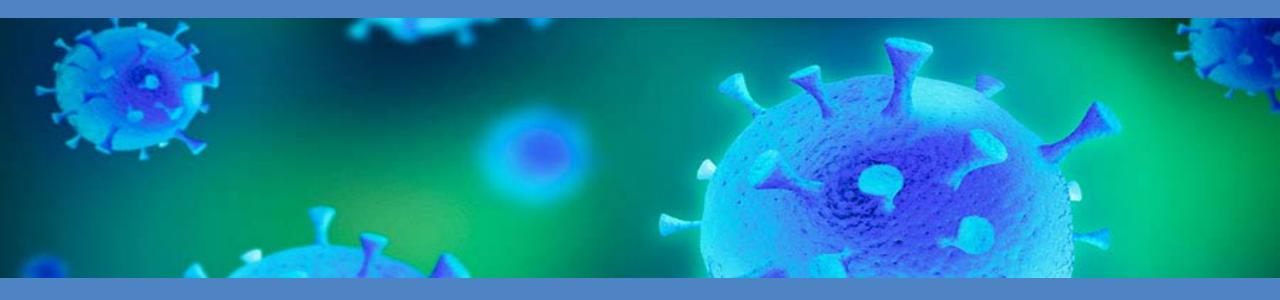
### VCHIP / CHAMP / VDH COVID-19 UPDATES



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









### **Technology Notes**

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 licon or press Enter to send.

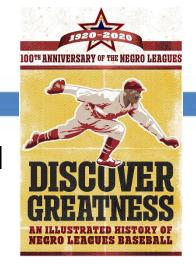






### Overview

- 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]

June 29, 2020

## Situation update

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
Last Updated: 6/29/2020, 10:48:29

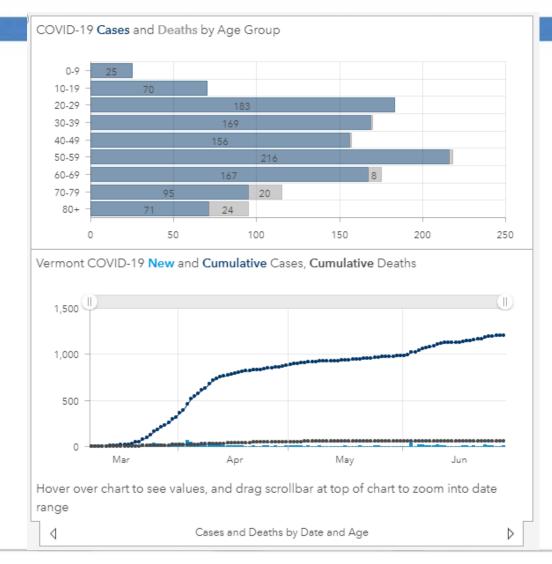
- Weekend (new) cases not associated with outbreaks.
- Fairhaven: significant community testing over weekend with *no positives*.

https://www.healthvermont.gov/response/coronavirus-covid-19/current-activity-vermont#dashboard



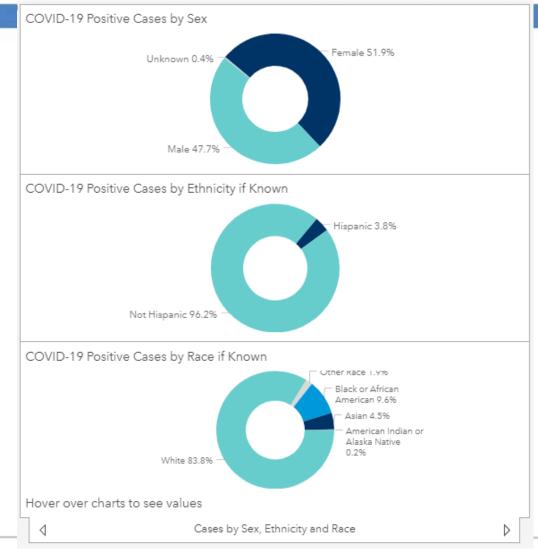


# Situation update





# Situation update







June 29, 2020

# **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
- Technical Report: Electronic Documentation in Pediatrics: The Rationale and Functionality Requirements
  - Aim/goal: "drive electronic documentation improvement initiatives & maximize the benefits while mitigating potential negative aspects."





# Today's Media Briefing

### Governor Scott:

- □ Friday (6/26/20): updated travel policy
  - https://dfr.vermont.gov/about-us/covid-19/modeling
- 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.







# Practice Issues

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

Drs. Bill Raszka and Ben Lee, Pediatric Infectious Diseases UVM Children's Hospital



University of Vermont Children's Hospital



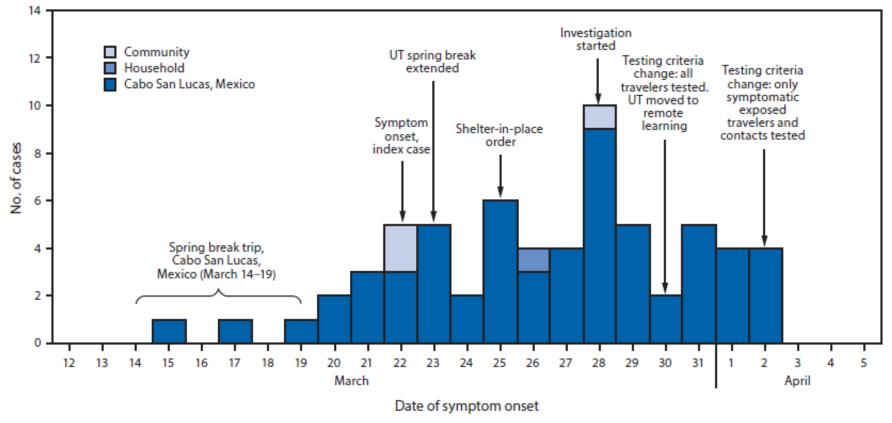




# Ben and Bill's COVID-19 Update June 29

- Outbreaks
- Serology
- Vaccines

FIGURE. COVID-19 cases (n = 64) following a spring break trip to Cabo San Lucas, Mexico, by exposure source and date of symptom onset,\* and public health investigation — Austin, Texas, March 12–April 5, 2020



One fifth of whom were asymptomatic when tested

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

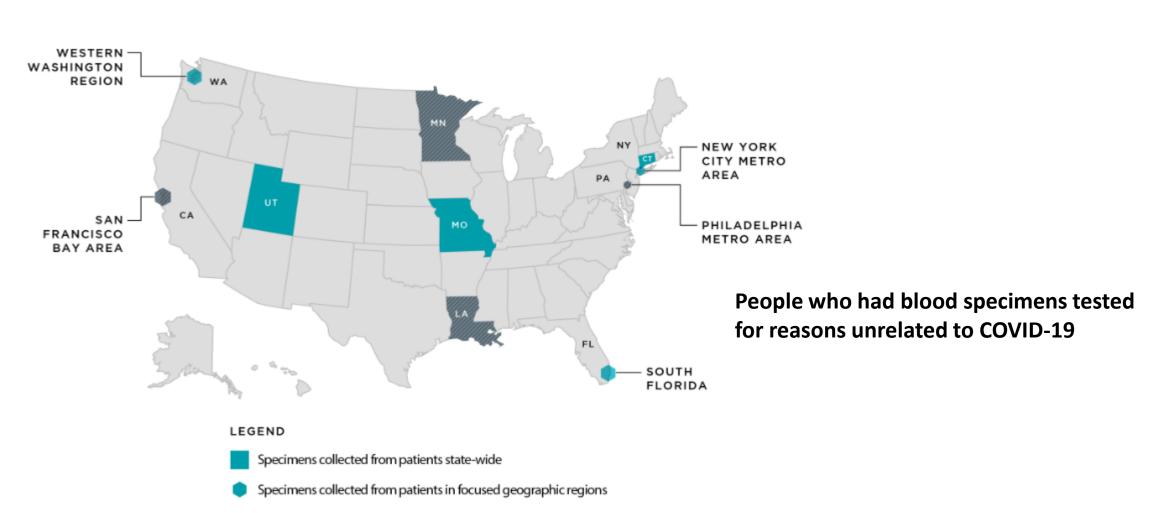
Asymptomatic persons or those with mild symptoms likely play an important role in sustaining SARS-CoV-2 transmission during outbreaks

#### Do not congregate together!

#### Commercial Laboratory Seroprevalence Survey Site Locations as of June 25, 2020

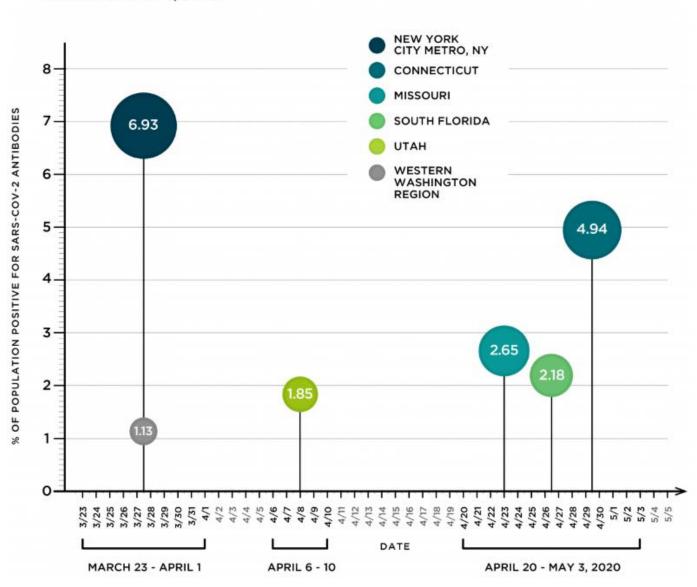
Future specimens collected from patients state-wide

Future specimens collected from patients in focused geographic regions



#### 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 Region

6.93%

Seroprevalence estimate

Mar 23 - Apr 1, 2020

When samples were collected

53,800

Cases Reported in that catchment area by April 1, 2020

641,800

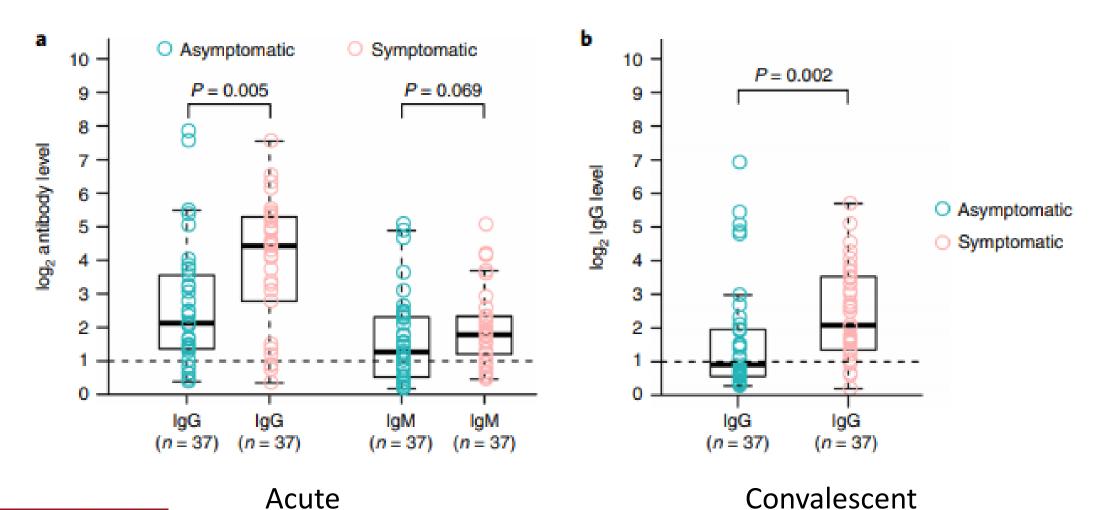
Estimated Cases based on Seroprevalence and catchment area population 12x higher ⊕

Difference between reported cases counts and estimated case count based on survey

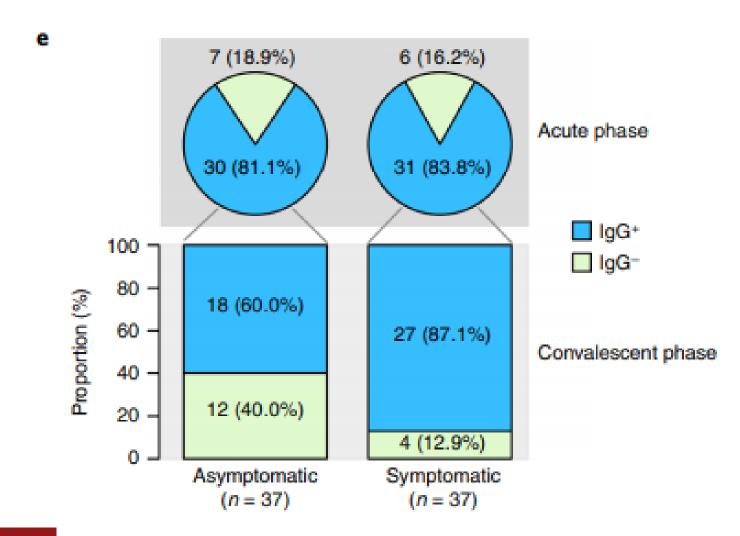
Range: 1.13 – 6.93%

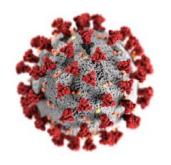
Range: 6- 24 x

# Neutralizing antibody titers in symptomatic and asymptomatic COVID+ Chinese adults



# 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:

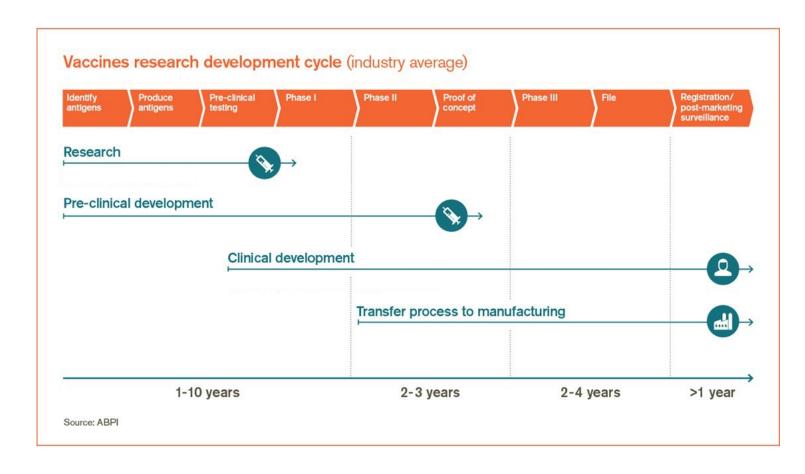
- Larger (100–300)
- Safety and immunogenicity

#### Phase III trials:

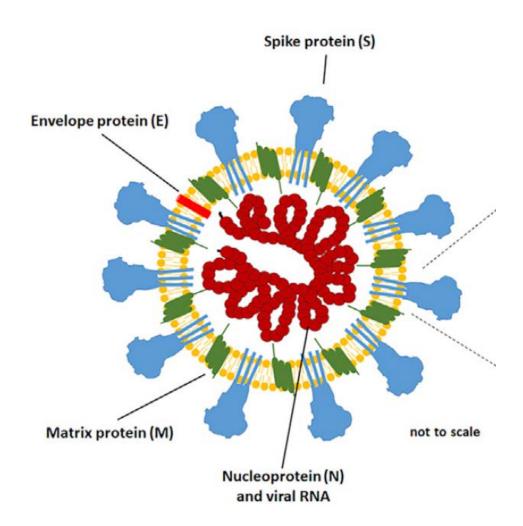
- Larger still (100s–10,000s)
- Safety, immunogenicity, efficacy

#### Phase IV trials:

 Post-marketing approval safety monitoring, effectiveness



### SARS-CoV-2



Receptor binding domain (RBD) Viral membrane

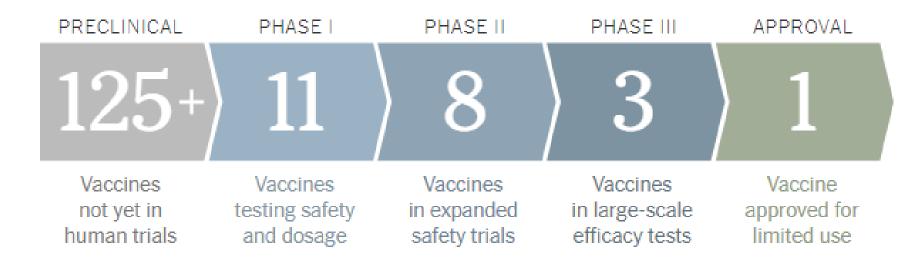
https://www.cell.com/immunity/pdf/S1074-7613(20)30120-5.pdf

https://science.sciencemag.org/content/367/6483/1260

### The New York Times

### Coronavirus Vaccine Tracker

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











**BCG** 





- 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)



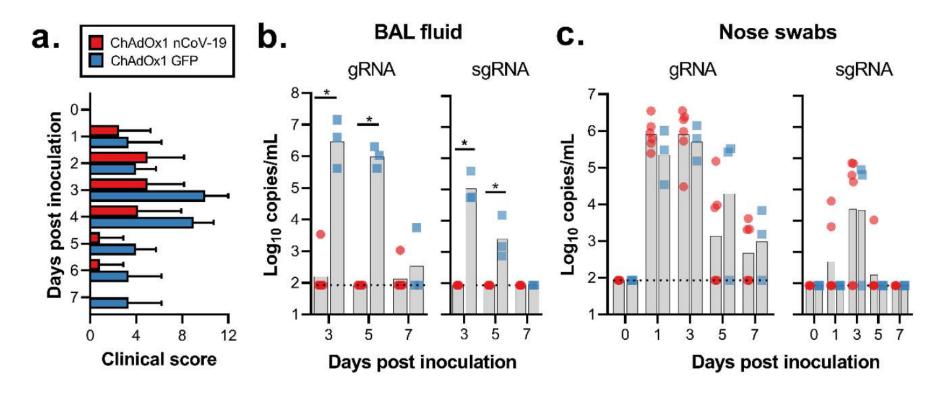


- Scaling up manufacturing capacity in parallel and at known risk
- Goal of 2 billion doses total (400 million to US and UK by September)!
- 1 billion doses to low- and middle-income countries via license to Serum Institute of India (400 million by end of 2020)





At least some cause for concern:



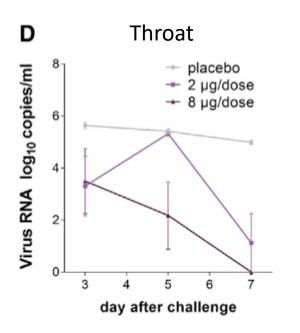
ChAdOx1 nCOV-19 vaccination prevents SARS-CoV-2 pneumonia in rhesus macaques. https://doi.org/10.1101/2020.05.13.093195doi:

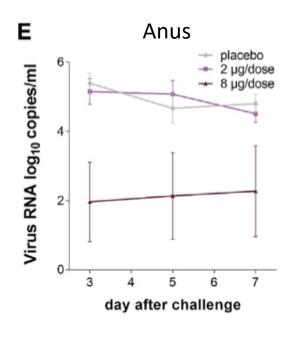


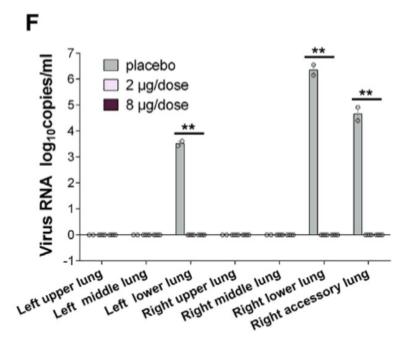
### 武汉生物制品研究所有限责任公司

WUHAN INSTITUTE OF BIOLOGICAL PRODUCTS CO., LTD.

- BBIBP-CorV: inactivated whole virus vaccine, 2 doses
  - Launching new phase 3 trial in UAE tomorrow















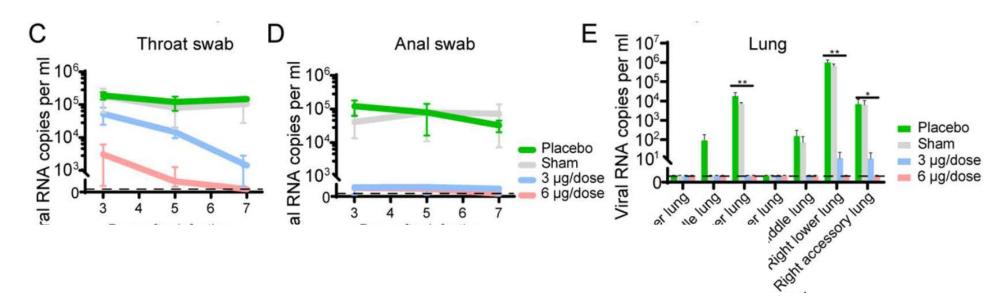






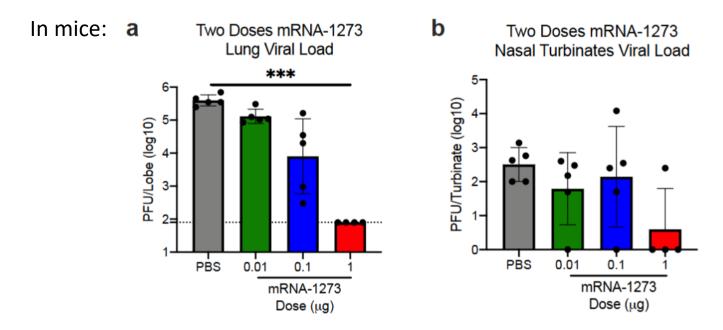


- PiCoVacc: inactivated whole virus, 3 doses
- Slightly more encouraging animal data (but numbers small)
- Phase 3 trial in Brazil planned (N=9000)





- 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



SARS-CoV-2 mRNA vaccine development enabled by prototype pathogen preparedness. https://doi.org/10.1101/2020.06.11.145920











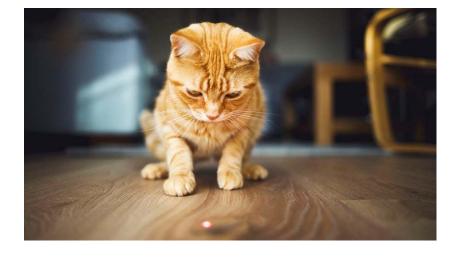




# Reasons for realism (aka pessimism)







# **WARP SPEED**

- 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

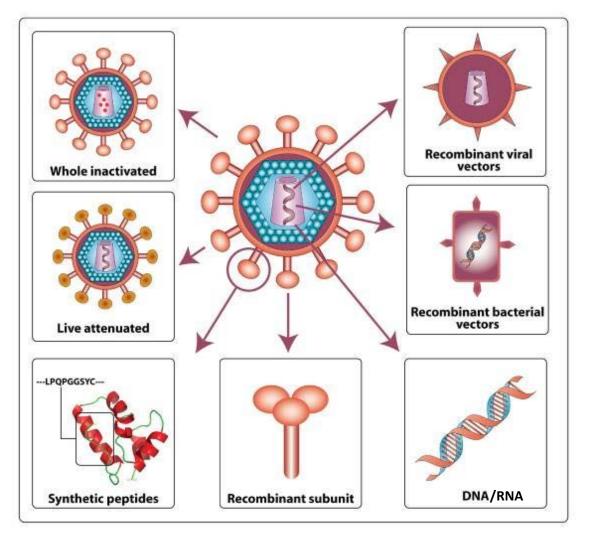
- Powerful incentives for rapid vaccine distribution with relative paucity of safety information
- Proper clinical trials design
  - Ethical issues: need for exposure to test vaccine efficacy
  - Inclusion of children? Will trials need to be powered to detect MIS-C, as rotavirus vaccine trials were powered 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)

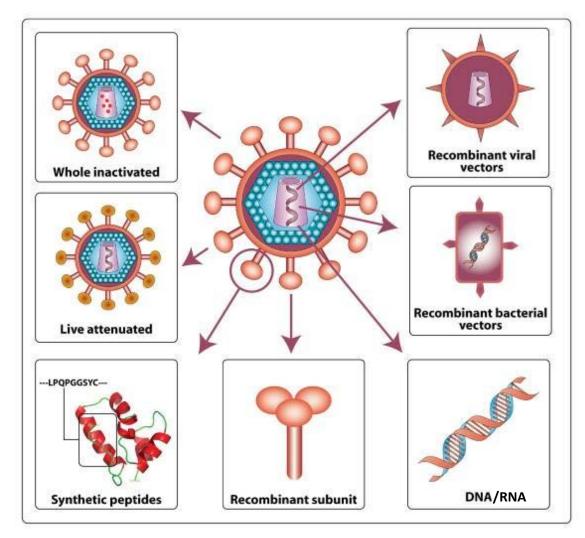


# Which approach?



# Which approach?

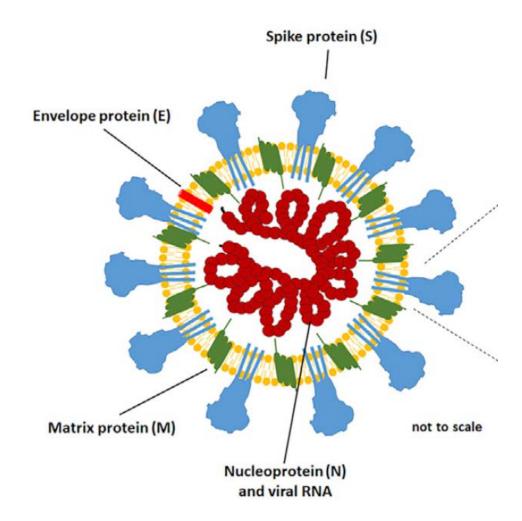
Very slow!



Very fast!

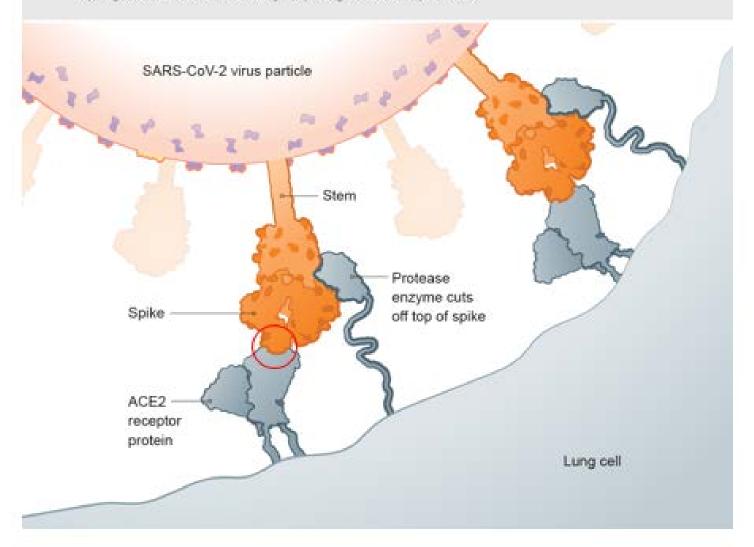
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2075523/

### 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.



# Topics We Are Following

- 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





### Questions/Discussion

- 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 <u>you</u> 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 4<sup>th</sup>!)
- 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



