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September COVID-19 Report

A study shows 9 in 10 recovered COVID-19 patients experience side-effects – September 29, 2020
https://nationalpost.com/pmn/health-pmn/nine-in-ten-recovered-covid-19-patients-experience-side-effects-study

- A preliminary study in South Korea showed that 9 in 10 coronavirus patients reported experiencing side-effects such as fatigue, psychological after-effects and loss of smell and taste after recovering from the disease
    - The study consisted of an online survey of 965 recovered COVID-19 patients
- Of the 965, 879 (91.1%) responded that they were suffering at least 1 side-effect
- Fatigue was the most common side-effect, follow by difficulty in concentration
- Other side-effects included: psychological or mental side-effects and loss of taste or smell

COVID Long-haulers are experiencing prolonged side effects – June 19, 2020
https://www.ctvnews.ca/health/coronavirus/my-brain-doesn-t-work-like-it-did-covid-19-long-hauler-describes-persistent-symptoms-1.5121902

- Scientists have found that some of the long-term effects of COVID-19 include heart damage as well as neurological issues like brain fog and difficulty thinking
- Others have reported hair loss, fatigue, and even painful lesions now commonly referred to as COVID toes
- Those who were affects by the virus have stated that new symptoms would appear, disappear, and then reappear with no warning
- Doctors are unsure why many of those who have recovered from COVID-19 continue to experience a range of symptoms
- To support each other, these people who are now referred to as the COVID long-haulers have started Facebook groups
- One of the busiest Slack channels is dedicated to people who have had symptoms for more than 30 days
- A recent survey of 640 long-haulers (not peer-reviewed or representative of the entire group) found that symptoms among respondents were not limited to cough, fever, and shortness of breath
    - The more widely reported symptoms included fatigue, body aches, headache, brain fog, gastrointestinal issues, dizziness, chills, sweats, and trouble sleeping
    - Interestingly, the majority of respondents were between ages 30 and 42
- Many COVID long-haulers never tested positive as testing was not yet readily available and when they did get tested, it was many weeks after they started exhibiting symptoms

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    - By this time, the virus may have already cleared the area
- Initially, COVID-19 was considered as respiratory illness but researchers know now that the virus can infect different organs or regions in the body, such as gastrointestinal areas and the neurological space
- The virus has been found in stool samples, in blood, and even in cerebral spinal fluid
- The reliability of nasal swabs are of concerns – there have been many cases of false positive and false negative test results
    - A false negative becomes more likely if the patients is tested a week after their first symptoms emerge
- Rob Kozak, a clinical microbiologist at Sunnybrook Hospital in Toronto who helped isolate the SARS Co-V-2 virus in March speculates several reasons for an abnormal immune response to the virus
    - Possibility that "molecular mimicry" is occurring: where proteins in the virus might resemble proteins in the person and the immune system has trouble distinguishing between them
    - The immune system recognizes proteins on the virus and goes out and attacks it but once the virus is cleared, it sees proteins in the host that look similar to the virus and think it is still fighting the virus
    - Another explanation: Even after the infection clears, viral RNA or genetic materials from the virus remains in the body and the immune system detects it and launches another attack
- The long-lasting symptoms in certain people could be the result of either explanation or a combination of both
    - However, there are so few cases and limited data that it is difficult to know what is really responsible for the various conditions
- People who contracted COVID-19 may also have lingering physical symptoms that are the result of the psychological trauma they have experienced during the crisis
- Doctors and researchers still need to study the viral pathogenesis before they can fully understand the long-term symptoms some are experiencing

Persistent Symptoms in Patients After Acute COVID-19 – July 9, 2020
https://jamanetwork.com/journals/jama/fullarticle/2768351

- 87.4% of patients who had recovered from COVID-19 reported persistence of at least 1 symptom – particularly fatigue and dyspnea
- Limitations of the study include lack of information on symptoms history before acute COVID-19 illness and the lack of details on symptoms severity
- This was a single-center study with a relatively small number of patients and without a control group of patients discharged for other reasons

Neurologic and Radiographic Findings Associated with COVID-19 Infection in Children – July 1, 2020

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https://jamanetwork.com/journals/jamaneurology/fullarticle/2767979

- Of the 27 children with COVID-19 pediatric multisystem inflammatory syndrome, 4 who were previously healthy had new-onset neurological symptoms
    - This included: encephalopathy, headaches, brainstem and cerebellar signs, muscle weakness, and reduced reflexes
- All 4 patients required ICU admission for the treatment of COVID-19 pediatric multisystem inflammatory syndrome
- Splenium signal changes were seen in all 4 patients on magnetic resonance imaging of the brain
- In the 2 patients whose cerebrospinal fluid was tested, samples were acellular, with no evidence of infection on polymerase chain reaction or culture and negative oligoclonal band test results
- In all 3 patients who underwent electroencephalography, a mild excess of slow activity was found
- In all 3 patients who underwent nerve conduction studies and electromyography, mild myopathic and neuropathic changes were seen
- Tests for N-methyl-D-aspartate receptor, myelin oligodendrocyte glycoprotein, and aquaporin-4-au-toantibodies had negative results in all patients
- Neurological improvement was seen in all patients with 2 making a complete recovery by the end of the study
- These neurological symptoms were present in the absence of respiratory symptoms

AstraZeneca gets partial immunity in low-cost EU vaccine deal – September 25, 2020
https://www.theguardian.pe.ca/business/reuters/exclusive-astrazeneca-gets-partial-immunity-in-low-cost-eu-vaccine-deal-501699/

- The European government has announced that they will pay claims above and agreed limit against AstraZeneca over side-effects from its potential COVID-19 vaccine
    - This will happen under different terms to a deal struck with Sanofi
- AstraZeneca has secured the EU's backing in a confidential agreement which reflects a lower price
- The speed at which a COVID-19 vaccine is being pursued increases the risks of unforeseen conditions
- The deal with AstraZeneca was struck in August
    - This deal shifts some of the risks involved in the roll-out of a vaccine to taxpayers
    - Under this deal, AstraZeneca would only pay legal costs up to a certain threshold
- In return for the higher price paid for its vaccine, French drugmaker Sanofi (working with GlaxoSmithKline as a partner) did not get any liability waiver
- AstraZeneca deal – EU countries have agreed to pay 2.5 euros per dose

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    - EU also made a non-refundable down payment of 336 million euros to AstraZeneca to secure 400 million doses
    - The contract with AstraZeneca included a narrow definition of side-effects that could limit the possibility of claiming compensation although the company remains liable for its vaccine
    - This deal was made before AstraZeneca paused late-stage trials of its vaccine candidate this month after a British volunteer developed neurological symptoms
    - EY governments would share compensation costs only if unexpected side-effects emerged after the AstraZeneca vaccine was approved
- Sanofi deal - EU countries will pay 10 euros per dose
    - The EU also made a non-refundable down payment of 324 million euros to Sanofi for 300 million doses
- The U.S. has granted immunity for liability for COVID-19 vaccines that receive regulatory approval
- Russia has stated that they will shoulder some of the legal liability should anything go wrong with the vaccine developed by Moscow's Gamaleya Institute

Trial of Chinese COVID-19 Vaccine in Russia Showed No Side-Effects – September 24, 2020
https://news.cgtn.com/news/2020-09-24/Trial-of-a-Chinese-COVID-19-vaccine-in-Russia-No-side-effects--U2Lmp4nZss/index.html

- People who got a Chinese COVID-19 vaccine candidate in a large-scale clinical trials in Moscow in early September have reported no side effects
- The vaccine, Ad5-nCoV was developed by Chinese company CanSino Biologicas in alliance with the Chinese military's research team
- Russia approved the Phase 3 trials of the vaccine in August and Russian pharmaceutical company Petrovax worked with CanSino to conduct the trial
- So far, they have received more than 3000 applications to get the vaccine
- The study participants who got vaccinated are expected to develop antibodies and cellular immune response to COVID-19
    - They will also be put under direct supervisions for nearly a month
    - They will have 4 interim face-to-face examinations and will undergo a control examination after 6 months
- Preliminary results of the study are expected to come out in November
- Once the vaccine is approved to enter the market after reliable results from the Phase 3 traisl, Petrovax has stated that they will be able to produce more than 4 million doses per month this year and 10 million doses per month in 2021
- CanSino's Ad5-nCoV is one of the most promising COVID-19 candidates currently in the final stage of clinical trials worldwide
- Phase 1 and 2, which involved more than 700 volunteers, were conducted in China this spring

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- Phase 3 trials of the vaccine has also launched in Saudi Arabia, involving 5000 subjects

NIH is Concerned about Serious Side Effect in Coronavirus Vaccine Trial – September 15, 2020
https://www.scientificamerican.com/article/nih-very-concerned-about-serious-side-effect-in-coronavirus-vaccine-trial/

- The FDA is currently weighing whether to follow British regulators in resuming a coronavirus vaccine trial led by AstraZeneca that was halted due to a participant who suffered spinal cord damage
- AstraZeneca has stated that the trial volunteered in question as now recovered from a severe inflammation of the spinal cord and is no longer hospitalized
    - They have not confirmed that the patient was afflicted with transverse myelitis although some neurologists believe this to be the case
- The NIH has yet to get tissue or blood samples from the British patient and its investigation is in the planning stages
- The FDA has not given a timeline on how long they will take before deciding whether to move forward
- They are worried about molecular mimicry – when some small piece of the vaccine is similar to tissue in the brain or spinal cord and results in an immune attack on that tissue in response to a vaccine component
    - If this is the case, another occurrence of transverse myelitis would be likely
- Health leaders have expressed frustration that AstraZeneca hasn't released more information about the health problem that led it to halt its U.K. trial
    - The company has stated that they are unable to provide more information about the health problem as it would violate patient privacy

Pfizer and the COVID vaccine Race – September 3, 2020
https://www.bnnbloomberg.ca/pfizer-s-covid-vaccine-trial-plan-may-beat-rivals-to-early-look-1.1497516

- Pfizer CEO has stated that the company will not submit a COVID-19 vaccine for approval or emergency use authorization if its scientists don't have data from large phase 3 trials showing safty and efficacy
- The FDA Commissioner Stephen Hahn, MD, has told the *Financial Times* that the agency would consider an approval application based on preliminary datad from a phase 3 trial
- The COVID-19 vaccine that Pfizer and BioNTech has developed tofethr is being evaluated in phase 3 trials in the US with approximately 23,000 people enrolled so far
- The companies hope to enroll 30,000 people with 15,000 receiving 2 doses of the mRNA-based vaccine and 15,000 control patients receiving a placebo
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Pfizer states COVID-19 vaccine showed Moderate Side Effects – September 16, 2020
https://www.clinicaltrialsarena.com/news/pfizer-covid-vaccine-tolerability-data/

- Pfizer is developing a COVID-19 vaccine in alliance with BioNTech
- Earlier this month, the companies secured regulatory approval from the Paul-Ehrlich-Institute in Germany to conduct a Phase 2/3 trial of their vaccine, BNT162b2
- Pfizer has stated that Phase 3 clinical trial participants were experiencing mild-to-moderate side effects with its investigational COVID-19 vaccine candidate
- There are more than 12,000 study participants who have received the second dose of the vaccine candidate
- In phase 3 data through Aug 27, trial participants who had received only the first dose experienced mostly fatigue and headache, with other cases of muscle pain, diarrhea, chills and joint pain reported
- Pfizer reported safety data for 5,664 people ages 18-64 and 1,816 people ages 65-85 who received one dose
- In the younger group, 38% reported fatigue afterward, while 35% reported headache and 16% had chills
    - 11% or fewer suffered joint pain, diarrhea or chills
    - The side effect percentages were lower among the older age group
- After their 2nd dose, 36% of trial participants aged 18-64 reported fatigue, 28% reported a headache and 18% reported muscle pain
    - Again, the data were blinded between placebo and the vaccine candidate
- Most side effects after the second dose were mild to moderate but some participants did experience severe or grade 4 side effects that could be life-threatening or disabling
- There were more severe side-effects after the 2nd dose as compared to the first dose
- Recently, the company submitted an amended protocol to the US FDA for the Phase 3 pivotal trial, seeking approval to expand enrolment to about 44,000 participants
    - The initial target was up to 30,000 subjects
    - They proposed that the expansion would enable increase of trial population diversity, recruit subjects aged as young as 16 and people with chronic, stable HIV, hepatitis C or hepatitis B infection
- The company has recruited more than 29,000 volunteers so far in 3 countries
- Pfizer is planning further enrollment in Germany, Turkey, and South Africa
- Amid the research effort, the drug maker has also set out to design a cold chain for distribution so that its vaccine can be properly stored – in extremely cold temperatures – until administered
- The company's distributions centers are equipped with ultra-lower temperature storage capabilities, and vaccine are shipped in thermal containers of between 200 and 1000 vials
    - Each container also contains a GPS-enabled temperature monitoring device

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- Pfzier and BioNTceh plan to deliver 100 million doses in 2020 and 1.3 billion in 2021

Pfizer's COVID Vaccine Trial Plan may Beat Rivals to Early Look – September 22, 2020
https://www.bnnbloomberg.ca/pfizer-s-covid-vaccine-trial-plan-may-beat-rivals-to-early-look-1.1497516

https://www.fiercepharma.com/vaccines/pfizer-sees-mostly-mild-to-moderate-safety-profile-phase-3-covid-vaccine-study

- Pfizer's trial was designed to evaluate its vaccine candidate as fast as possible
- They company has worked with government scientists to develop best practices for testing and based its schedule for interim analyses on the vaccine's strong profile in early human trials and animal tests
- The company has been open about the numbers since before the trial began in late July
- Case totals for interim analysis were based on probabilities of success and were not selected based on timeframes
- Pfizer has said that their study will likely yield results in October
- If Pfizer's vaccine were to receive emergency authorization based on results from October, most patients would have had less than 2 months of follow-up
    - At that point, there will be little known about its duration of protection and its impact on may not be clear
- Pfizer's trial reaches deeper into patients with mildly symptomatic cases
    - For example, it counts even a coronavirus-positive patient with fever alone, as a symptomatic case
    - This may allow Pfizer to tally cases faster
    - It could also mean an early result based mostly on mild cases
    - The rush for results may make it harder to get clear answers about how well the vaccine works

4th Large-Scale COVID-10 Vaccine Trial Begins in the U.S. – September 13, 2020
https://www.nih.gov/news-events/news-releases/fourth-large-scale-covid-19-vaccine-trial-begins-united-states

- A 4th Phase 3 clinical trial evaluating an investigational vaccine for COVID-19 has begun enrolling adult volunteers
- The trial is deigned to evaluate if the investigational Janssen COVID-19 vaccine (JNJ-78436725) can prevent symptomatic COVID-19 after a single dose regimen
- Up to 60,000 volunteers will be enrolled in the trial at up to nearly 125 clinical research sites in the U.S. and internationally
- The Janssen Pharmaceutical Companies of Johnson & Johnson developed the investigational vaccine (knowns as Ad.26.COV2.S) and is leading the clinical trials as regulatory sponsor

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- The National Institute of Allergy and Infectious Diseases, part of the NIG, and the Biomedical Advanced Research and Development Authority, part of the U.S Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response are funding the trial
- The Janssen vaccine candidate is a recombinant vector vaccine that uses a human adenovirus to express the SARD-COV-2 spike protein in cells
    - Adenoviruses are a group of viruses that cause the common cold
    - The Adenovirus vector used in the vaccine candidate has been modified so that it can no longer replicate in humans and cause disease
- They used the same vector in the first dose of its prime-boost vaccine regimen against Ebola virus disease that was recently granted marketing authorization by the European Commission
- Preclinical findings published in *Nature* show that the investigational Janssen COVID-19 vaccine induced neutralizing antibody responses in rhesus macaques and provided complete or near-complete protection against virus infection in the lungs and nose following SARS-CoV-2 challenge
- Positive interim results from a Phase 1/2a clinical study demonstrated that the safety profile and immunogenicity after a single vaccination were supportive of further development
- The Phase 3 trial is being conduced in collaboration with Operation Warp Speed (OWS)- a multi-agency collaboration overseen by HHS and the Department of Defense that aims to accelerate the development, manufacturing and distribution of medical countermeasures for COVID-19
- OWS and CoVPN are also assisting with additional COVID-10 preventative candidate vaccines, including mRNA-1273, an investigational vaccine co-developed by NIAID and the Cambridge, Massachusetts-based biotechnology company Moderna, Inc. and AZD1222, a vaccine candidate being developed by UK based biopharmaceutical company AstraZeneca
- For the study, volunteers must provide informed consent to participant in the trial
- After providing baseline nasopharyngeal and blood sample, participants will be assigned at random to receive either a single dose of the investigational vaccine or a saline placebo
- The trial is blinded – neither investigators nor participants will know who is receiving the investigational vaccine
- Participants will be followed closely for safety and will be asked to provide additional blood samples at specified time points after the injection and over 2 years
- Scientists will analyze the blood samples to detect and quantify immune response to COVID-19
- Specialized assays will be used that can distinguish between immunity as a result of natural infection and vaccine-induced immunity
- The trials is designed primarily to determine if the investigational vaccine can prevent moderate to severe COVID019 after a single dose

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    - It also aims to understand if the vaccine can prevent COVID-19 requiring medical intervention and if the vaccine can prevent milder cases of COVID-19 and asymptomatic SARD-CoV-2 infection

Sanofi and GSK sign COVID-19 Supply Dela with Canada – September 23, 2020
https://www.pharmaceutical-technology.com/news/sanofi-gsk-vaccine-canada/

- Sanofi and GlaxoSmithKline have signed a deal with the Government of Canada to supply up to 72 million doses of adjuvanted COVID-19 vaccine candidate from next year
- The companies launched a Phase ½ clinical trial on September 3, with initial data expected December
- If researchers obtain positive trial data, the companies will apply for regulatory approval in the first half of next year
- Sanofi and GSK are working to step-up manufacture of the antigen and adjuvant to produce up to 1 million doses annually worldwide
- GSK Said it does not expect to make a profit from COVID-29 vaccines during the pandemic
    - The company will invest any0short term income in research on coronavirus
- The Canadian government has further increased its confirmed order commitment to 20 million doses of Moderna's COVID-19 vaccine candidate- mRNA-1273

Evidence Builds that COVID-19 can damage the heart – September 15, 2020

- Cardiologist, Sam Mohiddin is taking on the role of a research subject to find out if those who suffered a mild or moderate bout of COVID-19 as he did, need to worry about their heat health
- Fears that COVID-19 can cause the cardiac inflammation called myocarditis have grown
- How the virus might damage hear muscle is a question that researchers are now probing
- In more than half of virus-induced cases, the heart inflammation resolves without incident
    - However, some cases lead to arrythmia and impaired heart function
- Whether SARS-CoV-2 induces cardiac injury including myocarditis more often than other viruses is still unclear
- Due to the fact that SARS-CoV-2 can trigger an intense immune response throughout the body us a possible explanation as to why survivors may be at heightened risk of cardiac inflammation
- Another theory suggests that COVID-19 patients might be prone to the condition because the virus enters cells by binding with the angiotensin-converting enzyme 2 receptor, which sits on heart muscle cells
    - This hypothesis however, is not tested

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- One reason why it is hard to say whether COVID-19 poses a special risk of myocarditis is uncertainty about its prevalence after other infections
- A cardiologist at University Hospital Frankfurt used MRI to scan the hearts of 100 COVID_19 patients an average of 71 days after they had tested positive
    - Scans showed cardiac abnormalities in 78 people, with 60 appearing to have active inflammation
    - Most also described lingering symptoms such as fatigue and milk shortness of breath
    - This led the team to wonder whether heart inflammation might be responsible
    - Their findings were published in July in *JAMA Cardiology*
- Due to the physical demands of sports, team doctors need to be on guard for myocarditis
    - A paper in *JAMA Cardiology* last week reported a study of 26 athletes at Ohio State University after COVID-19 and 4 had developed myocarditis
- Autopsies of heart tissue after COVID_19 have revealed inflammation in the heart's blood vessels instead of its muscle cells, the site of the inflammation caused by other infections
- Another autopsy study found scattered death of heart cells – however, the author noted the mechanism of injury was unknown
- Mohiddin is also running a trial that aims to recruit 140 people while they are hospitalized with COVID-19 or soon after, 20 with severe myocarditis, and the rest without
    - They will look for abnormal T cell levels in the blood of people with myocarditis
    - This could help explain whether and how the immune system is causing cardiac injury
    - He is also exploring whether immune cell patterns in the blood presage myocarditis later

Exercise could negative affect the heart in those who have been infected by the COVID-19 virus - September 15, 2002
https://www.wired.com/story/if-youve-just-had-covid-exercise-might-not-be-good-for-you/

- Data from initial outbreaks in China, New York City, and Washington state suggested that 2—30% of patients hospitalized with COVID-19 showed signs of cardiac injury
- New evidence suggests that the virus can cause heart damage even in people who have had mild symptoms or none at all, especially if they exercise while they're infected
- Viruses can jolt the body's immune system into attack mode, leading to inflammation

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    - If a person rests while they are ill and during recovery, most of the time the inflammation recedes and the heart muscle heals on its own
    - But strenuous activity while the heart is weakened can cause swelling in the legs, dizziness, shortness of breath, and in serious cases, irregular heartbeat, cardiac arrest, and sudden death
    - The more extreme outcomes are seen most often in competitive athletes
- Doctors at Ohio State University have developed a new protocol that requires any player diagnosed with COVID-19 to receive a clinical examination, blood test, electrocardiogram, and MRI before returning to play
- A larger observational study conducted in Germany earlier this summer followed 100 non-athlete COVID-19 patients and found lingering heart inflammation and other cardiac abnormalities in 78 of them
    - 12 of those people had no symptoms of COVID-19 at all
    - Conclusion of the study: even a mild course of COVID-19 could harm the heart
- Scientists still don't know if the inflammation observed in COVID-19 patients is collateral damage from the body's immune response or the virus directly infecting heart tissue
- Scientists at Gladstone Institute based on San Francisco found that the virus, when added to human cardiac cells in a petri dish, shredded the long muscle fibers that keep hearts beating
    - But more research is needed to better understand if that's representative of what is actually happening inside the bodies of those with COVID-19 infections
- Some doctors suggest that if you have tested positive for COVID-19, you should take a few week off before returning gradually to the level of training you were at before

College Athletes Experienced Heart Damage after COVID-19 Study – September 14, 2020
https://www.the-scientist.com/news-opinion/college-athletes-experienced-heart-damage-after-covid-19-study-67929

- COVID-19 has been linked with myocarditis at a higher frequency than other viruses have been, however this is based on limited studies and anecdotal evidence
- A recent study of 100 patients in Germany found that 60% suffered from myocarditis following their COVID=19 diagnoses independent of pre-existing conditions
- Among 26 athletes, 4 met a least 2 criteria consistent with a diagnosis of myocarditis
    - 8 showed inconclusive evidence of strain
    - Among the 4, all of which were men, 2 experienced symptoms while the other 2 were asymptomatic

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- This study was small and did not include controls, and did not test its participants at the same time interval following their diagnosis– therefore, it is difficult to apply the study's findings more broadly

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