VCHIP / CHAMP / VDH COVID-19 UPDATES

Wendy Davis, MD FAAP - Vermont Child Health Improvement Program, UVM
Breena Holmes, MD FAAP – Director of Maternal & Child Health, Vermont Department of Health
June 29, 2020
1) **All participants will be muted upon joining the call.**

   If you dialed in or out, unmute by pressing #6 to ask a question (and press *6 to mute).

   Presenters: Please avoid the use of speakerphone and make sure your computer speaker is muted if you dialed in via phone.

2) **To ask or respond to a question using the Chat box, type your question and click the 📣 icon or press Enter to send.**
Launch of the “Tipping Your Cap” campaign by Major League Baseball (#TipYourCap2020)
- June 25, 1978: inaugural unfurling of the Rainbow Flag (at S. F. Pride)
- Today is also *Please Take My Children to Work Day*

This week: **REVISED call schedule Mon & Wed ONLY**

- Situation and AAP updates
- Today’s Media Briefing
- Practice Issue: **Update on COVID-19 Outbreaks, Serology, & Vaccines**
  - Drs. Bill Raszka and Ben Lee, Pediatric Infectious Diseases, UVM Children’s Hosp.
- Q & A, Discussion

*Please note: the COVID-19 situation continues to evolve very rapidly – so the information we’re providing today may change quickly*
Situation update

- Weekend (new) cases **not associated with outbreaks**.
- Fairhaven: significant community testing over weekend with **no positives**.

[Table with statistics]

- Total Cases: 1,208 (6 New)
- Currently Hospitalized: 2
- Hospitalized Under Investigation: 11
- Total People Recovered: 949
- Deaths: 56
- People Tested: 64,993
- Travelers Monitored: 1,571
- Contacts Monitored: 59
- People Completed Monitoring: 1,526

Situation update

COVID-19 Positive Cases by Sex
- Female 81.9%
- Male 47.7%
- Unknown 0.4%

COVID-19 Positive Cases by Ethnicity if Known
- Hispanic 3.8%
- Not Hispanic 96.2%

COVID-19 Positive Cases by Race if Known
- White 83.2%
- Black or African American 0.6%
- Asian 4.5%
- American Indian or Alaska Native 0.2%

Hover over charts to see values

AAP Updates

New guidance and policy this week:

- COVID-19 Planning Considerations: Guidance for School Re-entry
- HealthyChildren.org: Return to School During COVID-19
- Policy Statement: Electronic Documentation in Pediatrics: The Rationale and Functionality Requirements

Aim/goal: “drive electronic documentation improvement initiatives & maximize the benefits while mitigating potential negative aspects.”
Governor Scott:

- Friday (6/26/20): updated travel policy

- Today: recognition of State of Vermont agencies & partners:
  - **Legislature** – (temporary) end of session 6/26/20 evening
  - **State employees** (159 d. since Health Operations Center opened; 109 days since fully activated State Emergency Operations Center; extended team of 700: Health, Safety, Emergency Response workers).
  - **Many other state agencies**
Today’s Media Briefing

VDH Commissioner Levine:

- Recap of current data: maintaining slope VT epi curve.
- 10 new cases over weekend (none assoc. w/outbreaks); abundant testing. Percent positive remains low.
  - Weekend community testing Fairhaven: well over 200 tests all negative.
- Rest of U.S. ~65% upsurge over past weeks, w/record one-day totals:
  - E.g., FL (10K new cases on a day VT had 6 new cases), NV, SC, TX, CA
- Reminder of social/physical distancing; consider “exposure budget.”
- Definition of “recovered”: individual being monitored reports to VDH “recovered.” OR, if >30 days since onset of illness.
Today’s Media Briefing

VDH Commissioner Levine (cont’d.):

- VT HCWs w/pos. tests: 1/5 self-identify as HCW. 35% associated w/outbreaks. Others occurred late March/early April.
  - Ages 20-50 y.o. (somewhat younger than other cases); 70% F; 84% symptomatic; 92% not hospitalized.
- Hard to find states w/comparison data.
  - WA state: 37% cases reported employment in healthcare sector.
- Why? Increased risk to front-line workers; more frequent testing; HCWs comprise significant proportion of VT workforce.
- **Recognizing Vermont’s entire healthcare workforce.**

June 29, 2020
Practice Issue: Update on COVID-19 Outbreaks, Serology, Vaccines

Drs. Bill Raszka and Ben Lee, Pediatric Infectious Diseases
UVM Children’s Hospital
Ben and Bill’s COVID-19 Update June 29

• Outbreaks
• Serology
• Vaccines
One fifth of whom were asymptomatic when tested

Importance of testing both symptomatic and asymptomatic persons after a known COVID-19 exposure

Asymptomatic persons or those with mild symptoms likely play an important role in sustaining SARS-CoV-2 transmission during outbreaks

Do not congregate together!
People who had blood specimens tested for reasons unrelated to COVID-19
Percentage of Population Positive for SARS-CoV-2 Antibodies in Samples from Areas in 6 States

MARCH 23 - MAY 3, 2020

NEW YORK: CITY METRO, NY
CONNECTICUT
MISSOURI
SOUTH FLORIDA
UTAH
WESTERN WASHINGTON REGION

% OF POPULATION POSITIVE FOR SARS-COV-2 ANTIBODIES

MARCH 23 - APRIL 1
APRIL 6 - 10
APRIL 20 - MAY 3, 2020
## New York City Metro Region

<table>
<thead>
<tr>
<th>Seroprevalence estimate</th>
<th>Mar 23 - Apr 1, 2020</th>
<th>Difference between reported cases count and estimated case count based on survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.93%</td>
<td></td>
<td>12x higher</td>
</tr>
<tr>
<td>53,800</td>
<td>641,800</td>
<td></td>
</tr>
<tr>
<td>Cases Reported in that catchment area by April 1, 2020</td>
<td>Estimated Cases based on Seroprevalence and catchment area population</td>
<td>Range: 1.13 – 6.93%</td>
</tr>
</tbody>
</table>

Neutralizing antibody titers in symptomatic and asymptomatic COVID+ Chinese adults

Acute

Convalescent
Persistence of neutralizing Ab titers
COVID-19 Vaccine Progress

Benjamin Lee
06/29/20
Clinical evaluation of new vaccines

- **Phase I trials:**
  - First in humans
  - Small numbers (20–80)
  - Safety

- **Phase II trials:**
  - Larger (100–300)
  - Safety and immunogenicity

- **Phase III trials:**
  - Larger still (100s–10,000s)
  - Safety, immunogenicity, efficacy

- **Phase IV trials:**
  - Post-marketing approval safety monitoring, effectiveness
SARS-CoV-2

Receptor binding domain (RBD)


https://science.sciencemag.org/content/367/6483/1260
Coronavirus Vaccine Tracker

By Jonathan Corum, Denise Grady, Sui-Lee Wee and Carl Zimmer  Updated June 29, 2020

<table>
<thead>
<tr>
<th>Stage</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinical</td>
<td>125+</td>
<td>Vaccines not yet in human trials</td>
</tr>
<tr>
<td>Phase I</td>
<td>11</td>
<td>Vaccines testing safety and dosage</td>
</tr>
<tr>
<td>Phase II</td>
<td>8</td>
<td>Vaccines in expanded safety trials</td>
</tr>
<tr>
<td>Phase III</td>
<td>3</td>
<td>Vaccines in large-scale efficacy tests</td>
</tr>
<tr>
<td>Approval</td>
<td>1</td>
<td>Vaccine approved for limited use</td>
</tr>
</tbody>
</table>

The New York Times
• AZD1222: non-replicating adenovirus vector (ChAdOx1), 1 dose
• Pacing the field right now ($1.2 billion from US helps...)
• Trials in progress
  • Phase 2/3 in England, target N=10,000
  • Phase 3 trials in Brazil and South Africa (dosing this week), target N=2000 each
• US study planned for Sep, proposed N=30,000
• Pediatric trial also reportedly being planned (but no details)
• Scaling up manufacturing capacity in parallel and at known risk
• Goal of 2 billion doses total (400 million to US and UK by September)!
• 1 billion doses to low- and middle-income countries via license to Serum Institute of India (400 million by end of 2020)
At least some cause for concern:

ChAdOx1 nCOV-19 vaccination prevents SARS-CoV-2 pneumonia in rhesus macaques.

https://doi.org/10.1101/2020.05.13.093195doi:
• BBIBP-CorV: inactivated whole virus vaccine, 2 doses
  • Launching new phase 3 trial in UAE tomorrow

Development of an inactivated vaccine candidate, BBIBP-CorV, with potent protection against SARS-CoV-2.
• PiCoVacc: inactivated whole virus, 3 doses
• Slightly more encouraging animal data (but numbers small)
• Phase 3 trial in Brazil planned (N=9000)

Development of an inactivated vaccine candidate for SARS-CoV-2.
https://science.sciencemag.org/content/early/2020/05/06/science.abc1932
mRNA-1273: prefusion stabilized spike trimer, 2 doses
Fast: first in humans 66 days after release of SARS-CoV-2 sequence!
Plan for phase 3 trial next month

In mice:

SARS-CoV-2 mRNA vaccine development enabled by prototype pathogen preparedness.
https://doi.org/10.1101/2020.06.11.145920
Discovery/Preclinical → Phase 1 → Phase 2 → Phase 3 → Licensure

INOVIO
POWERING DNA MEDICINES

Beth Israel Lahey Health
Beth Israel Deaconess Medical Center
Johnson & Johnson

MERCK
iavi

The University of Queensland
CSL
gsk
Reasons for realism (aka pessimism)
• Inovio
  • DNA vaccine

• U. Oxford/AstraZeneca
  • Non-replicating viral vector (ChAdOx1)

• U. Queensland/GlaxoSmithKline
  • Purified recombinant prefusion spike protein
  • “Molecular clamp” technology

• U. Oxford/AstraZeneca
  • Non-replicating viral vector (ChAdOx1)

• Moderna
  • RNA vaccine

• Pfizer
  • RNA vaccine

• Merck
  • VSV vector (used in Ebola vaccines)

• Johnson & Johnson
  • Non-replicating viral vector (Ad26)
There is no substitute for human data!

- CanSino biologics: first phase I results published, to general disappointment (neutralizing antibodies lower than desired)
- Most efficacy trials performed over years, not months
- Rare safety signals usually cannot be detected in phase 3 trials—but may become a big problem post-licensure (RotaShield?)
- Biggest, most established vaccine manufacturers taking a slower approach...
Real challenges, part I

• Immune enhancement
  • Cell-mediated
    • Early RSV vaccine candidates
    • Early SARS vaccine candidates
  • Antibody-dependent
    • Dengue virus infection (and Dengvaxia vaccine)

• In children, MIS-C pathogenesis not understood
• Immune correlates of protection not defined
• Duration of immunity not understood
Real challenges, part II

• Powerful incentives for rapid vaccine distribution with relative paucity of safety information

• Proper clinical trials design
  • Ethical issues: need for exposure to test vaccine efficacy
  • Inclusion of children? Will trials need to be powered to detect MIS-C, as rotavirus vaccine trials were powered to detect intussusception?

• Controlled human infection models (CHIMs)
  • Volunteers may actually not be an issue
  • However, developing a reliable model typically takes years-decades
My opinions

• A widely available vaccine with solid safety and efficacy data is unrealistic to expect before fall/winter 2021, and maybe beyond

• Too much emphasis is being placed on rapid deployment of novel technologies without enough support for “tried and true” methods (despite longer development time)
Which approach?

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2075523/
Which approach?

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2075523/

Very fast!

Very slow!
SARS-CoV-2

1 **BIND TO A LUNG CELL**

When a virus spike protein latches onto an ACE2 receptor, a protease enzyme slices off the spike's head. This releases fusion machinery, part of the spike's stem that is compressed in a springlike state. ACE2 normally helps regulate blood pressure.

Join us **Wednesday, 7/1/20** for update on Children’s Integrated Services delivery (following VDH guidelines for in-person services, telehealth, new referrals, etc.) in response to your questions.

- AAP-VT Task Force on Race and Health Equity
- Immunization strategies/policy: catch-up, flu, COVID-19 (?)
- Health care “restart” details, incl. telehealth/telephone coverage
  - Federal and state plans for COVID-19 financial relief
- MIS-C (Multi-System Inflammatory Syndrome in Children)
- Summer camps/other recreational activities
- OneCare Vermont all-payer model adjustments
Q & A Goal: monitor/respond in real time – record/disseminate later as needed (and/or revisit next day).

For additional questions, please e-mail:
  - vchip.champ@med.uvm.edu
  - What do you need – how can we be helpful (specific guidance)?

VCHIP CHAMP VDH COVID-19 website:
https://www.med.uvm.edu/vchip/projects/vchip_champ_vdh_covid-19_updates

Next CHAMP call: **Wednesday, July 1, 12:15-12:45** (same webinar/call information – invitation to follow). **No call Friday, July 3, 2020 (Happy 4th!)**

Please tune in to VMS call with Commissioner Levine:
  
  **Tomorrow, Tuesday, June 30, 12:15-12:45**
  Phone: 1-802-552-8456
  Conference ID: 993815551