NMCP COVID-19 Literature Report #77: Friday, 24 September 2021

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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The Big Picture

News in Brief

Grim Milestones

"1 in 500 Americans have died of Covid-19" (WP).

COVID-19 has overtaken the 1918 Spanish flu as deadliest disease in American history (STAT).

"American Samoa, one of the last places without coronavirus, has first infection" (WP).

Heads Up

BLUF from DHS: "Here's what we've learned about COVID-19—an update" (DHS; see also: Master Question List [pdf]).

"Six things to understand about the pandemic now — The rules of the pandemic keep changing, but these principles can guide your thinking through the seasons to come" (Atlantic).

"Winter is coming, again: What to expect from Covid-19 as the season looms" (STAT).

The current surge combined with supply chain stress is causing widespread shortages of medical equipment such as exam tables, defibrillators, and crutches (Reuters).

Research Concerns

"Preprint advocates must also fight for research integrity — Efforts to share research with the public must include mechanisms to prevent harm resulting from low-quality work" (Nature).

"Swedish research misconduct agency swamped with cases in first year. The newly formed government organization tackled 46 research-fraud investigations in 2020 — three times as many as expected" (Nature). *Ed note: If you like podcasts, check out Dr. Death season 3 — this agency was created after the events covered in that series.*

Long read: "How the pandemic is changing the norms of science — Imperatives like skepticism and disinterestedness are being junked to fuel political warfare that has nothing in common with scientific methodology" (Tablet).

Journal Articles

PNAS: Excess mortality from COVID and non-COVID causes in minority populations (28 September 2021; online 21 September 2021)

> "The 2020 US mortality totaled 2.8 million after early March, which is 17.3% higher than age-population–weighted mortality over the same time interval in 2017 to 2019, for a total excess death count of 413,592. We use data on weekly death counts by cause, as well as life

> tables, to quantify excess mortality and life years lost from both COVID-19 and non–COVID-19 causes by race/ethnicity, age, and gender/sex. Excess mortality from non–COVID-19 causes is substantial and much more heavily concentrated among males and minorities, especially Black, non-Hispanic males, than COVID-19 deaths. Thirty-four percent of the excess life years lost for males is from non–COVID-19 causes. While minorities represent 36% of COVID-19 deaths, they represent 70% of non–COVID-19 related excess deaths and 58% of non–COVID-19 excess life years lost. Black, non-Hispanic males represent only 6.9% of the population, but they are responsible for 8.9% of COVID-19 deaths and 28% of 2020 excess deaths from non–COVID-19 causes. For this group, nearly half of the excess life years lost in 2020 are due to non–COVID-19 causes."

Clin Infect Dis: Is COVID-19 Less Deadly Now? -- Trends of In-Hospital Mortality Among Hospitalized COVID-19 Patients in the United States (17 September 2021)

> "After an initial decline from April through June 2020 (from 22.2% to 11.9%), adjusted in-hospital mortality in COVID-19 inpatients peaked twice and was significantly higher than June 2020 for subsequent months except in July and October 2020. Adjusted mortality trends differed across age groups between November 2020 and February 2021."

SARS-CoV-2 Virus and Variants

News in Brief

"'Delta has been brutal': Covid-19 variant is decimating rural areas already reeling from the pandemic" (STAT).

Virus Origins

"Closest known relatives of virus behind COVID-19 found in Laos — Studies of bats in China and Laos show southeast Asia is a hotspot for potentially dangerous viruses similar to SARS-CoV-2" (Nature; see also: preprint at Research Square).

"Did the coronavirus jump from animals to people twice? A preliminary analysis of viral genomes suggests the COVID-19 pandemic might have multiple animal origins — but the findings still have to be peer reviewed" (Nature; see also: preprint from virological.org).

"SARS-like viruses may jump from animals to people hundreds of thousands of times a year — Study pinpoints Asian regions that could spark the next coronavirus pandemic" (Science; see also: medRxiv preprint).

Long read: "A virus-hunter's advice on dealing with China's resistance on Covid: Hardball is the wrong technique to get China to open up about the early spread of the pandemic. A successful but little-known global disease program offers a much smarter approach" (Politico).

Journal Articles

MMWR: Outbreak of SARS-CoV-2 B.1.617.2 (Delta) Variant Infections Among Incarcerated Persons in a Federal Prison — Texas, July–August 2021 (24 September 2021)

> "What is already known about this topic? Incarcerated populations have experienced disproportionately higher rates of COVID-19–related illness and death.
>
> What is added by this report? During a COVID-19 outbreak involving the Delta variant in a highly vaccinated incarcerated population, transmission rates were high, even among vaccinated persons. Although attack rates, hospitalizations, and deaths were higher among unvaccinated than among vaccinated persons, duration of positive serial test results was similar for both groups. Infectious virus was cultured from vaccinated and unvaccinated infected persons.
>
> What are the implications for public health practice? Even with high vaccination rates, maintaining multicomponent prevention strategies (e.g., testing and masking for all persons and prompt medical isolation and quarantine for incarcerated persons) remains critical to limiting SARS-CoV-2 transmission in congregate settings where physical distancing is challenging."

COVID-19 Vaccines

News in Brief

The FDA has authorized a single booster dose of the Pfizer COVID-19 vaccine in patients over 65 years old, in people aged 18-64 at high risk of severe COVID-19, or in individuals aged 18-64 whose risk of exposure puts them at high risk of serious complications from COVID-19 (FDA).

"In a statement released early Friday [24 September 2021], the [CDC] said those at high risk of occupational exposure, such as healthcare workers, may receive the Pfizer booster shot at least 6 months after the two-dose primary series, based on their individual benefits and risks. On Thursday [23 September 2021], the ACIP voted 6-9 against recommending a booster in this population" (Medpage).

"The tangled history of mRNA vaccines — Hundreds of scientists had worked on mRNA vaccines for decades before the coronavirus pandemic brought a breakthrough" (Nature).

Shots in Arms

"The US was a world leader in vaccination. What went wrong? How most of Europe caught up to — and then surpassed — the US in their Covid-19 vaccine drives" (Vox).

"Many unvaccinated people are not opposed to getting a shot. The challenge is trying to get it to them" (WP).

Boosters

"J&J says second dose of their COVID vaccine boosts protection — Efficacy data promising, but confidence intervals wide" (Medpage; see also: medRxiv preprint).

"What will the Covid-19 booster rollout look like? Public health groups plan as they await details" (STAT).

Immune Response

"A preprint study using blood samples suggested that mutant-specific T-cell responses were stronger after vaccination than they were in individuals who had been infected with SARS-CoV-2 up to a year ago" (Medpage; see also: medRxiv preprint).

"COVID vaccine immunity is waning — how much does that matter? As debates about booster shots heat up, what's known about the duration of vaccine-based immunity is still evolving" (Nature).

In Kids

"Pfizer Covid-19 vaccine generates robust antibody response in children, without serious safety issues, company says" (STAT; see also: Pfizer news release).

Events

WHAT: Developing the Oxford AstraZeneca COVID-19 vaccine: Elizabeth Blackwell Annual Public Lecture 2021 with Professor Dame Sarah Gilbert – free event

WHEN: Wednesday, 06 October 2021 0800-0900 ET

ABOUT: "Dame Sarah Gilbert is Professor of Vaccinology in the Nuffield Department of Medicine at the University of Oxford, and is the Oxford Project Leader for ChAdOx1 nCoV-19, the leading UK coronavirus vaccine.

> In this talk, Dame Sarah will take us on a journey from the moment she first heard about a serious new illness affecting people in China, to her team designing a successful COVID-19 vaccine which would save the lives of millions of people. You will hear the behind-the-scenes story of how the AstraZeneca COVID-19 vaccine - both cheaper and easier to distribute than some other vaccines - was developed and approved at a pace, while the public waited eagerly for science to find a way out of this major global health challenge.
>
> She will look at the reasons some people are hesitant to get vaccinated and discuss how people's trust in science can be affected by how science is communicated. What can we learn from this pandemic and the ways it could help us plan for future health crises, as we look towards a post-COVID world?"

REGISTER: https://www.eventbrite.co.uk/e/dame-sarah-gilbert-developing-the-oxford-astrazeneca-covid-19-vaccine-registration-162416757895

Journal Articles

Recommendations

MMWR: Use of Pfizer-BioNTech COVID-19 Vaccine in Persons Aged ≥16 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, September 2021 (24 September 2021)

> "What is already known about this topic? On August 23, 2021, the Food and Drug Administration granted full approval of the Pfizer-BioNTech COVID-19 vaccine for persons aged ≥16 years.
>
> What is added by this report? On August 30, 2021, after a systematic review of the data, the Advisory Committee on Immunization Practices revised its interim recommendation to a standard recommendation for use of the Pfizer-BioNTech COVID-19 vaccine in persons aged ≥16 years for the prevention of COVID-19.
>
> What are the implications for public health practice? Continued use of the Pfizer-BioNTech COVID-19 vaccine, now fully approved by the FDA in persons aged ≥16 years, is recommended based on increased certainty that its benefits (prevention of asymptomatic infection, COVID-19, and associated hospitalization and death) outweigh vaccine-associated risks."

Effectiveness

MMWR: Comparative Effectiveness of Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) Vaccines in Preventing COVID-19 Hospitalizations Among Adults Without Immunocompromising Conditions — United States, March–August 2021 (24 September 2021)

> "What is already known about this topic? Two 2-dose mRNA COVID-19 vaccines (from Pfizer-BioNTech and Moderna) and a 1-dose viral vector vaccine (from Janssen [Johnson & Johnson]) are currently used in the United States.
>
> What is added by this report? Among U.S. adults without immunocompromising conditions, vaccine effectiveness against COVID-19 hospitalization during March 11–August 15, 2021, was higher for the Moderna vaccine (93%) than the Pfizer-BioNTech vaccine (88%) and the Janssen vaccine (71%).
>
> What are the implications for public health practice? Although these real-world data suggest some variation in levels of protection by vaccine, all FDA-approved or authorized COVID-19 vaccines provide substantial protection against COVID-19 hospitalization."

Lancet Infect Dis: Infections, hospitalisations, and deaths averted via a nationwide vaccination campaign using the Pfizer–BioNTech BNT162b2 mRNA COVID-19 vaccine in Israel: a retrospective surveillance study (22 September 2021)

> "Background: On Dec 20, 2020, Israel initiated a nationwide COVID-19 vaccination campaign for people aged 16 years and older and exclusively used the Pfizer–BioNTech BNT162b2 mRNA COVID-19 vaccine (tozinameran). We provide estimates of the number of SARS-CoV-2 infections and COVID-19-related admissions to hospital (ie, hospitalisations) and deaths averted by the nationwide vaccination campaign.
>
> Methods: In this retrospective surveillance study, we used national surveillance data routinely collected by the Israeli Ministry of Health from the first 112 days (Dec 20, 2020, up to our data cutoff of April 10, 2021) of Israel's vaccination campaign to estimate the averted burden of four outcomes: SARS-CoV-2 infections and COVID-19-related hospitalisations, severe or critical hospitalisations, and deaths. As part of the campaign, all individuals aged 16 years and older were eligible for inoculation with the BNT162b2 vaccine in a two-dose schedule 21 days apart. We estimated the direct effects of the immunisation programme for all susceptible individuals (ie, with no previous evidence of laboratory-confirmed SARS-CoV-2 infection) who were at least partly vaccinated (at least one dose and at least 14 days of follow-up after the first dose). We estimated the number of SARS-CoV-2 infection-related outcomes averted on the basis of cumulative daily, age-specific rate differences, comparing rates among unvaccinated individuals with those of at least partly vaccinated individuals for each of the four outcomes and the (age-specific) size of the susceptible population and proportion that was at least partly vaccinated.

Findings: We estimated that Israel's vaccination campaign averted 158 665 (95% CI 144 640–172 690) SARS-CoV-2 infections, 24 597 (18 942–30 252) hospitalisations, 17 432 (12 770–22 094) severe or critical hospitalisations, and 5532 (3085–7982) deaths. 16 213 (65·9%) of 24 597 hospitalisations and 5035 (91·0%) of 5532 of deaths averted were estimated to be among those aged 65 years and older. We estimated 116 000 (73·1%) SARS-CoV-2 infections, 19 467 (79·1%) COVID-19-related hospitalisations, and 4351 (79%) deaths averted were accounted for by the fully vaccinated population.

Interpretation: Without the national vaccination campaign, Israel probably would have had triple the number of hospitalisations and deaths compared with what actually occurred during its largest wave of the pandemic to date, and the health-care system might have become overwhelmed. Indirect effects and long-term benefits of the programme, which could be substantial, were not included in these estimates and warrant future research."

NEJM: Effectiveness of mRNA Covid-19 Vaccine among U.S. Health Care Personnel (22 September 2021)

"Background: The prioritization of U.S. health care personnel for early receipt of messenger RNA (mRNA) vaccines against severe acute respiratory disease coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (Covid-19), allowed for the evaluation of the effectiveness of these new vaccines in a real-world setting.

Methods: We conducted a test-negative case-control study involving health care personnel across 25 U.S. states. Cases were defined on the basis of a positive polymerase-chain-reaction (PCR) or antigen-based test for SARS-CoV-2 and at least one Covid-19-like symptom. Controls were defined on the basis of a negative PCR test for SARS-CoV-2, regardless of symptoms, and were matched to cases according to the week of the test date and site. Using conditional logistic regression with adjustment for age, race and ethnic group, underlying conditions, and exposures to persons with Covid-19, we estimated vaccine effectiveness for partial vaccination (assessed 14 days after receipt of the first dose through 6 days after receipt of the second dose) and complete vaccination (assessed ≥7 days after receipt of the second dose).

Results: The study included 1482 case participants and 3449 control participants. Vaccine effectiveness for partial vaccination was 77.6% (95% confidence interval [CI], 70.9 to 82.7) with the BNT162b2 vaccine (Pfizer-BioNTech) and 88.9% (95% CI, 78.7 to 94.2) with the mRNA-1273 vaccine (Moderna); for complete vaccination, vaccine effectiveness was 88.8% (95% CI, 84.6 to 91.8) and 96.3% (95% CI, 91.3 to 98.4), respectively. Vaccine effectiveness was similar in subgroups defined according to age (<50 years or ≥50 years), race and ethnic group, presence of underlying conditions, and level of patient contact. Estimates of vaccine effectiveness were lower during weeks 9 through 14 than during weeks 3 through 8 after receipt of the second dose, but confidence intervals overlapped widely.

Conclusions: The BNT162b2 and mRNA-1273 vaccines were highly effective under real-world conditions in preventing symptomatic Covid-19 in health care personnel, including those at risk for severe Covid-19 and those in racial and ethnic groups that have been disproportionately affected by the pandemic."

NEJM: Efficacy of the mRNA-1273 SARS-CoV-2 Vaccine at Completion of Blinded Phase (22 September 2021)

"Background: At interim analysis in a phase 3, observer-blinded, placebo-controlled clinical trial, the mRNA-1273 vaccine showed 94.1% efficacy in preventing coronavirus disease 2019 (Covid-19). After emergency use of the vaccine was authorized, the protocol was amended to include an open-label phase. Final analyses of efficacy and safety data from the blinded phase of the trial are reported.

Methods: We enrolled volunteers who were at high risk for Covid-19 or its complications; participants were randomly assigned in a 1:1 ratio to receive two intramuscular injections of mRNA-1273 (100 µg) or placebo, 28 days apart, at 99 centers across the United States. The primary end point was prevention of Covid-19 illness with onset at least 14 days after the second injection in participants who had not previously been infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The data cutoff date was March 26, 2021.

Results: The trial enrolled 30,415 participants; 15,209 were assigned to receive the mRNA-1273 vaccine, and 15,206 to receive placebo. More than 96% of participants received both injections, 2.3% had evidence of SARS-CoV-2 infection at baseline, and the median follow-up was 5.3 months in the blinded phase. Vaccine efficacy in preventing Covid-19 illness was 93.2% (95% confidence interval [CI], 91.0 to 94.8), with 55 confirmed cases in the mRNA-1273 group (9.6 per 1000 person-years; 95% CI, 7.2 to 12.5) and 744 in the placebo group (136.6 per 1000 person-years; 95% CI, 127.0 to 146.8). The efficacy in preventing severe disease was 98.2% (95% CI, 92.8 to 99.6), with 2 cases in the mRNA-1273 group and 106 in the placebo group, and the efficacy in preventing asymptomatic infection starting 14 days after the second injection was 63.0% (95% CI, 56.6 to 68.5), with 214 cases in the mRNA-1273 group and 498 in the placebo group. Vaccine efficacy was consistent across ethnic and racial groups, age groups, and participants with coexisting conditions. No safety concerns were identified.

Conclusions: The mRNA-1273 vaccine continued to be efficacious in preventing Covid-19 illness and severe disease at more than 5 months, with an acceptable safety profile, and protection against asymptomatic infection was observed."

NEJM: Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months (15 September 2021)

> "Background: BNT162b2 is a lipid nanoparticle-formulated, nucleoside-modified RNA vaccine encoding a prefusion-stabilized, membrane-anchored severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) full-length spike protein. BNT162b2 is highly efficacious against coronavirus disease 2019 (Covid-19) and is currently approved, conditionally approved, or authorized for emergency use worldwide. At the time of initial authorization, data beyond 2 months after vaccination were unavailable.
>
> Methods: In an ongoing, placebo-controlled, observer-blinded, multinational, pivotal efficacy trial, we randomly assigned 44,165 participants 16 years of age or older and 2264 participants 12 to 15 years of age to receive two 30-μg doses, at 21 days apart, of BNT162b2 or placebo. The trial end points were vaccine efficacy against laboratory-confirmed Covid-19 and safety, which were both evaluated through 6 months after vaccination.
>
> Results: BNT162b2 continued to be safe and have an acceptable adverse-event profile. Few participants had adverse events leading to withdrawal from the trial. Vaccine efficacy against Covid-19 was 91.3% (95% confidence interval [CI], 89.0 to 93.2) through 6 months of follow-up among the participants without evidence of previous SARS-CoV-2 infection who could be evaluated. There was a gradual decline in vaccine efficacy. Vaccine efficacy of 86 to 100% was seen across countries and in populations with diverse ages, sexes, race or ethnic groups, and risk factors for Covid-19 among participants without evidence of previous infection with SARS-CoV-2. Vaccine efficacy against severe disease was 96.7% (95% CI, 80.3 to 99.9). In South Africa, where the SARS-CoV-2 variant of concern B.1.351 (or beta) was predominant, a vaccine efficacy of 100% (95% CI, 53.5 to 100) was observed.
>
> Conclusions: Through 6 months of follow-up and despite a gradual decline in vaccine efficacy, BNT162b2 had a favorable safety profile and was highly efficacious in preventing Covid-19."

JAMA Netw Open: Safety and Antibody Response After 1 and 2 Doses of BNT162b2 mRNA Vaccine in Recipients of Allogeneic Hematopoietic Stem Cell Transplant (14 September 2021)

> "This cohort study examines safety and antibody responses after 1 and 2 doses of BNT162b2 mRNA vaccine in recipients of allogeneic hematopoietic stem cell transplant (HSCT). …
>
> Despite the limitations inherent to an observational analysis and the fact that the cohort was small and from a single center, this study found a high response rate of 83% in this cohort of allogeneic HSCT recipients after 2 doses of BNT162b2 vaccine. Of note, 62% of the patients achieved the highest IgG titer also reached by a concomitant healthy cohort."

In Kids

Clin Infect Dis: Safety and immunogenicity of a recombinant adenovirus type-5-vectored COVID-19 vaccine with a homologous prime-boost regimen in healthy participants aged 6 years and above: a randomised, double-blind, placebo-controlled, phase 2b trial (22 September 2021)

> "Background: We assessed the safety and immunogenicity of a recombinant adenovirus type-5 (Ad5)-vectored COVID-19 vaccine with homologous prime-boost regimens in healthy participants aged 6 years and above.
>
> Methods: In this randomised, double-blind, placebo-controlled trial, participants received low-dose vaccine, middle-dose vaccine or placebo. Prime-booster regimens were given intramuscularly 56 days apart. ELISA antibodies to the receptor binding domain (RBD) and pseudovirus neutralising antibodies were detected. Adverse events were monitored for 28 days following each vaccination.
>
> Results: A total of 430 participants were enrolled in the study, with 30 participants aged 18-55 years (MID cohort), 250 participants aged 56 years and older (OLD cohort), and 150 participants aged 6-17 years (MIN cohort). Ad5-vectored COVID-19 vaccine induced significant RBD-specific ELISA antibodies which decreased with increasing age, with geometric mean titres (GMTs) of 1037.5 in MIN cohort, 647.2 in MID cohort, and 338.0 in OLD cohort receiving 5×10 10 viral particles on day 28 following boost vaccination. Pseudovirus neutralising antibodies showed a similar pattern, with GMTs of 168.0 in MIN cohort, 76.8 in MID cohort, and 79.7 in OLD cohort. A single dose in children and adolescents induced higher antibody responses than that elicited by two doses in adults, with GMTs of 1091.6 and 96.6 in ELISA antibody and neutralising antibody, respectively. Homologous prime-boost vaccination was safety and tolerable.
>
> Conclusions: Ad5-vectored COVID-19 vaccine with a single dose was safe and induced robust immune responses in children and adolescents aged 6-17 years. A prime-boost regimen needs further exploration for Ad5-vectored COVID-19 vaccine."

Boosters

NEJM: Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel (15 September 2021)

> "Background: On July 30, 2021, the administration of a third (booster) dose of the BNT162b2 messenger RNA vaccine (Pfizer-BioNTech) was approved in Israel for persons who were 60 years of age or older and who had received a second dose of vaccine at least 5 months earlier. Data are needed regarding the effect of the booster dose on the rate of confirmed coronavirus 2019 disease (Covid-19) and the rate of severe illness.

Methods: We extracted data for the period from July 30 through August 31, 2021, from the Israeli Ministry of Health database regarding 1,137,804 persons who were 60 years of age or older and had been fully vaccinated (i.e., had received two doses of BNT162b2) at least 5 months earlier. In the primary analysis, we compared the rate of confirmed Covid-19 and the rate of severe illness between those who had received a booster injection at least 12 days earlier (booster group) and those who had not received a booster injection (nonbooster group). In a secondary analysis, we evaluated the rate of infection 4 to 6 days after the booster dose as compared with the rate at least 12 days after the booster. In all the analyses, we used Poisson regression after adjusting for possible confounding factors.

Results: At least 12 days after the booster dose, the rate of confirmed infection was lower in the booster group than in the nonbooster group by a factor of 11.3 (95% confidence interval [CI], 10.4 to 12.3); the rate of severe illness was lower by a factor of 19.5 (95% CI, 12.9 to 29.5). In a secondary analysis, the rate of confirmed infection at least 12 days after vaccination was lower than the rate after 4 to 6 days by a factor of 5.4 (95% CI, 4.8 to 6.1).

Conclusions: In this study involving participants who were 60 years of age or older and had received two doses of the BNT162b2 vaccine at least 5 months earlier, we found that the rates of confirmed Covid-19 and severe illness were substantially lower among those who received a booster (third) dose of the BNT162b2 vaccine."

NEJM: SARS-CoV-2 Neutralization with BNT162b2 Vaccine Dose 3 (15 September 2021)

This study " details the results of administration of a third Pfizer vaccine dose to 11 participants 18 to 55 years old and 12 participants 65 to 85 years 8 to 9 months after receipt of the second dose.…

A team led by University of Rochester researchers in New York collected serum samples before each of the three doses and 7 days and 1 month after. From 7 days after dose 2 to before dose 3, SARS-CoV-2 neutralizing antibody mean concentrations fell far faster in the subgroup of phase 1 participants than vaccine effectiveness declined in phase 2/3 trial participants.

But by 1 month after the third vaccine dose, antibody concentrations against the wild-type virus rose five times as high as the concentrations 1 month after the second dose in the group aged 18 to 55 years and seven times as high in the group aged 65 to 85.

Neutralizing antibody levels against the Beta (B1351) variant were more than 15 times higher after the third dose than after the second dose compared with antibodies against the wild-type virus in the younger group and more than 20 times higher in the older group.

Antibody concentrations declined from 7 days to 1 month after the second dose but increased from 7 days to 1 month after the third dose. A comparable pattern of broader neutralization and higher antibody concentrations against a combination of the Delta spike

protein and a wild-type genetic background were observed after the third dose." (summary taken from CIDRAP)

Adverse Events / Side Effects

JAMA Netw Open: Assessment of Allergic and Anaphylactic Reactions to mRNA COVID-19 Vaccines With Confirmatory Testing in a US Regional Health System (17 September 2021)

"Question: What risk factors and mechanisms can help explain documented allergic reactions to Food and Drug Administration–authorized mRNA COVID-19 vaccines?

Findings: In this case series of 22 patients with suspected vaccine allergy receiving clinical skin prick testing (SPT) and basophil activation testing (BAT) to the whole vaccine and key components (ie, polyethylene glycol [PEG] and polysorbate 80), none exhibited immunoglobulin (Ig) E–mediated allergy to components via SPT. However, most had positive BAT results to PEG, and all had positive BAT results to their administered mRNA vaccine, with no patient sample having detectable PEG IgE.

Meaning: These findings suggest that non–IgE-mediated allergic reactions to PEG may be responsible for many documented cases of allergy to mRNA vaccines."

Vaccine Development

iScience: Single-dose Intranasal Vaccination Elicits Systemic and Mucosal Immunity Against SARS-CoV-2 (24 September 2021; online 26 August 2021)

"Despite remarkable progress in the development and authorization of vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there is a need to validate vaccine platforms for broader application. The current intramuscular vaccines are designed to elicit systemic immunity without conferring mucosal immunity in the nasal compartment, which is the first barrier that SARS-CoV-2 virus breaches before dissemination to the lung. We report the development of an intranasal subunit vaccine that uses lyophilized spike protein and liposomal STING agonist as an adjuvant. This vaccine induces systemic neutralizing antibodies, IgA in the lung and nasal compartments, and T-cell responses in the lung of mice. Single-cell RNA sequencing confirmed the coordinated activation of T/B-cell responses in a germinal center-like manner within the nasal-associated lymphoid tissues, confirming its role as an inductive site to enable durable immunity. The ability to elicit immunity in the respiratory tract can prevent the establishment of infection in individuals and prevent disease transmission."

Breakthrough Infections, Reinfections, and Coinfections

Journal Articles

Clin Infect Dis: Prior infection and age impacts antibody persistence after SARS-CoV-2 mRNA vaccine (22 September 2021)

> "Determining the duration of immunity to SARS-CoV-2 vaccines is critical for informing the timing of booster immunization. Many host factors could influence both the magnitude and persistence of the antibody response. Here, we showed that SARS-CoV-2 infection before vaccination and age affected the decay of antibody responses to the SARS-CoV-2 mRNA vaccine."

Emerg Infect Dis: Multinational Observational Cohort Study of COVID-19–Associated Pulmonary Aspergillosis (15 September 2021)

> "We performed an observational study to investigate intensive care unit incidence, risk factors, and outcomes of coronavirus disease–associated pulmonary aspergillosis (CAPA). We found 10%–15% CAPA incidence among 823 patients in 2 cohorts. Several factors were independently associated with CAPA in 1 cohort and mortality rates were 43%–52%."

Lancet Regional Health: Vaccination reduces need for emergency care in breakthrough COVID-19 infections: A multicenter cohort study (09 September 2021)

> "Background: While recent literature has shown the efficacy of the SARS-CoV-2 vaccine in preventing infection, its impact on need for emergency care/hospitalization in breakthrough infections remain unclear, particularly in regions with a high rate of variant viral strains. We aimed to determine if vaccination reduces hospital visits in breakthrough COVID-19.
>
> Methods: This observational cohort analysis compared unvaccinated (UV), partially vaccinated (PV), and fully vaccinated (FV) adult patients with SARS-CoV-2 infection requiring emergency care(EC)/hospitalization within an eight-hospital system in Michigan. Demographic and clinical variables were obtained from the electronic record. Vaccination data was obtained from the Michigan Care Improvement Registry and Centers for Disease Control vaccine tracker. Primary endpoint was rate of emergency care/hospitalization encounters among patients diagnosed with COVID-19. Secondary outcome was severe disease-composite outcome (ICU, mechanical ventilation, or in-hospital death).
>
> Findings: Between December 15,2020 and April 30,2021, 11,834 EC encounters were included:10,880 (91.9%) UV, 825 (7%) PV, 129 (1.1%) FV. Average age was 53.0 ± 18.2 and 52.8% were female. Accounting for the SARS-CoV-2 vaccination population groups in Michigan, the ED encounters/hospitalizations rate relevant to COVID-19 was 96% lower in FV versus UV (multiplicative effect:0.04, 95% CI 0.03 to 0.06, $p < 0.001$) in negative binomial regression. COVID-19 EC visits rate peaked at 22.61, 12.88, and 1.29 visits per 100000 for

the UV, PV, and FV groups, respectively. In the propensity-score matching weights analysis, FV had a lower risk of composite disease compared to UV but statistically insignificant (HR 0.84, 95% CI 0.52 to 1.38).

Interpretation: The need for emergency care/hospitalization due to breakthrough COVID-19 is an exceedingly rare event in fully vaccinated patients. As vaccination has increased regionally, EC visits amongst fully vaccinated individuals have remained low and occur much less frequently than unvaccinated individuals. If hospital-based treatment is required, elderly patients with significant comorbidities are at high-risk for severe outcomes regardless of vaccination status."

Treatments and Management

News in Brief

"Remdesivir reduces Covid hospitalizations when given early, study shows" (STAT; see also: Gilead press release).

Around the Country

Alaska joins Idaho in shifting to crisis standards of care because of the volume of covid cases needing medical intervention (CIDRAP).

One in four hospitals in the south have more than 95% of its ICU beds are occupied (NYT).

"Tennessee limiting monoclonal antibody treatment to unvaccinated residents" (NBC).

Animals Get Care, Too

"Gorillas at Zoo Atlanta are being treated after initial tests showed they were positive for the coronavirus — and the zoo plans to vaccinate them once they recover" (WP).

"9 lions and tigers at the National Zoo are being treated for COVID" (NPR).

Events

WHAT:	COVID-19 and Crisis Standards of Care: The Fourth Wave and the Future Webinar
WHEN:	held 17 September 2021, 2 hours long
DETAILS:	"COVID-19 has fundamentally changed the delivery of health care services worldwide, forcing difficult choices on health professionals and laying bare many pre-existing health, medical, and public health sector frailties. A fourth wave of

the pandemic, driven by the Delta variant, extreme shortages of key resources have again brought the necessity of crisis standards of care to the forefront of the minds of many clinicians and patients.

This webinar featured discussions on past and current challenges in ethically allocating scarce resources in the face of surging demand, the health care staffing crisis seen across the country, and identify possible solutions to real-time issues and ways to ensure fair decisions are made even when systems are strained."

WATCH: Links to YouTube channel and more at https://nam.edu/event/covid-19-and-crisis-standards-of-care-the-fourth-wave-and-the-future-webinar/

Journal Articles

Diving Hyperb Med: Efficacy and safety of hyperbaric oxygen treatment in SARS-COV-2 (COVID-19) pneumonia: a systematic review (30 September 2021; accessed 24 September 2021)

"Introduction: The need for intubation and mechanical ventilation among COVID-19 patients is associated with high mortality rates and places a substantial burden on the healthcare system. There is a strong pathophysiological rationale suggesting that hyperbaric oxygen treatment (HBOT), a low-risk and non-invasive treatment, may be beneficial for COVID-19 patients. This systematic review aimed to explore the potential effectiveness and safety of HBOT for treating patients with COVID-19.

Methods: Medline, Embase, Scopus, and Google Scholar were searched from December 2019 to February 2021, without language restrictions. The grey literature was searched via an internet search engine and targeted website and database searches. Reference lists of included studies were searched. Independent reviewers assessed studies for eligibility and extracted data, with disagreements resolved by consensus or a third reviewer. Risk of bias was assessed using the Newcastle Ottawa Scale. Data were summarised descriptively.

Results: Six publications (one cohort study, five case reports/series) met the inclusion criteria with a total of 37 hypoxaemic COVID-19 patients treated with HBOT. Of these 37 patients, the need for intubation and mechanical ventilation and in-hospital survival were assessed for 26 patients across three studies. Of these 26 patients, intubation and mechanical ventilation were not required for 24, and 23 patients survived. No serious adverse events of HBOT in COVID-19 patients were reported. No randomised trials have been published.

Conclusions: Limited and weak evidence from non-randomised studies including one propensity-matched cohort study suggests HBOT is safe and may be a promising

intervention to optimise treatment and outcomes in hypoxaemic COVID-19 patients. Randomised controlled studies are urgently needed."

Clin Infect Dis: A Multi-center, Prospective, Observational-cohort controlled study of Clinical Outcomes following COVID-19 Convalescent plasma therapy in hospitalized COVID-19 patients (21 September 2021)

"Background: The SARS-CoV2 pandemic has caused high inpatient mortality and morbidity throughout the world. COVID19 convalescent plasma has been utilized as a potential therapy for patients hospitalized with COVID19 pneumonia. This study evaluated the outcomes of hospitalized COVID19 patients treated with COVID19 convalescent plasma in a prospective, observational multicenter trial.

Methods: From April 2020 through August 2020, hospitalized COVID19 patients at 16 participating hospitals in Colorado were enrolled and treated with COVID19 convalescent plasma (CCP) and compared to hospitalized patients with COVID19 who were not treated with convalescent plasma. Plasma antibody levels were determined following the trial given that antibody tests were not approved at the initiation of the trial. CCP-treated and untreated COVID19 hospitalized patients were matched using propensity scores followed by analysis for length of hospitalization and inpatient mortality.

Results: 542 total hospitalized COVID19 patients were enrolled at 16 hospitals across the region. A total of 468 hospitalized COVID19 patients were entered into propensity score matching with 188 patients matched for analysis in the CCP-treatment and control arms. Fine-Gray models revealed increased length of hospital stay in CCP-treated patients and no change in inpatient mortality compared to controls. In subgroup analysis of CCP-treated patients within 7 days of admission, there was no difference in length of hospitalization and inpatient mortality.

Conclusions: These data show that treatment of hospitalized COVID19 patients with CCP did not significantly improve patient hospitalization length of stay or inpatient mortality."

Clin Infect Dis: Randomized study of rivaroxaban vs. placebo on disease progression and symptoms resolution in high-risk adults with mild COVID-19 (15 September 2021)

"Background: SARS-CoV-2 infection may be associated with a prothrombotic state, predisposing patients for a progressive disease course. We investigated whether rivaroxaban, a direct oral anticoagulant factor Xa inhibitor would reduce COVID-19 progression.

Methods: Adults (N=497) symptomatic with mild COVID-19 and at high-risk for COVID-19 progression based on age, body mass index, or comorbidity were randomized 1:1 to either daily oral rivaroxaban 10 mg (N=246) or placebo-equivalent (N=251) for 21 days and followed to Day 35. Primary endpoints were safety and progression to moderate or severe

disease, per the Gates MRI scale. Absolute difference in progression risk was assessed using a stratified Miettinen and Nurminen method.

Results: The study was terminated after 497 of target 600 participants were enrolled due to a pre-specified interim analysis of the first 200 participants which crossed the futility boundary for the primary efficacy endpoint in the Intent to Treat population. Enrollees were 85% aged < 65 years old, 60% female, 27% Hispanic, Black or other minorities and 69% with ≥2 comorbidities. Rivaroxaban was well-tolerated. Disease progression rates were 46/222 (20.7%) in rivaroxaban vs. 44/222 (19.8%) in placebo groups, with a risk difference of -1.0, 95% CI, -6.4 to 8.4; P = 0.78.

Conclusions: Our study did not demonstrate an impact of rivaroxaban on disease progression in high-risk adults with mild COVID-19. There remains a critical public health gap in identifying scalable effective therapies for high-risk people in the outpatient setting to prevent COVID-19 progression."

Lancet Infect Dis: Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DisCoVeRy): a phase 3, randomised, controlled, open-label trial (14 September 2021)

"Background: The antiviral efficacy of remdesivir against SARS-CoV-2 is still controversial. We aimed to evaluate the clinical efficacy of remdesivir plus standard of care compared with standard of care alone in patients admitted to hospital with COVID-19, with indication of oxygen or ventilator support.

Methods: DisCoVeRy was a phase 3, open-label, adaptive, multicentre, randomised, controlled trial conducted in 48 sites in Europe (France, Belgium, Austria, Portugal, Luxembourg). Adult patients (aged ≥18 years) admitted to hospital with laboratory-confirmed SARS-CoV-2 infection and illness of any duration were eligible if they had clinical evidence of hypoxaemic pneumonia, or required oxygen supplementation. Exclusion criteria included elevated liver enzymes, severe chronic kidney disease, any contraindication to one of the studied treatments or their use in the 29 days before random assignment, or use of ribavirin, as well as pregnancy or breastfeeding. Participants were randomly assigned (1:1:1:1:1) to receive standard of care alone or in combination with remdesivir, lopinavir–ritonavir, lopinavir–ritonavir and interferon beta-1a, or hydroxychloroquine. Randomisation used computer-generated blocks of various sizes; it was stratified on severity of disease at inclusion and on European administrative region. Remdesivir was administered as 200 mg intravenous infusion on day 1, followed by once daily, 1-h infusions of 100 mg up to 9 days, for a total duration of 10 days. It could be stopped after 5 days if the participant was discharged. The primary outcome was the clinical status at day 15 measured by the WHO seven-point ordinal scale, assessed in the intention-to-treat population. Safety was assessed in the modified intention-to-treat population and was one of the secondary outcomes. This

trial is registered with the European Clinical Trials Database, EudraCT2020-000936-23, and ClinicalTrials.gov, NCT04315948.

Findings: Between March 22, 2020, and Jan 21, 2021, 857 participants were enrolled and randomly assigned to remdesivir plus standard of care (n=429) or standard of care only (n=428). 15 participants were excluded from analysis in the remdesivir group, and ten in the control group. At day 15, the distribution of the WHO ordinal scale was: (1) not hospitalised, no limitations on activities (61 [15%] of 414 in the remdesivir group vs 73 [17%] of 418 in the control group); (2) not hospitalised, limitation on activities (129 [31%] vs 132 [32%]); (3) hospitalised, not requiring supplemental oxygen (50 [12%] vs 29 [7%]); (4) hospitalised, requiring supplemental oxygen (76 [18%] vs 67 [16%]); (5) hospitalised, on non-invasive ventilation or high flow oxygen devices (15 [4%] vs 14 [3%]); (6) hospitalised, on invasive mechanical ventilation or extracorporeal membrane oxygenation (62 [15%] vs 79 [19%]); (7) death (21 [5%] vs 24 [6%]). The difference between treatment groups was not significant (odds ratio 0·98 [95% CI 0·77–1·25]; p=0·85). There was no significant difference in the occurrence of serious adverse events between treatment groups (remdesivir, 135 [33%] of 406 vs control, 130 [31%] of 418; p=0·48). Three deaths (acute respiratory distress syndrome, bacterial infection, and hepatorenal syndrome) were considered related to remdesivir by the investigators, but only one by the sponsor's safety team (hepatorenal syndrome).

Interpretation: No clinical benefit was observed from the use of remdesivir in patients who were admitted to hospital for COVID-19, were symptomatic for more than 7 days, and required oxygen support."

Nat Commun: New-onset IgG autoantibodies in hospitalized patients with COVID-19 (14 September 2021)

"COVID-19 is associated with a wide range of clinical manifestations, including autoimmune features and autoantibody production. Here we develop three protein arrays to measure IgG autoantibodies associated with connective tissue diseases, anti-cytokine antibodies, and anti-viral antibody responses in serum from 147 hospitalized COVID-19 patients. Autoantibodies are identified in approximately 50% of patients but in less than 15% of healthy controls. When present, autoantibodies largely target autoantigens associated with rare disorders such as myositis, systemic sclerosis and overlap syndromes. A subset of autoantibodies targeting traditional autoantigens or cytokines develop de novo following SARS-CoV-2 infection. Autoantibodies track with longitudinal development of IgG antibodies recognizing SARS-CoV-2 structural proteins and a subset of non-structural proteins, but not proteins from influenza, seasonal coronaviruses or other pathogenic viruses. We conclude that SARS-CoV-2 causes development of new-onset IgG autoantibodies in a significant proportion of hospitalized COVID-19 patients and are positively correlated with immune responses to SARS-CoV-2 proteins."

Pre-Existing Conditions, Comorbidities, and Impact on Other Health Issues

News in Brief

"Alabama heart patient dies after hospital contacts 43 ICUs in 3 states — 'He would not want any other family to go through what his did,' his family said" (NBC).

"A boy went to a COVID-swamped ER. He waited for hours. Then his appendix burst — Non-COVID patients are paying a price as the delta variant and low-vaccination rates overwhelm hospitals across the country. 'Wait times can now be measured in days,' said an expert" (ProPublica).

Journal Articles

JAMA Netw Open: Trends in Outpatient Antibiotic Prescriptions in the United States During the COVID-19 Pandemic in 2020 (22 September 2021)

> "This cross-sectional study examines the prescription fills of commonly prescribed outpatient antibiotics in the US through the end of 2020."

JAMA Netw Open: Association of Health Care Factors With Excess Deaths Not Assigned to COVID-19 in the US (13 September 2021)

> "In this cross-sectional study, a greater proportion of excess deaths were not assigned to COVID-19 in counties with reduced access to health insurance and primary care and in counties with more at-home deaths. Reduced access to health care may prevent a patient from receiving COVID-19 testing and diagnosis, which may reduce the probability of valid cause-of-death assignment. Counties in which residents were more likely to die at home may have been places where indirect deaths, such as deaths from drug overdose, were more likely to have occurred; however, these factors were beyond the scope our study."

Long COVID / Post-COVID Period

News in Brief

"'Post-vax COVID' is a new disease — Eventually we might all have to deal with COVID-19—but a shorter, gentler version, thanks to vaccines" (Atlantic).

"Study of up to 40,000 people will probe mysteries of Long Covid — Award of $470 million from the National Institutes of Health will enroll volunteers with long-term symptoms after coronavirus infection" (Science).

Upcoming Events

WHAT: Evaluating and Supporting Patients Presenting With Fatigue Following COVID-19 – free; can earn continuing education

WHEN: Thursday, 30 September 2021 1400-1500 ET

OVERVIEW: "During this COCA Call, presenters will discuss Post-COVID conditions (PCC), an umbrella term for the wide range of health consequences present four or more weeks after infection with SARS-CoV-2, which includes Long-COVID. It can be difficult to distinguish symptoms of fatigue and post-exertional malaise caused by PCC from symptoms that occur for other reasons. The American Academy of Physical Medicine and Rehabilitation (AAPM&R) has recently published a Multi-Disciplinary Collaborative Consensus Guidance Statement on the Assessment and Treatment of Fatigue in PCC. It provides practical guidance to clinicians when assessing and treating individuals with fatigue and a history consistent with PCC. The burden of PCC is expected to reflect the disproportionate burden of infection by race, ethnicity, and socioeconomic status and to highlight ongoing inequities in healthcare. The Health Equity Work Group of the AAPM&R has developed guidance to highlight the central role that principles of diversity, equity, and inclusion play in delivering quality healthcare."

WEBSITE: https://emergency.cdc.gov/coca/calls/2021/callinfo_093021.asp

Journal Articles

JAMA Netw Open: Clinical Characteristics of Multisystem Inflammatory Syndrome in Adults: A Systematic Review (22 September 2021)

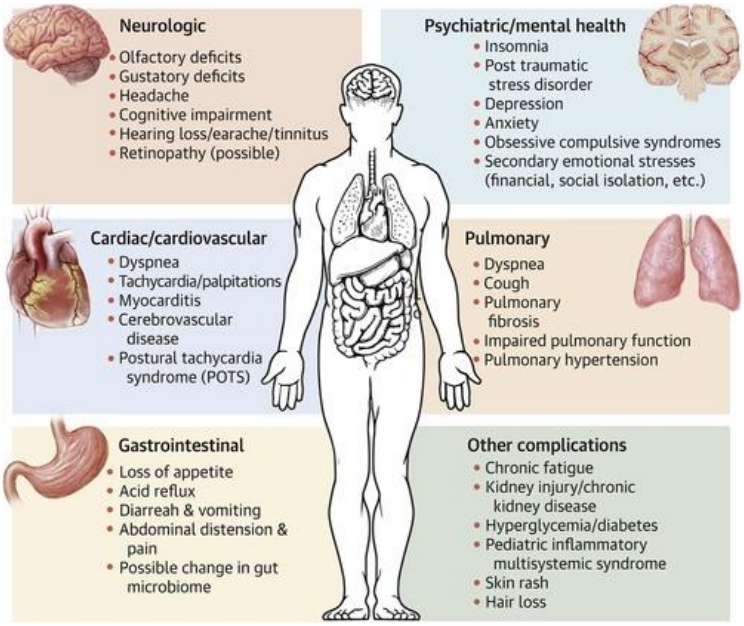
> "Question: What are the clinical characteristics of multisystem inflammatory syndrome in adults (MIS-A)?
>
> Findings: This systematic review of patients with MIS-A reported in the literature and to the US Centers for Disease Control and Prevention identified 221 patients worldwide. The syndrome presented approximately 4 weeks after acute COVID-19 with hyperinflammation and extrapulmonary multiorgan involvement that may be difficult to discern from acute biphasic COVID-19 and postacute sequelae of SARS-CoV-2 infection.
>
> Meaning: These findings suggest that MIS-A occurs in the postacute COVID-19 period with a heterogeneous clinical presentation likely owing to a dysregulated immune response."

MMWR: Post-Acute Sequelae of SARS-CoV-2 Infection Among Adults Aged ≥18 Years — Long Beach, California, April 1–December 10, 2020 (17 September 2021)

> "What is already known about this topic? The term “long COVID” is used to describe post-acute sequelae and long-term symptoms that can be experienced from weeks to months by persons recovering from COVID-19.
>
> What is added by this report? In a random sample of recovered COVID-19 patients in Long Beach, California, one third of participants reported post-acute sequelae 2 months after their positive test result, with higher rates reported among persons aged ≥40 years, females, persons with preexisting conditions, and Black persons.
>
> What are the implications for public health practice? Identification of populations disproportionately affected by COVID-19 and long COVID can help guide efforts to prioritize prevention and treatment."

JACC Basic Transl Sci: Postacute Sequelae of Severe Acute Respiratory Syndrome Coronavirus 2 Infection: A State-of-the-Art Review (15 September 2021)

> "The vast majority of patients (>99%) with severe acute respiratory syndrome coronavirus 2 survive immediate infection but remain at risk for persistent and/or delayed multisystem. This review of published reports through May 31, 2021, found that manifestations of postacute sequelae of severe acute respiratory syndrome coronavirus 2 infection (PASC) affect between 33% and 98% of coronavirus disease 2019 survivors and comprise a wide range of symptoms and complications in the pulmonary, cardiovascular, neurologic, psychiatric, gastrointestinal, renal, endocrine, and musculoskeletal systems in both adult and pediatric populations. Additional complications are likely to emerge and be identified over time. Although data on PASC risk factors and vulnerable populations are scarce, evidence points to a disproportionate impact on racial/ethnic minorities, older patients, patients with preexisting conditions, and rural residents. Concerted efforts by researchers, health systems, public health agencies, payers, and governments are urgently needed to better understand and mitigate the long-term effects of PASC on individual and population health."



Women's Health, Pregnancy, and Perinatal Care

Journal Articles

Clin Infect Dis: Congenital infection of SARS-CoV-2 with intrauterine foetal death: a clinicopathological study with molecular analysis (23 September 2021)

> "Observations of vertical transmission of SARS-CoV-2 infection from mother to foetus have recently been described in the literature. However, the consequences of such transmission, whether foetal or neonatal, are poorly understood. From a case of in utero foetal death at 24 +2 weeks of gestation that occurred seven days after the diagnosis of symptomatic SARS-CoV-2 infection in the mother, we isolated the incriminating virus by immunochemistry and molecular techniques in several foetal tissues, with a variant analysis of the SARS-CoV-2 genome. Moreover, the foetal demise could be explained by the presence of placental histological lesions, such as histiocytic intervillositis and trophoblastic necrosis, in addition to foetal tissue damage. We observed mild foetal growth retardation and visceral damage to the liver, causing hepatocellular damage and haemosiderosis. To the best of our knowledge, this is the first report in the literature of foetal demise secondary to maternal-foetal transmission of SARS-CoV-2 with a congenital infection and a pathological description of placental and foetal tissue damage. SARS-CoV-2 was identified in both specimens by three independent techniques (immunochemistry, RT-qPCR and RT-dPCR). Furthermore, the incriminating variant has been identified."

JAMA Netw Open: Factors Associated With Changes in Pregnancy Intention Among Women Who Were Mothers of Young Children in New York City Following the COVID-19 Outbreak (15 September 2021)

> "Question: Were there changes in pregnancy intentions among women who were mothers of young children around the peak of the first wave of COVID-19 in New York City?
>
> Findings: In this cross-sectional study of 1179 women in New York City who were mothers of young children, nearly half of those who had been attempting to become pregnant and more than a third who had been thinking about trying before the COVID-19 pandemic stopped in the first few months of the outbreak. Women who responded to a survey during the lockdown were more likely to cease attempts or plans to become pregnant.
>
> Meaning: The results of this study suggest that the outbreak of the COVID-19 pandemic was associated with fewer women planning or attempting to become pregnant; these findings may have long-term effects on fertility rates."

Pediatric Population

News in Brief

The Pfizer vaccine could be authorized for children aged 5-11 as early as October, according to sources (Reuters).

"Covid likely led to a rare disorder that left 8-year-old girl paralyzed" (NBC).

The CDC has developed print materials on multisystem inflammatory syndrome in children to educate physicians and fact sheets for parents (CDC).

"We know students are struggling with their mental health. Here's how you can help" (NPR).

"Scientists examine kids' unique immune systems as more fall victim to Covid" (KHN).

Journal Articles

MMWR: Longitudinal Trends in Body Mass Index Before and During the COVID-19 Pandemic Among Persons Aged 2–19 Years — United States, 2018–2020 (17 September 2021)

> "What is already known about this topic? The COVID-19 pandemic led to school closures, disrupted routines, increased stress, and less opportunity for physical activity and proper nutrition, leading to weight gain among children and adolescents.
>
> What is added by this report? Among a cohort of 432,302 persons aged 2–19 years, the rate of body mass index (BMI) increase approximately doubled during the pandemic compared to a prepandemic period. Persons with prepandemic overweight or obesity and younger school-aged children experienced the largest increases.
>
> What are the implications for public health practice? Obesity prevention and management efforts during and following the COVID-19 pandemic could include health care provider screening for BMI, food security, and social determinants of health, and increased access to evidence-based pediatric weight management programs and food assistance resources."

JAMA Ophthalmol: Rates of Myopia Development in Young Chinese Schoolchildren During the Outbreak of COVID-19 (16 September 2021)

> "Question: Were environmental changes during the outbreak of COVID-19 associated with increased development of myopia in young schoolchildren in China?
>
> Findings: In this observational study longitudinally monitoring 2114 students from grade 2 to grade 3, myopia incidence doubled from November and December 2019 to November and December 2020 compared with the same period from 2018 to 2019. The proportion of children without myopia and with spherical equivalent refraction greater than −0.50 D and

less than or equal to +0.50 D in grade 3 had increased by 18% by November and December 2020 compared with the same period in 2019.

Meaning: These data suggest that development of myopia in young Chinese schoolchildren may have increased during the COVID-19 outbreak; the long-term impact of environmental changes during the COVID-19 outbreak period on the development of myopia in children needs further investigation."

J Hosp Med: Factors Associated With COVID-19 Disease Severity in US Children and Adolescents (15 September 2021)

"BACKGROUND: Little is known about the clinical factors associated with COVID-19 disease severity in children and adolescents.

METHODS: We conducted a retrospective cohort study across 45 US children's hospitals between April 2020 to September 2020 of pediatric patients discharged with a primary diagnosis of COVID-19. We assessed factors associated with hospitalization and factors associated with clinical severity (eg, admission to inpatient floor, admission to intensive care unit [ICU], admission to ICU with mechanical ventilation, shock, death) among those hospitalized.

RESULTS: Among 19,976 COVID-19 encounters, 15,913 (79.7%) patients were discharged from the emergency department (ED) and 4063 (20.3%) were hospitalized. The clinical severity distribution among those hospitalized was moderate (3222, 79.3%), severe (431, 11.3%), and very severe (380, 9.4%). Factors associated with hospitalization vs discharge from the ED included private payor insurance (adjusted odds ratio [aOR],1.16; 95% CI, 1.1-1.3), obesity/type 2 diabetes mellitus (type 2 DM) (aOR, 10.4; 95% CI, 8.9-13.3), asthma (aOR, 1.4; 95% CI, 1.3-1.6), cardiovascular disease, (aOR, 5.0; 95% CI, 4.3-5.8), immunocompromised condition (aOR, 5.9; 95% CI, 5.0-6.7), pulmonary disease (aOR, 5.3; 95% CI, 3.4-8.2), and neurologic disease (aOR, 3.2; 95% CI, 2.7-5.8). Among children and adolescents hospitalized with COVID-19, greater disease severity was associated with Black or other non-White race; age greater than 4 years; and obesity/type 2 DM, cardiovascular, neuromuscular, and pulmonary conditions.

CONCLUSIONS: Among children and adolescents presenting to US children's hospital EDs with COVID-19, 20% were hospitalized; of these, 21% received care in the ICU. Older children and adolescents had a lower risk for hospitalization but more severe illness when hospitalized. There were differences in disease severity by race and ethnicity and the presence of selected comorbidities. These factors should be taken into consideration when prioritizing mitigation and vaccination strategies."

Healthcare Workers

News in Brief

"CDC to invest $2.1 billion to protect patients and healthcare workers from COVID-19 and future infectious diseases" (CDC).

"Cincinnati area hospitals boost security against 'violence, vile words,' key leader says" (Cincinnati Enquirer; see also: Health Security review articles, below).

The Pause app, based on a movement introduced by Jonathan Bartels RN, is to "honor a patient and the caregiver team" by offering a 15-30 second period of silence after a death (Pause app).

Special Reports and Other Resources

JHCHS: Mental Health and Social Support for Healthcare and Hospital Workers During the COVID-19 Pandemic (23 September 2021)

> "Healthcare and hospital workers providing care and support to infected patients during a pandemic are at increased risk for mental distress. Factors impacting their mental health include high risk of exposure and infection, financial insecurity due to furloughs, separation from and worries about loved ones, a stressful work environment due to surge conditions with scarce supplies, traumatic experiences due to witnessing the deaths of patients and colleagues, and other acute stressors. Finding ways for institutions to support the mental wellbeing of healthcare and hospital workers in an acute pandemic-related crisis situation is of critical importance. The factors affecting mental health are deeply connected to work-related motivation and attendance. Willingness to come to work is multifactorial and is dependent upon an individual's self-perception of risk, as well as having the skills and resources necessary to perform work tasks given the nature of the public health emergency. Social and material support for healthcare workers in a variety of high-stress and high-risk settings is important for supporting workers' mental health and in maintaining their commitment in challenging conditions.
>
> The impact of the COVID-19 pandemic on healthcare workers has been profound, characterized by death, disability, and an untenable burden on mental health and wellbeing. Lost on the Frontline, a report published by The Guardian and Kaiser Health Network in April 2021, revealed that more than 3,600 healthcare workers in the United States had died of COVID-19. While the median age of death due to COVID-19 was 78 years, in healthcare workers, it was 59. Two-thirds of deceased healthcare workers were people of color, revealing the deep inequities tied to race, ethnicity, and economic status in America's healthcare workforce. Lower-paid workers who handled everyday patient care, including nurses, support staff, and nursing home employees, were far more likely to die in the

pandemic than physicians. Only 30% of the deaths were among hospital workers, with few employed by well-funded academic medical centers. Healthcare workers were 3 times more likely to contract COVID-19 than the general public. Detrimental effects also experienced by healthcare and hospital workers included financial hardship, stress related to known and unknown information, and fear of the uncertainty regarding continued progression of the pandemic. As of August 2021, the COVID-19 pandemic is far from over and its full impact upon hospital and healthcare workers remains unknown.

The Johns Hopkins Health System (JHHS) operates in 2 states and the District of Columbia. Johns Hopkins Medicine (JHM) is the robust partnership between JHHS and the Johns Hopkins University School of Medicine, with a workforce of approximately 53,000 employees and a very limited number of contract workers. JHHS and JHM have played a leadership role during the COVID-19 response both nationally, by producing and sharing data to inform decisionmaking and evidence-based guidelines for response, and regionally, in accepting large numbers of patients during the surge. Prior to the onset of the pandemic, JHHS and JHM leadership had established a commitment to employee mental health and wellbeing through substantial investments and the implementation of numerous programs to support employees. However, even with the presence of these dedicated resources, clinical and nonclinical staff have reported high levels of stress, anxiety, and burnout.

To identify the issues most critical to healthcare workers' mental health, wellbeing, and motivation during the COVID-19 pandemic, we conducted a cross-sectional survey (1,189 responses) and 73 semistructured interviews with individuals currently employed at JHHS and JHM hospitals located in Maryland and the District of Columbia. Our study population included healthcare providers and direct support services staff, including workers in frontline environmental services, food services, and security.

The responses from our survey and interviews revealed that the trauma of witnessing COVID-19 death was exacerbated by the general stress of working during the pandemic and that the significant mental health burden created by the pandemic/infectious disease environment itself was characterized by the ongoing uncertainty and ambiguity about the scientific understanding of the virus. Additionally, stressors negatively impacting employee mental health stemmed from the workplace, resulting in reduced trust of and increased perceptions of betrayal in the institution.

Although our findings are specific to one academic health system, they may be relevant to other hospitals and health systems. Studies such as this offer an important window into learning more about employee health from the unique stress and trauma of the COVID-19 pandemic and can facilitate progress toward a health system that communicates value and prioritizes safety for all staff."

Journal Articles

Infect Control Hosp Epidemiol: COVID-19 Vaccine Hesitancy among Physicians, Physician Assistants, Nurse Practitioners, and Nurses in Two Academic Hospitals in Philadelphia (20 September 2021)

> "Objective: To evaluate COVID-19 vaccine hesitancy among health care personnel (HCP) with significant clinical exposure to COVID-19 at two large, academic hospitals in Philadelphia.
>
> Design, setting and participants: HCP were surveyed between November-December 2020 about their intention to receive the COVID-19 vaccine.
>
> Methods: The survey measured the intent among HCP to receive a COVID-19 vaccine, timing of vaccination, and reasons for or against vaccination. Among patient-facing HCP, multivariate regression evaluated the associations between healthcare positions (MD, NP/PA, RN) and vaccine hesitancy (intending to decline, delay, or were unsure about vaccination), adjusting for demographic characteristics, reasons why or why not to receive the vaccine, and prior receipt of routine vaccines.
>
> Results: Among 5,929 HCP (2,253 MDs/DOs, 582 NPs, 158 PAs, and 2,936 nurses), a higher proportion of nurses (47.3%) were COVID-vaccine hesitant compared with 30.0% of PAs/NPs and 13.1% of MDs/DOs. The most common reasons for vaccine hesitancy included concerns about side effects, the newness of the vaccines, and lack of vaccine knowledge. Regardless of position, Black HCP were more hesitant than White HCP (OR∼5) and females were more hesitant than males (OR∼2).
>
> Conclusion: Although a majority of clinical HCP intended to receive a COVID-19 vaccine, intention varied by healthcare position. Consistent with other studies, hesitancy was also significantly associated with race/ethnicity across all positions. These results underline the importance of understanding and effectively addressing reasons for hesitancy, especially among frontline HCP who are at increased risk of COVID exposure and play a critical role in recommending vaccines to patients."

Disaster Med Public Health Prep: Occupational Health and Safety Measures in Healthcare Settings During COVID-19: Strategies for Protecting Staff, Patients and Visitors (14 September 2021)

> "The COVID-19 (SARS-CoV-2) pandemic has profoundly impacted almost every aspect of healthcare systems worldwide, placing the health and safety of frontline healthcare workers at risk and still continues to remain an important public health challenge. Several hospitals have put in place strategies to manage space, staff, and supplies in order to continue to deliver optimum care to patients while at the same time protecting the health and safety of staff and patients. However, the emergence of the second and third waves of the virus with

the influx of new cases continue to add an additional level of complexity to the already challenging situation of containing the spread and lowering the rate of transmission and thus pushing healthcare systems to the limit.

In this narrative review paper we describe various strategies including administrative controls, environmental controls and use of personal protective equipment implemented by occupational health and safety departments for the protection of healthcare workers, patients and visitors from SARS-CoV-2 virus infection. The protection and safeguard of the health and safety of healthcare workers and patients through the implementation of effective infection control measures, adequate management of possible outbreaks and minimization of risk of nosocomial transmission is an important and effective strategy of SARS-CoV-2 pandemic management in any healthcare facility. High quality patient care hinges on ensuring that the care providers are well protected and supported so they can provide the best quality of care to their patients."

Threats

Health Secur: Terrorist Attacks Against Vaccinators: A Review (16 September 2021)

"Vaccinators fulfill an important role in a nation's public health by reducing the burden of disease on the population. Understanding patterns of attack employed against vaccinators is important to determine how to protect them. We conducted a search of the Global Terrorism Database for terrorist attacks against vaccinators that occurred between the years 1970 and 2018.

Using the search terms "hospital," "healthcare," "clinic," "doctor," "nurses," "vaccinators," and "vaccinations," 2,322 healthcare-related entries were identified. We then manually searched the dataset for incidents related to attacks on vaccinators, which resulted in the identification of 133 attacks against vaccinators. The majority (128 out of 133) of attacks occurred during or after 2010. Every attack except one has occurred in the Middle East, South Asia, or sub-Saharan Africa. Pakistan has seen the most attacks against vaccinators, with 112 incidents recorded. Vaccinators continue to be vulnerable to terrorist attacks. Protection of healthcare personnel during mass vaccination efforts is critical so that they can continue their life saving mission."

See also: Terrorist Attacks Against Healthcare Facilities: A Review

Disparities and Health Equity

News in Brief

Long read: "'Health equity tourists': How white scholars are colonizing research on health disparities" (STAT).

Upcoming Events

WHAT: 13th Annual Fighting Asthma Disparities Summit
Collaborating to Break Down Barriers in Pediatric Asthma Care

WHEN: Tuesday, 05 October 2021 0830–1400 EDT
– free, virtual event

ABOUT: "The Virtual 13th Annual Fighting Asthma Disparities Summit will focus on breaking down barriers in pediatric asthma care. Experts will discuss the physical and emotional impact of housing insecurity on children's health as well as environmental asthma triggers in urban schools. A thorough overview of SMART therapy, a relatively novel approach to managing asthma, will also be presented.

Breakout Session Topics:

- Caring for a child with asthma during the pandemic
- How Medicaid Managed Care Organizations are navigating the pandemic
- Improving asthma outcomes through structural home repairs
- Coordinating home- and school-based asthma care - prior to the pandemic"

Register at: https://www.eventbrite.com/e/13th-annual-fighting-asthma-disparities-summit-tickets-169177050111

Journal Articles

JAMA Health Forum: Disparities in SARS-CoV-2 Vaccination-to-Infection Risk During the COVID-19 Pandemic in Massachusetts (17 September 2021)

> "In this cohort study, analysis of SARS-CoV-2 vaccination indicated structural disparity in vaccine distribution with lower vaccine coverage to infection risk in communities with increased socioeconomic vulnerability and larger proportions of Black and Latinx individuals."

JAMA Health Forum: Prioritizing Equity and Diversity in Academic Medicine Faculty Recruitment and Retention (10 September 2021)

> "This essay examines groups that are underrepresented in the medical workforce, how the COVID-19 pandemic may affect these groups, and suggests strategies for addressing these issues."

Risk, Transmission, and Exposure

News in Brief

"FDA authorizes bamlanivimab and etesevimab monoclonal antibody therapy for post-exposure prophylaxis (prevention) for COVID-19" (FDA; see also: Lilly press release).

"Israel's struggles to contain COVID-19 may be a warning for other nations — Widespread boosters don't dent case rate as schools, holidays foster spread" (Science).

Travel

"Coronavirus-sniffing dogs unleashed at Miami airport to detect virus in employees" (WP).

"TSA is doubling fines for those who refuse to wear a mask while flying" (NPR).

"Can 'zero COVID' countries continue to keep the virus at bay once they reopen? Successful strategies used in Asia and the Pacific may not be sustainable in the long run" (Science).

Journal Articles

Clin Infect Dis: Risk of SARS-CoV-2 Transmission among Air Passengers in China (21 September 2021)

> "Background: Modern transportation plays a key role in the spread of SARS-CoV-2 and new variants. However, little is known about the exact transmission risk of the virus on airplanes.
>
> Methods: Using the itinerary and epidemiological data of COVID-19 cases and close contacts on domestic airplanes departing from Wuhan city in China before the lockdown on January 23, 2020, we estimated the upper and lower bounds of overall transmission risk of COVID-19 among travellers.
>
> Results: 175 index cases were identified among 5797 passengers on 177 airplanes. The upper and lower attack rates (ARs) of a seat were 0.60% (34/5622, 95%CI 0.43%-0.84%) and 0.33% (18/5400, 95%CI 0.21%-0.53%), respectively. In the upper- and lower-bound risk

estimates, each index case infected 0.19 (SD 0.45) and 0.10 (SD 0.32) cases respectively. The seats immediately adjacent to the index cases had an AR of 9.2% (95%CI 5.7%-14.4%), with a relative risk 27.8 (95%CI 14.4-53.7) compared to other seats in the upper limit estimation. The middle seat had the highest AR (0.7%, 95%CI 0.4%-1.2%). The upper-bound AR increased from 0.7% (95%CI 0.5%-1.0%) to 1.2% (95%CI 0.4%-3.3%) when the co-travel time increased from 2.0 hours to 3.3 hours.

Conclusions: The ARs among travellers varied by seat distance from the index case and joint travel time, but the variation was not significant between the types of aircraft. The overall risk of SARS-CoV-2 transmission during domestic travel on planes was relatively low. These findings can improve our understanding of COVID-19 spread during travel and inform response efforts in the pandemic."

Clin Infect Dis: Infectious SARS-CoV-2 in Exhaled Aerosols and Efficacy of Masks During Early Mild Infection (14 September 2021)

"Background: SARS-CoV-2 epidemiology implicates airborne transmission; aerosol infectiousness and impacts of masks and variants on aerosol shedding are not well understood.

Methods: We recruited COVID-19 cases to give blood, saliva, mid-turbinate and fomite (phone) swabs, and 30-minute breath samples while vocalizing into a Gesundheit-II, with and without masks at up to two visits two days apart. We quantified and sequenced viral RNA, cultured virus, and assayed sera for anti-spike and anti-receptor binding domain antibodies.

Results: We enrolled 49 seronegative cases (mean days post onset 3.8 ±2.1), May 2020 through April 2021. We detected SARS-CoV-2 RNA in 45% of fine (≤5 µm), 31% of coarse (>5 µm) aerosols, and 65% of fomite samples overall and in all samples from four alpha-variant cases. Masks reduced viral RNA by 48% (95% confidence interval [CI], 3 to 72%) in fine and by 77% (95% CI, 51 to 89%) in coarse aerosols; cloth and surgical masks were not significantly different. The alpha variant was associated with a 43-fold (95% CI, 6.6 to 280-fold) increase in fine aerosol viral RNA, compared with earlier viruses, that remained a significant 18-fold (95% CI, 3.4 to 92-fold) increase adjusting for viral RNA in saliva, swabs, and other potential confounders. Two fine aerosol samples, collected while participants wore masks, were culture-positive.

Conclusion: SARS-CoV-2 is evolving toward more efficient aerosol generation and loose-fitting masks provide significant but only modest source control. Therefore, until vaccination rates are very high, continued layered controls and tight-fitting masks and respirators will be necessary."

Health Messaging and Misinformation

News in Brief

"No, vaccinated people are not 'just as likely' to spread the coronavirus as unvaccinated people. This has become a common refrain among the cautious—and it's wrong" (Atlantic).

"Doctors warn consuming Betadine won't cure COVID, could be deadly" (OKC Fox; see also: JAMA Otolaryngol Head Neck article that could be problematic and misunderstood).

Nebulized hydrogen peroxide is also being pushed on Facebook and other groups (@oneunderscore Twitter thread).

"How ivermectin became the new focus of the anti-vaccine movement" (NPR).

Misinfo and Docs

"Oregon doc loses license for not wearing a mask, spreading misinformation" (Medpage).

Meanwhile… "Ohio Medical Board renews license of Sherri Tenpenny, doctor who claims vaccines make you magnetic" (USA Today).

And… "This doctor spread false information about COVID. She still kept her medical license" (NPR).

In Florida, the new surgeon general opposes mask and vaccine mandates (Miami Herald).

Journal Articles

JAMA Psychiatry: Ways That Mental Health Professionals Can Encourage COVID-19 Vaccination (23 September 2021)

> "This Viewpoint reviews what little is known about mental health and vaccination behavior and addresses 3 areas for intervention by mental health professionals, based on the Increasing Vaccination Model. …
>
> Although mental health is not the first thing that comes to mind when thinking about vaccination, strategic use of mental health professionals' expertise could provide new opportunities to encourage COVID-19 vaccination. A better understanding of how mental health affects receipt of COVID-19 vaccines and better defining how mental health professionals can help, particularly for disproportionately affected communities, is fundamentally important now and could strengthen vaccination efforts."

Commun: Disinformation about COVID-19 Preventions and Treatments: Analysis of USFDA Warning Letters (20 September 2021)

> "COVID-19 poses a challenge beyond the virus itself, in that lockdown has been associated increased use of the internet and social media. Disinformation about prevention and treatment strategies for COVID-19 can have lethal consequences. The United States Food and Drug Administration (USFDA) is currently monitoring the compliance of manufacturing firms as well as medicinal product advertisers to the Federal Food, Drug, and Cosmetic Act, 21 USC § 321(h) regulations. In the event of noncompliance in the form of advertising products without prior USFDA approval for specific indications, doses, or route of administration, warning letters (WLs) are issued. WLs are intended to address the concerns identified by USFDA and encourage the recipient to take corrective steps to avoid similar instances in the future. We analyzed 182 WLs that were issued for noncompliance with drugs/devices related to either treatment, prevention, or testing of COVID-19 infections. The medicinal product website was identified as the major source of disinformation, followed by disseminated information on Facebook, Twitter, and Instagram. Nearly four-fifths were related to drugs, followed by devices and biologicals. Several biologicals, as well as allopathic, herbal, and non-herbal drugs were identified in the WLs. We observed that noncompliance with the USFDA regulations in terms of advertising a variety of products for prevention and treatment of COVID-19 infection was widely prevalent. More efforts are required by the respective national drug regulatory authorities to initiate or continue their monitoring of disinformation that may have lethal consequences."

Other Infectious Diseases and Public Health Issues

News in Brief

The CDC has issued guidance to clinicians who are caring for Afghan refugees (CDC).

By executive order, measles is now on the list of quarantinable communicable diseases (WH.gov).

Speaking of measles, Nigeria reported 10K suspected cases since beginning of the year (ONT).

Officials have reported 2 new cases of Alaskapox, a novel orthopox first reported in Fairbanks in 2015 (ADHSS [pdf]).

Thirty cases of pneumonic plague have been reported in Madagascar (ECDC [pdf]); there was also one (assumed to be unrelated) case reported in Wyoming in a person who had contact with sick pet cats (WDH).

Dozens of people, many of them children, have died in a dengue outbreak in India (Al Jazeera).

Also in India: "Why the world should be more than a bit worried about India's Nipah virus outbreak" (NPR).

"The next health threat is here — action is needed on anti-microbial resistance" (Hill).

"Artemisinin-resistant malaria detected in Uganda" (CIDRAP; see also: NEJM article).

"Two-dose J&J Ebola vaccine gives strong immune response" (CIDRAP; see also: Lancet Infect Dis article 1, article 2, and commentary).

Some good news: "Guinea declares end of Marburg virus disease outbreak" (WHO).

Journal Articles

Philos Trans R Soc Lond B Biol Sci: The future of zoonotic risk prediction (20 September 2021)

> "In the light of the urgency raised by the COVID-19 pandemic, global investment in wildlife virology is likely to increase, and new surveillance programmes will identify hundreds of novel viruses that might someday pose a threat to humans. To support the extensive task of laboratory characterization, scientists may increasingly rely on data-driven rubrics or machine learning models that learn from known zoonoses to identify which animal pathogens could someday pose a threat to global health. We synthesize the findings of an interdisciplinary workshop on zoonotic risk technologies to answer the following questions. What are the prerequisites, in terms of open data, equity and interdisciplinary collaboration, to the development and application of those tools? What effect could the technology have on global health? Who would control that technology, who would have access to it and who would benefit from it? Would it improve pandemic prevention? Could it create new challenges?"
>
> NOTE: This article is part of the theme issue 'Infectious disease macroecology: parasite diversity and dynamics across the globe'.

Emerg Infect Dis: Novel Outbreak-Associated Food Vehicles, United States (15 September 2021)

> "Novel outbreak-associated food vehicles (i.e., foods not implicated in past outbreaks) can emerge as a result of evolving pathogens and changing consumption trends. To identify these foods, we examined data from the Centers for Disease Control and Prevention Foodborne Disease Outbreak Surveillance System and found 14,216 reported outbreaks with information on implicated foods. We compared foods implicated in outbreaks during 2007–2016 with those implicated in outbreaks during 1973–2006. We identified 28 novel food vehicles, of which the most common types were fish, nuts, fruits, and vegetables; one third were imported. Compared with other outbreaks, those associated with novel food

vehicles were more likely to involve illnesses in multiple states and food recalls and were larger in terms of cases, hospitalizations, and deaths. Two thirds of novel foods did not require cooking after purchase. Prevention efforts targeting novel foods cannot rely solely on consumer education but require industry preventive measures."

Nature: Resurgence of Ebola virus in 2021 in Guinea suggests a new paradigm for outbreaks (15 September 2021)

"Seven years after the declaration of the first epidemic of Ebola virus disease in Guinea, the country faced a new outbreak—between 14 February and 19 June 2021—near the epicentre of the previous epidemic. Here we use next-generation sequencing to generate complete or near-complete genomes of *Zaire ebolavirus* from samples obtained from 12 different patients. These genomes form a well-supported phylogenetic cluster with genomes from the previous outbreak, which indicates that the new outbreak was not the result of a new spillover event from an animal reservoir. The 2021 lineage shows considerably lower divergence than would be expected during sustained human-to-human transmission, which suggests a persistent infection with reduced replication or a period of latency. The resurgence of *Zaire ebolavirus* from humans five years after the end of the previous outbreak of Ebola virus disease reinforces the need for long-term medical and social care for patients who survive the disease, to reduce the risk of re-emergence and to prevent further stigmatization."

Nat Commun: Twenty-year trends in antimicrobial resistance from aquaculture and fisheries in Asia (10 September 2021)

"Antimicrobial resistance (AMR) is a growing threat to human and animal health. However, in aquatic animals—the fastest growing food animal sector globally—AMR trends are seldom documented, particularly in Asia, which contributes two-thirds of global food fish production. Here, we present a systematic review and meta-analysis of 749 point prevalence surveys reporting antibiotic-resistant bacteria from aquatic food animals in Asia, extracted from 343 articles published in 2000–2019. We find concerning levels of resistance to medically important antimicrobials in foodborne pathogens. In aquaculture, the percentage of antimicrobial compounds per survey with resistance exceeding 50% (P50) plateaued at 33% [95% confidence interval (CI) 28 to 37%] between 2000 and 2018. In fisheries, P50 decreased from 52% [95% CI 39 to 65%] to 22% [95% CI 14 to 30%]. We map AMR at 10-kilometer resolution, finding resistance hotspots along Asia's major river systems and coastal waters of China and India. Regions benefitting most from future surveillance efforts are eastern China and India. Scaling up surveillance to strengthen epidemiological evidence on AMR and inform aquaculture and fisheries interventions is needed to mitigate the impact of AMR globally."

Statistics

	Total Cases	*Total Deaths*	*Total Vaccine Doses Administered*
Global	230,706,705	4,730,896	6,057,700,104
United States	42,674,611	684,367	386,435,012

JHU CSSE as of 1000 EDT 24 September 2021

Virginia	Total cases (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	849,865	26,864	13,970	19,005	22,747	11,683	10,082	46,668
Hospitalizations	36,132	1,226	623	723	1,396	856	630	2,436
Deaths	12,511	327	214	269	301	219	210	487

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