Antimicrobial Steward Call
April 14, 2020
Tennessee Department of Health
Healthcare Associated Infections and Antimicrobial Resistance Program
Adobe Connect Housekeeping

- All lines have been muted
- Press *6 to unmute your line
- Also can use the chat box to ask questions/comment
Announcements
TDH AU Point Prevalence Survey

- Deadline for Q1 data will be April 30, 2020
Reminder: NHSN AU Reporting Deadlines

- Bed size of >250 – First month submitted by **January 1, 2021**
  - Outreach to non-reporters this Spring
  - Effects of COVID Pandemic

- Bed size between 100–250 – First month submitted by **January 1, 2022**

- Bed size of < 100 and Critical Access Hospitals – First month submitted by **January 1, 2023**
Novel Coronavirus Update and TDH Response
First...a disclaimer

- There are NO antiviral drugs proven to work against COVID-19 in humans
  - RCT ongoing
- There are no drugs currently approved by the FDA to prevent or treat COVID-19
Hydroxychloroquine and Chloroquine

- Increases endosomal pH of virus and interferes with glycosylation of cellular receptors
- In vitro studies show activity at both entry and post-entry stages of infection
- FDA issued Emergency Use Authorization for use against COVID-19 on March 28
- Liver, ocular, and cardiac toxicity
  - Prolongs QT interval
  - HCQ probably better tolerated
Comparison of HCQ + Azithro vs. HCQ along vs. Control

TWENTY patients showed significant reduction in viral carriage at day 6.
Results

• Viral “Eradication” Rates at Day 6:
  – HCQ + Azithro – 6/6 (100%)
  – HCQ along – 8/14 (57%)
  – Control – 2/16 (13%)

• Study started with 26 patients in HCQ and 16 controls
  – Six patients not evaluable at day 6
    • 3 transferred to ICU while still PCR positive
    • 1 died (PCR negative)
    • 1 left the hospital (PCR negative)
    • 1 withdrew due to nausea (PCR positive)

https://doi.org/10.1016/j.ijantimicag.2020.105949
Jason Pogue’s Twitter Account:
https://twitter.com/jpogue1/status/1241138975802359813
Statement from ISAC

Statement on IJAA paper

Official Statement from International Society of Antimicrobial Chemotherapy (ISAC)

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial (Gautret P et al. PMID 32205204)

ISAC shares the concerns regarding the above article published recently in the International Journal of Antimicrobial Agents (IJAA). The ISAC Board believes the article does not meet the Society’s expected standard, especially relating to the lack of better explanations of the inclusion criteria and the triage of patients to ensure patient safety.

Despite some suggestions online as to the reliability of the article’s peer review process, the process did adhere to the industry’s peer review rules. Given his role as Editor in Chief of this journal, Jean-Marc Rolain had no involvement in the peer review of the manuscript and has no access to information regarding its peer review. Full responsibility for the manuscript’s peer review process was delegated to an Associate Editor.

Although ISAC recognises it is important to help the scientific community by publishing new data fast, this cannot be at the cost of reducing scientific scrutiny and best practices. Both Editors in Chief of our journals (IJAA and Journal of Global Antimicrobial Resistance) are in full agreement.

Andreas Voss
ISAC President

HCQ – Randomized Controlled Trial

- 62 patients randomized to either HCQ 400mg/day x5d + SOC vs. SOC alone

- Endpoints at day 5
  - Time to clinical recovery
  - Clinical characteristics
  - Radiological results

- Shorter time to clinical resolution of symptoms

- Not Peer Reviewed

doi: https://doi.org/10.1101/2020.03.22.20040758
Results

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All</th>
<th>Control</th>
<th>HCQ</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases, n</td>
<td>62</td>
<td>31</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>44.7 (15.3)</td>
<td>45.2 (14.7)</td>
<td>44.1 (16.1)</td>
<td>0.8809</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.7991</td>
</tr>
<tr>
<td>Male</td>
<td>29 (46.8%)</td>
<td>15 (48.3%)</td>
<td>14 (45.2%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>33 (53.2%)</td>
<td>16 (51.7%)</td>
<td>17 (54.9%)</td>
<td></td>
</tr>
<tr>
<td>Fever, day (SD)</td>
<td>2.6 (1.0)</td>
<td>3.2 (1.3)</td>
<td>2.2 (0.4)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Cough, day (SD)</td>
<td>2.4 (1.3)</td>
<td>3.1 (1.5)</td>
<td>2.0 (0.2)</td>
<td>0.0016</td>
</tr>
<tr>
<td>Progressed to severe illness</td>
<td>4 (6.5%)</td>
<td>4 (12.9%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Adverse effects</td>
<td>2 (3.2%)</td>
<td>0</td>
<td>2 (6.4%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Characteristics of patients in this trial.

22 patients in the HCQ treatment group, 17 patients in the control group with a fever one day before the intervention. 22 patients in the HCQ treatment group, 15 patients in the control group with a cough one day before the intervention. Abbreviations: SD, standard deviation; HCQ, hydroxychloroquine; CT, computed tomography.

<table>
<thead>
<tr>
<th>Group</th>
<th>All</th>
<th>Exacerbated</th>
<th>Unchanged</th>
<th>Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
<td>Significant</td>
<td>Total</td>
</tr>
<tr>
<td>All</td>
<td>62</td>
<td>11 (17.7 %)</td>
<td>9 (14.5 %)</td>
<td>18 (29.0 %)</td>
</tr>
<tr>
<td>Control, n (%)</td>
<td>31</td>
<td>6 (20.0 %)</td>
<td>5 (16.1 %)</td>
<td>12 (38.7 %)</td>
</tr>
<tr>
<td>HCQ, n (%)</td>
<td>31</td>
<td>2 (6.5 %)</td>
<td>4 (12.9 %)</td>
<td>6 (19.4 %)</td>
</tr>
<tr>
<td>P value</td>
<td>0.0476</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Absorption of pneumonia on chest CT.

Abbreviations: HCQ, hydroxychloroquine.

doi: https://doi.org/10.1101/2020.03.22.20040758
Lopinavir/Ritonavir

- Lopinavir is a protease inhibitor that blocks viral replication by inhibiting viral proteinase (vital role in protein processing and virus maturation)
- Ritonavir “boosts” lopinavir concentration
- May be effective when used in combination with other drugs
- Beware DDI
• RCT in 199 hospitalized adult patients with confirmed COVID-19.
• 400/100mg BID x14 days plus SOC vs. SOC alone
• Mortality and detectable viral RNA were similar in both groups
• More GI ADR in tx group
Federal Stockpile of HCQ

HHS accepts donations of medicine to Strategic National Stockpile as possible treatments for COVID-19 patients

FOR IMMEDIATE RELEASE
March 29, 2020

Contact: ASPR Press Office
202-254-9117
asprmedia@hhs.gov

HHS accepts donations of medicine to Strategic National Stockpile as possible treatments for COVID-19 patients

FDA issues emergency use authorization for donated hydroxychloroquine sulfate, chloroquine phosphate

The U.S. Department of Health and Human Services (HHS) today accepted 30 million doses of hydroxychloroquine sulfate donated by Sandoz, the Novartis generics and biosimilars division, and one million doses of Resochin (medical grade chloroquine phosphate) donated by Bayer Pharmaceuticals, for possible use in treating patients hospitalized with COVID-19 or for use in clinical trials. These and other companies may donate additional doses, and companies have ramped up production to provide additional supplies of the medication to the commercial market.

Regional Emergency Coordinators (RECs) assigned to each of the HHS regions throughout the country are working directly with states to determine PPE, ventilator and MCM needs and to submit their requests to HHS. For areas of intense COVID-19 transmission, the REC may submit a request from the state for additional supplies. This strategic coordination is important to manage simultaneous requests for supplies.

https://www.phe.gov/emergency/events/COVID19/SNS/Pages/requesting.aspx
WE NEED YOUR HELP WITH PANDEMIC RESPONSE!

We are collecting information from facilities who would like to collaborate with the Tennessee Department of Health during a pandemic response. This survey should not be interpreted as pending availability of these resources. The purpose of this survey is to allow TDH to be prepared to distribute resources should they become available.

At this time, we are preparing for any scenario and are working to identify providers who could distribute anti-viral medication, personal protective equipment (PPE), and vaccine once developed.

Partnering providers are asked to consider their facility’s capacity to store and administer or distribute pandemic supplies to eligible members of the public and/or to the population they serve. Vaccines may require storage under freezing or refrigerated temperatures. Medications may require refrigeration or climate-controlled storage space. This survey assists us in understanding your estimated capacity to assist in pandemic response. We understand your answers will be rough estimates of your capacity and may vary by season. Please provide responses that would reflect your "average" capacity for storage of supplies.

The survey will be closed on April 13.

Please submit only ONE pandemic survey per facility/physical location to avoid duplicate information.
Pandemic Response Survey

• You may open the survey in your web browser by clicking the link below:
  – https://redcap.health.tn.gov/redcap/surveys/?s=wCscjhf4Zc

• Email questions to:
  – VPDIP.Pandemic@tn.gov
Convalescent Plasma

- Reports on 5 critically ill patients with COVID-19 and ARDS given convalescent plasma containing neutralizing antibody and had an improvement in clinical status

• Logistics and Process???
Remdesivir

- Available for investigational use only
- Adenosine-analog antiviral that inhibits RNA synthesis
- Activity against MERS-CoV, SARS, Ebola
- Study dose in adults: RDV 200 mg loading dose on day 1 is given, followed by 100 mg iv once-daily maintenance doses for 9 days
- Compassionate vs. investigational use
• 61 patients (53 analyzed)
• No control group
• Severe respiratory disease due to SARS-CoV-2
• 36/53 (68%) showed clinical improvement in median followup of 18d.
• 7 deaths

Grein et al. NEJM; April 10, 2020. DOI: 10.1056/NEJMoa2007016
Expanded Access Programs

- Expanded access ("compassionate use") may be appropriate when all the following apply:
  - Patient has a serious disease or condition, or whose life is immediately threatened by their disease or condition.
  - There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.
  - Patient enrollment in a clinical trial is not possible.
  - Potential patient benefit justifies the potential risks of treatment.
  - Providing the investigational medical product will not interfere with investigational trials that could support a medical product’s development or marketing approval for the treatment indication.
Gilead is transitioning the provision of emergency access to remdesivir from individual compassionate use requests to expanded access programs. This approach will both accelerate access to remdesivir for severely ill patients and enable the collection of data from all participating patients. These programs are currently under rapid development in conjunction with national regulatory authorities worldwide. More details on how to participate in the expanded access programs will be forthcoming.

During this transition period, we are unable to accept new individual compassionate use requests due to an overwhelming demand over the last several days. We are focused now on processing previously approved requests and anticipate the expanded access programs will initiate in a similar expected timeframe that any new requests for compassionate use would have been processed.

Exceptions will be made only for pregnant women or children less than 18 years of age with confirmed COVID-19 and severe manifestations of disease.

Given the importance of data generation, we urge you to enroll patients in clinical trials if reasonably possible rather than pursue an emergency treatment request. Please refer to the links below for information on current clinical trials investigating the use of remdesivir in COVID-19:

- NCT04280705
- NCT04292730
- NCT04292899
- 2020-000936-23

Thank you for your understanding as we work through this transition as rapidly as possible. We are grateful for all that you are doing to serve patients in your community as we work collectively to respond to this global health crisis.
12 Remdesivir Trials on Clintrials.gov

- Most are recruiting or in process
- Useful info to obtain before reaching out:
  - Prescriber name, address, email, and phone number associated with the treatment center
  - Professional designation (ie, MD) or qualifications of requester including medical license number
  - Institution/ hospital name, address, email, and phone number
  - Shipping information (including pharmacy hours)
  - Patient case information, including previous or current treatments and clinical status

Tocilizumab + Steroids

- Interleukin-6 inhibitor
- May be helpful in cytokine storm associated with severe disease
  - After other therapies have failed?
Evidence in Small Studies

- 20 severe or critical patients
- All received lopinavir, methylpred and supportive care plus tocilizumab 400mg IV once
- Fever in all patients returned to normal by day following treatment
- 75% had improved oxygen intake
- Improvements in CRP and WBC in all but two patients.

- 15 patients (7 critically ill)
- Used in combination with methylpred in 8 patients
- 5 patients received more than once
- All patients had increases in CRP ameliorated
- Serum IL-6 spiked then declined in 10 patients
  - 4 patients who failed had dramatically increased IL-6

Other non-specific treatment questions:

- Initial and Daily Lab Monitoring
  - Lactate
  - Ferritin
  - IL-6
  - Troponin-I

- Thromboembolism in COVID-19 patients
Ways Pharmacists Can Help

• Be a role model and educate others about infection prevention basics
• Provide guidance to patients and customers
• Offer strategies for symptom management
• Direct people to reliable resources
• Keep up to date
Good Treatment Resources

• Coronavirus Information for Pharmacists

• IDSA Guidelines on Treatment and Management of Patients with COVID-19

• SIDP Review of Early and Emerging Options
https://TN.Gov/Health

- For the Public
- Health Care Providers
- Laboratories
- Public Health
- Preparedness Tools
- Resources for Educational Organizations
- Resources for Congregate Care, Homeless, and Correctional Facilities
For the Public

- Learn more about this disease
- What to Expect After Being Diagnosed
  - What to Expect After Being Diagnosed (Spanish)
- What to Expect If You Were Possibly Exposed
  - What to Expect If You Were Possibly Exposed (Spanish)
- What to Expect After Being Tested
  - What to Expect After Being Tested (Spanish)
- CDC Guidance for Travelers
- Facility Visitor Guidance
- Interim Guidelines: Businesses & Employers
- Interim Guidelines: Mass Gatherings/Large Community Events
- Guidance for Faith-Based Organizations
  - Guidance for Faith-Based Organizations (Spanish)
Prevent introduction into facility

COVID-19 is a new disease caused by a novel coronavirus. Due to this evolving public health situation, the Tennessee Department of Health requests that you take the following precautions to help protect our communities and state.

**STOP**

- People with fever, cough, sore throat, or other flu-like symptoms are not permitted to visit.
- People who have traveled to a high-risk area for COVID-19 or had contact with a person known to be infected with COVID-19 are not permitted to visit.

**PROCEED WITH CAUTION**

- As a healthy visitor, please follow these recommendations:
  - Wash your hands with soap and water or alcohol-based hand rub before and after your visit.
  - Cover your sneeze or cough with your elbow or a tissue.

These restrictions are put in place to protect our facility and our community. We appreciate your understanding and cooperation.

This is a rapidly evolving situation. Up-to-date information is available online:


TDH: [https://www.tn.gov/health/cdews/cov.html](https://www.tn.gov/health/cdews/cov.html)

March 2, 2020
Health Care Providers

- TDH COVID-19 Webinars for Health Care Providers (held every Friday at noon!)
- Triage and assessment
- Clinical information about this disease
- Report a case of this disease
- Submit a specimen for laboratory testing
- Strategies for Optimizing the Supply of N95 Respirators
- PPE Conservation Guidance
- Application for Executive Order
- Guidance for Healthcare Workers Diagnosed with COVID
- Guidance for Healthcare Workers Returning to Work after COVID Illness
- Extended Use and Re-Use of N95s
- Extended Use and Re-Use of Facemasks
- Extended Use and Re-Use of Eye Protection
Additional resources

- Infection preventionist training:  
  - https://www.cdc.gov/longtermcare/index.html
- CDC Resources for Long-Term Facilities:  
- CDC Preparedness Checklist for LTC:  
- CDC COVID-19 Update and Information for LTCFs:  
- CDC FAQ for COVID-19:  
- Infection control toolkit for bedside licensed nurses and nurse aides:  
- Infection control and Prevention regulations and guidance: 42 CFR 438.80, Appendix PP of the State Operations Manual. See F-tag 880:  
Regional Healthcare Coalition Contacts

Heather Fortner | 901-222-8216 | heather.fortner@shelbycountytn.gov

WATCH (West Area Healthcare Coalition)
Josh Moore | 731-421-5383 | josh.moore@tn.gov
Wayne Arnold | warnold@madisoncountytn.gov

TN Highland Rim Healthcare Coalition - [https://tnrhcc.com/](https://tnrhcc.com/)
Tabitha Finney | 615-650-7000 | Tabitha.Finney@tn.gov
Madelyn McCormick | Madelynn.McCormick@nashville.gov

South Central Region Healthcare Coalition - [https://www.scrhcccoalition.org/](https://www.scrhcccoalition.org/)
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Kenneth Tartar | 423-634-1957 | Kenneth.T.Tartar@tn.gov
Jenny Wolverton | 423-209-8066 | VirginiaW@HamiltonTN.gov

John Brinkley | 865-215-5456 | John.Brinkley@knoxcounty.org
Wanda Roberts 865-549-5294 | Wanda.Roberts@tn.gov

Northeast/Sullivan Healthcare Coalition - [https://nethealtheightalcation.org/](https://nethealtheightalcation.org/)
Merenda Belcher | 423-279-2691 | mbelcher@sullivanelth.org
Anthony Wright | 423-979-4633 | anthony.c.wright@tn.gov

Kristi Langford | 931-646-7547 | Kristi.langford@tn.gov
Next Steps

• Next Call
  – June 9 at 2pm Eastern/1pm Central Time
  – Vancomycin AUC Dosing

• Feedback always appreciated
  – Christopher.evans@tn.gov