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June/July 2022 Report

COVID booster shot updates

https://www.cbc.ca/news/health/fda-vaccine-omicron-1.6505039 - June 29, 2022

- The FDA's Vaccines and Related Biological Products Advisory Committee voted 19-2 that the next wave of COVID booster shots should include a component that targets the Omicron variant of the coronavirus
- The agency plans to decide by early July on what the design of the boosters should be
- The CDC states that the BA.4 and BA.5 sub-variants of Omicron are estimated to make up a combined 52 per cent of the coronavirus cases in the United States as of June 25
- Moderna has said that they can be ready with a couple hundred million of double-targeted vaccines designed to combat BA.1 by September, however that if they need to design a vaccine targeting the newer sub variants, it would be late October of early November
- Prize and BioNTech have also stated that they have a significant amount of BA.1 vaccine ready and are preparing to produce a large amount of vaccine targeting BA.4 and BA.5
    - Either could be ready by early October
    - They have also said that their BA.1-inclusive vaccines generated a better immune response against Omicron than their current shots, which were designed for the original virus

BioNTech, Pfizer's universal vaccine for coronaviruses

https://www.reuters.com/business/healthcare-pharmaceuticals/biontech-pfizer-starting-testing-universal-coronavirus-vaccine-h2-2022-06-29/ - June 29, 2022
https://www.medicalnewstoday.com/articles/pfizer-and-biontech-to-test-universal-covid-19-vaccine-candidate - July 7, 2022

- While 2 doses of an mRNA COVID-19 vaccine were 85% effective in preventing hospital admission for infection with the Alpha and Delta variants of SARS-CoV-2, they were only 65% effective in doing so following an Omicron infection
- To try and overcome waning COVID-19 vaccine efficacy, researchers at Pfizer and BioNTech are developing a universal COVID-19 vaccine The 2 companies announced a new clinical trial for universal COVID-19 vaccine candidates in the second half of 2022
- Their experimental work on shots include T-cell-enhancing shots designed to primarily protect against severe disease and pan-coronavirus shots that protect against the broader family of viruses and its mutations
- The hope is that a universal coronavirus vaccine has the potential to better protect against future variants of SARS-CoV-2 as well as other coronaviruses
- However, just how universal such a vaccine would be is debatable
- BioNTech has also announced that they are independently working on precision antibiotics that kill superbugs that have grown resistant to currently available anti-infectives

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- They will be leaning on the technology of PhagoMed, which they acquired backed in October last year

Moderna COVID-19 Vaccine

- Moderna's COVID-19 vaccine may pose a higher risk of heart inflammation in some age groups than Pfizer-BioNTech's shot
- The CDC however has said that the findings on myocarditis and pericarditis, types of heart inflammation linked to both the mRNA shots, were not consistent across all of the U.S. vaccine safety monitoring systems
- Based on data from the Vaccine Safety Datalink (VSD) system, the incidence of heart inflammation was 97.3 cases per million doses for males aged 18-39 following a second dose of Moderna's shot, versus 81.7 cases per million Pfizer vaccine doses
- Available information suggests that most people with myocarditis after mRNA COVID-19 vaccination recover over time

COVID-19 Vaccine for Children Aged 6 Months to 4 Years

https://www.cbc.ca/news/health/fda-authorizes-covid-19-vaccines-kids-under-five-us-1.6492142

- On June 17th, the FDA accepted its advisory panel's unanimous recommendation for the paediatric shorts from Moderna and Pfizer-BioNTech
- Kids between 6 months and 4-years and a half in the U.S will now be eligible for their first COVID-19 vaccinations
- Paediatric deaths from COVID-19 have been higher than what is generally seen from the flue each year
- Studies from Moderna and Pfizer show that possible vaccine side effects including fever and fatigue were most minor
- Pfizer's vaccine for kids younger than 5 will be 1/5th of the adult dose
    - 3 shots are needed - the first 2 given 3 weeks apart and the last at least 2 months later
- Moderna's is 2 shorts, each a quarter of its adult dose, given about 4 weeks apart for kids under 6
- On July 28th, Health Canada also approved Moderna's paediatric shot

Emergency use authorization of Novavax

https://www.ctvnews.ca/health/coronavirus/u-s-fda-gives-emergency-use-authorization-to-novavax-s-covid-19-vaccine-1.5986356 - July 13, 2022
https://www.yalemedicine.org/news/novavax-covid-vaccine - July 20, 2022

- The U.S. FDA has authorized Novavax's COVID-19 vaccine for emergency use in adults
- This is the 4th coronavirus vaccines available in the U.S.
- The vaccine will be available as a 2-dose primary series for people 18 and older
- Novavax's vaccine is a protein-based vaccine which uses harmless protein fragments of the virus to teach the immune system how to spot the virus and fight it off

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    - It was created out of a genetic sequence of the first strain of the coronavirus
- Last-stage trials found that the efficacy of the vaccine against mild, moderate and severe disease is 90.4%
- There is no sufficient evidence to evaluate the impact of the vaccine on transmission of the virus
- The company announced that its vaccine shows broad immune response to currently circulating variants including Omicron sub variants BA.4/5
- The Novavax vaccine is being used in 40 other countries, including Canada
- In the clinical trial, the most commonly reported side effects were pain/tenderness, redness and swelling at the injection site, fatigue, muscle pain, headache, joint pain, nausea/vomiting, and fever
- Myocarditis occurred in a handful of Novavax clinical trial participants, all of whom were men, but there is insufficient evidence to establish a causal relationship between the vaccine and the contain so the FDA decided the benefits of the vaccine outweigh the risks
- Similar reports have risen around the mRNA vaccines and the FDA has issued a warning label on both the Pfizer and Moderna vaccines regarding myocarditis and pericarditis in adolescents and young adults

COVID-19 Vaccines and Pregnancy
https://hms.harvard.edu/news/covid-19-vaccines-pregnancy
- Pregnant individuals and newborns may face elevated risks of developing more severe cases of COVID-19 following SARS-CoV-2 infection, but research suggests that COVID-19 vaccination during pregnancy can help protect both the person giving birth and the child
- A new study led by investigators at Harvard Medical School, Massachusetts General Hospital, and Brigham and Women's Hospital and published June 28 in Nature Communications examined how different COVID-19 vaccines and the timing of vaccination during pregnancy may impact the extent of this protection
- The team also evaluated the transfer of protective SARS-CoV-2 antibodies via the placenta from the pregnant person to the fetus by analyzing blood from the umbilical cord and the person giving birth in 175 pairs
- The research revealed that the Johnson & Johnson vaccine induced lower-functioning SARS-CoV-2-specific antibodies than the Moderna and Pfizer-BioNTech vaccines
- The Moderna vaccine provided subtle advantages in antibody levels and function compared with the Pfizer-BioNTech vaccine
- Additionally, the mRNA-based vaccines induced higher levels and functions of antibodies against SARS-CoV-2 variants of concern, including alpha, beta, delta, and gamma
- All three vaccines also induced antibodies that demonstrated neutralizing activity against omicron
- Pregnant people vaccinated during the first and third trimesters had enhanced immune responses compared with second trimester vaccination
- SARS-CoV-2-specific antibodies were most efficiently transferred to the fetus through the placenta following vaccination during the first and second trimesters

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- Additional studies are needed to understand how to optimize maternal and neonatal immunity induced by vaccines in general during pregnancyInvestigators stressed the need for more research on this topic.

COVID-19 During Pregnancy: Increased Risk of Preterm Delivery and Infancy Neurodevelopmental Issues - June 27, 2022
https://www.forbes.com/sites/williamhaseltine/2022/06/27/covid-19-during-pregnancy-increased-risk-of-preterm-delivery-and-infant-neurodevelopmental-issues/?sh=60a015d5358b

- Pregnant women are at a high risk contracting disease, including COVID-19
- Researchers at the University College London suggest that mothers who catch COVID-19 during their first trimester are more likely to have an early miscarriage
- Another study led by a group at Harvard Medical School found that infants born to mothers who had COVID-19 during pregnancy are more likely to receive a neurodevelopmental diagnosis in the first 12 months following delivery
- Maternal vaccination has shown to help cut down many of the risks associated with SARS-CoV-2 infection during pregnancy
- Between May and December of 2020, Balachandren et al. recruited 3500 women via social media to help participate in the COVID-19 Contraception and Pregnancy Study
    - All women had conceived during the pandemic and were within the first 12 weeks of pregnancy
    - The team of researchers asked the women to report on any current or prior pregnancy complications and their medical history
    - The participants were also asked every trimester whether they or anyone in their household had been diagnosed with SARS-CoV-2 infection
    - Depending on their answer, the women were filtered into one of three groups: those who self-reported a SARS-CoV-2 infection within the first trimester (“presumed infected”), those who had symptoms or were exposed to household contacts with symptoms but had no official diagnosis (“uncertain”), and those who had neither symptoms nor household contacts with symptoms (“presumed uninfected”)
    - After accounting for age, body mass index (BMI), number of previous miscarriages, ethnicity, and smoking status, Baachandren and his colleagues discovered that the risk of early miscarriage was around 1.7 times higher in the “presumed infected” group — a rate of 14%, compared to 8% in the “presumed uninfected” group and 5% in the “uncertain” group
- How SARS-CoV-2 infection during the first trimester contributes to early miscarriage is not entirely clear
    - Researchers propose that cytokines may be involved as coronaviruses have also been shown to induce a pro-inflammatory cytokine storm in the body
- The researchers stress that they have not established a strict causal relationship between Covid-19 and early miscarriage, but rather a correlation between the two
    - Further research will be needed to prove that SARS-CoV-2 is directly at fault

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Pregnant women and booster dose

https://www.nihr.ac.uk/news/covid-19-vaccine-study-calls-on-pregnant-women-to-help-build-upon-booster-dose-guidance/30869 - July 19, 2022

- An on-going national COVID-19 vaccine study in the UK, Preg-CoV study, is urging more pregnant women across the UK to help researchers discover the most effective use of booster vaccines during pregnancy
- They currently have around 300 pregnant women taking part
- The study is led by researchers at St. George's University of London
- It is comparing vaccine currently being used for the UK vaccination programs (Pfizer/ BioNTech and Moderna) as well as new vaccines as they are approved for use, such as Novavax
- The study will also provide vital clinical trial data on the immune response to booster vaccination with different doses of vaccines as well as the immune response to different intervals between doses given in pregnancy
- COVID-19 vaccines are safe and effective for pregnant women, and there is a clinical consensus that it is the best way to protect pregnant women and their babies from COVID-19

PhagoMed Biopharma GmbH

https://www.mobihealthnews.com/news/emea/biontech-acquires-eit-health-startup-fight-against-bacterial-infections
https://amr-conference.com/news/biontech-acquires-vienna-based-start-up-phagomed/

- A Vienna-based biotech company that was developing novel synthetic lysin technology for precision antimicrobial treatments
    - Lysin are enzymes produced by bacteriophages that break down bacterial cell walls and kill bacteria
    - The advantages of lysins is that they are very precise and therefore only kill specific groups of bacteria
- PhagoMed's Lysin builder platform allows for the development of synthetic lysins that create targeted antibacterials
    - The Lysin Builder uses prediction algorithms to design novel precision antibiotics that target and kill select groups of bacteria
- As a result of antimicrobial resistance, some infections are much harder to treat or respond to treatment
    - Therefore, science and innovation are needed to find new and alternative solutions to antibiotics that are losing effectiveness
- PhagoMed joined the European Institute for Innovation and Technology's Gold Track programme in June 2020 and were supported over a period of 12 months
- The company's lead lysin candidate is PM-477, which targets Gardnerella app for the treatment of recurrent bacteria vaginosis
- On November 10th, 2021, PhagoMed was acquired by BioNTech
    - Terms of the transaction were not disclosed

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- This acquisition can be interpreted as their entry into the microbiome field

Phage Therapy Case Studies show success rate of more than half
https://www.genengnews.com/topics/translational-medicine/infectious-diseases/phage-therapy-case-studies-show-success-rate-of-more-than-half/ - June 10, 2022

- A research team led by scientists from the University of Pittsburgh and the University of California San Diego reported 20 new case studies on the use of phage therapy, showing success in more than half of the patients
- It is reportedly the largest ever set of published case studies for therapy using bacteriophages
- Each patient in the study was seeking care for an infection of one or more strains of Mycobacterium, a group of bacteria that can cause deadly, treatment-resistant infections in those with compromised immune systems or with cystic fibrosis
- While some show great outcomes, others are complicated, however, the 20 case studies show compelling evidence that the phages are contributing to favourable outcomes in patients who have no other alternatives
- Bacteriophage therapy represents a potentially novel approach to treating non-tuberculous Mycobacterium infections
- Mycobacterium isolates from 200 culture-positive patients with symptomatic disease were screened for phage susceptibilities and one or more lytic phages were identified for 55 isolates
- Phages were administered intravenously, by aerosolization, or both to 20 patients on a compassionate use basis and patients were monitored for adverse reactions, clinical and microbiologic responses, the emergence of phage resistance, and phage neutralization in serum, sputum, or bronchoalveolar lavage fluid
- No adverse reactions attributed to therapy were seen in any patient regardless of the pathogen phages administered, or the route of delivery
- Favourable clinical or microbiological responses were observed in 11 patients
- Neutralizing antibodies were identified in serum after initiation of phage delivery intravenously in eight patients, potentially contributing to lack of treatment response in four cases but were not consistently associated with unfavourable responses in others
- Phage treatment of *Mycobacterium* infections is challenging due to the limited repertoire of therapeutically useful phages, but favourable clinical outcomes in patients lacking any other treatment options support continued development of adjunctive phage therapy for some mycobacterial infections
- In 11 cases, researchers were unable to find more than 1 kind of phage that could kill the patient's infection
    - While standard practice is to inject a cocktail of different viruses, they did not observe failure of treatment from resistance even when using only a single phage
- Some patients' immune systems attacked the viruses, but only in a few cases did their immune systems render the virus ineffective

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- In some instances, the treatment was still successful despite such an immune reaction

Personalized bacteriophage therapy to treat pandrug-resistant spinal *Pseudomonas aeruginosa* infection

https://www.nature.com/articles/s41467-022-31837-9 - July 22, 2022

- Bone and joint infections (BJI) are one of the most difficult-to-treat bacterial infection, especially in the era of antimicrobial resistance
- Lytic bacteriophages are considered to have a high therapeutic potential for the treatment of severe bacterial infections and especially BJI, as they also target biofilms
- Lytic bacteriophages can rapidly and selectively target and kill bacteria whilst producing new phage particles in an exponential and self-sustained reaction
- A 74-year-old man with melanoma treated with anti-PD1 (pembrolizumab) experienced a catheter-related bacteremia due to multidrug-resistant P. aeruginosa
- A unique academic collaboration between universities and hospitals located in three different European countries (Switzerland, Belgium, and France) allowed researchers to identify three different lytic phages active on the patient initial P. aeruginosa isolate, to produce them separately, and to administer them as a pre-assembled personalized three-phage cocktail to the patient, in the shortest possible time
- The phage cocktail was locally administered (same volume and phage concentration) before insertion of the intersomatic cages at L2-L3 and L3-L4 level
- As the cultures revealed persistence of the *P. aeruginosa*, phages were also added intravenously over 3-h infusions (30 mL, phage titers 106 pfu/mL) every day for 21 days
- Under this treatment, the patient experienced abdominal pain related to gall stone migration and relapsing *C. difficile* infection
- No adverse event potentially related to phage therapy was noticed
- The outcome was favorable during the follow-up (21 months), without implant loosening nor clinical signs of infection (Fig. 2C, D), and the patient was walking without pain