Updates to COVID-19 Immunity and Epidemiology to Inform Vaccine Policy

Megan Wallace, DrPH, MPH

ACIP Meeting
October 30, 2020
Outline

- Overview of U.S. COVID-19 epidemiology
- COVID-19 post-infection immunity
- COVID-19 reinfection
- Epidemiology of COVID-19 in pregnant women
Overview of U.S. COVID-19 Epidemiology
Trends in Number of COVID-19 Cases in the US
January 22 to October 29, 2020

8,834,393
TOTAL CASES

+81,599 New Cases

CDC | Updated: Oct 29 2020 12:47PM

https://www.cdc.gov/covid-data-tracker/index.html#trends
Trends in COVID-19 Case Rate by Urban/Rural Classification
January 22 to October 20, 2020

*Non-core counties are nonmetropolitan counties that are not in a micropolitan statistical area and may be thought of as the most rural areas.
Number of Specimens Tested and Percent Positive for SARS-CoV-2: Combined Laboratories Reporting to CDC

March 1, 2020 – October 17, 2020

6.3% Week 42

Weekly COVID-19-associated Hospitalization Rates by Age Group

COVID-NET, March 1–October 17, 2020

United States COVID-19 Deaths by County
January 22 to October 29, 2020

227,045 TOTAL DEATHS
+1,660 New Deaths

CDC | Updated: Oct 29 2020 12:47PM

Trends in Number of COVID-19 Deaths in the US
January 22 to October 29, 2020

USA

227,045
TOTAL DEATHS

+1,060 New Deaths

CDC | Updated: Oct 29 2020 12:47PM

https://www.cdc.gov/covid-data-tracker/index.html#trends
Trends in Pneumonia, Influenza and COVID-19 Mortality
Data through the week ending October 17, 2020

COVID-19 Post-infection Immunity
What happens to anti-SARS-CoV-2 antibodies after infection?
Rhesus macaques challenged with SARS-CoV-2 developed binding and neutralizing antibody responses.

Chandrashekar et al, Science. 20 May 2020
Re-challenge of rhesus macaques boosted SARS-CoV-2 antibody responses.

Red lines reflect mean responses. P values reflect two-sided Mann-Whitney tests.
Chandrashekar et al, Science. 20 May 2020
In humans with SARS-CoV-2 infection, serum antibodies decline between acute phase and 2 months post discharge.

Declines seen in:
- Acute phase: 93%
- Convalescent phase: 97%
- Acute phase: 81%
- Convalescent phase: 62%
In healthcare workers with a history of mild SARS-CoV-2 infection, serum antibodies waned 2 months post-infection.

Manish Patel, Wesley Self, Melissa Coughlin, CDC MPIR lab, IVY investigators, manuscript in preparation
Among hospitalized persons with SARS-CoV-2 neutralizing antibody titers demonstrated little to no decrease over 75 days since symptom onset.

Data from 88 samples from 15 individuals collected between 0- and 75-days post-symptoms. Each point represents a measurement of 50% neutralizing titer (NT50). Lines connect measurements from the same individual and a loess smooth function is shown in blue. Iyer et al. Science immunology. October 8, 2020.
Do persons infected with SARS-CoV-2 mount cellular immune responses?
In symptomatic COVID-19 patients, SARS-CoV-2 memory B cells did not wane at the same rate as serum antibodies.

Serum antibodies

Memory B cells

*DAF: Days following onset of symptoms
Recovered COVID-19 patients have SARS-CoV-2 – specific CD4+ T cells and CD8+ T cells.

Grifoni et al. Cell. 181: 1489-1501
Conclusions

▪ Repeat exposure to SARS-CoV-2 may cause boosting of immune response.

▪ Several studies have observed waning of serum antibodies in COVID-19 patients after a few months. The implications for protection are unknown.

▪ Neutralizing antibody titers demonstrated little or no decrease at 75 days post-symptom onset.

▪ SARS-CoV-2 specific cellular B and T cell responses detected in COVID-19 patients. Memory B cells did not wane as fast as serum antibody titers.
COVID-19 Reinfection
COVID-19 Reinfection

- Infection with SARS-CoV-2 following recovery from previous documented SARS-CoV-2 infection.

- Reinfections occur with other human coronaviruses and become more common over time.
  - Likely as a function of both waning immunity and increased exposure.
15 volunteers inoculated with HCoV-229E

10 had subsequent live viral shedding, of which 8 had clinical colds.

6 of 9 previously infected volunteers were re-infected on repeat challenge. All asymptomatic

In this experimental model, reinfection with live viral shedding occurred for most subjects 1 year after initial inoculation. Reinfection occurred in spite of raised antibody titers.

10 adult male volunteers had blood drawn every 3-6 months for > 10 years between 1985–2020.

Antibodies against each of the 4 seasonal coronaviruses were measured.

≥ 1.4 fold change in antibody optical density was considered an infection event.

Reinfection with seasonal coronaviruses – 10 volunteers, 35 years of observation

Reinfection with seasonal coronaviruses – 10 volunteers, 35 years of observation

Interval Between Seasonal Coronavirus Reinfection

White dots: reinfections without an intermediate decrease in antibody levels;
Black vertical lines: median reinfection times
https://doi.org/10.1038/s41591-020-1083-1
Based on the current evidence for SARS-CoV-2, reinfections are likely uncommon within 3 months.
Hong Kong Case of Reinfection

33-year-old with no pre-existing conditions

MAR 23rd – developed productive cough, sore throat, fever, headache

MAR 26th (Day 3) – RT-PCR POS

MAR 29th (Day 6) – hospitalized (per policy), but with improving symptoms.

APR 2nd (Day 10) – IgG NEG

APR 14th (Day 22) – RT-PCR NEG x 2

APR 14th (Day 22) – discharged from hospital

APR 14th (Day 22) – IgG NEG

APR 15th (Day 22) – RT-PCR NEG x 2

APR 14th (Day 22) – discharged from hospital

AUG 15th (Day 145) – RT-PCR POS

AUG 16th (Day 146) – IgG NEG

AUG 20th (Day 151) – IgG POS

AUG – vacation to London and Spain.

AUG 15th (Day 145) – returned to Hong Kong, underwent entry screening; asymptomatic. Hospitalized again (per policy), chest imaging negative; CRP elevated at 8.6 mg/L.

To et al, Clinical Infectious Diseases, 25 August 2020, https://doi.org/10.1093/cid/ciaa1275
# Review of 5 reports of suspected cases of SARS CoV-2 Reinfection

<table>
<thead>
<tr>
<th>Report</th>
<th>Days from 1st course onset</th>
<th>Features of 2nd clinical course</th>
<th>Evidence for reinfection/Contribution to literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>To et al. – Healthy 33M from Hong Kong (Aug 25)</td>
<td>145 days</td>
<td>Asymptomatic</td>
<td><strong>Strongest evidence published case</strong> – demonstrated evidence for acute, substantial infection (high viral load, serological conversion after) as well as substantial genome differences (23 nucleotides, different clades/lineages).</td>
</tr>
<tr>
<td>Van Eslande et al – 52F on inhaled corticosteroids from Belgium (Sep 05)</td>
<td>93 days</td>
<td>Symptomatic w/ similar but milder URI symptoms</td>
<td><strong>Intermediate evidence</strong> - demonstrated RT-PCR positive (Ct value = 33 on reinfection) and genomic difference &gt; expected molecular clock (11 nucleotides).</td>
</tr>
<tr>
<td>Tillet et al. – 25M from Reno, Nevada (Aug 31)</td>
<td>43 days</td>
<td>Atypical pneumonia w/ hypoxemia; 2nd course worse than 1st</td>
<td><strong>Lesser degree of evidence</strong> – demonstrated distinct viral genomes from 2 episodes (7 nucleotides) but did not demonstrate significant viral burden (Ct =35).</td>
</tr>
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<td>Raddad. et al – migrant workers in Qatar (Aug 26)</td>
<td>Median of 65 days</td>
<td>Unknown clinical course, uses location of swab (health facility vs survey) as proxy</td>
<td><strong>First attempt at quantifying reinfection</strong> – searched for repeat positive RT-PCR &gt;45 days among 133K cases. 35 (0.03%) of which had Ct values &lt;30 on the 2nd specimen.</td>
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<td>CDC Reinfection Investigation</td>
<td>Initial 3 months after primary infection</td>
<td>Recurrent COVID-19 like symptoms with positive SARS-CoV-2 RT-PCR, but no alternate etiology identified for their symptoms.</td>
<td>26 cases with specimens available for both illness episodes. All specimens from the second episode of infection had Ct values &gt;30 and no replication-competent virus isolated.</td>
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Conclusions

- Reinfections occur with other human coronaviruses and become more common over time.

- Reinfection for SARS-CoV-2 is possible, but likely uncommon within 3 months.
Epidemiology of COVID-19 in Pregnant Women
Possible groups for Phase 1 vaccination

From prior ACIP Discussions:

Phase 1a:
- HCP

Phase 1b:
- Essential Workers
- High Risk Med Conditions
- Adults ≥ 65 years old

High Risk Medical Conditions
>100M

Essential workers
~80M

Healthcare personnel
~20M

Adults ≥ 65 years old
~53M
75% of the healthcare workforce are women.

Women are a majority among the largest healthcare personnel groups

- **Registered Nurses**: 88%
- **Healthcare support workers**: Nursing, psychiatric, and personal and home health aides, 86%

From 2019 Census Data
Around 330,000 healthcare personnel expected to be pregnant or recently postpartum

https://data.census.gov/cedsci/table?q=registered%20nurse&tid=ACSDT1Y2019_B24010&tp=false&hidePreview=true
Risks of COVID-19 During Pregnancy
Pregnant women with COVID-19 have an increased odds of ICU admission compared with non-pregnant women of reproductive age.

Pregnant women with COVID-19 have increased odds of invasive ventilation compared with non-pregnant women of reproductive age.

Pregnant women with COVID-19 have no increased odds of death compared with non-pregnant women of reproductive age.

Preliminary and unpublished U.S. data can add to the evidence base.
Women of Reproductive Age with COVID-19 by Pregnancy Status — January 22 – October 3, 2020

From CDC COVID-19 Case Surveillance Data
Inclusion Criteria
• Women aged 15-44 years
• Laboratory-confirmed SARS-CoV-2 infection
• 50 states, NYC, DC, & territories
• Reported to CDC January 22–October 3, 2020

*Includes women reported as asymptomatic and those with unknown/missing symptom status
Increased risk for ICU admission, mechanical ventilation and death during pregnancy

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<th>Outcomes of Interest</th>
<th>No. (%)*</th>
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<td>Nonpregnant women (N = 431,410)</td>
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<td>ICU Admission</td>
<td>274 (0.9)</td>
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<td>120 (&lt;0.1)</td>
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<td>1.9 (1.1-3.2)</td>
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<td>Death</td>
<td>45 (0.2)</td>
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* Percentages calculated among total in pregnancy status group; those with missing data on outcomes were counted as not having the outcome
† Adjusted for age, race/ethnicity, and presence of underlying conditions. Nonpregnant women are the referent group.
Extracorporeal membrane oxygenation
Increased risk for ICU admission, mechanical ventilation and death during pregnancy

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Extracorporeal membrane oxygenation
Neonates of mothers with COVID-19 are at increased risk for preterm birth before 37 weeks compared to those without COVID-19.

COVID-19 and Breastfeeding

- Although samples of breast milk have tested positive by RT-PCR, current evidence indicates it is not likely a route of transmission.
- Rate of infection is no greater when a baby is breastfed or remains with the mother.
- Breast milk is the optimal source of nutrition for most infants, even those born to mothers with suspected or confirmed COVID-19.
  - Precautions to avoid spreading the virus to her infant should be taken.

Gro BR. Lancet. Detection of SARS-CoV-2 in human breastmilk
Chambers. JAMA. Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women
Conclusions

- We expect around 330,000 healthcare personnel to be pregnant or recently postpartum at the time a vaccine becomes available.
- Data demonstrate increased risks of severe maternal illness and preterm birth due to COVID-19.
- Although samples of breast milk have tested positive by RT-PCR, there is no evidence that this is an important risk for transmission, and breastfeeding is still recommended.
Summary

▪ **Overall**: As of October 29, over 8.8 million cases of COVID-19 diagnosed and over 227,000 COVID-19-associated deaths reported in the United States.

▪ **Post-infection Immunity**: Data on post-infection immunity are limited but suggests that antibodies wane over time. SARS-CoV-2 cellular immunity has been detected in COVID-19 patients.

▪ **Reinfection**: Data are limited but suggests that reinfection is unlikely within 3 months of infection.

▪ **Pregnancy**: Data demonstrate increased risks of severe maternal illness and preterm birth.
Acknowledgments

- COVID-19 post-infection immunity
  - Natalie Thornburg
  - Manish Patel
  - CDC MPIR lab
  - Wes Self and IVY investigators

- COVID-19 reinfection
  - Deblina Datta
  - James Lee

- Epidemiology of COVID-19 in pregnant women
  - AAP
  - ACOG
  - CDC PILOT
  - CDC Vaccine TF Leadership
  - CDC COVID-19 Response Leadership
  - NIH
For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Waning of passively transferred measles antibodies in infants occurs at approximately same rate, but time to seronegativity dependent upon initial titer.

Leuridan et al, BMJ 340:c1626
**Increased Risk for ICU admission, Mechanical Ventilation and Death for Symptomatic Pregnant Women Compared to Symptomatic Nonpregnant Women of Reproductive Age**

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<td>Symptomatic Nonpregnant women with COVID-19 (N = 386,028)</td>
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<tr>
<td>ICU Admission</td>
<td>245 (1.1)</td>
<td>1,492 (0.4)</td>
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§ Extracorporeal membrane oxygenation
Strengths and Limitations of the Case Surveillance Data

**Strengths**
- Population-level data
- Large sample size with power to study rare outcomes like maternal deaths

**Limitations**
- Large proportion of cases with missing data
- Representativeness of data and generalizability of findings
- Inability to distinguish between hospitalization for COVID-19 from hospitalization for non-COVID-19 reasons
- Incomplete ascertainment of outcomes
- Does not capture data on pregnancy/birth outcomes and trimester of infection
Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET) — Adaptation for COVID-19

Inclusion Criteria

- Women with laboratory confirmed SARS-CoV-2 infection (PCR+) at any point during pregnancy, up to and including the day of delivery

Jurisdictions Reporting Birth and Infant Outcome Data, October 14, 2020 — 5,047 Pregnant Women with SARS-CoV-2 Infection

Pregnant Women with SARS-CoV-2 Infection by Trimester of Infection* — SET-NET, 16 Jurisdictions, March 29–October 14, 2020

*Excludes 1231 pregnant women with missing data on trimester of infection

Preliminary Unpublished Data
Birth and Infant Outcomes Among Pregnant Women with Laboratory-Confirmed SARS-CoV-2 Infection — SET-NET, 16 Jurisdictions, March 29–October 14, 2020

- N=4242 women with SARS-CoV-2 infection in pregnancy as of October 22
  - 9% asymptomatic, 52% symptomatic, 39% missing symptom status

- Of 3912 live births with reported gestational age, 12.9% (n=506) were preterm (<37 weeks)
  - 9.1% (n=357) Late preterm (34 to <37 weeks)
  - 1.3% (n=50) Moderate preterm (32 to <34 weeks)
  - 1.8% (n=69) Very preterm (28 to <32 weeks)
  - 0.8% (n=30) Extremely preterm

Preliminary Unpublished Data
Fever During Pregnancy

- Studies have shown possible associations between maternal fever during early pregnancy and certain birth defects, including:

  - Neural tube defects
  - Orofacial clefts
  - Heart defects