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April/May 2022 Report

Placental Tissue Destruction and Insufficiency From COVID-19 Causes Stillbirth and Neonatal Death From Hypoxic-Ischemic Injury: A Study of 68 Cases With SARS-CoV-2 Placentitis From 12 Countries
https://meridian.allenpress.com/aplm/article/doi/10.5858/arpa.2022-0029-SA/477699/Placental-Tissue-Destruction-and-Insufficiency - February 10, 2022

- The objective of the study was to evaluate the role of the placenta in causing stillbirth and neonatal death following maternal infection with COVID-19 and confirmed placental positivity for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
- This was a case-based retrospective clinicopathologic analysis by a multinational group of 44 perinatal specialists from 12 countries of placental and autopsy pathology findings from 64 stillborns and 4 neonatal deaths having placentas testing positive for SARS-CoV-2 following delivery to mothers with COVID-19
- SARS-CoV-2 placentitis, as defined by the coexistent occurrence of 3 microscopic findings —chronic histiocytic intervillositis, increased fibrin deposition, and trophoblast necrosis —was identified in 65 of 68 placentas (97%) in this study
- Of the 3 findings constituting SARS-CoV-2 placentitis, all 68 placentas had increased fibrin deposition and villous trophoblast necrosis and 66 had chronic histiocytic intervillositis
- Sixty-three placentas had massive perivillous fibrin deposition
- Severe destructive placental disease from SARS-CoV-2 placentitis averaged 77.7% tissue involvement
- Other findings included multiple intervillous thrombi (37%; 25 of 68) and chronic villitis (32%; 22 of 68)
- The majority (19; 63%) of the 30 autopsies revealed no significant fetal abnormalities except for intrauterine hypoxia and asphyxia
- Four autopsied stillborns had SARS-CoV-2 identified in internal organs
- The pathology abnormalities composing SARS-CoV-2 placentitis cause widespread and severe placental destruction resulting in placental malperfusion and insufficiency and in these cases intrauterine and perinatal death likely results directly from placental insufficiency and fetal hypoxic-ischemic injury
- However there was no evidence that SARS-CoV-2 involvement of the fetus had a role in causing these deaths
- Studies performed at the beginning phase of the current pandemic found that although pregnant women in China could develop infection with the newly identified coronavirus, the large majority of infected mothers had either mild or nonexistent symptoms and did not become more ill than did nonpregnant women of the same age, and that, except for a reported increase in premature delivery, there was little or no excess perinatal mortality
- Eventually, COVID-19 was found to be associated with adverse pregnancy outcomes including severe maternal illness as well as neonatal complications
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- Anecdotal experiences by pathologists and clinicians together with some published reports suggested that increasing numbers of pregnant women infected with SARS-CoV-2 were having stillbirths
- This was supported in April 2021 when a cluster of 6 stillborn fetuses and 1 miscarriage occurred in mothers with COVID-19 from Ireland, and then in May 2021 when a population-based cohort study from England demonstrated an increased risk among pregnant women infected with SARS-CoV-2 for having a fetal death
- The association of SARS-CoV-2 infection and stillbirth was confirmed on November 26, 2021, when the US Centers for Disease Control and Prevention reported a population-based study showing that pregnant women with COVID-19 had an increased risk for stillbirth compared with uninfected women, and that the strength of this association was highest during the period of the SARS-CoV-2 B.1.617.2 (delta) variant predominanc
- Data from these 68 cases support previous case reports suggesting that placental insufficiency is responsible for perinatal deaths occurring with SARS-CoV-2 placentitis
- SARS-CoV-2 placentitis can cause extensive placental damage as a result of destructive lesions, and that the damage can be further exacerbated by additional pathology abnormalities
    - Increased fibrin and MPFD, chronic histiocytic intervillositis, and trophoblast necrosis result in sizable destruction of the villous capillary bed accompanied by obstruction of the intervillous space, causing placental malperfusion and insufficiency that are incompatible with intrauterine survival
    - The fetal hypoxia that ensues can lead to a hypoxic-ischemic fetal demise or neonatal death
- Fortunately this sequence of events develops in only a small percentage of pregnant women having COVID-19

Study shows persistent antibodies in infants after COVID-19 vaccination in pregnancy
https://www.sciencedaily.com/releases/2022/02/220207124816.htm - February 7, 2022

- A recent study from Massachusetts General Hospital showed vaccination during pregnancy resulted in more lasting antibody levels in infants, when compared to babies born to unvaccinated COVID-infected mothers
    - The study was published in *The Journal of the American Medical Association (JAMA)*
- Titers were higher in vaccinated mothers and their umbilical cord blood at delivery than in those study participants infected with COVID at 20 to 32 weeks' gestation
- After two months, 98% of the infants (48 of 49) born to vaccinated mothers had detectable levels of the protective Immunoglobulin G (IgG), the most common antibody found in blood
- At six months, the researchers looked at 28 of the infants born to vaccinated mothers and found 57% (16 of 28) still had detectable IgG
    - This was compared with just 8% (1 of 12) born to infected mothers
- Limitations to the study: small study cohort, delays in follow-up with the infected group, reporting of tigers as opposed to clinical outcomes

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Moderna aims for fall release of COVID-19 Omicron vaccine
https://globalnews.ca/news/8768889/moderna-omicron-covid-19-vaccine-fall-release/ - April 19, 2022
- Moderna hopes to offer updated COVID-19 boosters in the fall that combine its original vaccine with protection against the Omicron variant
- Both Moderna and Pfizer are testing bivalent shots - a mix of each company's original vaccine and an Omicron-targeted version

FDA authorizes first COVID-19 breath test
https://www.nbcnews.com/health/health-news/fda-authorizes-first-covid-19-breath-test-rcna24497 - April 14, 2022
https://www.ctvnews.ca/health/first-covid-19-test-using-breath-samples-authorized-by-u-s-fda-1.5862795 - April 14, 2022
https://globalnews.ca/news/8764652/covid-breath-test-explainer/ - April 16, 2022
- InspectIR Covid-19 Breathalyzer test is the first COVID-10 test that uses breath samples
- It needs to be done by a trained operator under the supervision of a licensed health-care provider
- To collect the sample, the person exhales through their mouth into a tube or single-use straw connected to the testing kit
- An algorithmic software analyzes the subject's breath to look for specific chemistry associated with COVID-19 and can provide a result in around 3 min.
    - The InspectIR Covid-19 Breathalyzer utilizes an instrument called gas chromatography gas mass spectrometry to separate and identify chemical mixtures and quickly detect five Volatile Organic Compounds linked with the COVID-19 infection
    - According to the Centre of Public Environmental Oversight, the GC-MS is one of the most accurate tools for analyzing environmental samples
- A green square on the information screen indicates a negative test result and red means the person is COVID-positive
    - If this tests positive, it is recommended that one follows up with a molecular test
- With a sensitivity of 91%, the breath test is more accurate than the rapid antigen test
- The InspectIR Covid-19 Breathalyzer was tested in a study of more than 2400 individuals
- The tests uses equipment about the size of a piece of carry-on luggage and can be used for testing in places such as day-care centres, schools, long-term homes, and just outside an operating room
- The breath test however does not provide information regarding specific variants
    - It is also unknown if it will pick up new variants
- InspectIR has not yet released is proving model at his time
- The company expects to be able to produce approximately 100 instruments per week, which can each be used to evaluate approximately 160 samples per day
- The validity of the InspectIR Covid-19 Breathalyzer was tested in a study of 2409 people, both with and without COVID-19 symptoms

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  - The test was shown to have 91.2% sensitivity (per cent of positive samples accurately recognized by the test) and 99.3% specificity in the research (per cent of negative samples the test correctly identified)
  - In a follow-up clinical research focused on the Omicron variant, it was found that the test had equal sensitivity
- The FDA however has noted that results from InspectIR Covid-19 Breathalyzer should not be used as the sole basis for treatment or patient management decisions

Biden Administration expands availability of COVID antiviral pill Paxlovid
https://www.ctvnews.ca/health/coronavirus/biden-administration-expands-availability-of-covid-antiviral-pill-1.5876305- April 26, 2022
https://theconversation.com/what-is-paxlovid-and-how-will-it-help-the-fight-against-coronavirus-an-infectious-diseases-physician-answers-questions-on-the-covid-19-pill-181998 - April 28, 2022

- The Biden Administration is not taking steps to raise awareness of Paxlovid and making it easier to access
- As part of this initiative, they announced that the drug will now be distributed directly to pharmacies, in addition to existing distribution channels run by states
- Paxlovid has been proven to bring about a 90% reduction in hospitalization and deaths among high risk patients when taken within 5 days of symptoms appearing
  - Paxlovid is made up of 2 protease inhibitors, including one used in treating HIV as a booster medicine
  - These protease inhibitors block enzymes that viruses need to replicate
  - Therefore, the combination in Paxlovid prevents the coronavirus from completing its like cycle
- It is currently authorized for adults and children age 12 or older with a positive COVID-19 test and early symptoms who face the highest risk of severe outcomes - including those with conditions like obesity and heart disease
  - However, the drug is not recommended for patients with severe kidney or liver problems
- The U.S. has ordered enough supply of the pills for 20 million people - it is estimated that this will last for several months
- The administration is also working to expand the number of tets-to-treat sites that provide a one-stop shop for those with COVID-19 to get tested, consult wit ha medical professional, and fill a prescription for Paxlovid on site
  - There are currently 2200 locations nationwide
- Some caveats to Paxlovid:
  - It was studied only in unvaccinated patients so it is unclear how well it works in a vaccinated population - unsure how much additional benefit it gives on top of vaccination
  - Some who could most benefit from Paxlovid are also at highest risk for drug interaction with Paxlovid

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Covid symptoms returning for some after taking Paxlovid
https://www.nbcnews.com/health/health-news/covid-symptoms-may-return-taking-paxlovid-antiviral-pills-rare-cases-rcna25581- April 27, 2022
https://www.aarp.org/health/conditions-treatments/info-2022/paxlovid-covid-rebound.html

- The FDA is evaluating rare reports that patients treated for COVID-19 with Paxlovid experience a second round of the disease shortly after recovering
- Infectious disease experts stress that such cases of apparent viral rebound are not cause for alarm as patient who report a return of symptoms are not experiencing severe symptoms
- So far, there are only anecdotal reports
- Scientific documentation about post-Paxlovid relapse has actually been available since last fall
    - In the placebo-controlled clinical trial, which included 2,246 participants, they noted that several subjects appeared to have a rebound in SARS-CoV-2 RNA levels around Day 10 or Day 14 after beginning treatment
- People who experience such a rebound can relay their experience to Pfizer's portal for reporting Paxlovid-related adverse events
- One theory is that a 5-day course of Paxlovid lows the amount of virus in the body, but does not remove it all and in the meantime, the immune system takes a back seat while the antiviral treatment leads the charge
    - However, when the Paxlovid stops, the virus has a chance to resurrect itself
- Researchers are looking into whether extending the course of the drug might solve the issue
- They are also exploring whether variants play a role in the newly reported rebound cases, since Paxlovid was tested when the delta strain was dominant
- There is currently no evidence that additional treatment with Paxlovid or other anti-SARD-CoV-2 therapies is needed in cases where COVID-19 rebound is suspected

Early pandemic survivors still report symptoms 2 years later
https://www.medicalnewstoday.com/articles/long-covid-half-of-patients-still-report-at-least-1-symptom-2-years-on - May 25, 2022

- Since the first cases of COVID-19 were reported in December 2019, many COVID-19 survivors have reported lingering health issues or symptoms that suddenly appear months and even a year after the initial infection
    - These are mainly in people who experienced COVID-19 before vaccines were developed
- A recent study looked into the current conditions of COVID-19 patients from Wuhan 2 years later
    - The 2.469 participants in the study had all been discharged from Jin Yin-tan Hospital between January 7 and May 29, 2020

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    - At 6 months after acute infection, 68% of participants reported symptoms of long COVID and by 2 years, that number dropped to 55%
    - Long COVID symptoms at 2 years were related to decreased quality of life, lower exercise capacity, abnormal mental health, and increased use of healthcare after discharge
    - The most common long COVID symptoms after 2 years were muscle weakness or fatigue and sleep difficulties - reported by 31% of participants
    - After 2 years, 89% of participants had returned to their original work
- Long-term sequelae of COVID-19 may be dependent on a number of factors: treatments that patients got when they were acutely ill, number and type of vaccinations they received prior to contracting COVID-19, dose of the virus, host response, as well as the variant, so it is difficult to predict the medical future of COVID-19 survivors

https://globalnews.ca/news/8869117/long-covid-vaccination-older-people/ - May 25, 2022

- New U.S research on long COVID-19 provides evidence that it can happen even after breakthrough infections in vaccinated people and that older adults face higher risks for the long-term effects
- In a study of 13 million veterans published in Nature Medicine (aged 60 on average), 1% experienced breakthrough infections and of that, 32% showed signs of long COVID
    - This is compared with 36% of unvaccinated veterans who had been infected and develop long COVID
    - Of the 13 million, 3 million had been vaccinated
    - The study was done before the highly contagious omicron variant appeared and thus, researchers presume that the number of breakthrough infections have likely increased
    - Breakthrough infections and long COVID symptoms were more common among those who have received Johnson & Johnson's single-dose shot compared with 2 doses of either Moderna of Pfizer vaccines
        - Whether any had recovered booster shots is not known
- A separate reports from the Centers for Disease Control and Prevention found that up to a year after an initial coronavirus infection, 1 in 4 adults aged 65 and older had at least one potential long COVID health problem, compared with 1 in 5 younger adults
- Long COVID refers to any of more than 2 dozens symptoms that linger, recur or appear at least one month after a coronavirus infection
- Vaccinated reduced the chances for any long COVID symptoms by about 15%, although it cut the risk in half for lingering respiratory or clotting problems
- An infectious disease expert who runs a centre for long COVID patients at the Cleveland Clinic said that the Nature Medicine study mirror what she sees at her clinic
- A CDC reported that was recently released used medical records for almost 2 million U.S. adults form the start of the pandemic in March 2020 to November 2021
    - The included 353,000 who had COVID-10

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- Patients were tracked for up to a year to determine if they developed any of 26 health conditions that have been attributed to long COVID
- Those who had COVID were much more likely than other adults without COVID to develop at least one of these conditions and risks were greatest for those aged 65 and older
- Breathing problems and muscle aches were among the most common conditions
- Older adults' risks were higher for certain conditions, including strokes, brain fog, kidney failure and mental health problems
- Information on vaccination, sex and race was not included

A study deliberately infected healthy volunteers with the SARS-CoV-2 virus was published in journal Nature Medicine

https://www.ctvnews.ca/health/coronavirus/first-covid-19-human-challenge-study-yields-valuable-insights-1.5843948 - April 1, 2022

- Findings from a research study that deliberately infected healthy volunteers with the SARS-CoV-2 virus was published in journal Nature Medicine
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- The study began in March 2021 and included 36 volunteers between the ages of 18 and 30
    - All participants were screened for any risk factors for severe COVID-19
- The first 10 infected volunteers got the antiviral drug remdesivir to reduce their chances of progressing to severe disease
- Researchers also had monoclonal antibodies at the ready in case anyone took a turn for the worse but ultimately, the remdesivir proved unnecessary, and researchers never had to give anyone antibodies
- The volunteers got a tiny drop of fluid containing the originally detected strain of the virus through a long, thin tube inserted into their nose
- They were medically monitored 24 hours a day and stayed for two weeks in rooms at London's Royal Free Hospital that had special air flow to keep the virus from escaping
- A total of 18 participants became infected, 2 of whom never developed symptoms
- Among those who got sick, their illnesses were mild - stuffy nose, congestion, sneezing and sore throats
- Most of the study participants -83% - lost their sense of smell to some degree
    - 9 could not smell at all
    - This got better for most people, but six months after the study ended, there's one person whose sense of smell isn't back to normal but is improving
    - Researcher have given this participants cognitive tests to check their short-term memory and reaction time and believe these tests will be quite informative
- None of the volunteers develop lung involvement in their infections
- Findings from the study:
    - Just a tiny virus-laden droplet, about the width of a human blood cell, was enough to infect someone with COVID-19

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    - COVID-19 has a very short incubation period -it takes about two days after infection for a person to start shedding virus
    - People shed high amounts of virus before they show symptoms
        - On average, the young, healthy study volunteers shed virus for 6½ days, but some shed virus for 12 days
    - Infected people can shed high levels of virus without any symptoms
    - About 40 hours after the virus was introduced, it could be detected in the back of the throat
    - It took about 58 hours for virus to show up on swabs from the nose, where it eventually grew to much higher levels
    - Lateral flow tests, the rapid at-home kind, work really well for detecting when a person is contagious
        - The study found that these kinds of tests could diagnose infection before 70 per cent to 80 per cent of viable virus had been generated
- Everyone was screened for antibodies to closely related viruses, like the original SARS virus, meaning it wasn't cross-protection that kept them safe; it was something else
- Blood and tissue samples collected for the study will continue to be analyzed for years to com
- Researchers who conducted this challenge study plan to do another one with vaccinated people infected with the Delta variant to study their immune response