evidence-based practice
WORKSHOP
April 28-30, 2021
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Disclosures:

Workshop Course Directors have nothing to disclose and have no conflicts of interest.

In fact… none of our faculty had any relevant disclosures, that is no conflicts of interest.
2003: 1st National EBM Workshop

2019: 17th year
EBM Fundamental Principles

• Not all evidence is created equal

  A hierarchy of evidence helps us differentiate information more likely to be valid or true

• Evidence alone is never enough

  Decisions are informed and guided by patient and societal values and preferences.
Meta-analysis

RCT

Observational Studies
  Prospective
  Retrospective

Case-Control

Case Series

Nonsystematic Clinical Experience

Summary Methodology
  Experimental Design
    Less error
      Less error
        Comparison
          Uncontrolled
How to Frame Clinical Questions

- **P**: Patient, population, problem
- **I**: Intervention, exposure, prognostic factor
- **C**: Comparison (if applicable)
- **O**: Outcome
- **T**: Type of question (e.g. therapy, harm, prognosis, diagnosis)
- **T**: Type of study design (e.g. RCT, cohort, case-control)
EBM Fundamental Principles

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• Clinicians make recommendations
  Clinicians make recommendations “For” or “Against” a particular course of action and those recommendations can be “Weak” or “Strong”
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COVID-19

3-28-2020: FDA issued an Emergency Use Authorization

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of COVID-19 when administered as described in the Scope of Authorization (section II) meet the criteria for issuance of an authorization under Section 564(c) of the Act, because:

1. The SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that chloroquine phosphate and hydroxychloroquine sulfate may be effective in treating COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of chloroquine phosphate and hydroxychloroquine sulfate when used to treat COVID-19 outweigh the known and potential risks of such products; and

3. There is no adequate, approved, and available alternative to the emergency use of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of COVID-19.
Background And Rationale

Effects of chloroquine on viral infections: an old drug against today’s diseases?

Andrea Savarino, Johan R Boelaert, Antonio Cassone, Giancarlo Majori, and Roberto Cauda.

THE LANCET Infectious Diseases Vol 3 November 2003 http://infection.thelancet.com

• Numerous in vitro studies suggest chloroquine and HCQ have unique antiviral properties
• Alteration of endosome pH inhibiting early replication pathway
• Immunomodulatory effects, decreasing TNF-alpha, IL-6
Available Evidence

- EUA 3-28-2020: No specific studies or data referenced
- In vivo data on potential benefit

Journal Pre-proof 2-28-2020

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial

Philippe Gautret, Jean-Christophe Lagier, Philippe Parola, Van Thuan Hoang, Line Meddeb, Morgane Mailhe, Barbara Doudier, Johan Courjon, Valérie Giordanengo, Vera Esteves Vieira, Hervé Tissot Dupont, Stéphane Honoré, Philippe Colson, Eric Chabrière, Bernard La Scola, Jean-Marc Rolain, Philippe Brouqui, Didier Raoult

DOI: https://doi.org/10.1016/j.ijantimicag.2020.105949
Open-label Non-Randomized Trial

- Hospitalized COVID-19 patients in France
  - Intervention group: 26 patients agreeing to take HCQ (200 mg tid x 10 d) as part of study
  - Exclusion criteria: allergy to HCQ / CQ, retinopathy, G6PD deficiency, QT prolongation, breast feeding or pregnant
  - Control group: patients who refused or who met exclusion criteria, or patients from a different center who did not receive HCQ
Open-label Non-Randomized Trial

• Hospitalized COVID-19 patients in France
  • “Lost to follow up”: Excluded 6 HCQ patients in analysis- 3 went to ICU, 1 died, 1 stopped treatment, 1 left the hospital

• Primary Outcome: nasopharyngeal clearance at day #6
% Patients PCR+ on day #6

Controls 14/16 still PCR-positive

Treated 6/20 still PCR-positive

Does not include 6 patients, 3 in ICU, 1 died, 1 left, 1 d/c HCQ

Nonrandom, groups not equal at baseline
Relative risk (95% CI) not reported
Surrogate Outcome (not patient important)
Known Harms of HCQ

- **Cardiovascular:** Prolonged QT interval, Torsades de pointes
- **Endocrine metabolic:** Hypoglycemia (Severe)
- **Hematologic:** Agranulocytosis, Anemia, Aplastic anemia, Hemolysis, Pancytopenia, Thrombocytopenia
- **Musculoskeletal:** Disorder of muscle
- **Neurologic:** Extrapyramidal disease
- **Ophthalmic:** Retinal disorder
- **Otic:** Hearing loss
- **Other:** Angioedema
Case-Control

Observational Studies

Case Series

Nonsystematic Clinical Experience

RCT

Prospective

Retrospective

Summary Methodology

Experimental Design

Less error

Comparison

Uncontrolled

Meta-analysis
Is this Sheri being too critical?

Commentary

Hydroxychloroquine for COVID-19 Study Did Not Meet 'Expected Standard'

Retraction Watch Staff

Disclosures | April 08, 2020

Editor's note: Find the latest COVID-19 news and guidance in Medscape's Coronavirus Resource Center.

The paper that appears to have triggered the Trump administration's obsession with hydroxychloroquine as a treatment for infection with the novel coronavirus has received a statement of concern from the society that publishes the journal in which the work appeared.
Is this Sheri being too critical?

World Health Organization

**Recommendation against**

We recommend against administering hydroxychloroquine or chloroquine for treatment of COVID-19.

*Remark: This recommendation applies to patients with any disease severity and any duration of symptoms.*

IDSA

**Overview of IDSA COVID-19 Treatment Guidelines**
*Version 4.1.0 – March 5, 2021*

<table>
<thead>
<tr>
<th>Setting and severity of illness</th>
<th>Ambulatory care: mild-to-moderate disease</th>
<th>Hospitalized: mild-to-moderate disease without need for suppl. oxygen</th>
<th>Hospitalized: severe but non-critical disease (spO₂ &lt;94% on room air)</th>
<th>Hospitalized: critical disease (e.g., in ICU needing MV, or septic shock, ECMO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Hydroxy-chloroquine (HCQ)*</td>
<td>NA</td>
<td>Recommend against use</td>
<td>Recommend against use</td>
<td>Recommend against use</td>
</tr>
<tr>
<td>2 HCQ* + azithromycin</td>
<td>NA</td>
<td>Recommend against use</td>
<td>Recommend against use</td>
<td>Recommend against use</td>
</tr>
</tbody>
</table>
Man dies after taking chloroquine in an attempt to prevent coronavirus

The man and his wife thought the ingredient, used to treat sick fish, could prevent the disease.

The man's wife told NBC News she'd watched televised briefings during which President Trump talked about the potential benefits of chloroquine. Even though no drugs are approved to prevent or treat COVID-19, the disease caused by the coronavirus, some early research suggests it may be useful as a therapy.

The name "chloroquine" resonated with the man's wife, who asked that her name not be used to protect the family's privacy. She'd used it previously to treat her koi fish.

"I saw it sitting on the back shelf and thought, 'Hey, isn't that the stuff they're talking about on TV?'"

The couple – both in their 60s and potentially at higher risk for complications of the virus – decided to mix a small amount of the substance with a liquid and drink it as a way to prevent the coronavirus.

RETRACTED ON 2 JUNE 2020

RETRACTED

RETRACTED

RETRACTED

RETRACTED
2021… We are Back!
Who are we?

- 80 participants
- 47 tutors, tutor-trainees, Librarians
  - Administrative team: Erin, Sierra
Who are we?

- 30 institutions
- 14 with multiple participants
  - Lahey 10
  - Duke 7
  - Henry Ford 7
  - Univ. of Miami / Jackson 7
  - Cincinnati Children's 6
  - Morristown 4
  - Mayo 4
  - UNC 4
  - Emory 3
  - Rochester 3
  - Zucker Hillside 3
  - Akron Children’s 2
  - Kaiser Permanente 2
  - Riverside Methodist 2

- 16-ish disciplines
  - Anesthesia
  - Advanced Practice - PA
  - Emergency Medicine
  - Hospital Medicine
  - Internal Medicine
  - Librarians
  - Medicine-Pediatrics
  - Nursing
  - Pediatric Critical Care
  - Pediatric Emergency Med
  - Pediatrics
  - Psychiatry
  - Perfusion Medicine
  - Pharmacy
  - Primary Care
  - Rheumatology
Participants from 17 States & DC

- California
- Florida
- Georgia
- Illinois
- Kentucky
- Massachusetts
- Maryland
- Michigan
- Minnesota
- New York
- North Carolina
- Ohio
- Oregon
- South Carolina
- Texas
- Virginia
- Washington DC
- Wisconsin
Course Objectives

• Practice the evidence cycle
  • Assess patient’s dilemma
  • Ask well framed question
  • Acquire information
  • Appraise for validity
  • Apply based on values/ preferences
Course Objectives

• Exposure to Core Curricular areas
  • Therapy (RCT)
  • Harm (Case-Control)
  • Prognosis (Cohort)
  • Diagnosis (Prospective Comparison to Reference Standard)
  • Systematic Review / Meta-analysis
Course Objectives

• Modeling interactive teaching

• Create opportunities for networking and interaction with educator colleagues

• Practice teaching and critical appraisal skills
Schedules

- Large Group Sessions
- Small Group Sessions
- Concurrent Sessions
- Self-Directed Study Period (during the day and after 5 pm)
- Networking Opportunities
Breaks and in-Session Stretches

• Long sessions may have mini-breaks – camera off if you like, but please come back when due

• Facts of life in a virtual session
  • I don’t know where your bathroom is
  • Food: yes, as much as you like
Materials

• User’s Guide to the Medical Literature Ed. 3
• Box (Think Virtual Binder)**
  https://duke.app.box.com/s/lghynr4vcxqe1ps6ptxyxk3fecfzf9ns
• PDF “Fillable” documents – MUST BE DOWNLOADED
• Web-based content
  • Duke Workshop Manual
  • Slides from large groups posted within a week of the workshop
  • McMaster University modules
• http://sites.duke.edu/ebmworkshop/materials/

** Shout out to VA Folks and others with firewalls**
Materials

• Access to electronic resources will be through your own library or work with your librarian

• Sharing articles or small group materials
  • Use pdf and share in your Box folder or via the chat
  • If you can’t get hold of an article, work with your librarian to get what you need
Welcome & Logistics
Sheri Keitz, MD, PhD

Large Group (LG): Introduction to EBP
Sheri Keitz, MD, PhD

10:30 AM - 30 Minute Break

LG: Therapy (RCTs)
Kenneth Goldberg, MD

12:30 PM - 60 Minute Lunch / Virtual Networking

Small Group (SG): Introductions and Tutor “See One” Presentations

2:30 PM - 15 Minute Break

2:45 SG: Librarian Presentation
3:45 SG: Planning the Week

4:00 PM – 15 Minute Reflection / Tutor Debrief

Independent Study or Concurrent Sessions
  Session 1: Randomization
  Juan Lozano, MD
  Session 2: Tips & Apps for EBP at the Bedside
  Sarah Cantrell, MLIS

5:15 End of Day / Faculty Huddle
9:00  LG: Study Designs and Harm/Risk  
Sheri Keitz, MD, PhD and Nancy Skehan, MD

10:30 AM - 30 Minute Break

11:00  LG: Diagnosis (Cohort Studies)  
James Fox, MD

12:30 PM - 60 Minute Lunch / Virtual Networking

1:30  Small Group Session

2:30 PM - 15 Minute Break

2:45  Small Group Session

4:00 PM – 15 Minute Reflection / Tutor Debrief

4:15  Independent Study or Concurrent Sessions  
Session 1: EBP Curriculum Development  
Matthew Tuck, MD  
Session 2: Non-Inferiority Trials  
Daniella Zipkin, MD

5:15  End of Day / Faculty Huddle
LG: Systematic Reviews, Meta-analysis, and GRADE Criteria
Sheri Keitz, MD, PhD and Larry Young, MD

10:30 AM - 30 Minute Break

Small Group Session

1:00 PM - 30 Minute Lunch

LG: Bringing it Home

Wrap-up and Final Evaluation
Required for CME

End of Workshop / Faculty Huddle

Friday April 30
On-line Evaluations

• PLEASE…

• ….And Thank you!

• We are doing the evaluations in real time and online. At the end of each session you can give us feedback session by session.
Small Groups and Self-Study

The great end of life is not knowledge, but action.

T.H. Huxley
Small Groups: Workshop Core

• Tutorial Team facilitate
• Small Group Members take responsibility for the majority of the group teaching / learning
• Much less time than usual for Small Group
• Recommend each person present at least twice
• Encourage planning of to cover a variety of ‘core curriculum’ topics
• BOX for Small Groups

You can view and download workshop files via Box at bit.ly/EBP_Files
You can upload files for your small group members via Box at bit.ly/EBP_ShareFiles
Group 1: Keitz, Blevins
Group 2: Fox, Dunnick, Konieczny
Group 3: Young, Shidfar, Menard
Group 4: Zipkin, Flowers, Cyrus
Group 5: Bartlett, Jackson, Carlson
Group 6: Goldberg, Zamor, Graves
Group 7: Kaminetzky, Feeney, Ledbetter
Group 8: Tuck, Marcantonio, Cantrell
Group 9: Kushinka, Skehan, Stellrecht
Group 10: Stephany, Subramanian, Hendren
Group 11: Ribeiro, George, Kaplan
Group 12: Cearras, Herdy Varella, Brennan
Group 13: Ashley, Taldone. von Isenburg
Group 14: Gagliardi, Hernandez, Baltich Nelson
Group 15: Brown, Robbins, Nicholson
Group 16: Lozano, Clifton/Posey
Logistics…

• Moving “rooms” -- you will move yourself
• Breakout Rooms
  • 2 each afternoon on Wed and Thurs
  • Rooms are Concurrent Session 1 and 2
• Networking – catch up, connect, network during lunch and breaks
Breakout Sessions within Large Group

• Handouts will be in the large group folder on Box and may also be shared in the Chat

• Breakouts will be with your small group team (group 1 to 16).

• Please select a spokesperson willing to report out when we return to Large Group
The Watch Animation…. (Hope this works)
Logistics...

• **Zoom hardware / software**
  - Desktop / laptop with camera and microphone
  - Update zoom version ([https://zoom.us/download](https://zoom.us/download))
  - Technology Help: Request assistance from Erin or Sierra and visit breakout room called Technical Support**

• **Camera status**
  - On for small group
  - On or off for large group BUT it will be interactive

• **Microphone status**
  - OFF unless speaking (prevent feedback, background noise)

**Seek help if you are joining by phone**
Logistics…

• Please do NOT record large or small group
  • pdf and materials will be posted
  • Set ground rules in small group regarding recording / screen shots

• Teaching with Zoom
  • Annotation for interactivity
  • Chat Box for comments / questions
  • You will NOT be able to do polls within zoom during your small group
How to Use Annotation Function

• Hover at the top of your screen and select drop down “view options”

• Select Annotate which will open a toolbar

• Note: if you are sharing your screen, you select annotate from the bottom of the screen.
Annotation Station:
Practice! Rank Order Ice Cream Flavors

1ST Choice
Chocolate

2nd Choice
Vanilla

Cookie Dough
Annotation Station:
Should we all use Jamie’s Credit Card for Lunch Delivery?
What is your recommendation?

Weak | For | Strong
--- | --- | ---
Weak | Against | Strong
Up next...

LG: Case Introduction
Sheri Keitz, MD, PhD

9:30