## Today’s Agenda

<table>
<thead>
<tr>
<th>Topic</th>
<th>Presenter(s)</th>
<th>Approximate Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Welcome, Announcements, Introductions</td>
<td>Lachelle Smith, Director, ECHO Idaho</td>
<td>5 minutes</td>
</tr>
<tr>
<td>Idaho Epidemiology Curves and Public Health Updates</td>
<td>Carolyn Buxton Bridges, MD FACP</td>
<td>5 minutes</td>
</tr>
<tr>
<td>Public Health to Clinical Practice – Infection Control and Prevention Practices: PPE, UV light, Vaccination</td>
<td>Megan Dunay, MD MPH</td>
<td>10 minutes</td>
</tr>
<tr>
<td>The Basic Science Aspects of COVID-19: Virology and Immunology</td>
<td>Ranya Miura, PhD</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Review of Clinical Pearls and Q&amp;A</td>
<td>Sky Blue, MD</td>
<td>20 minutes</td>
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<tr>
<td></td>
<td>Tanya Miura, PhD</td>
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<td></td>
<td>Cathy Oliphant, PharmD</td>
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<td>Andrea Christopher, MD MPH</td>
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<td></td>
<td>Megan Dunay, MD MPH</td>
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<tr>
<td>Closing, Announcements, Call to Action</td>
<td>Megan Dunay, MD MPH</td>
<td>5 minutes</td>
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<td></td>
<td>Lachelle Smith, Director, ECHO Idaho</td>
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Microbiology of COVID-19 and the Infectious Disease Clinical Perspective

April 7, 2020

Sky Blue, MD
Tanya Miura, MD
Cathy Oliphant, PharmD
Carolyn Buxton Bridges, MD
Andrea Christopher, MD, MPH
Megan Dunay, MD, MPH
Idaho Public Health Updates

Carolyn Buxton Bridges, MD FACP
Governor’s Coronavirus Working Group, Former CDC Public Health Physician and Researcher
COVID-19 in Idaho

• At least 83 (7.1%) hospitalized
• At least 21 (1.8%) ICU
• At least 87 (7.4%) healthcare personnel

Confirmed Cases: 1,170
New Cases Today: 69 (4/6)
Deaths: 13

Data are preliminary and subject to change.

https://coronavirus.idaho.gov

Idaho has 1,170 reported cases of COVID-19 in 31 of 44 Idaho counties.
(hover over map for more info)
• Idaho Stay-at-Home order started on March 25.
• To be re-assessed before April 15.
SARS-CoV-2 Testing in Idaho

• 117% (2.17 times) increase in testing at commercial labs in 7 days.

• Reminder of high priority for IBL
  • Hospitalized patients
  • Symptomatic healthcare workers
  • Symptomatic patients in long-term care facilities

• Notify your local public health district within 24 hours of shipment for high priority specimens for IBL.

<table>
<thead>
<tr>
<th>Date</th>
<th>Number of people tested through the Idaho Bureau of Laboratories (IBL)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/30</td>
<td>1,567</td>
</tr>
<tr>
<td>4/2</td>
<td>1,851</td>
</tr>
<tr>
<td>4/6</td>
<td>2,263</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Number of people tested through commercial laboratories**</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/30</td>
<td>4,145</td>
</tr>
<tr>
<td>4/2</td>
<td>6,094</td>
</tr>
<tr>
<td>4/6</td>
<td>8,983</td>
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</tbody>
</table>

N95 vs Masks vs Cloth Facial Coverings

- REMINDER: Preserve PPE were possible — CDC PPE strategy page
- NEW CDC recommendation on use of cloth facial coverings
  - Not a substitute for social distancing (SD) and is NOT PPE
  - Considered for use in settings with difficult to maintain SD
  - Level of benefit is unclear
    - N=4 person study in Annals of Internal Medicine found not difference in virus in room with mask vs cloth, but significant methodologic issues

- NEW systematic review of N-95 vs surgical masks for non-high risk procedures (Bartoszko, et al)
  - 4 RCT’s among HCW – no difference in lab confirmed viral respiratory illnesses or ILI.

The Gap

Public Health, Basic Sciences, Clinical Medicine

...and the space between

Megan Dunay, MD MPH, Geriatrician, Boise VA and Medical Director for Geriatrics and Extended Care for VA Pacific Northwest Region
Mind the Gap
The way the world should be

<table>
<thead>
<tr>
<th>Clinical Care Consideration</th>
<th>Ideal Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>How do we determine who has COVID-19?</td>
<td>• Highly sensitive point of care test</td>
</tr>
<tr>
<td>How do we prevent the spread of COVID-19?</td>
<td>• Wear specific equipment</td>
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<tr>
<td></td>
<td>• Isolate patients who are positive in a consistent manner</td>
</tr>
<tr>
<td>How do we treat COVID-19 with antimicrobials?</td>
<td>• Prevent via vaccination</td>
</tr>
<tr>
<td></td>
<td>• Treat with a highly-effective antiviral</td>
</tr>
<tr>
<td></td>
<td>• Prevent Immune-mediated sequelae</td>
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</tbody>
</table>
The way the world is

<table>
<thead>
<tr>
<th>Clinical Care Consideration</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>How do we determine who has COVID-19?</td>
<td>• RT-PCR: virons, sub-cellular viral particles, cellular particles; 70% sensitivity at best?</td>
</tr>
<tr>
<td></td>
<td>• Antibody Testing: detectable 10-12 days after onset of symptoms</td>
</tr>
<tr>
<td>How do we prevent the spread of COVID-19?</td>
<td>• Virons in respiratory droplets?</td>
</tr>
<tr>
<td></td>
<td>• Virons aerosolized?</td>
</tr>
<tr>
<td>How do we treat COVID-19 with antimicrobials?</td>
<td>• Trials confounded by steroids</td>
</tr>
<tr>
<td></td>
<td>• Trials confounded by ECMO</td>
</tr>
<tr>
<td></td>
<td>• Patient selection</td>
</tr>
<tr>
<td></td>
<td>• Outcomes that matter</td>
</tr>
<tr>
<td></td>
<td>• Viral-mediated syndrome; immune-mediated syndrome</td>
</tr>
</tbody>
</table>
# Making sense of our world

<table>
<thead>
<tr>
<th>Philosophy of Science</th>
<th>Morality: The way the world should be</th>
<th>Rationality: The way the world is</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epistemology</strong></td>
<td><strong>Rousseau, John Locke</strong></td>
<td><strong>Thomas Hobbes, Ayn Rand</strong></td>
</tr>
<tr>
<td><strong>Empiricism: Pierre Duhem</strong></td>
<td>We should only accept observable evidence</td>
<td></td>
</tr>
<tr>
<td><strong>Induction: Francis Bacon</strong></td>
<td>Individual examples → Generalizations</td>
<td></td>
</tr>
<tr>
<td><strong>Deduction: Rene Descartes</strong></td>
<td></td>
<td>Premises → Logical conclusions</td>
</tr>
<tr>
<td><strong>Falsification: Karl Popper</strong></td>
<td>Evidence can only be used to rule out ideas, not to support them</td>
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</tbody>
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- How do we accept things as true?
- How do we justify that acceptance?
The Basic Science of COVID-19: Virology and Immunology

This much I know is true (at least for today...)

Tanya Miura, PhD
Microbiology, Associate Professor, University of Idaho
A timeline of coronavirus infections in humans

1965

HCoV-229E
HCoV-OC43
‘common cold viruses’

2004: HCoV-NL63
2005: HCoV-HKU1
colds, bronchiolitis, pneumonia

2002

SARS-CoV
New introduction into humans

2012

MERS-CoV

2019

SARS-CoV-2

SARS = Severe Acute Respiratory Syndrome
November 2002 – July 2003
8,273 Cases/775 Deaths (~10%)

MERS = Middle East Respiratory Syndrome
June 2012 - Present
2,519 Cases/866 Deaths (~34%)
Saudi Arabia 2,121/788
S Korea 2015: 186/36

COVID-19 = SARS-CoV-2
November 2019 – Current
1,346,299 Cases/74,679 Deaths (~5%)??

confirmed cases
largely untested
Coronaviruses: Structure and Replication

<table>
<thead>
<tr>
<th>mRNA Segment</th>
<th>Replication Enzymes</th>
<th>Structural &amp; Accessory</th>
</tr>
</thead>
<tbody>
<tr>
<td>5' - rep 1a</td>
<td>76%</td>
<td>72/32, 95, 91, 69, 85, 81, 40, 73, 94</td>
</tr>
<tr>
<td>rep 1b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3'</td>
<td>76-100% similar to SARS-CoV</td>
<td></td>
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</tbody>
</table>

76-100% similar to SARS-CoV

RNA replication enzymes

Structural & Accessory

76% 72/32 95 91 69 85 81 40 73 94
Coronaviruses: Structure and Replication

ACE2

TMPRSS2

or endosomal pathway

Attachment and entry

Spike protein

Viral release

Uncoating

Genomic RNA (positive)

Translation of ORF1a and ORF1b

RNA-dependent RNA polymerase

Transcription

Replication

Exocytosis

Vesicle

Golgi

Rough ER

Spike (S)

Membrane (M)

Nucleocapsid (N)

Envelope (E)

Genome RNA
Angiotensin Converting Enzyme 2 (ACE2) is the entry receptor for SARS-CoV-2

SARS-CoV-2 is better than SARS-CoV at binding ACE2

Shang, J. et al., 2020
Nature
Immune responses to coronaviruses: evasion of innate antiviral response

**Recognition**
- CoV
- ORF4a
- dsRNA
- Nsp16
- Host translation

**Signal transduction**
- RIG-I
- MDA-5
- MAVS
- IKKα
- IKKβ
- NFκB

**Translation**
- ssRNA
- Nsp1

**Signal transduction**
- IFNα/β receptor
- JAK1
- STAT1, STAT2
- Nsp1
- pSTAT1, pSTAT2
- ORF3b

**Transcription of antiviral genes**
- ISRE

**Nucleus**
- Proinflammatory cytokines
- IFN β
Immune responses to coronaviruses: immune-mediated damage

Source: Gralinski & Baric 2015
Journal of Pathology
Immune responses to CoV: dysregulated inflammation

**Pathogenic/dysregulated inflammation**
- Robust virus replication
- Delayed IFN response
- Inflammatory monocyte-macrophage and neutrophil infiltration
- Proinflammatory cytokines and chemokines

**Consequences:**
- Enhanced epithelial and endothelial cell apoptosis
- Increased vascular leakage
- Sub-optimal T cell and antibody responses
- Impaired virus clearance

**Outcome:**
- ALI
- ARDS
- Death

**Protective/regulated inflammation**
- Non-robust virus replication
- Early IFN response
- Inflammatory monocyte-macrophage and neutrophil infiltration
- Proinflammatory cytokines and chemokines

**Consequences:**
- Minimal epithelial and endothelial cell apoptosis
- Reduced vascular leakage
- Optimal T cell and antibody responses
- Effective virus clearance

**Outcome:**
- Protective immunity
- Host Survival

Source: Channappanavar & Perlman 2017 Seminars in Immunopathology
Review of Clinical Pearls

&

Q & A

Sky Blue, MD  Infectious Disease Medicine
Tanya Miura, PhD,  Microbiology, University of Idaho
Cathy Oliphant, PharmD,  Infectious Disease, Professor and Interim Chair, ISU College of Pharmacy
More to come...

• Friday, April 10 – Goals of Care: Difficult Conversations and Clinical Palliative Care for COVID-Positive Patients

**Opioid Addiction and Treatment Series**

• Thursday, April 9 – Managing Common Psychiatric Conditions and Substance Use Disorder through COVID-19