Welcome to the Front Lines of the Fight Against COVID-19

A TOWN HALL CONVERSATION

We will begin at 9:30 a.m.

Houston Methodist
Leading Medicine
COVID-19 Town Hall

Marc L. Boom, MD
April 17, 2020
Four Features Of COVID-19 Combine To Create A Perfect Pandemic Storm

(And Why This Is Not The Common Cold Or Flu)

1. It’s highly contagious (more so than the flu, but less so than measles).

2. It’s new, so few people have immunity.

3. It causes infection without symptoms in some people, who can unknowingly infect others.

4. It can latch on to receptors in the lung, causing severe pneumonia much more frequently (perhaps 10 times more) than seasonal flu.

By Drs. David S. Ludwig and Richard Malley, NY Times 03.30.2020
https://www.nytimes.com/2020/03/30/opinion/obesity-us-health-coronavirus.html
Houston Region: Confirmed Cases

Coronavirus cases in the Houston region by date

These are all the known cases, by date, for the eight counties that comprise the Houston region.

https://public.flourish.studio/visualisation/1586543/?utm_source=showcase&utm_campaign=visualisation/1586543

Data as of April 15, 2020
Flattening the Curve

Flattening the curve

- Daily number of cases
- Delay outbreak peak
- Reduction in peak of outbreak
- Health care system capacity
- Time since first case
- Cases without protective measures
- Cases with protective measures

Source: CDC
Flattening the Curve

The Power of Social Distancing

- **NOW**
  - 1 PERSON infects
  - 5 DAYS: 2.5 PEOPLE infected
  - 30 DAYS: 406 PEOPLE infected

- **50% LESS EXPOSURE**
  - 1 PERSON infects
  - 5 DAYS: 1.25 PEOPLE infected
  - 30 DAYS: 15 PEOPLE infected

- **75% LESS EXPOSURE**
  - 1 PERSON infects
  - 5 DAYS: .625 PEOPLE infected
  - 30 DAYS: 2.5 PEOPLE infected

@SignerLab @garywarshaw
COVID-19 Outbreak: Houston Modeling

Modeling – March 30, 2020
• Peak of Curve – 4/24/20
• Cumulative cases at peak – 62,000
• Total cases by June 15 – 115,000

Modeling – April 13, 2020
• Peak of Curve – 4/28/20
• Cumulative cases at peak – 31,000
• Total cases by June 13 – 55,000

Source: Email communication, April 4, 2020 and April 13, 2020
Eric Boerwinkle, Ph.D
Dean, UT School of Public Health
COVID-19 Outbreak: Texas Modeling – IHME – April 3

34 days until peak resource use on
May 6, 2020

Resources needed for COVID-19 patients on peak date

- All beds needed: 17,221 beds
- ICU beds needed: 2,568 beds

- All beds available: 28,633 beds
- ICU beds available: 2,259 beds

- Bed shortage: 0 beds
- ICU bed shortage: 309 beds

Invasive ventilators needed: 2,055 ventilators

Data as of April 3, 2020

https://covid19.healthdata.org/
TMC Modeling

- Maximum Social Distancing – 1% prevalence
- Moderate Social Distancing – 2% prevalence
- Minimal Social Distancing – 15% prevalence
TMC ICU BEDS ACROSS THE 9 GREATER HOUSTON COUNTIES

Texas Medical Center ICU bed capacity modeling

Peak ICU bed requirements
- Minimal social distancing
- Moderate social distancing
- Maximum social distancing

+81% ICU beds already planned for surge
38% ICU available, without surge
23% Currently occupied COVID-19
39% Currently occupied non-COVID-19

Surge capacity: ~1,450
Base capacity: 573
Today: 559
1,187

Data as of April 14, 2020

Key Messages

COVID-19 related patients already account for 23% of ICU beds.

TMC has already identified ~80% incremental ICU surge capacity.

TMC is preparing personnel to address surge capacity needs

This document is solely intended to share insights and best practices rather than specific recommendations. Individual institution data is shown as reported and has not been independently verified.

TMC | TEXAS MEDICAL CENTER
# Current Houston Methodist ICU Bed Surge Planning

<table>
<thead>
<tr>
<th>Surge Response</th>
<th>Staffing</th>
<th>Beds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surge I</td>
<td>Standard Staffing</td>
<td>Existing ICU Capacity: 302 ICU Beds</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak: Maximum Social Distancing ~290</td>
</tr>
<tr>
<td>Surge II</td>
<td>Modified Staffing</td>
<td>Surge II 592 ICU Beds</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak: Moderate Social Distancing ~580</td>
</tr>
<tr>
<td>Surge III</td>
<td>Stretched Staffing</td>
<td>Surge III 750-800 ICU Beds</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak: Minimal Social Distancing ~2,520</td>
</tr>
</tbody>
</table>

- **FEMA National Guard**
  - Field Hospitals Utilize Closed Facilities
- **Pandemic Staffing**
  - ORs, ECCs, Cath Lab, Acute Care as ICU. Conf. Rooms for Acute Care
- **Modified Pandemic Staffing**
  - Add Additional PACUs, IMUs as ICUs
- **Stretched Staffing**
  - Add Closed ICUs and PACUs as ICUs
- **Standard Staffing**
  - Usual
“To gradually move away from a reliance on physical distancing as our primary tool for controlling future spread, we need:

1. Better data to identify areas of spread and the rate of exposure and immunity in the population;

2. Improvements in state and local health care system capabilities, public-health infrastructure for early outbreak identification, case containment, and adequate medical supplies;

3. Therapeutic, prophylactic, and preventive treatments and better-informed medical interventions to better protect the most vulnerable people and help rescue those who may become very sick.”
Road Map to Reopening

Phase I: Slow the Spread

Phase II: Reopen, State by State

Phase III: Establish Protections; Then Lift All Restrictions

Phase IV: Rebuild Our Readiness for the Next Pandemic

Trigger for Moving to Phase II:

- Sustained reduction in cases for at least 14 days
- Hospitals in the state are safely able to treat all patients requiring hospitalization without resorting to crisis standards of care
- The state is able to test all people with COVID-19 symptoms; and
- The state is able to conduct active monitoring of confirmed cases and their contacts.
COVID-19 Testing by State

Test per 1 M Population

<table>
<thead>
<tr>
<th>State</th>
<th>Number Tested per 1M Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>KS</td>
<td>5,043</td>
</tr>
<tr>
<td>TX</td>
<td>5,444</td>
</tr>
<tr>
<td>CA</td>
<td>5,502</td>
</tr>
<tr>
<td>VA</td>
<td>5,520</td>
</tr>
<tr>
<td>OH</td>
<td>6,146</td>
</tr>
<tr>
<td>KY</td>
<td>6,379</td>
</tr>
<tr>
<td>NE</td>
<td>6,470</td>
</tr>
<tr>
<td>AZ</td>
<td>6,523</td>
</tr>
<tr>
<td>GA</td>
<td>6,592</td>
</tr>
<tr>
<td>IA</td>
<td>6,600</td>
</tr>
<tr>
<td>NY</td>
<td>8,340</td>
</tr>
<tr>
<td>LA</td>
<td>10,700</td>
</tr>
<tr>
<td>RI</td>
<td>13,000</td>
</tr>
</tbody>
</table>

Data as of April 16, 2020

https://www.worldometers.info/coronavirus/#countries
Trigger for Moving to Phase II:

- Sustained reduction in cases for at least 14 days
- Hospitals in the state are safely able to treat all patients requiring hospitalization without resorting to crisis standards of care
- The state is able to test all people with COVID-19 symptoms; and
- The state is able to conduct active monitoring of confirmed cases and their contacts.

Road Map to Reopening

[Link to Road Map to Reopening](https://www.aei.org/wp-content/uploads/2020/03/National-Coronavirus-Response-a-Road-Map-to-Recovering-2.pdf)
The Frontlines...
INNOVATION

DEVELOPING STORY

NEW TOOLS HELPING PATIENTS & HEALTHCARE WORKERS
HM IP&C COVID-19 Response

Firas R. Zabaneh MT(ASCP), CIC, CIE, MBA
Director, System Infection Prevention and Control
System IP&C COVID Response

- Training – train the trainer, in-person training
- Learning tools – tip sheets, videos
- Visual tools – PPE posters, isolation signs
- Innovation – Reduce reliance on disposable personal protective equipment

CDC: Controlling exposures to occupational hazards

Hierarchy of Controls

1. Elimination
2. Substitution
3. Engineering Controls
4. Administrative Controls
5. PPE

Most effective

Least effective
Innovation – N95 Mask Reprocessing

Steam Sterilization
- Multiple N95 brands and models tested
- All biological and chemical indicators passed
- Seven-minute quantitative fit testing performed before and after sterilization
- Manuscript accepted for publication in ICHE

UV Light Disinfection
- Collaborative initiative with EnMed
- Methodology validated for all N95 masks and surgical masks

Hydrogen Peroxide disinfection
- Recently approved by the FDA
- Most N95 masks can be reprocessed 10 times with no impact on mask integrity
- Most viable option at this time
Innovation – Personal Protective Pod

Isolating people from the hazard
Innovation – Sample Collection Pod

Isolating people from the hazard while reducing reliance on disposable PPE

Device deployed at HM remote collection clinics
Innovation – Future Projects

• OB aerosol containment device
• N95 fit testing App
• Reusable N95 masks
• Neonatal ICU intubation box
• Modifying aerosol containment device to be adapted for other settings
  o Pathology
  o OR
  o Cath lab
Houston Methodist and Covid-19 Research

April 17, 2020
Controlling Infectious Disease

- Control of Disease
- Treatment
- Testing
- Vaccination
Controlling Infectious Disease

Control of Disease

Testing

Treatment

Vaccination
Drug Treatment for Covid-19

Tocilizumab
Sarilumab
Binds IL-6 receptor
Prevents IL-6 receptor activation
Inhibits IL-6 signaling

Camostat mesylate
Inhibits TMPRSS2
Prevents viral cell entry

Arbidol
Targets S protein/ACE2 interaction
Inhibits membrane fusion of the viral envelope

Chloroquine
Hydroxychloroquine
Inhibits viral entry and endocytosis by multiple mechanisms as well as host immunomodulatory effects

Lopinavir
Darunavir
Inhibits 3-chymotrypsin-like protease

Ribavirin
Remdesivir
Favipiravir
Inhibits viral RdRp

RNA synthesis
Translation
Nonstructural proteins
Proteolysis
Polypeptides
Translation
Structural proteins
Assembly
Exocytosis

Published online April 13, 2020.
Antibody Treatment for Covid-19

- Hyperimmune globulin
- Convalescent Plasma
- Monoclonal antibodies
1. Convalescent plasma infusion
   - 28 patients infused (6 discharged)
   - Possible future work:
     - Compassionate use in TMC
     - Mayo-led multicenter clinical trial (plan to collaborate)
     - HM protocol for treatment of less severe patients

2. Remdesivir
   - severely ill patients – 40 patients (16 discharged)
   - moderately ill patients – 6 patients (4 discharged)

Subject to rapid change
Projects in the Pipeline at Houston Methodist

1. Bioengineered antibodies
   • Collaboration with US Army & UT Austin

2. Cytokine release syndrome ("cytokine storm")
   a. Cell therapies (Mesenchymal stem cells, CAR-T cells)
   b. Monoclonal antibody (anti-GM-CSF)

3. Hydroxychloroquine
   • High risk with positive COVID-19 test to prevent hospitalization

4. RNA vaccine project – Collaboration with Gene One Life Sciences

5. Surveillance Testing of Health Care Workers

Subject to rapid change
Panelists

- **Jenny C. Chang, MD**
  - Emily Herrmann Chair in Cancer Research
  - Director, Houston Methodist Cancer Center

- **James M. Musser, MD, PhD**
  - Fondren Presidential Distinguished Chair, Research Institute
  - Chair, Department of Pathology & Genomic Medicine
COVID-19
Cytokine Release Syndrome
Work Group

Jenny C Chang
Houston Methodist Cancer Center
April 17, 2020
COVID-19 Cytokine Storm

Hematology/BMT
Ravi Pingali
Jasleen Randhawa
Shilpan Shah
Malcolm Brenner
Helen Heslop
George Carrum

ICU/Critical Care
Faisal Masud
Deepa Gotur

Infectious Diseases
Ashley Drews
Kevin Grimes
William Musick

Solid Organ Transplant
Osama Gaber
Howard Huang
Stages of Cytokine Release Syndrome

- **Stage I (Early Infection):**
  - Viral response phase
  - Clinical Symptoms: Mild constitutional symptoms, Fever >99.6°F, Dry Cough, diarrhea, headache

- **Stage II (Pulmonary Phase):**
  - IIA
  - IIB
  - Host inflammatory response phase
  - Clinical Signs: Shortness of Breath, Hypoxia (PaO2/FiO2<300mmHg), Lymphopenia, increased prothrombin time, increased D-Dimer and LDH (mild), Abnormal chest imaging, Transaminitis, Low-normal procalcitonin

- **Stage III (Hyperinflammation Phase):**
  - ARDS, SIRS/Shock, Cardiac Failure
  - Clinical Signs: Elevated inflammatory markers (CRP, LDH, IL-6, D-dimer, ferritin), Troponin, NT-proBNP elevation

- **Potential Therapies:**
  - Remdesivir, chloroquine, hydroxychloroquine, convalescent plasma transfusions
  - Reduce immunosuppression
  - Corticosteroids, human immunoglobulin, IL-6 inhibitors, IL-2 inhibitors, JAK inhibitors
Cytokine Storm Causes Direct Organ Injury

Cytokine Storm
- Clotting
- Renal Failure
- Shock
- Immune Paralysis
- Lung Injury
- Cell Death

Cytokines
- CD28SA (e.g., TGN1412)
- CD28
- CD11b
- ICAM1
- FcγR

Induction phase
- T cell
- Endothelial cell adhesion

Immuno-pathogenesis
- Cytokine storm
  - TNFα, IFNγ
  - IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12
- Capillary leak syndrome
  - Endothelial damage

End-organ damage
- Multiple organ failure
  - Pulmonary infiltrates
  - Lung injury
  - Acute respiratory distress syndrome
  - Cardiovascular shock
  - Disseminated intravascular coagulant
  - Renal failure
Consequences of Cytokine Release Syndrome
SITC Statement on anti-IL-6/IL-6R for COVID-19

Insights from immuno-oncology: The Society for Immunotherapy of Cancer statement on access to IL-6-targeting therapies for COVID-19

Algorithm for Treatment of **Severe Cytokine Release Syndrome**

**Confirmed POSITIVE SARS-CoV-2(COVID-19) PCR**

**Acute Care**
- **Mild S/Sx**
  - Supportive Care & Close Monitoring
  - Consult Infectious Diseases and/or Pulmonology
  - Risk Factors for Progression:
    - ≥ 60yO
    - ALC <800
    - DM
    - CAD/HF
    - ESRD/ESLD
    - Lactate >2
    - Morbid Obesity (BMI>40)
    - Pre-existing Lung Disease
    - Immunocompromised

**Moderate S/Sx**
- No Risk Factors
- HCQ

**Critical Care**
- **Severe S/Sx**
  - Consult Infectious Diseases and/or Pulmonology
  - **Inflammatory Lab Bundle**
    - IgG, IL-6, Ferritin, CRP, D-Dimer, LDH, Triglycerides, Fibrinogen
  - HCQ (+) RBV
    - Adjuvant: Neb Interferon-α or Azithromycin

**Immune Modulation**
- (see COVID CRS Score – left)
- Consider Tocilizumab
- Evaluate patient for inclusion in study protocols (over)

Upon admission to ICU:
- Lactate, LFTs, blood cross & type, Troponin, EKG (baseline QTc)
- Daily:
  - CRP, Ferritin, LDH, LFTs, Mg, Phos, CBC c Diff, BMP
  - EKG if on multiple agents that prolong QTc

**HM COVID CRS SCORE**

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>Score</th>
<th>Inflammatory Markers</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>P/F ratio (on PEEP=5)</td>
<td>0</td>
<td>CRP (≥10 mg/dl)</td>
<td>1</td>
</tr>
<tr>
<td>200 - 300</td>
<td>1</td>
<td>LDH (≥350 U/L)</td>
<td>1</td>
</tr>
<tr>
<td>100 - 200</td>
<td>2</td>
<td>D-Dimer (≥10 μg/ml)</td>
<td>0.5</td>
</tr>
<tr>
<td>&lt;100</td>
<td>3</td>
<td>Triglycerides (≥350 mg/dl)</td>
<td>0.5</td>
</tr>
<tr>
<td>MAP &gt;70</td>
<td>1</td>
<td>Fibrinogen (≥200 mg/dl)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

**SCORE**
- C ≥ 2 + IM ≥ 2: Suggest immune modulation - Tocilizumab
- +18-24 hrs, re-assessment: No clinical improvement - repeat Tocilizumab
- >36-48 hrs, re-assessment: No clinical improvement - escalate to Anakinra + Infliximab
Algorithm for Treatment of Moderate Cytokine Release Syndrome

SARS-COV-2 POSITIVE

IP on Medical floor
≥ 3 risk factors (Table 1)

- Tocilizumab*^  
- Glucocorticoids**

---

Table 1. Risk factors for Severe CoVID-19 disease

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Labs</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR ≥ 100/min</td>
<td>D-Dimer &gt;10</td>
</tr>
<tr>
<td>RR &gt;24/min</td>
<td>Δ CRP (≥10mg/dl) in 24 hr Or CRP (≥20mg/dl)</td>
</tr>
<tr>
<td>SpO2 &lt;90% on RA</td>
<td>Δ IL-6 (≥25 pg/mL) in 24 hr Or IL-6 (≥50pg/mL)</td>
</tr>
<tr>
<td>Worsening lung imaging</td>
<td>LDH &gt; 2x ULN</td>
</tr>
<tr>
<td>Age &gt;60 years</td>
<td>ALC &lt;800</td>
</tr>
<tr>
<td>Pre-existing lung disease</td>
<td>Ferritin &gt;1000</td>
</tr>
<tr>
<td>Immunosuppression/Chemotherapy</td>
<td>Triglycerides &gt; 4 mmol</td>
</tr>
<tr>
<td>CKD ≥ Stage 3</td>
<td>Fibrinogen &lt; 200 mg/dL</td>
</tr>
</tbody>
</table>

*^Tocilizumab-400 mg IV x 1. Repeat another dose after 12 hours if clinically indicated.  
Siltuximab 11mg/kg IV x1 is an alternative to Tocilizumab  
^ Daily CRP and Twice a week IL-6 level after Tocilizumab infusion
Plasma therapy for HMH patients

SARS-CoV-2 molecular diagnostics

Antibody tests: healthcare workers + patients + Houston residents
• Fancy name for giving a patient the fluid part of blood that contains antibodies that kill the SARS-Cov-2 virus.
• Concept is >100 years old: diphtheria and Nobel Prize.
• We obtain it from COVID-19 patients who have recovered and then transfuse it to very sick patients.
• Methodist was the first hospital in the United States to give patients this innovative treatment.
• We have treated 28 patients; very large team effort.
• It is safe. It is experimental. We are very cautiously optimistic.
• Much, much more to be done.
Let’s Talk Antibody Testing: Is It the Answer?

- This is an extremely complicated but important topic.
- Our hope is that the presence of antibody against the SARS-CoV-2 virus means that we are immune to it.
- Sometimes it does, sometimes it doesn’t – this depends on the pathogen.
- Regardless, we need a high-throughput strategy to determine precise antibody levels in >100,000 people.
- Fusion of robotics, collaboration, and informatics.
- Health care workers, patients, Houston citizens from all walks of life and all neighborhoods.
- Stay tuned. More to come...
What needs to be achieved in the near and longer term?

- We need to understand precisely who is and who is not at risk of catching COVID-19 disease.
- We need to significantly expand our molecular and antibody testing. Many external supply chain problems.
- We need proven curative therapies. We are largely flying blind right now. We need a recipe for the secret sauce.
- We need an effective vaccine – likely 18 to 24 months for large-scale deployment.
- Physician-scientists are uniquely able to solve the COVID-19 problem.
Special Thank You To...

- Infectious Diseases Research Challenge Initiative and its visionary leaders, and all of our very generous donors.
- Our extraordinarily dedicated technologists in the Methodist Molecular Diagnostic Laboratory.
- Dr. Masud and his outstanding team.
- Our ~60 plasma donors thus far. They are all heroes.
- Collaborators at the US ARMY Futures Command and University of Texas Austin.
- Drs. Boom, Sostman, Phillips, and Schwartz
THANK YOU FOR ATTENDING OUR TOWN HALL CONVERSATION.

To continue the conversation, please reach out to foundation@houstonmethodist.org

Take care and be well