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

A TOWN HALL CONVERSATION

We will begin at 10 a.m.

HOUSTON Methodist
LEADING MEDICINE
Review of Questions

• How are our transplant patients doing? Organ dependent?
• Are transplant patients impacted more or less than non-transplant? Outcomes? Is the hospital seeing more transplant patients?
• Can COVID survivors (recovered) be organ donors?
• Will “at risk” populations such as transplant patients have early access to the COVID vaccine once approved?
J.C. Walter Jr. Transplant Center
Transplant Waitlist Heatmap
All Organs – 1/1/2016 to 8/2020

Pre-Transplant

Houston Methodist
J.C. Walter, Jr.
Transplant Center
Total Transplant Volume

UNOS Total Transplants

- 2006: 174
- 2007: 195
- 2008: 234
- 2009: 308
- 2010: 362
- 2011: 418
- 2012: 462
- 2013: 396
- 2014: 420
- 2015: 421
- 2016: 446
- 2017: 494
- 2018: 497
- 2019: 525
- 2020 YTD: 570

Growth:
- 2006: +12%
- 2007: +20%
- 2008: +32%
- 2009: +17.5%
- 2010: +15.5%
- 2011: +10.5%
- 2012: +14.2%
- 2013: -6.0%
- 2014: +10.7%
- 2015: +6.0%
- 2016: +1.0%
- 2017: +6.0%
- 2018: +5.6%
- 2019: +8.6%

National Rankings:
- 2006: 13th
- 2007: 9th
- 2008: 7th
- 2009: 13th
- 2010: 7th
- 2011: 13th
- 2012: 9th
- 2013: 7th
- 2014: 13th
- 2015: 9th
- 2016: 7th
- 2017: 13th
- 2018: 9th
- 2019: 7th
- 2020 YTD: 13th
In 2019, only 4 centers landed in top 25 volumes for the 4 key organ programs.

Ranked #1 for Transplant volumes in 2019

- Did not land in top 25 for lung or heart
- Kidney made up 67% of volumes (HM, 48%)

<table>
<thead>
<tr>
<th>Hospital System</th>
<th>Kidney</th>
<th>Liver</th>
<th>Heart</th>
<th>Lung</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCLA</td>
<td>408</td>
<td>168</td>
<td>58</td>
<td>91</td>
<td>5</td>
<td>730</td>
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<tr>
<td>University of Pennsylvania</td>
<td>241</td>
<td>135</td>
<td>57</td>
<td>80</td>
<td>22</td>
<td>535</td>
</tr>
<tr>
<td>Houston Methodist Hospital</td>
<td>252</td>
<td>151</td>
<td>41</td>
<td>61</td>
<td>20</td>
<td>525</td>
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<tr>
<td>University of Colorado</td>
<td>284</td>
<td>134</td>
<td>43</td>
<td>44</td>
<td>10</td>
<td>515</td>
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</table>

<table>
<thead>
<tr>
<th>Hospital System</th>
<th>Kidney</th>
<th>Liver</th>
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<th>Lung</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jackson Memorial</td>
<td>502</td>
<td>155</td>
<td>24</td>
<td>22</td>
<td>44</td>
<td>747</td>
</tr>
</tbody>
</table>
2019 Transplant Activity Funnel

- 5501 Referrals
- 1959 Evaluations
- 1649 MRB Presented
- 907 Listings
- 687 End Organ Interventions

- 525 Transplants
- 118 Live Donations
- 44 VADs

Growth from 2018:
- 13.7% ↑
- 2.7% ↑
- 10.7% ↑
- 1.2% ↑
COVID and Transplantation

- COVID transplant task force
- Follow CMS guidelines
- Increased transplantation rate after a brief slow period
- Implementation of strict guidelines for the transplant population
- COVID clinic
## Post Transplant COVID – Cumulative

<table>
<thead>
<tr>
<th>Trending</th>
<th>Post Transplant Percent Positivity</th>
<th>&lt; 1 Yr Post Txp (death)</th>
<th>1-3 Yr Post Txp (death)</th>
<th>&gt;3 Ys Post Txp (death)</th>
<th>Post Txp COVID Positive Deaths</th>
<th>Case Fatality Rate (CFR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/19/2020</td>
<td>120/843 (14.2%)</td>
<td>20 (2)</td>
<td>32 (3)</td>
<td>68 (5)</td>
<td>10</td>
<td>8.3%</td>
</tr>
<tr>
<td>7/26/2020</td>
<td>130/894 (14.5%)</td>
<td>20 (2)</td>
<td>34 (3)</td>
<td>76 (7)</td>
<td>12</td>
<td>9.2%</td>
</tr>
<tr>
<td>8/02/2020</td>
<td>136/932 (14.6%)</td>
<td>23 (2)</td>
<td>35 (4)</td>
<td>78 (7)</td>
<td>13</td>
<td>9.6%</td>
</tr>
<tr>
<td>8/09/2020</td>
<td>137/982 (14.0%)</td>
<td>23 (3)</td>
<td>37 (4)</td>
<td>78 (8)</td>
<td>15</td>
<td>11.0%</td>
</tr>
<tr>
<td>8/16/2020</td>
<td>143/1031 (13.9%)</td>
<td>25 (3)</td>
<td>37 (4)</td>
<td>81 (8)</td>
<td>15</td>
<td>10.5%</td>
</tr>
<tr>
<td>8/23/2020</td>
<td>147/1087 (13.4%)</td>
<td>25 (3)</td>
<td>38 (4)</td>
<td>84 (9)</td>
<td>16</td>
<td>10.9%</td>
</tr>
<tr>
<td>8/30/2020</td>
<td>150/1126 (13.3%)</td>
<td>25 (4)</td>
<td>38 (4)</td>
<td>87 (9)</td>
<td>17</td>
<td>11.3%</td>
</tr>
<tr>
<td>9/7/2020</td>
<td>153/1167 (13.1%)</td>
<td>26 (5)</td>
<td>38 (4)</td>
<td>89 (10)</td>
<td>19</td>
<td>12.4%</td>
</tr>
<tr>
<td>9/13/2020</td>
<td>155/1198 (12.9%)</td>
<td>27 (5)</td>
<td>38 (4)</td>
<td>90 (10)</td>
<td>19</td>
<td>12.2%</td>
</tr>
<tr>
<td>9/20/2020</td>
<td>158/1231 (12.8%)</td>
<td>27 (6)</td>
<td>38 (4)</td>
<td>93 (10)</td>
<td>20</td>
<td>12.7%</td>
</tr>
<tr>
<td>9/27/2020</td>
<td>159/1259 (12.6%)</td>
<td>28 (6)</td>
<td>38 (4)</td>
<td>93 (11)</td>
<td>21</td>
<td>13.2%</td>
</tr>
<tr>
<td>10/4/2020</td>
<td>161/1301 (12.4%)</td>
<td>28 (6)</td>
<td>39 (4)</td>
<td>94 (11)</td>
<td>21</td>
<td>13.0%</td>
</tr>
<tr>
<td>10/11/2020</td>
<td>167/1348 (12.4%)</td>
<td>31 (7)</td>
<td>41 (4)</td>
<td>95 (11)</td>
<td>22</td>
<td>13.2%</td>
</tr>
<tr>
<td>10/18/2020</td>
<td>169/1388 (12.2%)</td>
<td>31 (7)</td>
<td>41 (4)</td>
<td>97 (11)</td>
<td>22</td>
<td>13.0%</td>
</tr>
<tr>
<td>10/25/2020</td>
<td>173/1430 (12.1%)</td>
<td>31 (8)</td>
<td>42 (4)</td>
<td>100 (11)</td>
<td>23</td>
<td>13.3%</td>
</tr>
<tr>
<td>11/1/2020</td>
<td>176/1462 (12.0%)</td>
<td>32 (8)</td>
<td>43 (4)</td>
<td>101 (11)</td>
<td>23</td>
<td>13.0%</td>
</tr>
<tr>
<td>11/8/2020</td>
<td>180/1496 (12.0%)</td>
<td>32 (8)</td>
<td>44 (4)</td>
<td>104 (11)</td>
<td>23</td>
<td>12.8%</td>
</tr>
<tr>
<td>11/15/2020</td>
<td>188/1526 (12.3%)*</td>
<td>34 (8)</td>
<td>44 (4)</td>
<td>110 (12)</td>
<td>24/188</td>
<td>12.8%**</td>
</tr>
</tbody>
</table>
Post Transplant COVID – Cumulative

COVID-19 Positive Tests by Organ:
Kidney (94), Liver (27), Lung (19), Heart (18),
Kidney/Pancreas (9), Liver/Kidney (8), Heart/Kidney (4),
Heart/Liver (1), Heart/Lung (1), Pancreas (1), PAK (2),
Multi-Organ Other (4)

COVID-19 Positive Deaths by Organ:
Kidney (12), Liver (4), Lung (5), Heart (1),
Kidney/Pancreas (1), Heart/Kidney (1)
<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Deaths</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.</td>
<td>11,439,011</td>
<td>248,462</td>
<td>2.2%</td>
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<tr>
<td>Transplant</td>
<td>188</td>
<td>24</td>
<td>12.3%</td>
</tr>
</tbody>
</table>
Review of Questions

- Can COVID survivors (recovered) be organ donors?
  Not sure, long-term effects not clear

- Will “at risk” populations such as transplant patients have early access to the COVID vaccine once approved?
  Hope so
Clinical characteristics and risk factors associated with COVID-19 disease severity in patients with cancer in Wuhan, China: a multicentre, retrospective, cohort study

Jianjie Tian*, Xiaofen Yuan*, Jun Xia*, Qiang Zhang*, Chengxiang Yang*, Bo Li*, Xinmin Cai*, Zequing Li*, Jing Wang, Yanan Wang, Shaoqin Liu, Biao Cheng, Jin Wang, Ming Zhang, Lu Wang, Sijun Shi, Zhi Yao, Xiongbo Deng, Fan Zhou, Wei Wei, Qianli Li, Xiu Chen, Wenhong Chen, Qin Yang, Shijun Wu, Jiquan Fan, Bo She, Zhiquan Hu, Shuangliang Wang, Xiangping Yang, Wenhao Li, Xixiao Mi and Zhihua Wang*

Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study

To identify potential prognostic factors for mortality and severe illness in cancer patients with COVID-19

COVID-19 and Cancer Consortium (CCC19) – USA, Canada, Spain

1035 patients included

Most common cancers were breast (21%) and prostate (16%)
COVID-19: CANCER

- **Age** (odds ratio 1.84, 95% CI 1.53-2.21)
- **Male** sex (odds ratio 1.63, 95% CI 1.07-2.48)
- **Smoking** status (odds ratio 1.60, 95% CI 1.03-2.47)
- Number of **co-morbidities** (odds ratio 4.50)
- **Poor Performance** ECOG (odds ratio 3.89)
- **Active cancer** (odds ratio 5.20)
CYTOKINE STORM: CYTOKINE RELEASE SYNDROME

SARS-CoV2 → COVID-19 infection

Epithelial cells → ROS → Cell death

Immune invasion

Epithelial cells → Macrophages → Activated T cells

Macrophages → Neutrophils

Cytokines

↑ IL-1, ↑ IL-2, ↑ IL-6, ↑ TNF-α, ↑ IFN-γ

Cytokine storm

PRR activation

PAMPs + DAMPs

Tissue damage

Inflammatory cascade → Bacterial infection → Acute respiratory distress syndrome → Sepsis → Multi-organ dysfunction syndrome

Lungs

Dry/productive cough, rhinorrhea, sneezing, sore throat, dyspnoea, haemoptysis, increasing fever

Gastrointestinal tract

Nausea, vomiting, diarrhoea, infection of lower GI

Brain

Headache, impaired consciousness, confusion, acute cerebrovascular diseases (stroke), skeletal muscle injury, anosmia, hypogeusia, brain inflammation

Cardiovascular system

Heart palpitations, chest tightness, blood clots, heart attacks, cardiac inflammation

Liver

Raised AST

Kidneys

Oliguria, haematuria, proteinuria, rapid fall in blood pressure

Microcirculation

Hypoxemia

Eyes

Conjunctivitis
CHANGES IN BLOOD INFLAMMATORY MARKERS

- LDH Levels
- CRP Levels
- Ferritin Levels
- IL6 Levels

Graphs showing changes over time from tocilizumab dose.
CYTOF ANALYSIS
MUTIPLE INFLAMMATORY PATHWAYS

SARS-CoV-2
- Spike protein
- Viral RNA

ACE2

New infecting SARS-CoV-2

Host cell ribosomes

Genomic RNA release

Genomic RNA replication

Translation

Multiple proteins

Proteolysis

Direct activation, lectin pathway

Immune complexes, classical pathway

Toll-like receptor

Toll-like receptors, alternative pathway

Complement activation

C5

C3

C5a

C3a

Neutrophil

Macrophage

Cytokine release syndrome and accumulation of neutrophils and monocytes/macrophages

Day 0

Virus entry

ACE inhibitors?

Remdesivir
Ritonavir/lopinavir

1-2

Virus replication in the airway cells

3-5

Activation of innate immunity in the lung: maladaptive inflammatory response

Pathway-specific inhibitors

Anti-C3

Anti-C5

5-7

ARDS

7-14

Anti-IL-6
Anti-IL-1?
Anti-IFN?
MULTIPRONG APPROACH

Day 0
- Virus entry
  - ACE inhibitors?
    - Remdesivir
    - Ritonavir/lopinavir

1-2
- Virus replication in the airway cells
  - T

3-5
- Activation of innate immunity in the lung: maladaptive inflammatory response
  - T
  - Pathway-specific inhibitors
    - Anti-C3
  - Anti-C5
  - Anti-IL-6
  - Anti-IL-1?
  - Anti-IFN?

5-7
- Anti-C3
- Anti-C5
- Anti-IL-6
- Anti-IL-1?
- Anti-IFN?

7-14
- ARDS

= Tocilizumab
= Anakinra
= Infliximab
MULTIPRONG APPROACH

COVID-19 Subject

1- MSCs are safe

2- When delivered systemically, MSCS home to the lungs

3- MSCs are ‘immune privileged’

ARDS, ALI, Inflammation, Fever

ARDS

Macrophage

Chemokines Cytokines

IL-6
IL-8
TNF-α

Activated Neutrophil

SARS-CoV-2

Alveolar cells

Capillary

MSC

4- Immunomodulation: via IL-10, TGFβ, IDO, PGE2

5- Antimicrobial: via LL-37, MicroRNAs

6- Regeneration via VEGF, KGF, EGF

Injured endothelial Cell

Red blood cell

Cell debris

Leaky endothelium
# Analysis of the Implementation of Telehealth Visits for Care of Patients With Cancer in Houston During the COVID-19 Pandemic

## Table 1. Patient Characteristics and Associations with Utilization of MyChart Video Visits

<table>
<thead>
<tr>
<th>Demographics</th>
<th>No. of Patients (%) or Mean</th>
<th>No. of Patients Accepted (%) or Mean</th>
<th>No. of Patients Declined (%) or Mean</th>
<th>P (accepted vs. declined)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>N=1782</td>
<td>61.4 (17-98)</td>
<td>60.2 (17-98)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Median Income (in $1k)</td>
<td>N=1782</td>
<td>71.45 (8.5-154)</td>
<td>72.32 (8.5-154)</td>
<td>66.86 (2.1-241.9)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>585 (33.2)</td>
<td>476 (32.2)</td>
<td>109 (38.2)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>1177 (66.8)</td>
<td>1001 (67.8)</td>
<td>176 (61.8)</td>
</tr>
<tr>
<td>Ethnicity/race</td>
<td>White</td>
<td>1061 (60.8)</td>
<td>877 (59.9)</td>
<td>184 (65.7)</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>312 (17.9)</td>
<td>270 (18.4)</td>
<td>42 (15.0)</td>
</tr>
<tr>
<td></td>
<td>Hispanic</td>
<td>227 (13.1)</td>
<td>192 (13.1)</td>
<td>35 (12.5)</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>103 (5.9)</td>
<td>91 (6.2)</td>
<td>12 (4.3)</td>
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<tr>
<td></td>
<td>Other</td>
<td>41 (2.3)</td>
<td>34 (2.3)</td>
<td>7 (2.5)</td>
</tr>
<tr>
<td>Insurance Type</td>
<td>Commercial Insurance</td>
<td>1037 (59.4)</td>
<td>926 (63.3)</td>
<td>111 (39.2)</td>
</tr>
<tr>
<td></td>
<td>Medicare/Medicaid</td>
<td>643 (36.8)</td>
<td>489 (33.4)</td>
<td>154 (54.4)</td>
</tr>
<tr>
<td></td>
<td>Other (Tricare, VA, self-pay)</td>
<td>67 (3.8)</td>
<td>49 (3.3)</td>
<td>18 (6.4)</td>
</tr>
</tbody>
</table>

Figure 1. It illustrates and multivariate analysis, a lower age (A, B), a higher median income (B, D) and having commercial insurance (C, D) are associated with participation in telemedicine video visits. In multivariate analysis, female sex is associated with participation but this association is not statistically significant in multivariate analysis (B). Age and median income are depicted as continuous variables and type of insurance is categorical.
The COVID-19 and Cancer Consortium

Please click the button below to report on a cancer patient with COVID-19. See below for eligibility.

ACCESS THE SURVEY
THANKS

Katherine Perez
Deepa Gotur
Susan Miller
William Musick
Faisal Masud
Asma Zainab
Prakruthi Voore

Jasleen Randhawa
S Ravi Pingali
Shilpan Shah
Malcom Brenner
Helen Heslop
Tejaswini Reddy
Liliana Guzman
Jessica Bronstad
Stephen Wong
Akshjot Puri
Eric Bernicker
Jorge Darcourt

All our frontline physicians, nurses, care providers

To and for our patients
COVID-19 Testing

Houston Methodist Town Hall

11/19/2020
SARS-CoV-2

Viral composition

- Nucleocapsid Protein (1000 copies)
- Spike Protein (100 copies)
- Membrane Protein (2000 copies)
- Envelope Protein (20 copies)
- ssRNA
- Affinity to ACE2-R
  Kd: 1-30 nM
- Lipid Membrane
- Host Cell

Ralph Weissleder, Hakho Lee, Jina Ko, Mikael J. Pittet, 2020
Testing for COVID-19

- Viral RNA
- Proteins (Antigen)
- Immune response
  - Antibody
  - T-cell
Laboratory Testing for COVID-19

- Sample
  - “Go to where the money is”
- Infects epithelia and other cells

- Nasopharyngeal*
- Nasal*
- Oropharyngeal
- Sputum
- Bronchoalveolar Lavage
- Tracheal aspirates
- Saliva

- Discrepancies
  - Viral concentrations
COVID-19 Testing

• There are no FDA approved tests

• Two avenues for tests to be available for clinical use
  – Laboratory developed test
    • Only one lab, not marketed
  – Emergency Use Authorization from FDA
    • Expedited review of validation data by FDA
    • Can be marketed

  – Houston Methodist uses EUA assays
Viral composition

- Nucleocapsid Protein (1000 copies)
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- Envelope Protein (20 copies)
- ssRNA
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COVID-19 Nucleic Acid Amplification Tests

a) sample collection

b) RNA extraction

c) Reverse transcription

d) RT-PCR amplification

e) Results
Current Testing at Houston Methodist

• Nucleic acid amplification tests
  – Reverse Transcriptase Real Time-PCR (RT-PCR)

• Multiple platforms (all concordant)
  – Fastest turnaround time is Cepheid with on-board time of 75 minutes
    • Reagents very limited by vendor allocation
    • Reserved for STAT situations
  – Average turnaround time (all platforms aggregated) in past 7 days is 5.4 hours from receipt in laboratory
  – Specimens: NP, OP, NS, BAL, sputum and Tracheal aspirations
• Statistics 262,741 tests
  – 27,985 positive
    • 10.07% cumulative positive
    • 2.5% of TX positives have been diagnosed at HM
  – Maximum throughput over 7,500 per day

– as of 11/16/2020
Antigen Tests

• Seven antigen assays
  – All but one detect nucleocapsid protein
  – Sampinite detects Receptor Binding Domains of Spike protein
  – Instrument read except BinaxNow and CareStart (visual)

• Sofia 2 SARS Antigen FIA (Quidel)
• BD Veritor System SARS-CoV-2
• LumiraDx SARS-CoV-2 Ag Test
• BinaxNOW COVID-19 Ag Card
• Sofia 2 Flu + SARS Antigen FIA
• CareStart COVID-19 Antigen test
• Sampinite™ COVID-19 Antigen MIA

• Note: BinaxNOW is totally under government control and not available from the vendor
Antigen Tests

- FDA indicates that each antigen test is unique
- All have decreased sensitivity relative to NAAT

**Negative test result:**
- BD and CareStart – all negative results are presumptive
- Sofia (Quidel), LumiraDx and Sampinite – presumptive after certain time from symptom onset or exposure

**Positive test result:**
- Treat as positive
- However, false positives (FP) do occur
- Different algorithms are suggested for identification of FP and their resolution
Antigen Tests

• FDA issued warning letter 11/03/2020
  – False positives occur
  – Highlighted areas of concern
  – Must adhere to manufacturer’s instructions
  – Correlate with clinical symptoms especially in long-term care facilities
• We evaluated several other SARS-CoV-2 tests

  – Collected NP sample and tested by HM current method

  – Collected specimen for other test and/or also tested NP on candidate system per manufacturer’s directions
Of 100 patients positive by NP Swab by an HMH RT-PCR:
– 63 will be positive by nasal swab via RT-PCR
– 47 will be positive on Abbott ID Now
– 40 will be positive on Sofia (Quidel) Antigen test

All patients negative on HMH RT-PCR were negative by other tests and/or with other specimen type

Others ongoing
Influenza Season?

• Minimal Influenza in Southern Hemisphere in 2020 world-wide

• At Houston Methodist, there have been a total of 18 cases of Influenza A/Influenza B since September 15, 2020

• [https://flu.houstonmethodist.org/](https://flu.houstonmethodist.org/)

• COVID-19 plus Influenza tests are available
COVID-19 Antibodies

Viral composition

- Nucleocapsid Protein (1000 copies)
- Spike Protein (100 copies)
- Membrane Protein (2000 copies)
- Envelope Protein (20 copies)
- ssRNA
- Lipid Membrane

Affinity to ACE2-R
Kd: 1-30 nM

Host Cell

Ralph Weissleder, Hakho Lee, Jina Ko, Mikael J. Pittet, 2020
COVID-19 Antibody Development

https://www.globalbiotechinsights.com/articles/20247/the-worldwide-test-for-covid-19
Antibodies to SARS-CoV-2

• Not for acute diagnosis
• Can demonstrate previous exposure/infection
• Immune status
  – Post-vaccination
• Convalescent plasma
  – Ortho Vitros assay is used to qualify convalescent plasma
Post-vaccination Testing

• Post-vaccination Antibodies
  – Quantitative antibody levels tested at some frequency
  – Quantitative assay will be available at Houston Methodist

• T-cell Immunity
  – For those without post-vaccination antibody response
  – Methods are not easy or scalable
  – Active area of research
THANKS

• Dr. Musser, Chairman

• Molecular team
  – Drs. Olsen, Thomas, Li

• Microbiology team
  – Drs. Long and Olsen

• Serology team
  – Drs. Eagar and Yi

• Dr. Boom
  – Drs. Roberta Schwartz, Sostman and Phillips

• Many lab techs, staff, collectors, admin, etc.
New reported deaths by day in the United States

National Hotspot Map

Trend of COVID-19 Compared to Mask Usage by State

Masking up
Fewer covid-19 symptoms reported in states with higher rates of mask use.

Percentage of people who know someone with covid-19 symptoms

Percentage of people wearing masks in public all or most of the time

Data as of Oct. 19
Source: Delphi CovidCast, Carnegie Mellon University

Texas Hotspot Map

Average daily cases per 100,000 people in past week

Few or no cases

Texas COVID-19 Stats

Daily reported new cases
15,000 cases

Daily reported deaths
300 deaths

Daily reported specimens tested
150,000 tests

Hospitalizations
10,000
**DAILY NEW COVID-19 POSITIVE CASES**

*Greater Houston Area*[^1]

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**Monitoring threshold:**
Threshold is exceeded by the occurrence of a positive daily growth rate (averaged over 7 days) in the new daily case trend.

**Current status:**
12 days of positive daily growth rate (averaged over 7 days) in the new daily case trend.

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[^1]: [COVID-19 Case Trends](https://www.dshospitals.org/coronavirus)
Houston Methodist Testing Trend

Confirmed COVID-19 Lab Tests

Positive COVID-19 Tests
7 Day Rolling Average of Percent of Positive Tests
TMC Daily New COVID-19 Hospitalizations

Monitoring threshold:
Threshold is exceeded by the occurrence of a positive daily growth rate, averaged over 7 days

Current status: 0.8% daily growth rate (averaged over 7 days) in the COVID-19 daily hospital admissions trend

Notes:
While new daily cases may fluctuate for a variety of reasons (e.g., testing), the daily hospitalization trend shows an objective view of how COVID-19 impacts hospital systems

This document is solely intended to share insights and best practices rather than specific recommendations. All information presented is shown as reported and has not been independently verified.
Houston Methodist COVID-19 Cases by Day

Houston Methodist COVID-19 Patients by Day

- Med/Surg Pos + Now Neg
- ICU Pos + Now Neg
- Total Pos + Now Neg
- IMU Pos + Now Neg
Current status: 80% total daily growth rate

2.6% ICU daily growth rate

4.6% Med Surg daily growth rate

COVID-19 patients in TMC hospitals (averaged over 7 days) in hospitals

November 17, 2020

Notes:

While daily cases may fluctuate for a variety of reasons (e.g., testing), the number of COVID-19 positive patients being treated in med surg and ICU shows an objective view of how COVID-19 impacts hospital systems.
How do you account for the $R(t)$'s continuing to hover a little above 1, but the case count and positivity rate keep increasing?
Houston Area Rt Estimate Trend

Rt estimate

This graph shows the R(t) over time. R(t) is a measure of contagiousness or how many people one COVID19 person infects. If R(t)>1, the epidemic is increasing. If R(t)<1, the epidemic is declining. There is higher alert if the whole interval is above the horizontal line at 1. For **Q - Houston**, the rate of contagiousness is **1.10**; the epidemic is increasing.

https://sph.uth.edu/dept/bads/covid19-dashboard; similar BCM site: https://ictr.github.io/covid-19-county-R0/
What is the best way to approach family gatherings at the holidays? Advice for flying?
1. Science, especially biological science, is messy in real time.
2. Hospitals together must work on their “Sacred AND”
3. Our political leaders must work together on society’s “Sacred AND”
4. Our social lives must take a backseat to the “Sacred AND”
5. Masks are a means to accomplish the “Sacred AND”
COVID-19 Precautions – Holiday Safety

“The safest way to celebrate Thanksgiving this year is to celebrate with people in your household. If you do plan to spend Thanksgiving with people outside your household, take steps to make your celebration safer.”

Safest Options

- Gather only with those in your household
- Host a virtual celebration

Least Safe Options

- Create a “holiday bubble” using social distancing and testing
- Bubble is only as strong as the weakest link

- Gather with individuals outside your “bubble”
- At a minimum, follow CDC recommendations

COVID-19 Precautions –
Holiday Safety

Hosting a Thanksgiving Gathering

If having guests to your home, be sure that people follow the steps that everyone can take to make Thanksgiving safer. Other steps you can take include:

- Have a small outdoor meal with family and friends who live in your community.
- Limit the number of guests.
- Have conversations with guests ahead of time to set expectations for celebrating together.
- Clean and disinfect frequently touched surfaces and items between use.
- If celebrating indoors, make sure to open windows.
- Limit the number of people in food preparation areas.
- Have guests bring their own food and drink.
- If sharing food, have one person serve food and use single-use options, like plastic utensils.

COVID-19 Precautions – Holiday Safety

Thanksgiving Travel

Travel increases your chance of getting and spreading COVID-19. Staying home is the best way to protect yourself and others.

If you do travel

- Check travel restrictions before you go.
- Get your flu shot before you travel.
- Always wear a mask in public settings and on public transportation.
- Stay at least 6 feet apart from anyone who is not in your household.
- Wash your hands often or use hand sanitizer.
- Avoid touching your mask, eyes, nose, and mouth.
- Bring extra supplies, such as masks and hand sanitizer.
**What are the most promising treatments?**

Methodist has one of the lower death rates of any hospital. Does Methodist have a ‘COVID best practices’ that they share with other hospitals? If a loved one were to get sick at another hospital, is there a particular ‘formula’ to the treatment of patients that has been shared?
HM Treatment Protocols

HM SARS-CoV-2 / COVID-19 Treatment Algorithm

This is a guidance document only and is not a replacement for clinical judgement in a multidisciplinary collaborative.

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

All COVID-19 patients should receive chemical VTE prophylaxis unless contraindicated - HM COVID Anticoagulation Guide

Acute Care

Mild S/Sx
Fevers, cough, URI

Supportive Care
& Close Monitoring

Mild-Patient COVID-guide

Moderate S/Sx
SpO2 > 94% RA

Evaluate for Remdesivir Using HM Formulary Approved Criteria*

Inclusion:
- Confirmed COVID PCR within ≤4 days & symptoms ≤10 days
- Radiographic evidence of Pulmonary Infiltrates
- Requires supplemental O2 to maintain SpO2 ≥94%

Exclusion:
- ALT or AST > 5x ULN
- Creatinine Clearance < 30mL/min

*Note: Remdesivir is RESTRICTED to Infections Disease, Pulmonology and Critical Care providers. Limited product availability may necessitate additional restrictions.

Severe S/Sx
SpO2 <94% RA, RR >24, Supplemental O2, Inminent Resp Fail, Shock

Critical Care

Please Note:
Available literature suggests a low proportion of bacterial co-infections in admitted COVID-19 patients (< 10%).

Risk Factors for Progression:
≥ 60yo
ESRD/EOLD
ALC <800
Morbid Obesity (BMI>40)

Consider Infectious Disease and/or Pulmonology Consult in these cases or if COVID Rx is needed.

With ANY Risk Factors:
Assess Inflammatory Lab Bundle
IgG, IL-6, Ferritin, CRP, D-Dimer, Fibrogenin, PT, aPTT, LDH, TG

**Check serum HCG in females of child-bearing potential

Contact William Musick, PharmD (832-747-4749, wemusick@houstonmethodist.org) with questions and/or updates.

Inflammatory Lab Bundle
IgG, IL-6, Ferritin, CRP, D-Dimer, Fibrogenin, PT, aPTT, LDH, TG

Consider Infectious Diseases and/or Pulmonology Consult

Immune Modulation

- Consider Dexamethasone
- IF ≥ 7 DAYS from onset of symptoms
  (DO NOT start Dex if NOT requiring supplemental oxygen)

Upon admission to ICU:
Lactate, LFTs, blood cross & type, Troponin, EKG (Baseline QTc), serum HCG if indicated
Daily: CRP, Ferritin, LFTs, Mg, Phos, CBC, c Dfll, BMP
EKG if on multiple agents that prolong QTc
Monoclonal Antibody Results

• Regeneron (Press release)
  – Dual mAb “cocktail” in 275 outpatients
    • Greater effect with poor native antibody response, high viral load
    • Reduced medical visits (4.9% low dose / 7.7% high dose vs. 15.2% placebo)
    • Infusion reactions: 2 in placebo group, 1 in antibody group
  – Inpatient trial
    • Pause for “unfavorable risk / benefit”
    • No details yet
Monoclonal Antibody Results

- **Lilly**
  - Single mAb in 452 outpatients (NEJM October 2020)
    - Hospitalization / ER visits: 1.7% treated vs. 6% placebo (RR = .28)
    - 8% resistant mutants in treated group vs. 6% in placebo
    - EUA November 2020 for high-risk outpatients
  - Dual mAb “cocktail” in 268 outpatients (Press release)
    - Hospitalization / ER visits: 0.9% treated vs. 5.8% placebo (RR = .15)
    - No resistant mutants in treated group
  - Inpatient trial halted for futility (Press release)
    - No details yet
U.S. reaches deal with Eli Lilly for experimental SARS-CoV-2 antibody treatment

Reuters (10/28) reports the U.S. “will pay as much as $1.19 billion to Eli Lilly and Co to secure nearly 1 million doses of its experimental [SARS-CoV-2] antibody treatment.” The company “will start delivering 300,000 doses of the treatment, for which it is being paid $375 million, within two months of receiving an emergency use authorization.” According to HHS, the federal government then “has an option to buy an additional 650,000 vials for $812.5 million.”

Initial allocation for Texas = 5,780 vials / week
Will you take the vaccine? Is the vaccine safe?

There have been concerns about safety and efficacy of new vaccines due to reports of safety shortcuts and reduced testing standards. Please share your thoughts on Pfizer, its manufacturing processes and testing with regard to safety and clinical trials.

Is COVID-19 here to stay? How likely is it that the (eventual) vaccine will become part of normal childhood/adult inoculations?
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Antibody Response</th>
<th>T Cell Response</th>
<th>Species</th>
<th>N of Doses</th>
<th>Protection (Monkeys)</th>
<th>EUA Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna</td>
<td>100% (2x – 8x CP)</td>
<td>100%</td>
<td>Human</td>
<td>2</td>
<td>Infection</td>
<td>December 2020</td>
</tr>
<tr>
<td>Pfizer / BioNTech</td>
<td>100% (5x – 30x CP)</td>
<td>94%</td>
<td>Human</td>
<td>2</td>
<td></td>
<td>November 2020</td>
</tr>
<tr>
<td>J &amp; J</td>
<td>100%</td>
<td>82%</td>
<td>Human</td>
<td>1</td>
<td>Infection</td>
<td>Q1 2021</td>
</tr>
<tr>
<td>Oxford / Astra Zeneca</td>
<td>100% (= CP)</td>
<td>100%</td>
<td>Human</td>
<td>2</td>
<td>Disease</td>
<td>December 2020</td>
</tr>
<tr>
<td>Novavax</td>
<td>100% (2x CP)</td>
<td>100% (subgroup)</td>
<td>Human</td>
<td>2</td>
<td></td>
<td>Q1 2021</td>
</tr>
</tbody>
</table>

CP = convalescent plasma
Vaccine Updates

• Pfizer
  – 43,538 enrolled and randomized to vaccine or placebo
  – 170 infections so far / 95% protection with vaccination
  – 10 severe cases, 9 in placebo group
  – Appears to be effective in all ages and ethnicities
  – Unknowns
    • Infection vs. disease
    • Duration of protection
  – Safety profile appears very good (2-4% headache / fatigue)
  – Logistics: Two doses & extreme cold chain needed
  – mRNA technology appears to work
  – Phase 1 & pre-clinical data suggest other vaccines will also be effective
Vaccine Updates

• Moderna
  – > 30,000 enrolled and randomized to vaccine or placebo
  – 95 infections so far / 95% protection with vaccination
  – 11 severe cases – all in placebo group
  – Similar efficacy in all subgroups (preliminary review)
  – Unknowns
    • Infection vs. disease
    • Duration of protection
  – Safety profile appears very good
  – Logistics: Two doses & cold chain needed
  – Phase 1 & pre-clinical data suggest other vaccines will also be effective
Vaccine Updates

How mRNA Vaccines Work
The vaccine spurs healthy cells to produce viral proteins that stimulate a potent immune response

1. Scientists generated an mRNA sequence that codes for the virus spike protein
2. The RNA sequence, a blueprint for making the spike, is swathed in a lipid coating for delivery
3. Once it arrives, cells read the information in the mRNA sequence to produce millions of copies of the spike protein
4. The protein fragments spur the immune system to produce antibodies that can protect when a real virus enters the body

Sources: Pfizer, Bloomberg research
Hypotheses
- Coronavirus is an easy target
- Cross reactivity from other HCoV – is every dose a booster?
- mRNA technology may just be that good
  - note the Ab responses for Pfizer and Moderna compared with viral vector (AstraZeneca)
Vaccine Updates

- **J & J**
  - Trial re-started

- **AstraZeneca**
  - Trial re-started
  - Analysis of phase 1-2 data shows good immunogenicity > 55 yo
  - Reactogenicity was lower in > 55 yo
  - 1 death in Brazil – placebo group
Obstacles?

- Reluctance to accept vaccination
  - Political issues
  - Concerns about potential side effects
- Logistics Challenges
  - Supplies (borosilicate glass vials, needles, syringes, etc.)
  - Cold chain of refrigeration
  - Air freight capacity (8,000 jumbo jets)
  - Paperwork, customs, health regulations, etc.
  - Organizing administration sites, records, personnel
  - Monitoring safety, side effects
THANK YOU FOR ATTENDING OUR TOWN HALL CONVERSATION

If you would like more information about Transplant, Cancer, Testing, or The Society for Leading Medicine, please contact foundation@houstonmethodist.org

Take care and be well