COVID-19 Science Update

From the Office of the Chief Medical Officer, CDC COVID-19 Response, and the CDC Library, Atlanta, GA.
Intended for use by public health professionals responding to the COVID-19 pandemic.

***** Available on-line at https://www.cdc.gov/library/covid19 *****

Epidemiology

PEER-REVIEWED

Geographic access to United States SARS-CoV-2 testing sites highlights healthcare disparities and may bias transmission estimates. Rader *et al.* Journal of Travel Medicine (May 15, 2020).

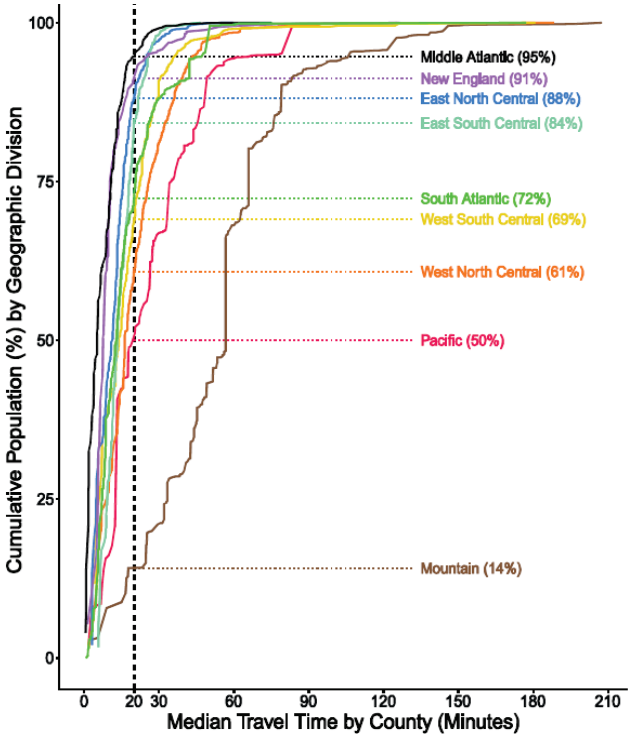
Key findings:

- Almost one-third of the US population resides in a county that has a median travel time of over 20 minutes to SARS-CoV-2 testing sites (Figure).
- Median travel time is longer in counties with lower population density, a higher percentage of racial/ethnic minorities (i.e., not non-Hispanic white), and a higher percentage of persons with no health insurance.

Methods: A modeling analysis to assess associations between sociodemographic factors and median travel time to 6,236 SARS-CoV-2 testing locations, by county. *Limitations*: Non-geographic barriers to SARS-CoV-2 testing access (e.g., economic) were not examined.

Implications: Geographic access to SARS-CoV-2 testing sites varies substantially by county in the US, which might influence healthcare disparities and reported case estimates.

Figure:



Note: From Rader *et al*. Median travel time by county versus the cumulative population for each geographic region. **Vertical dashed line** indicates 20-minute median travel time. Horizontal dotted lines indicate cumulative population percentage in that region (in parenthesis) residing in counties with <20 minutes median travel time. Licensed under CC-BY-NC-SA.

Modeling & Transmission

PEER-REVIEWED

Assessment of proficiency of N95 mask donning among the general public in Singapore. Yeung *et al.* JAMA Network Open (May 20, 2020).

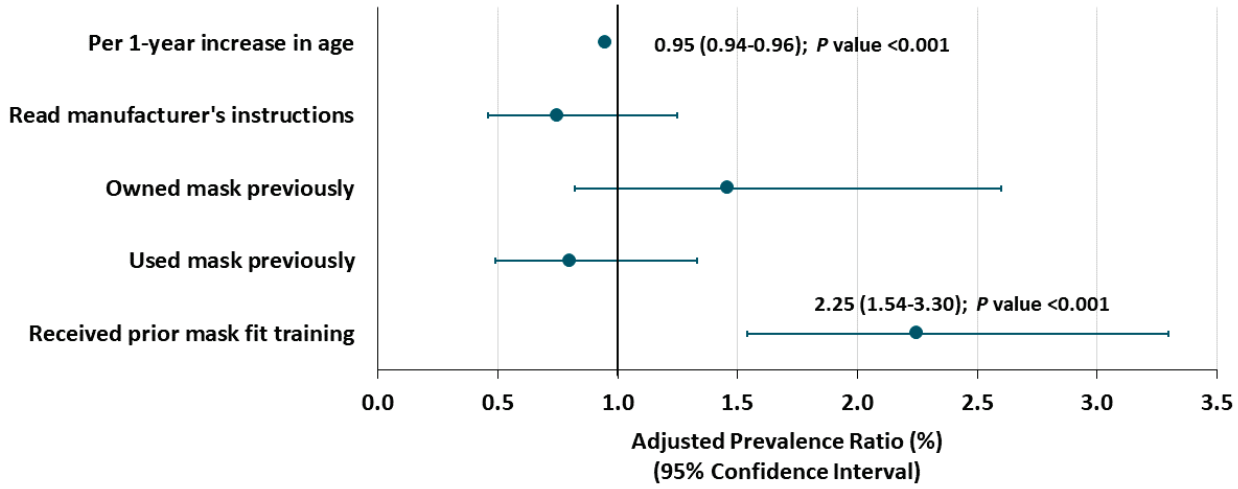
Key findings:

- In 2015, a very low proportion of the general public in Singapore correctly wore N95 masks
  - Only 12.6% of participants (90/714) passed the visual mask fit (VMF) test.
- Younger adults and those with previous mask-fit training had higher likelihood of passing the VMF test (Figure).

Methods: A 2015 cross-sectional study of Singapore residents who experienced the 2013 episode of severe smoky haze from nearby fires to assess proficiency donning N95 masks. Participants aged ≥21 years were recruited by simple random sampling without replacement from 2,231 eligible households and were provided N95 masks and multilingual pictorial instructions. Persons from 714 (32%) households agreed to be interviewed. Interviewers administered a VMF test. *Limitations*: Non-response bias.

Implications: The general public exhibited poor proficiency properly donning N95 masks with a good fit and may be falsely assured of protection when using them. Any recommendations for mask use by the general public may benefit from being coupled with effective training materials.

Figure:



Note: Adapted from Yeung *et al*. Multivariable analysis of factors associated with passing visual mask fit test. The dots represent adjusted prevalence ratios, and the lines represent 95% CIs. Licensed under CC-BY.

Modeling COVID-19 latent prevalence to assess a public health intervention at a state and regional scale. Turk *et al.* JMIR Public Health and Surveillance (May 18, 2020).

Key findings:

- Following the implementation of statewide stay-at-home orders in North Carolina and using a susceptible-infected-removed (SIR) infectious disease model, investigators observed that:

    - Doubling time (days it took for COVID-19 case counts to double) increased from 2.94 days to 4.01 days.
    - The rate of infection decreased by 25%.
- Model results suggest that this wave of the outbreak may be over by mid-July.

Methods: Authors developed SIR infectious disease models to estimate cases of COVID-19 over time in North Carolina under 2 scenarios: (1) without the statewide stay-at-home order, and (2) with the statewide stay-at-home order that began March 30. Authors estimated the doubling time before and after the intervention, and efficacy of implementing the stay-at-home order on reducing the rate of infection. *Limitations*: Estimates highly dependent on modeling assumptions.

Implications: Modeling suggests that social distancing and the implementation of statewide stay-at-home order may curb the COVID-19 epidemic in North Carolina.

Transmission: Mother to Child

Studies of pregnant women infected with SARS-CoV-2 before or after giving birth can inform guidance to reduce the likelihood for mother-to-child (vertical) transmission, including through breastfeeding. The following two case series present findings on mothers with COVID-19 and their infants.

PEER-REVIEWED

A. Coronavirus disease 2019 among pregnant Chinese women: Case series data on the safety of vaginal birth and breastfeeding. Wu *et al.* British Journal of Obstetrics and Gynaecology (May 5, 2020).

Key findings:

- Among all 13 assessed pregnant women, vaginal samples were negative for SARS-CoV-2 RNA.
- Among newborns, throat and anal swabs were all negative for SARS-CoV-2 RNA.
- Breast milk samples from 1 of 5 women were transiently positive for SARS-CoV-2 RNA.

Methods: A case series of 13 pregnant women with mild COVID-19 and their 5 newborns at a single hospital in Wuhan, China. Among the 5 births, 4 women had cesarean section deliveries and 1 had a vaginal delivery. SARS-CoV-2 RNA testing was performed on vaginal and breast milk samples from the mothers, and throat and anal swabs from the newborns. *Limitations*: Small sample size; single hospital.

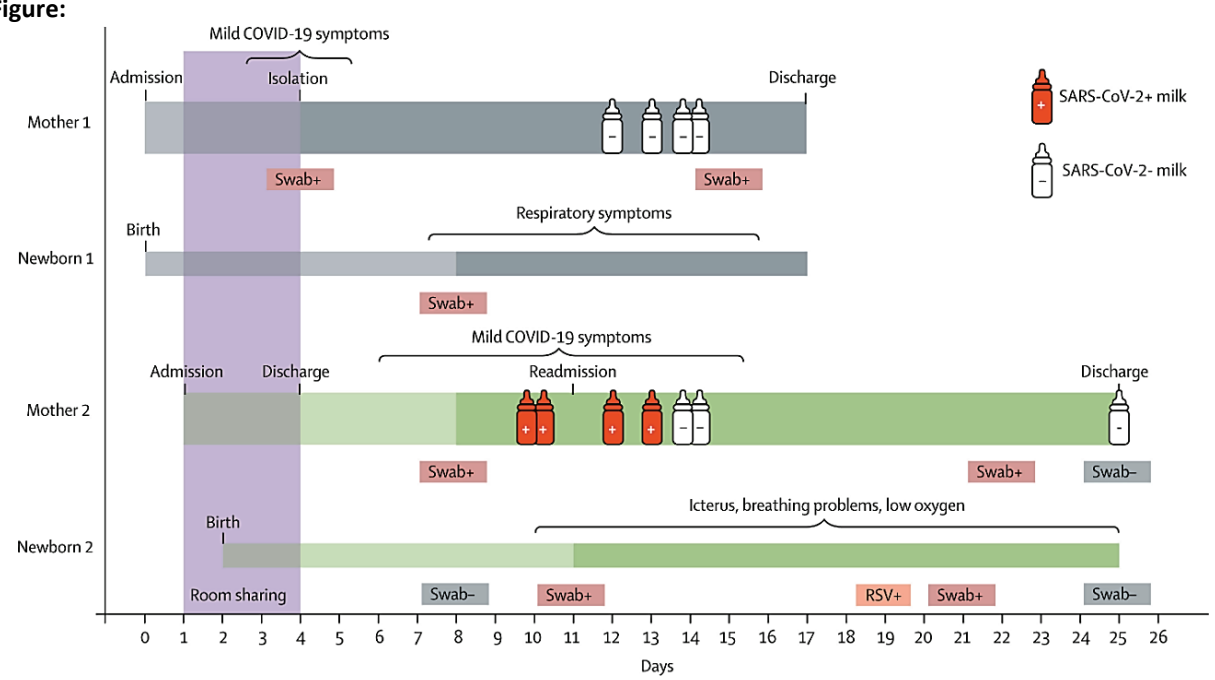
B. Detection of SARS-CoV-2 in human breastmilk. Groß *et al.* Lancet (May 21, 2020; Correction on September 12, 2020).

Key findings:

- Mother 1 tested positive for SARS-CoV-2 RNA shortly after delivery (day 4). Following isolation of Mother 1 from her newborn, Newborn 1 tested positive (day 8).
    - Breastmilk samples from Mother 1 were negative for SARS-CoV-2 RNA (Figure).
- Mother 2 and Newborn 2 stayed in the same room as Mother 1 and Newborn 1 until Mother 1 tested positive for SARS-CoV-2 RNA. Mother 2 tested positive on day 8; Newborn 2 tested positive on day 11.
    - Breastmilk samples from Mother 2 were positive for SARS-CoV-2 RNA on days 10–13 (Figure).

Methods: A case series of two postpartum women who developed mild COVID-19 after delivery. SARS-CoV-2 RNA testing was performed on breast milk samples and using oropharyngeal and nasopharyngeal swabs. *Limitations*: Small sample size; single hospital.

Figure:



Note: From Groß *et al.* Time course of SARS-CoV-2 infection of two mothers with newborn children. Darker **green** or **gray** shading indicates time from first SARS-CoV-2 positive oropharyngeal and nasopharyngeal swabs. Brackets indicate duration of COVID-19 symptoms. This article was published in Lancet, Vol 395, Groß *et al.*, Detection of SARS-CoV-2 in human breastmilk, P1757-1758, Copyright Elsevier 2020. This article is currently available at the Elsevier COVID-19 resource center: https://www.elsevier.com/connect/coronavirus-information-center.

Implications of both studies (Wu *et al.* & Groß *et al.*): There was no evidence of SARS-CoV-2 transmission from mother to newborn during pregnancy or delivery. However, transmission via breastfeeding, either through breast milk or close physical contact, is uncertain. Further studies are needed to assess the potential for vertical transmission from mother to newborn, including via breastfeeding.

Clinical Treatment & Management

PEER-REVIEWED

Early short course corticosteroids in hospitalized patients with COVID-19. Fadel *et al.* Clinical Infectious Diseases (May 19, 2020).

Key findings:

- Compared with those in the standard of care group, COVID-19 patients treated with a short course of corticosteroids <48 hours after presentation:
    - Were less likely to progress to poor outcomes (defined as ICU admission, mechanical ventilation, and death) after adjusting for sex, age, and disease severity: 34.9% vs 54.3%, OR 0.45 (95% CI 0.26–0.79).
    - Had lower median length of hospital stay (5 vs 8 days).

Methods: On March 20, 2020, clinical guidelines in a Michigan hospital system were changed such that patients with moderate to severe COVID-19 needing supplemental oxygen or mechanical ventilation were recommended to be prescribed a short course of corticosteroids <48 hours after presentation.

Among hospitalized adults with moderate to severe COVID-19, authors compared clinical outcomes of 81 patients who were admitted prior to the change in treatment guidelines (SOC group), with 132 patients who were admitted afterward (early corticosteroid group). *Limitations*: Patients in both groups may have received other medications; some baseline characteristics, including race/ethnicity, varied by treatment group; some providers may not have followed hospital guidelines; differences in other treatments may have affected outcomes by group; patients only followed for 14 days.

Implications: Early, short course corticosteroid treatment may improve clinical outcomes among patients with moderate to severe COVID-19. Clinical trials with larger samples are warranted to further explore this issue.

Urinary frequency as a possibly overlooked symptom in COVID-19 patients: Does SARS-CoV-2 cause viral cystitis? Mumm *et al.* European Urology (May 12, 2020).

Key findings:

- 7 males who tested positive for SARS-CoV-2 RNA in NP swabs reported increased urinary frequency, along with dry cough (n = 5), fever (n = 3), and shortness of breath (n = 3).
- These 7 patients did not have urinary infection, acute renal injury, or prostatitis.

Methods: Retrospective and prospective assessment of symptoms, including urinary frequency, on hospital admission in 57 COVID-19 patients in Germany. Urine analysis and ultrasound tests were conducted for persons with high urinary frequency. *Limitations*: Small sample size; retrospective symptom assessment may have been incomplete.

Implications: High urinary frequency may indicate viral cystitis from SARS-CoV-2 infection. Larger studies are warranted to assess the occurrence of this symptom.

Prevalence of putative invasive pulmonary aspergillosis in critically ill patients with COVID-19. Alanio *et al.* Lancet Respiratory Medicine. (May 20, 2020).

Key findings:

- One-third of ventilated COVID-19 patients had invasive pulmonary aspergillosis (IPA), a severe disease affecting the lungs that is caused by fungal (*Aspergillus*) infection.
- Compared with those without IPA, patients with IPA had higher rates of hypertension (6/9 vs. 6/18; p = 0.046) and similar mortality rates (4/9 vs 7/18; p = 0.99).

Methods: Prospective observational study in 27 critically ill COVID-19 patients. Traditional methods used in IPA diagnosis, such as a CT scan or bronchoalveolar lavage (BAL), are difficult to conduct in critically ill COVID-19 patients. Investigators broadened diagnostic criteria to include (1) positive BAL culture as a stand-alone criterion, or (2) two of the following: positive RT-PCR results for *Aspergillus fumigatus* in serum or respiratory samples, beta-d-glucan (a component of fungal cell walls) in serum samples, positive bronchial aspiration culture, or galactomannan (cell wall component of *Aspergillus*) in serum or respiratory samples. *Limitations*: Small sample size.

Implications: Although mortality rates were similar between IPA and non-IPA patients in this limited sample, the role of *Aspergillus* infection in COVID-19-related lung inflammation is unknown.

Laboratory Science

PEER-REVIEWED

Simulated sunlight rapidly inactivates SARS-CoV-2 on surfaces. Ratnesar-Shumate *et al.* Journal of Infectious Diseases (May 20, 2020).

Key findings:

- Exposure to ultraviolet B (UVB) light− like that found in sunlight− inactivated SARS-CoV-2 in minutes.
  - 90% of infectious virus was inactivated every 7 minutes in simulated sunlight that was equivalent to noon during summertime at the same latitude as New York City.
  - Slower inactivation occurred at lower levels of simulated sunlight.
- In darkness, infectious virus persisted.

Methods: Dried samples of SARS-CoV-2 in a solution mimicking saliva were exposed to various levels of simulated sunlight in an environmentally controlled chamber for 2-18 minutes, with measurement of recovered virus after exposure. Infectious dose of virus was plotted over time. *Limitations*: 5µL droplets were used, whereas a range of droplet sizes are present in humans and droplet size may affect virus survival.

Implications: Sunlight can inactivate SARS-CoV-2, and exposure risk may vary between indoor and outdoor environments. The extent of inactivation by sunlight will depend on time of year and the extent of cloud cover.

Figure 1

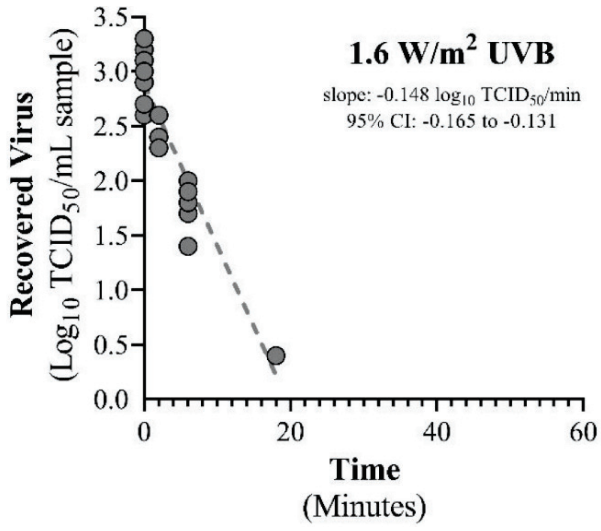
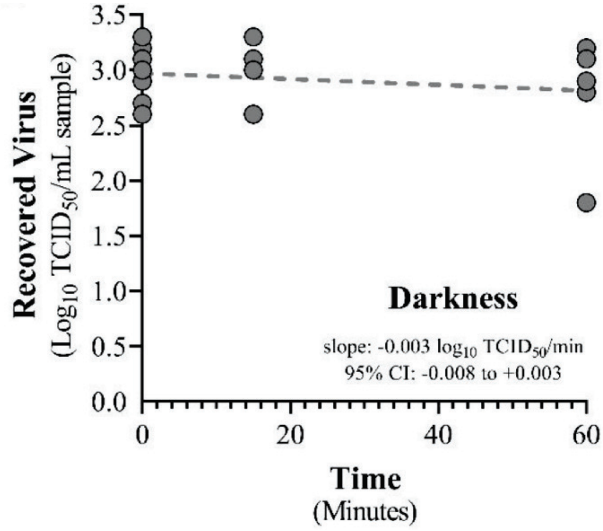


Figure 2



Note: Adapted from Ratnesar-Shumate *et al*. Linear regression fit for SARS-CoV-2 in simulated saliva and recovered following exposure to light (**Figure 1**) or dark (**Figure 2**). Watts per square meter (W/m^2) is a measurement of light intensity; viral concentration expressed as median tissue culture infectious dose ($TCID_{50}$) per mL of sample. Licensed under CC-BY-NC-ND.

Vaccine Studies in Rhesus Macaques

Development of a vaccine that confers immunity to SARS-CoV-2 is of high priority, but in preliminary stages. Animal models can help inform vaccine development. The following peer-reviewed papers describe the effects of inoculation with SARS-CoV-2 vaccine candidates, followed by SARS-CoV-2 infection, on the development of neutralizing antibodies and trajectory of viral loads among small samples of rhesus macaques.

PEER-REVIEWED

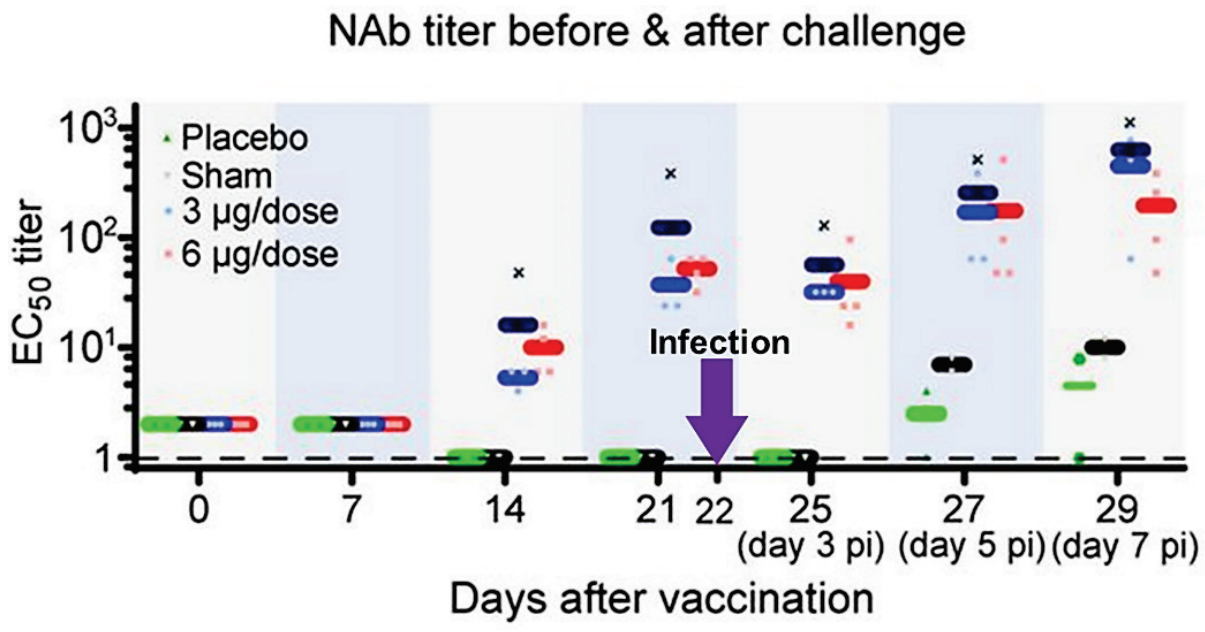
A. Development of an inactivated vaccine candidate for SARS-CoV-2. Gao *et al.* Science (May 6, 2020).

Key findings:

- 8 rhesus macaques immunized with an inactivated SARS-CoV-2 vaccine produced antibodies able to neutralize virus (neutralizing antibodies) at levels that correlated with the vaccine dose (Figure).
- When inoculated with SARS-CoV-2, the 8 vaccinated animals exhibited lower viral burdens (95–100% reduction) compared with unvaccinated controls.

Methods: 16 rhesus macaques were inoculated with 3 doses of either purified, inactivated SARS-CoV-2 vaccine (medium or high dose), placebo, or a sham dose that only contained components of the vaccine that enhance the immune response (adjuvant) (n = 4 in each group). 21 days after completing the series of injections, animals were inoculated with SARS-CoV-2. Neutralizing antibody levels and viral burden were quantified. *Limitations*: Animal study; post-vaccination assessments at later time points are necessary to determine if detrimental immune responses develop after antibodies wane.

Figure:



Adapted from Gao *et al*. SARS-CoV-2-specific neutralizing antibody levels (y axis) after vaccination (day 0, x axis) and subsequent challenge (**infection arrow**) with SARS-CoV-2 for **placebo**, **sham**, **medium vaccine dose**, and **high vaccine dose** groups (n = 4 macaques per group). SARS-CoV-2-specific neutralizing antibody levels were measured as half of the maximum effective neutralizing antibody concentration (EC_{50} titer). NAb - neutralizing antibody; pi - post infection. Licensed under CC BY 4.0.

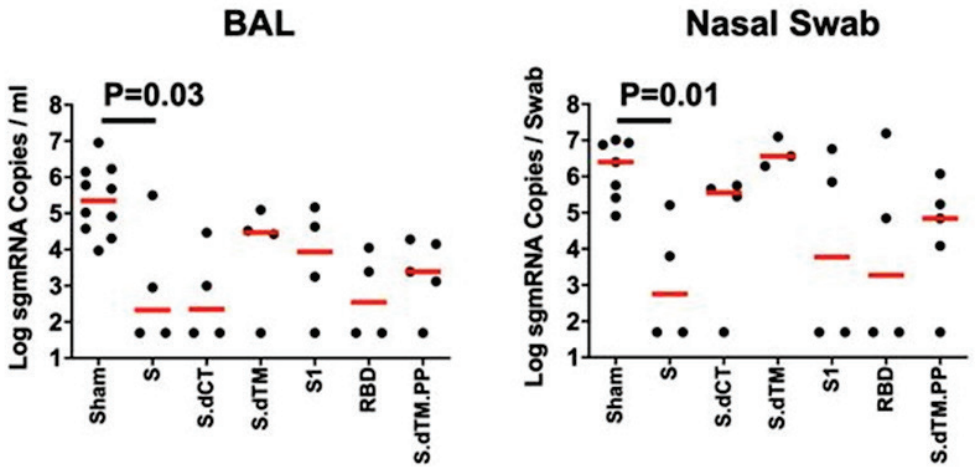
B. **DNA vaccine protection against SARS-CoV-2 in rhesus macaques.** Yu *et al.* Science (May 20, 2020).

Key findings:

- Five weeks after experimental vaccinations, neutralizing antibody titers in vaccinated macaques were comparable to titers described in macaques and humans that recovered from natural SARS-CoV-2 infection.
- Among vaccinated animals challenged with SARS-CoV-2, peak viral loads were lower than in macaques that received the sham dose (Figure).
    - 8/25 vaccinated macaques had no detectable viral RNA after SARS-CoV-2 challenge.

Methods: Thirty-five rhesus macaques were immunized with a vaccine candidate (without adjuvant) containing one of six variants of the SARS-CoV-2 spike protein (n = 25) or with a sham dose (control, n = 10) at week 0 and week 3. At week 5, neutralizing antibody levels were assessed. At week 6, all macaques were inoculated with SARS-CoV-2. Viral RNA was assessed through bronchoalveolar lavage (BAL) and nasal swabs for 14 days following exposure to the virus. *Limitations*: Small sample size; results should be corroborated in human clinical trials.

Figure:



Note: Adapted from Yu *et al*. Peak SARS-CoV-2 viral loads **(median shown in red)** during the 14 days following inoculation with SARS-CoV-2 virus at week 5, by vaccination group (receipt of one of six candidates containing a variant of the SARS-CoV-2 Spike protein or sham dose), from BAL (left) and nasal swab (right) samples taken from 35 rhesus macaques. The six vaccine candidates included S; S.dCT; S.dTM; S1; RBD; S.dTM.PP. Licensed under CC BY 4.0.

Implications (Gao *et al.* & Yu *et al.*): Some SARS-CoV-2 vaccine candidates may provide immunity against infection in primates. However, additional studies should be conducted to demonstrate efficacy and safety in humans.

In Brief

- Walker *et al*. **CONTAIN: An open-source shipping container laboratory optimised for automated COVID-19 diagnostics**. bioRxiv. Presents an approach to expand testing capacity by converting a shipping container into a BSL-2+ laboratory to automate RT-PCR testing.
- Whitcroft *et al*. **Olfactory dysfunction in COVID-19 diagnosis and management**. JAMA. COVID-19-associated olfactory dysfunction should prompt SARS-CoV-2 testing, self-isolation, and possible treatment if dysfunction extends beyond two weeks.

- Sittig *et al*. **COVID-19 and the need for a national health information technology infrastructure**. JAMA. Accurate, timely, and complete data are essential for guiding clinical management and treatment, and responding to the COVID-19 pandemic.
- Zhai *et al*. **Need for transparency and reliable evidence in emergency use authorizations for coronavirus disease 2019 (COVID-19) therapies**. JAMA Internal Medicine. There is a risk of damage associated with issuing an emergency use authorization for COVID-19 therapies based on insufficient evidence.
- Soliman *et al*. **COVID-19 virus case fatality rate: how to avoid errors in calculation of data during the outbreak?** Acta Biomedica. Authors present two methods for more accurate estimation of case fatality rates associated with COVID-19.
- Hsu *et al*. **How COVID-19 is accelerating the threat of antimicrobial resistance**. BMJ. Highlights the dangers in antibiotic misuse during treatment of COVID-19, which could increase antimicrobial resistance.
- Angulo *et al*. **Reopening society and the need for real-time assessment of COVID-19 at the community level**. JAMA. Real-time COVID-19 data, including community surveys and seroepidemiology data, are essential for understanding the epidemic, optimizing clinical treatment and management, and knowing how and when to reopen businesses.
- Bausch D. **Precision physical distancing for COVID-19: An important tool in unlocking the lockdown.** The American Journal of Tropical Medicine and Hygiene. Precision physical distancing may provide a sustainable long-term solution to resuming normal activities.
- Subbaraman N. **Refugee camps race to avert coronavirus catastrophe.** Nature. Researchers and aid workers are taking steps to protect refugees during the pandemic.
- Editorial. **Share lessons on lifting lockdowns.** Nature. Countries need to share best practices as they lift restrictions on movement.
- Metz T. **Is universal testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) needed on all labor and delivery units?** Obstetrics and Gynecology. Decisions regarding universal testing need to be made in the context of local COVID-19 prevalence.
- Zastrow M. **Coronavirus contact-tracing apps: Can they slow the spread of COVID-19?** Nature. New apps track movement of persons so that contract tracing can be automated. Privacy issues needs to be resolved and the efficacy of the apps needs to be verified.
- Venturini *et al*. **Severe neutropenia in infants with SARS caused by novel coronavirus**. Journal of Pediatrics. This is the first description of severe neutropenia in infants infected with SARS-CoV-2.
- Tullie *et al*. **Gastrointestinal features in children with COVID-19: an observation of varied presentation in eight children**. Lancet Child and Adolescent Health. Based on 8 children with COVID-19 presenting with atypical appendicitis, requiring hospitalization, recommends conducting imaging and RT-PCR testing in children presenting with fever and abdominal pain before surgical intervention, if appendicitis is suspected.