibodies in US Trials

IL‐6 Receptor Antibody

- Tocilizumab
- Sarilumab
- Clazakinumab

Favorable case series in China
Approved in China
Several approvals in US

Approved for RA in US

Convalescent Plasma for COVID‐19: Early Study

- 5 patients with ARDS and continuously high viral load
- SARS‐Cov‐2 binding titer > 1:1000 and neutralization titer > 40: all on mechanical ventilation
- Body temperature resolved within 3 days in 4
- Viral load negative 12 days after transfusion in all
- ARDS resolved by 12 days in 4
- 3 weaned off ventilator by end of week 2
- 3 discharged (>50 days) and 2 stable

Chen C et al. JAMA 2020
Investigative Agents for COVID-19 (Not All-Inclusive)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Company</th>
<th>Mechanism</th>
<th>Approved</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Remdesivir</td>
<td>Gilead</td>
<td>Nucleotide inhibitor</td>
<td>RA, SCA, juvenile arthritis, C57r/G6</td>
<td>None (studied for Ebola)</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>Roche</td>
<td>IL-6R inhibitor (mAb)</td>
<td>RA, SLE, Juvenile arthritis, CRS w/ CAR-T</td>
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</tr>
<tr>
<td>Sarilumab</td>
<td>Regeneron</td>
<td>IL-6R inhibitor (mAb)</td>
<td>RA</td>
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<tr>
<td>Clazakinumab</td>
<td>Vitaeris</td>
<td>IL-6R inhibitor (mAb)</td>
<td>None</td>
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</tr>
<tr>
<td>Tocilizumab</td>
<td>Sanofi-Aventis</td>
<td>None</td>
<td>None</td>
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</tr>
<tr>
<td>Hydroxychloroquine + Azithromycin</td>
<td>Sanofi-Aventis</td>
<td>Nucleotide inhibitor (Antiviral)</td>
<td>RA</td>
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<tr>
<td>Hydrazoles</td>
<td>None</td>
<td>3-nitroanilide, receptor antagonism, acidification of endosomes</td>
<td>RA, S44</td>
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<tr>
<td>Tocilizumab</td>
<td>Roche</td>
<td>IL-6R inhibitor (mAb)</td>
<td>RA, SLE, Juvenile arthritis, C57r/G6</td>
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<tr>
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<td>Regeneron</td>
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<td>None</td>
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</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>Generic</td>
<td>None</td>
<td>None</td>
<td></td>
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<td>Generic</td>
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HCV

- RNA virus (Flavivirus)
- Non-ionotropic
- Parenteral transmission
- Chronicity common
- Genotypes: clinical differentiator
- End stage disease takes years
- Slow evolution from nonspecific to specifically targeted direct-acting antiviral agents (DAA)
- Viral clearance was pivotal goal
- Resistance maintained until 2nd gen drugs
- No vaccine after 30 years

SARS-CoV2

- RNA virus (coronavirus)
- Zoonotic (“jump” from animals to humans)
- Respiratory droplet (airborne?), highly transmissible
- Does chronicity exist? (?)
- Genotypic variation: any clinical implications?
- End stage disease takes days
- Controversy about whether nonspecific Rx will work: immuno-modulatory or antiviral or both?
- Trials endpoints achieved quickly
- Success will be measured by viral suppression
- Resistance may not matter: short course, nucleotide (?), viral suppression may be enough
- Vaccine desperately needed

American College of Gastroenterology
Preparation

- Encourage your hospital or lab to scale up COVID-19 testing now
- Conserve PPE
- If possible, obtain N95s or equivalent
- Break down all procedures into elective, semi-elective, urgent

Procedure Classification

<table>
<thead>
<tr>
<th>Elective (Delay)</th>
<th>Semi-Elective (Perform)</th>
<th>Urgent (Perform)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening or surveillance endoscopy</td>
<td>Severe iron deficiency anemia and suspected GI source</td>
<td>Upper and Lower GI bleeding</td>
</tr>
<tr>
<td>- Screening or surveillance EGD in a patient with asymptomatic upper GI disease</td>
<td>- Significant weight loss - EGD</td>
<td>- Dysphagia impacting oral intake</td>
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<tr>
<td>- Evaluation of non-urgent symptoms, such as vague abdominal pain, nausea, GI bleeding, or other symptoms</td>
<td>- Placement - EUS/staging for malignancy - Pouches removal</td>
<td>- Cholangitis</td>
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<tr>
<td>- Non-urgent endoscopic procedures</td>
<td>- Endoscopic cyst or small submucosal lesions</td>
<td>- Symptomatic pancreaticobiliary disease</td>
</tr>
<tr>
<td>All motility procedures (esophageal/perianal manometry, jejunal)</td>
<td>- All motility procedures (esophageal/perianal manometry, jejunal)</td>
<td>- Palliation of GI obstruction</td>
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<tr>
<td>- Severe alarm symptoms</td>
<td>- EUS for pancreatic cyst or small submucosal lesions</td>
<td>- Any significant upper/lower GI symptom that will aid in diagnosis/management of suspected disease that the patient and physician believe cannot wait 3 months to evaluate</td>
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<td>- Upper and Lower GI bleeding</td>
<td>- Placement - EUS/staging for malignancy - Pouches removal</td>
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Waves of Deployment

| Wave 1 ICU | Critical care trained physicians currently not practicing in ICUs and non-medical ICU intensivists (Pulmonologists trained in critical care, Anesthesiologists trained in critical care, Cardiologists who cover the CCU, Surgeons who cover the surgical ICU) |
| Wave 2 ICU | Young physicians and volunteer senior fellows who receive additional training in ICU procedures and ventilator management. These physicians are board certified in Internal medicine and just a few years out from their ICU experience as residents. |
| Wave 3 ICU | Hospitalists who received additional ICU training |
| Wave 4 Medical Floors | Internists and subspecialists (gastroenterologists) who will act as medical attendings to backfill the vacant hospitalist positions. |
Two Tiers of the COVID Army

- Medical Attending
  - Acting as a hospitalist
  - Interns, resident, APPs
  - Responsible for overall medical management and clinical decisions
  - 12-15 patients
  - Internal medicine trained (often subspecialist)
- Supplemental medical attendings (Super Residents)
  - Part of a team of other supplemental medical attendings and housestaff
  - Overseen by a hospitalist
  - Average of 5 patients
  - Surgeons, Ophthalmologists, Dermatologists, OB/GYN

Other COVID-19 Tips:

- Uniform communication messaging wherever possible with staff and patients
- Plan for limited reopening of ASCs/Offices once the number of new cases begins to decline (May / June?)
  - Bring in the Semi-urgent patients first
- Self-monitoring for symptoms—test or retest for ANY symptoms
  - Test all doctors, nurses and other staff who are planning on working with patients
- Recognizing stress/anxiety for patients, staff, and MDs
  - Exacerbation of underlying anxiety and mental illness—all ramped up by severe limitations on “usual” activities
  - Uncertainty how long this will last
  - It is a marathon without knowing where the finish line is

Visit ACG’s COVID-19 Resource Page
www.gi.org/COVID19
How to Receive CME and ABIM MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR
ACG will send a link to a CME & ABIM MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2020 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2021 for this activity.

ACG will submit MOC points on the first of each month. Please allow 3-5 business days for your MOC credit to appear on your ABIM account.
ABIM MOC QUESTION

If you plan to claim ABIM MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.

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