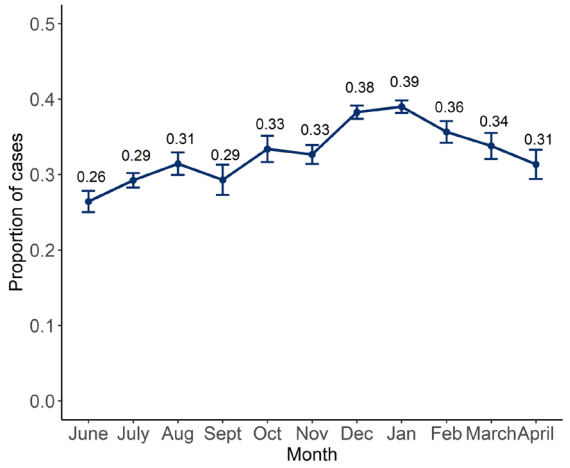


Figure 2. Proportion of COVID-19 cases that were part of a household cluster, Fulton County, June 2020–April 2021. Error bars denote 95% confidence interval around the point estimate.

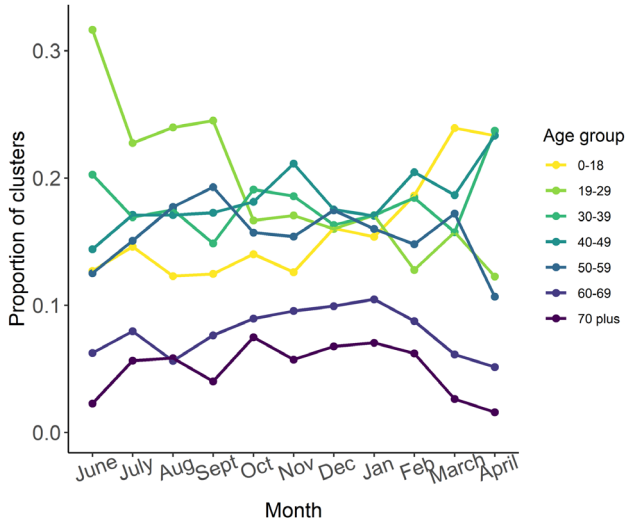


Figure 3. Age of first diagnosis among households with at least 2 cases diagnosed within 14 days

Conclusion. One-third of COVID-19 cases in Fulton County were part of a household cluster. The higher proportion of children in household clusters likely reflects higher probability of living in a home with an adult caregiver. Higher household clustering among Hispanic and Asian persons, regardless of age, may reflect larger households (supported by census data) or increased exposures outside the house. Timely testing for household members to prevent ongoing transmission remains essential.

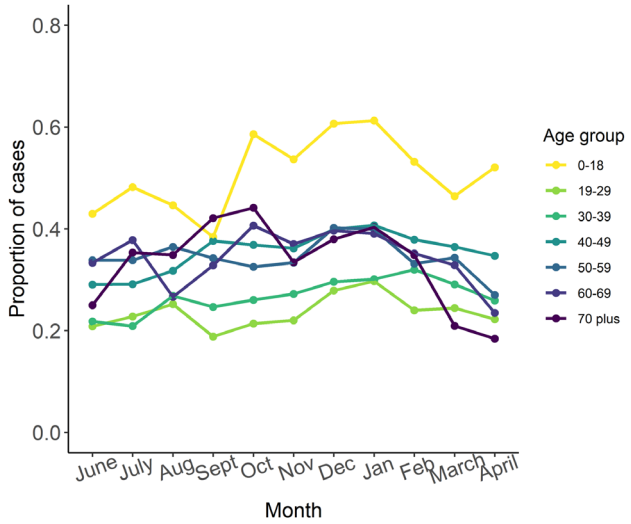
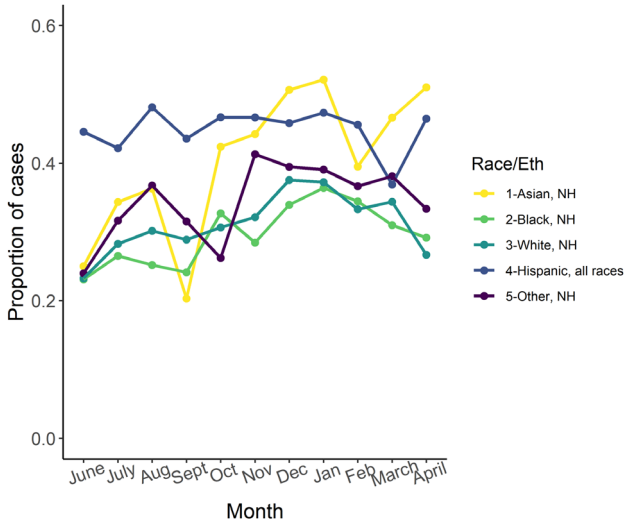


Figure 4. Proportion of COVID-19 cases that were part of a household cluster, by age – Fulton County, June 2020–March 2021



Proportion of COVID-19 cases that were part of a household cluster in Fulton County stratified by race/ethnicity over time

Disclosures. **All Authors**: No reported disclosures

188. Visualizing the Impact of a Wedding Leading to COVID-19 Outbreaks in Healthcare Settings, Washington State, July – August 2020

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Session: O-37. Updates in COVID Epidemiology

Background. Large social gatherings during the COVID-19 pandemic have been linked to extensive community transmission. Healthcare workers (HCW) that engage in these social gatherings pose a risk to the vulnerable patients they serve. Public Health—Seattle & King County identified a COVID-19 outbreak associated with a wedding in July 2020 when the 14-day incidence rate was 105 cases per 100,000 residents. HCW who attended the wedding were subsequently linked to 45 outbreaks in healthcare settings across three counties in the next month.

Methods. COVID-19 case interview data was used to identify HCW cases who reported the wedding as their exposure event. The Washington Disease Reporting System (WDRS), the state database in which COVID-19 cases and epi-linkages are tracked, was queried to identify healthcare outbreaks linked to the HCW wedding-attendee cases and the HCW that they infected. NodeXL was used to visualize the resulting chains of wedding-associated healthcare transmission using a Harel-Koren Fast Multiscale layout where the network visualization's directed arrows represent putative links and direction of transmission. Numbers of associated settings, cases, and deaths were calculated.

Results. Seven HCW wedding attendees were linked to outbreaks in healthcare facilities that they worked at while infectious; HCWs linked to as many as six subsequent healthcare outbreaks. In total, the wedding was connected to 45 healthcare facilities: adult family homes (N=1), hospitals (N=1), supported living agencies (N=7) and associated group homes (N=38), assisted living (N=1), home health services (N=1), behavioral health (N=2), and rehab centers (N=1). Across the settings, 277 cases were identified, including 15 deaths.

Conclusion. A series of COVID-19 healthcare outbreaks was traced back to a wedding. Cases worked in multiple homes, agencies, and other healthcare settings which likely facilitated rapid and wide transmission; the structure of these healthcare settings often do not facilitate a single job providing enough hours and income to support an individual. In terms of public health learnings, addressing these outbreaks require effective contact tracing, multijurisdictional coordination, and for supported living, interventions need to be applied across households sharing staff.

Disclosures. **All Authors**: No reported disclosures

189. Potential Tiger-to-Human Transmission of SARS-CoV-2 at a Tennessee Zoo: A One Health Approach to Outbreak Investigation

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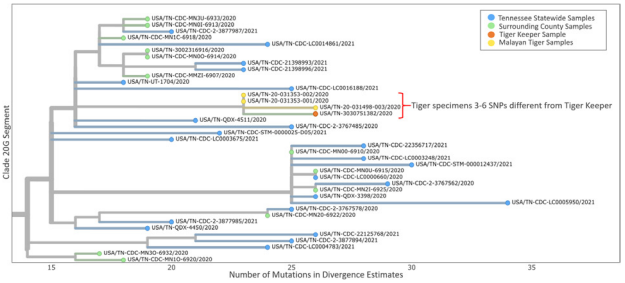
Session: O-37. Updates in COVID Epidemiology

Background. Human-to-feline and airborne transmission among cats of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has been described, though documented feline-to-human transmission has not been reported. In October 2020, all 3 Malayan tigers at a Tennessee AZA accredited zoo were diagnosed with symptomatic SARS-CoV-2 infection. We investigated to determine source and prevent further transmission.

Methods. Tiger nasal swab specimens were tested at the National Veterinary Services Laboratories (NVSL). An environmental assessment at the zoo was completed. We interviewed 18 staff who interacted with the tigers during the 2 weeks before animal symptom onset. Confirmed human cases were defined as persons testing positive for SARS-CoV-2 by RT-PCR during September 28–October 29, with tiger interaction during their 14-day incubation period. Interviewed staff had repeat SARS-CoV-2 RT-PCR and serum IgG testing on October 29. Tigers and staff testing positive had specimens sent to CDC for genomic sequencing. Tiger sequences were compared phylogenetically with 30 geographically associated human cases collected within 2 weeks of the outbreak and > 200 background sequences from TN.

Results. NVSL confirmed SARS-CoV-2 infection in all 3 tigers. Environmental assessment identified fencing between humans and animals allowing airflow and an open outdoor exhibit observation point above the habitat. Confirmed cases were identified in a tiger keeper and veterinary assistant; both developed symptoms after exposure to symptomatic tigers and one sample was genotyped. Staff did not report known contact with ill visitors. All staff were negative for SARS-CoV-2 IgG. The tigers and most temporally and geographically associated cases had genetic sequences in clade 20G and B.1.2. Tiger sequences were 3-6 single nucleotide polymorphisms different from the positive tiger keeper (Figure).

Figure. Whole-genome phylogenetic analysis.



Whole-genome phylogenetic analysis from a portion of clade 20G showing divergence estimates from SARS-CoV-2 Wuhan-Hu-1 reference genome with sequences from humans living in Tennessee and Malayan tigers sampled during the outbreak investigation in October 2020. Sequence analysis showed 3-6 single nucleotide polymorphisms (SNPs) differences between one human tiger keeper and all three tiger sequences. Differences are indicated by one-step edges (lines) between colored dots (individual SARS-CoV-2 sequenced infections). Numbers indicate unique sequences. Note not all analyzed sequences are shown in this figure.

Conclusion. Using a One Health approach, we concluded the index tiger was likely infected via transmission from an ill visitor at an exhibit observation point or unidentified asymptomatic staff. Infection spread to the other 2 tigers and tiger-to-human transmission to 2 staff is possible thereafter. The zoo was advised on infection control practices for humans and animals, and no additional cases were identified.

Disclosures. **William Schaffner, MD**, **VBI Vaccines** (Consultant)

190. Epidemiology of COVID-19 Breakthrough Infections in Dallas County, Texas, 2021

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Session: O-37. Updates in COVID Epidemiology

Background. From March 2020 through May 2021, Dallas County reported a total of 304,056 cases of COVID-19, including 4,073 deaths. During the month of December 2020, a post-holiday surge of cases led to peak daily average case rates of over 50 cases per 100,000. COVID-19 cases and deaths have since declined substantially following the rollout of COVID-19 vaccine delivery. As of June 8, 2021, about 1,831,588 Dallas County residents have received at least one COVID-19 vaccine dose and 910,067 are fully vaccinated. Recent county integration of immunization and case databases enabled identification and analysis of COVID-19 breakthrough infections.

Methods. A COVID-19 breakthrough infection was defined as a positive test (PCR or antigen) collected from an individual ≥ 14 days after receiving the full series of an FDA-authorized COVID-19 vaccine. Nationally, 10,262 vaccine breakthrough infections had been reported from 46 US states and territories, through April 2021. Vaccine breakthrough cases were reviewed and medical records abstracted to collect demographic information, clinical characteristics, and medical conditions. Data analysis was performed using R, version 4.0.2 (2020).

Results. Of the 700 vaccine breakthrough cases reported in Dallas County residents as of June 8, 2021, 304 (43%) were male and 396 (57%) female, with an average age of 53 years. The majority of the vaccine breakthrough cases were White (42%); 25% were Hispanic/Latino; and 20% were Black. Almost all breakthrough cases were confirmed with PCR testing, with 451 (64%) cases receiving the Pfizer vaccine. Of breakthrough cases, 49% were symptomatic; 52% (358) had underlying conditions including: tobacco use, obesity, or immunocompromised state; 68 (10%) were hospitalized; and 11 (1.6%) died. Whole genome sequencing was performed on 51 cases, with 14 (27.5%) variants identified, including: eight B.1.1.7, two B.1.429 and one P.1 variants.

Conclusion. Despite the high levels of vaccine efficacy documented in US vaccine trials, COVID-19 breakthrough infections, though currently uncommon, do occur and are important to investigate. Ongoing close public health surveillance of variants is needed to discern changes in patterns of vaccine efficacy and characteristics of populations at greatest risk of severe disease from COVID-19.

Disclosures. **All Authors**: No reported disclosures

191. High-Dose Rifampin-containing Regimens for the Treatment of TB Meningitis

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Session: O-38. Updates in Mycobacteria

Background. TB meningitis is the most severe form of tuberculosis (TB), associated with high morbidity and mortality. High-dose rifampin (35mg/kg/day) is safe in adults and substantially improves the bactericidal activity of standard TB regimen. However, there is conflicting data regarding its benefit in TB meningitis where outcomes may also be associated with intracerebral inflammatory responses.

Methods. A novel mouse and a validated rabbit model of TB meningitis utilizing intracranial *Mycobacterium tuberculosis* infections were used for these studies (**Fig. 1**). Animals received high-dose (35 mg/kg/day) or standard-dose (10 mg/kg/day) rifampin in combination with isoniazid, pyrazinamide and dexamethasone at human equipotent dosing. Bacterial burden, multi-modality positron emission tomography (PET) imaging, tissue drug concentrations, markers of neuroinflammation, and vascular leak were measured. Imaging data from a patient with TB meningitis was analyzed and correlated with the findings in animals.

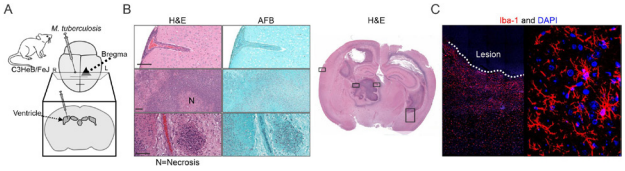

Figure 1. Mouse model of TB meningitis replicates human histopathology hallmarks. (A) Scheme of infection. (B) Histopathology hematoxylin-eosin (H&E) and acid-fast bacilli (AFB) staining in a representative M. tuberculosis-infected mouse shows regions of meningitis, ventriculitis, choroiditis, necrotizing and non-necrotizing granulomas. The bar represents 100μm. (C) Images show immunofluorescence of microglia activation in red (Iba-1) and nuclear stain in blue (DAPI). The rabbit model of TB meningitis has been described previously (Tucker et al. Dis Model Mech. 2016 and Tucker et al. Sci Transl Med. 2018). Animal studies were approved by the Johns Hopkins Animal Care and Use Committee.

Results. Administration of the high-dose rifampin regimen achieved four times higher brain concentration than the standard-dose regimen and displayed higher bactericidal activity in both mice and rabbits ($P < 0.01$) (**Fig. 2**). There were no differences in intracerebral microglial activation (^{124}I-DPA-713 PET and iDISCO) and pro-inflammatory cytokines during treatment in animals receiving high- or standard-dose rifampin regimens (**Fig. 3**). Whole-brain PET and immunolabeling demonstrated spatially compartmentalized inflammation, vascular leak and rifampin exposures (**Fig. 4**). Longitudinal imaging in the same animals showed a 40% decrease in vascular leak after two weeks of TB treatment. Spatially compartmentalized brain rifampin exposures and decreases in vascular edema over TB treatment were also noted in the TB meningitis patient.