COVID-19 Vaccines

Developed by Dr. Gauri Shah and Dr. Joan Robinson for PedsCases.com.
December 28, 2021

Introduction:

Hello everyone, my name is Dr. Gauri Shah, and today I will be presenting a podcast on COVID 19 vaccines in children. I am a pediatrician, and I trained in pediatrics in India and then did a Pediatric Infectious Diseases fellowship at the Stollery Hospital at the University of Alberta in Edmonton, Canada. I am very fortunate to be joined today by Dr. Joan Robinson, a pediatric infectious diseases specialist at the University of Alberta, Stollery Children's Hospital, Edmonton, Alberta. I will be doing this as an interview with an expert in this field.

Before we bring her in, let's learn some of the basics related to vaccines

In 2005, Dr. Katalin Karikó and colleagues (1) replaced uridine in the RNA with pseudouridine to make the mRNA model. They discovered that such a model effectively stimulated the innate immune response with lesser cytokines in mammalian cells. Little did they realize that this breakthrough invention would eventually be used to make one of the fastest developed and highly effective vaccines (mRNA vaccines) that would save countless lives.
Yes, we are talking about all vaccines against covid 19, focusing on pediatric vaccines.

Here are some objectives:

After listening to this podcast, the learner should be able to:

1) Learn the different types of vaccines available in Canada for covid 19
2) Understand which vaccines are appropriate in Children and why
3) Solve some of the questions related to side effects, effectiveness and concerns around them.
4) Deep dive into the present and future of the current pandemic with our expert.

As always, let's start with a case:

I suppose you remember seven-year-old Lily from my previous podcast. Well, she recovered fully from an acute COVID-19 infection and went home. It's been a year, and

now she learnt that they are vaccinating all children aged 5 to 11 years. Her older brother, who is 15, already got his shot and is doing great.

After having been through so much, she is excited that there's a vaccine but has lots of questions about them.

Vaccine Development

On December 9, 2020, the Pfizer BioNTech COVID-19 vaccine (Comirnaty®) was authorized by Health Canada (2) for use in adults above 16 years of age. This was then followed by approval for adolescents 12 to 15 years of age on May 5, 2021. Another type of RNA vaccine (Moderna or Spikevax®) was approved for children 12 years and above on August 27, 2021. After a long gap and extensive review, Health Canada approved the Pfizer BioNTech vaccine for children 5 to 11 years of age on November 19, 2021(3).

Many people have expressed concern about the pace of COVID-19 vaccine development. To help address these concerns, let's discuss the phases of vaccine development.

Vaccine development goes through a pre-clinical evaluation and three distinct clinical stages(4):

Phase 1 trials – These are designed to test vaccine safety profiles mainly. Dose-ranging studies are also included. Many vaccines never get past Phase 1.

Phase 2 trials – The safety and immunogenicity are studied in a larger population.

Phase 3 trials – These trials are designed to study the vaccine's efficacy to achieve a specific endpoint. The initial COVID vaccine trials used prevention of hospitalization due to COVID as their endpoint. More safety data is also obtained as Phase 3 vaccine trials enroll thousands of patients.

For unprecedented circumstances like the COVID-19 pandemic, the three phases were carried out very quickly due to the situation's urgency. The phase 3 trials were ready to start when the phase 2 trials were completed. Multiple countries were involved in phase 3 trials to allow for rapid enrollment. However, the sample sizes were not reduced, and the rigor of the scientific process was not compromised. Therefore, we have almost as much data as we would typically have when a vaccine is licensed. The only thing that is missing is long-term follow-up data. However, a vaccine is almost unheard of to cause a severe adverse event that becomes apparent more than two months after the vaccine is given.

Vaccine Monitoring and Safety:

Talking more about the long term effects of the vaccines, let me tell you a bit about vaccine monitoring and safety(5) :

All vaccines are continuously monitored for adverse effects by the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) surveillance program. This is run by Health Canada (HC) and the Public Health Agency of Canada (PHAC)2) There is a direct reporting system in place mandated by Health Canada as soon as any vaccine is marketed. This is called post-marketing surveillance. Here, the person giving the vaccine, be it a public health nurse, physician, or pharmacist, must report every vaccine-related adverse event (AEFI) that they become aware of.

In 1991, PHAC(5), in collaboration with the Canadian Pediatric Society (CPS), started an active surveillance program called IMPACT which stands for Immunization Monitoring Program ACTive. A trained nurse monitors every hospital admission at 13 children's hospitals across the country to look for the possibility that vaccine-related side effects led to that admission. For example, they look for children admitted for unexplained thrombocytopenia or neurological symptoms like seizures, acute encephalitis, or acute flaccid paralysis (including Guillain-Barré syndrome and aseptic meningitis). They then determine when that child last received a vaccine. Sometimes they identify a potential link between a vaccine and a hospitalization that was not appreciated by the medical team looking after the patient.

Types of Vaccines:

Before we move on to the questions, I would like to quickly tell you about five different technologies used in making vaccines. All are being used to develop COVID vaccines, but the last two are the ones that have been the most successful. (4)

The first is a Live attenuated vaccine – produced by developing genetically weakened wild-type of the virus. Examples are BCG & MMR. These are contraindicated in pregnancy, and immuno- compromised states. Live vaccines are being studied for COVID but are not yet licensed in Canada.

Second are Inactivated vaccines, produced by chemically inactivating the virus after growing it in cell cultures. Examples are Hepatitis B vaccine and the DPT vaccine. The Sinovac vaccine for COVID-19 made in China is an example. It is used in children in some countries but is not yet licensed for children or adults in Canada.

Third, protein subunit vaccines use, for example, the spike protein from SARS-CoV-2. Medicago has developed such a vaccine. It is yet to be licensed anywhere but may eventually be manufactured in Canada.

Fourth are viral Vector vaccines. These vaccines use a harmless virus to produce a protein antigen, leading to an immune response. Examples of this type of vaccine are the Astra Zeneca and J&J vaccines that have been licensed in Canada for adults only.

Finally, the recombinant DNA and mRNA vaccines, with the best example being the previously mentioned Pfizer and Moderna vaccines. These vaccines contain the mRNA of the spike protein of the SARS-COV 2 virus. The mRNA is then transcribed to produce spike proteins using the hosts own cells. This results in the patient's macrophages initiating the innate immune response.

Interview with Dr. Robinson:

After this brief background on vaccines, let me introduce the expert I will be interviewing today. Her name is Dr. Joan Robinson. She is a Pediatric infectious diseases specialist at the Stollery Children s hospital at the University of Alberta. She is currently the divisional director for pediatric infectious diseases at the University of Alberta and editor-in-chief for the Canadian Paediatric Society Journal *Paediatrics & Child Health*. She is an undifferentiated researcher interested in a wide variety of bacterial and viral diseases and in the optimal use of antimicrobials in both inpatients and outpatients. She has cared for patients with COVID 19 and MIS-C and researched both.

Hello Dr. Robinson, let us jump to the first question as the listeners are eager to hear your thoughts and recommendations.

Interview Questions:

1. What vaccines are approved in Canada for covid 19, and which ones are still under trial?
2. Why is it that only Pfizer BioNTech is approved in children 5-12 whereas, children above 12 can opt for either Pfizer or Moderna?
3. Why is a smaller dose (1/3 of adult) recommended in children between 5-12 years of age? Is it adequate?
4. Do people who had covid -19 infection /MIS-C need to be vaccinated, and when is the appropriate time to get vaccinated after recovery?
5. Speaking of adverse events, how much are we concerned about myocarditis in children like that reported in adolescents and young adults?
6. How will vaccinating the pediatric population make a difference, given that children don't get as sick to them and the overall pandemic?
7. What do we know about best dose interval? Also, can one take another type of vaccine, if available, for their second dose?
8. How much interval should be ideally kept between the covid 19 vaccine and other routine vaccines in children? Can they be given at the same time?
9. With the ongoing emergence of different variants of concern like the delta variant, how much do we know the vaccines provide protection?

10. How does the emergence of new variants like the Omicron affect the urgency of vaccination?
11. What are some of the tips you can give to Pediatricians or other health care providers dealing with Parents who have vaccine hesitancy?
12. Last question, what do you think we have learnt from these previous two years and what do you think will be the future of this virus?

Thank you so much, Dr. Robinson, for such an interesting interview. We learnt so much from this.

Take-Home Points:

Before we leave, let's conclude with some take-home points:

1) It is crucial to vaccinate everyone eligible for vaccination to prevent severe disease and life-threatening complications
2) The pediatric vaccine is safe and most effective if given at an interval of 8 weeks for a best immunological response even against variants of concern
3) Vaccine hesitancy is real, and good health advocacy backed up with solid data is the need of the time
4) Finally, although we cannot see the future, what we do know that equity of vaccine availability and information is the only way to move forward to beat this continuously mutating virus.

Thanks for listening! See you soon.

References:

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