
WICKED RISK:

HOW TO HAVE A CONVERSATION ADDRESSING VACCINE HESITANCY IN THE EMERGENCY DEPARTMENT

VACCINATIONS AND THE EMERGENCY DEPARTMENT

The ED provides a unique opportunity to address vaccine hesitancy as we routinely ask about a pediatric patient's vaccination status as part of our history. Parents or other caregivers who are vaccine hesitant or refusers are often guarded and defensive when asked this seemingly simple question. Emergency providers serve as an interface between the hospital and community settings and thus our conversations may either diffuse or entrench pre-existing beliefs about vaccinations depending on how we address the subject.

In 2018 the RCPSC included the following in its list of competencies for emergency medicine:

- “Principles of antimicrobial prophylaxis, antibiotic stewardship, and infection prevention and control”
 - Medical Expert 1.3.4 - July 2018
- “Communicate using a patient-centred approach that encourages patient trust and autonomy and is characterized by empathy, respect and compassion”
- “Recognize when the perspectives, values, or biases of patients, physicians or other health care professionals may have an impact on the quality of care, and modify their approach to the patient accordingly”
- “Manage disagreements and emotionally charged conversations”
 - Communicator 1.1, 1.3, & 1.5 – July 2018

Despite our obvious role as potential influencers for vaccination, little time, if any, in emergency medicine residency programs is dedicated to specifically address communicating with vaccine hesitant individuals. As emergency physicians and public health advocates, we need to be prepared to at least initiate what may be a difficult, frustrating, or awkward conversation with a vaccine hesitant family member for the good of the individual patient and for our communities.

Currently, there is no CAEP position statement on vaccinations or how to address this question. ACEP has a brief policy statement entitled “Immunization of Adults and Children in the Emergency Department” suggesting that we should consider vaccinating undervaccinated patients in the ED if there is no readily available resource for this, yet it fails to provide any guidelines as to how to discuss the subject.

The objective of this paper is to review the underlying causes of vaccine hesitancy and how we may best address this as emergency physicians.

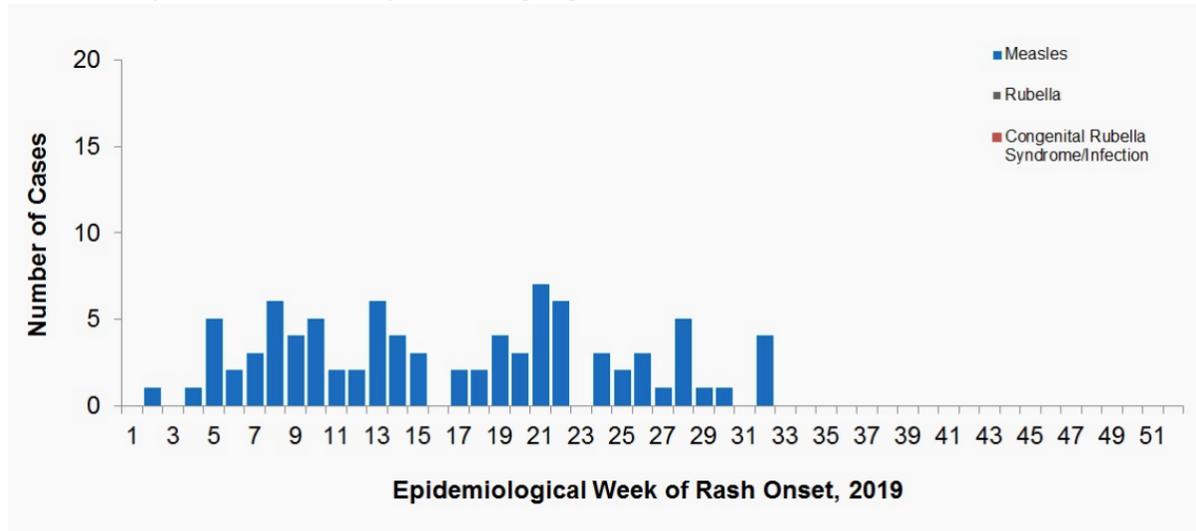
FAKE NEWS! A FEW CANADIAN FACTS ON VACCINATION AND MEASLES

Canada currently has no jurisdictions mandating vaccinations. Proof of vaccination is required in Ontario and New Brunswick to attend school however exceptions may be made for both medical and ideological reasons.³

As of September 2018, British Columbia has required mandatory reporting of immunizations to public health units for all students enrolled in public and private schools. MMR vaccinations in schools in the past year have resulted in 87.6% of children with the full 2 doses, and at least 95% of student have at least one of two doses with a target of a 95% immunization rate.⁴

- Endemic measles was eliminated in Canada in 1998
- Measles is highly contagious with 1 infected individual causing 12-18 infections in susceptible individuals
 - Influenza infection will only transmit 1-2 new infections in susceptible individuals
- Measles is a leading cause of vaccine-preventable deaths in children worldwide
 - In 2017 the global mortality of measles was reduced 80%, from 545 000 deaths in 2000 to 110 000 deaths
 - An estimated 21.1 million deaths were prevented by vaccinations in this time period
- Before the introduction of the measles vaccine in 1963-1964 there were 300 – 400 000 cases of measles annually in Canada
- ≥ 1 complication occurs in $\leq 30\%$ of individuals infected with measles
 - Diarrhea most common ($\leq 8\%$)
 - AOM especially in younger children
 - Immunosuppression and risk of co-infections with
 - Respiratory and gastrointestinal viruses
 - Secondary bacterial infections (Staph, Strep, Hib)
 - Pneumonia occurs in 6% and is the most common cause of measles-associated deaths
 - Encephalitis and Acute disseminating encephalomyelitis (ADEM) each occur in 1 in 1000 cases
 - Mortality for ADEM is 10-20%
 - Subacute Sclerosing Panencephalitis (SSPE) can occur 7-10 years after initial measles infection especially in children infected before the age of 2 years old and is fatal
- Vaccination confers $\sim 97\%$ of individuals immunity to measles

Figure 1: Number of cases of measles (n=88), rubella (n=0), and congenital rubella syndrome (n=0) ³ by week of rash onset, as reported to the Canadian Measles/Rubella Surveillance System (CMRSS) and Measles and Rubella Surveillance System (MARS), for the period ending August 17, 2019.



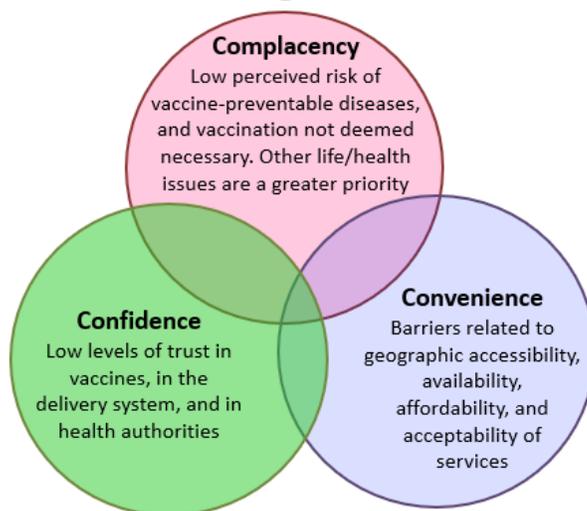
❖ <https://www.canada.ca/en/public-health/services/publications/diseases-conditions/measles-rubella-surveillance/2019/week-33.html>

WHAT IS VACCINE HESITANCY?

“Vaccine hesitancy refers to a delay in acceptance or refusal of vaccination despite availability of vaccination services. Vaccine hesitancy is complex and context specific, carrying across time, place and vaccines. It is influenced by factors such as complacency, convenience and confidence.”

- Noni MacDonald, the SAGE Working Group on Vaccine Hesitancy 2015

Factors contributing to vaccine hesitancy



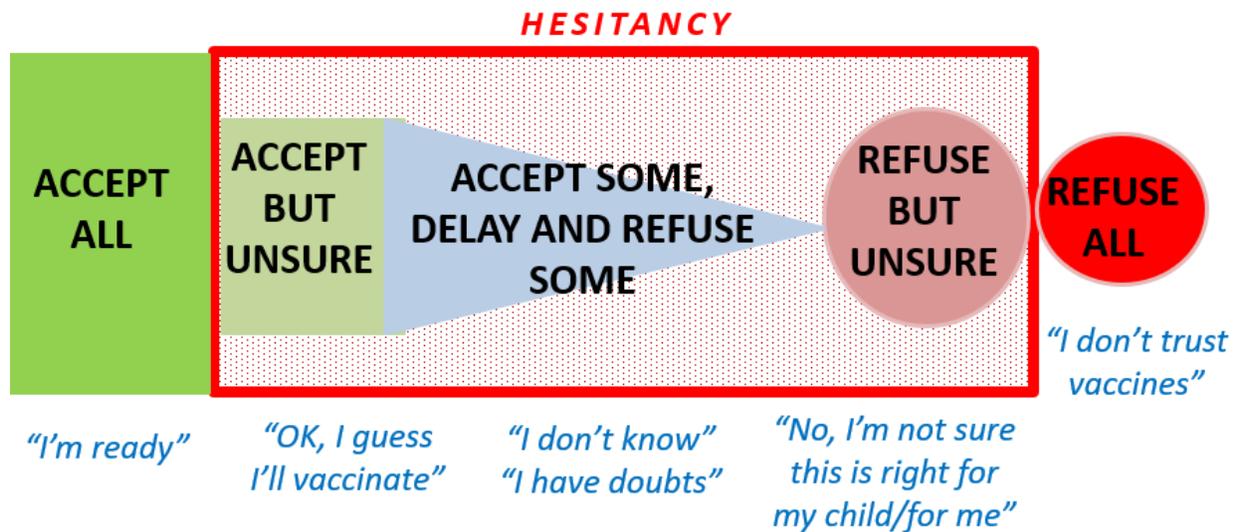
From: Dhawan, S. Conversations to build trust in vaccination: A training module for health workers. World Health Organization, May 2017¹

TO VACCINATE OR NOT TO VACCINATE – FACTORS INFLUENCING DECISION MAKING

According to the SAGE Working Group on Vaccine Hesitancy the following table comprises factors that influence the decisions on immunizations:^{1,5}

Contextual	Individual and Group Influences	Vaccine/Vaccination Specific Issues
Media and public communication	Beliefs and attitudes about health and disease prevention	Mode of administration
Local politics	Knowledge and awareness	Source of the vaccine
Religion and/or culture	Poor quality health service experience	Vaccination schedule
Accessibility of services		Any costs associated with the vaccination
Trust in authorities		Knowledge/attitudes of healthcare professionals

In Canada stanch vaccination refusal is low at approximately 3%, however beliefs and behaviours that constitute vaccine hesitancy is seen in up to 35% of Canadian parents.² Vaccine hesitancy constitutes a continuum that exists between complete vaccine acceptance and refusal with both hesitancy and refusal related to skepticism in vaccination.



Parents want what is best for their children. Health care providers want what is best for their patients and for their communities at large. Vaccination hesitancy is not simply about ignorance or stupidity on the part of parents, but about what influences personal, social, cultural, spiritual, religious, and political factors play on, what is still an individual decision, to vaccinate or not to vaccinate.

ADDRESSING SPECIFIC CONCERNS ABOUT VACCINATIONS:

The World Health Organization named vaccine hesitancy as a leading global health threat in 2019.⁶ Immunizations have always been controversial with its opponents claiming it is unnatural or

contaminating.⁷ The success of immunizations once was self-evident as campaigns were pushed to immunize against diseases that were a part of daily life and possessing a frighteningly high rate of morbidity and mortality. Today, however, even most physicians have never seen a case of measles or its complications; thus, to some extent, it is natural for the average human being to question whether the risks of vaccines outweigh the benefits.

The benefits of immunization to the community are established or threatened by the behaviour of individuals choosing whether to obtain vaccinations for themselves and their children.² Vaccine hesitant individuals comprise a heterogeneous group for whom paramount concerns include vaccination safety, when and how frequently vaccines should be given, questions of individual freedom, and skepticism of both medical professionals and the pharmaceutical industry.

In Canada up to 35% fall somewhere into the spectrum of behaviours and beliefs constituting vaccine hesitancy.² An Angus Reid online survey of 1000 Canadians with children aged five and younger was conducted in December 2015 posing questions about decisions on immunization of their children, and more specifically regarding views on the MMR vaccine. 92% of participants had their children immunized with MMR. Roughly half of the 6% that were not vaccinated stated the age the vaccine was given, was a primary factor. 3.9% had intentionally avoided having the vaccination: 25% due to fear of adverse reactions and 11% owing to dubiousness of effectiveness.²

Below is a summary of their findings:

Question	Agree	Disagree
Vaccines are safe and effective at preventing childhood illnesses.	>90%	
There is clear consensus among medical experts that vaccines are safe.	82%	
Vaccination is less important than it used to be because we have eradicated most childhood diseases.		83%
Vaccination is less important today than it was in the past.	17%	
Vaccines cause autism.	14% An additional 14% were unsure	
There is a strong likelihood that the MMR vaccine will produce serious adverse events.	>25% agreed or were unsure	
Should parents be able to choose whether their children are vaccinated?	44% 7% unsure	49%
Schools and daycare facilities should refuse children who are not vaccinated, except for those with medical exemptions.	65%	
Parents who do not have their children immunized (except in cases involving medical exemptions) are irresponsible.	66%	
Drug companies are behind the government's push for mandatory vaccinations.	33%	

A series of open ended, situational questions were also asked:

Question	Response	Percentage
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Which media sources do you most use for health news and information?	Online news and information sources (e.g. google, social media, websites, etc) Television or radio Specific sources (e.g. medical journals)	57% 29% 5%	
Where would parents go first and most often for information and guidance if an outbreak of VPD were to pose a risk to their community?	Website of major news organizations Official government website Television station Social media	33% 24% 19% 14%	
What are parents most trusted sources for health information overall		Trust	Do not trust
	Physicians	89%	7%
	Public health officials	83%	7%
	Academics	77%	15%
	Popular celebrities (e.g. Gwyneth Paltrow, Oprah Winfrey)	8%	82%
	Celebrity physicians (e.g. Dr. Oz)	25%	59%
	News media	46%	47%

In comparing those that were vaccinators to non-vaccinators there was a different level of trust in various groups to “do what is right”.

Group	Group	Trust	Do not trust
Physicians, public health authorities, and academics	Vaccinators	90%	6%
	Non-vaccinators	55%	37%
Pharmaceutical companies	Vaccinators		51%
	Non-vaccinators		80%
Celebrities			Equally distrust

Finally, surveyors posed the question to these parents of what messages would be most effective for public health officials to use in persuading vaccine hesitant parents to vaccinate. Although almost two-thirds agreed with the statement, “parents who do not have their children vaccinated are irresponsible,” nearly as many thought this shaming type message would be ineffective. The strongest support was for showing evidence of vaccine safety and efficacy, the likelihood of developing a serious disease without vaccination, and detailing the effects of these diseases. Reinforcing that vaccination is strongly

recommended while still leaving the decision to individual preference was also thought to aid. Also important was to debunk myths, demonstrate compassion, and communicate honestly about the risks.

Psychological research indicates that provider recommendation is a strong motivator for getting vaccinations.⁸ However, the uncertainty surrounding vaccine hesitancy is a “wicked” problem in that it is both difficult to define and to solve creating a communication dilemma for health care providers.² Refusal of all vaccines is more common among Caucasian children with older, university educated mothers of higher income households.² It is thus difficult to argue that this represents a merely stupid or ignorant cohort of parents. Radical antivaccine activists purposefully skew science, shift their hypotheses, suppress contradictory opinions, and attack their critics personally and in the courts as routine strategies. They use stories that are vivid and horrific to illustrate their views whereas physicians and scientists are loath to use similar strategies as they are not evidence based. These stories prey on the very real emotional response of anger, fear, and regret. In our current “post-truth” era, emotional arguments hold greater sway than facts, making these messages are even more powerful and dangerous.

Conversely, messages from official sources and medical professionals are generally factual, boring and forgettable. Vivid and horrific descriptions of diseases prevented by vaccines may illicit a fear response that in turn leads to anger and greater entrenchment of the views that vaccination is the wrong answer. Despite numerous studies, including a Cochrane review, looking at ways to specifically address communication by health care providers on vaccination, no approach has emerged as best practice. A sense of the risk of anticipated regret an individual would feel if their child was infected or harmed by a vaccine preventable disease (VPD) may be the most motivational factor related to vaccine behaviour.⁸

Openness, honesty, dialogue, empathy, compassion, and respect are foundational ethical and effective values in risk communication. The goal cannot be to change everyone’s mind. There has always been, and always will be individuals that are unwilling or unable to be vaccinated. It simply needs to be enough to maintain levels needed for effective community immunity.

COMMUNICATING WITH VACCINE HESITANT PARENTS IN THE EMERGENCY DEPARTMENT:

How do you respond to the parent of a child or infant presenting the emergency department when they state the child’s vaccines are not up to date? Does it change how you now approach this patient and their caregiver? Do you show outrage or disgust? Are you kind and compassionate? Do you shrug it off? Do you feel comfortable opening a dialogue about the subject? Do you know what to say and how to say it?

You have just been given an opportunity to assist this patient, this parent, your emergency department, and your community to curtail vaccine preventable diseases. Take it. Here’s how:

Begin by taking a moment to sit down, then gently and kindly asking why they have not chosen to vaccinate their child. Observe and listen to their response. Be prepared for, and accept, their defensiveness. Acknowledge that they have their child’s best interests at heart. Address the concerns directly and honestly, using facts and your own story.

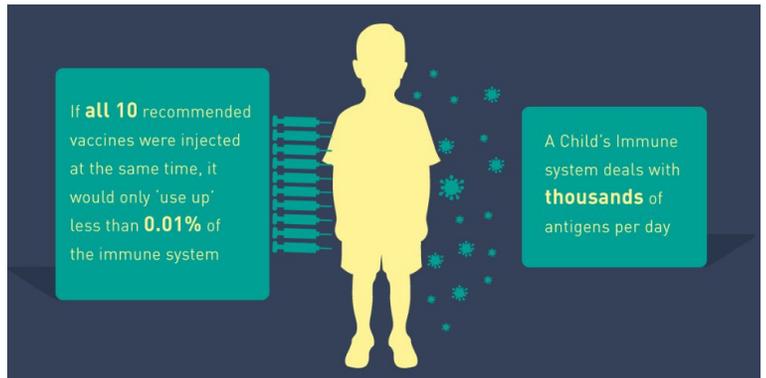
1. Concern:

My baby is too young to handle vaccinations. I've done research and it tells me that there are too many vaccinations and their immune system will be overwhelmed.

Response:

Vaccination teaches your body how to deal with disease. From birth, your baby has handled thousands and thousands of germs everyday. Whenever your baby puts something into their mouth the immune system to decide if its good or bad.

Vaccinations stimulate the immune system to recognize a bad germ and fight it in the same way. Scientists have estimated that babies can handle about 10000 germs at any time and they do that whenever they crawl or play on the floor. Giving many vaccinations at the same time does not give less protection than spacing them out and it means using a few needles as possible.



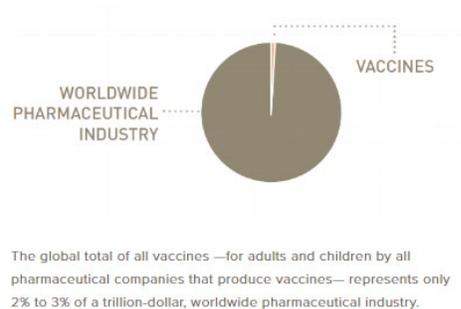
2. Concern:

I know you doctors make money from vaccines – you're being paid by the drug companies.

Response:

Actually, I get paid when you come into the emergency department with an illness. If I wanted to profit from people, I'd be better off telling you and everyone else not to vaccinated or not to wear your seatbelt so that you come in here really sick or hurt and I could make more money. I have enough work, though. What I truly want is for you and your child to be safe and healthy and out of the hospital living a good life.

Yes, vaccines cost money. And the profits and development costs are not necessarily transparent. But compared to the pharmaceutical industry, vaccines are just a drop in the bucket. And there are demonstrable economic benefits to being vaccinated that apply to each of us, including the cost associated with absenteeism from work or school, visits to health care providers, hospitalizations, and premature deaths.



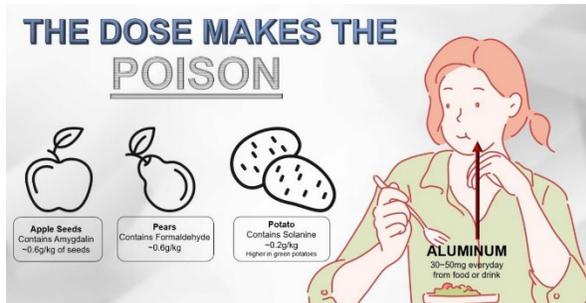
<https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-3-benefits-immunization.html#p1c2a3>

https://www.youtube.com/watch?time_continue=7&v=U45jcfULm2k

3. Concern:

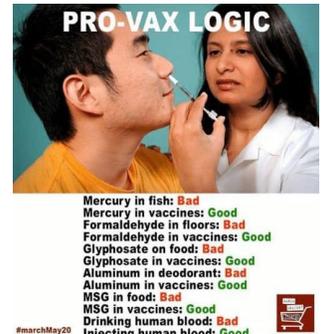
Vaccines contain toxic ingredients. How can they be safe?

Response:



It is true that there are substances in vaccines that could be toxic, but only at a much higher dosage.

Water can be toxic if you drink too much of it, too. The ingredients in vaccines help prevent them from becoming contaminated by bacteria and to help them work better.



Does this make sense to you??

Addressing Specific Toxins:

Aluminum

Response:

It is true that some vaccines contain aluminum. It is used to boost the immune system. There is also aluminum in the food we eat and the water we drink. The amount of aluminum in vaccines is similar to the amount in breast milk and formula.

Mercury or thimerosal

Response:

The mercury in vaccines is different than that found in fish. The kind in fish can build up in your body over time, the kind used in vaccines doesn't do that. It breaks down into something called ethylmercury that gets pooped out. It's not even used in childhood vaccinations anymore. The only vaccine it's used for is some flu vaccines to prevent contamination if the same bottle is being used for lots of doses.

Formaldehyde

Response:

Formaldehyde is used as preservative and is found in naturally in foods. You would eat more in a pear than you get from all the vaccines that we give to kids.

4. Concern:

I never got sick with anything and I didn't get vaccinated when I was a kid. My kid is fine.

Response:

It's true that your child may never need the protection of a vaccine, but you do not want them to be unprotected in the event of an outbreak. These do happen here, including for measles, mumps, and whooping cough. Do you ensure that you and your kids have their seatbelt on when you're driving somewhere? Nobody wants or plans to be in a collision – we put them on “just in case”. Vaccinations are similar.

5. Concern:

Vaccines don't really work. You can still get sick even if you are vaccinated.

Response:

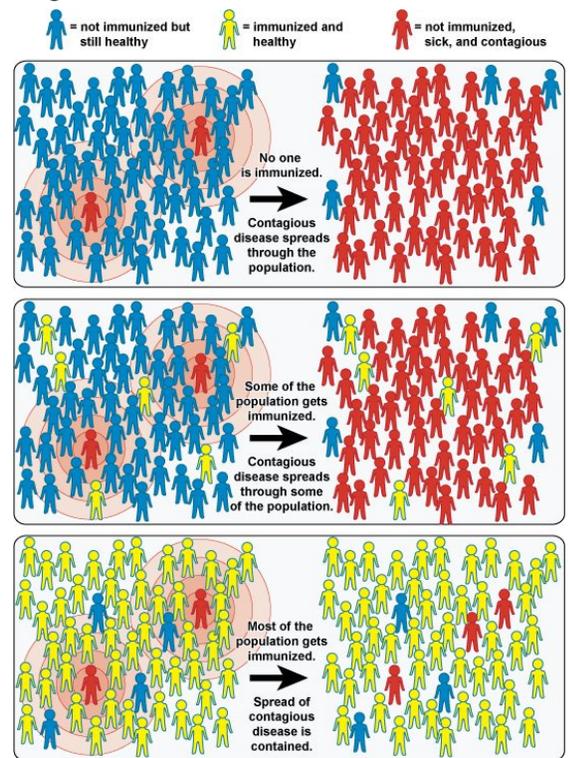
While that is true, it is very uncommon. 95-99% of children will develop immunity with the vaccination, and this improves with the boosters. Only the live vaccines, like MMR might be able to cause the disease and if it does, it is usually a very mild version.

Concern:

So, if vaccines work, why do vaccinated people get sick if there's an outbreak?

Response:

I want you and your child to be protected from these diseases. I also want all your neighbours and mine to be vaccinated. If almost everyone who can be vaccinated is vaccinated, it will prevent the spread of a disease. If there aren't enough people vaccinated a disease like measles, that is extremely contagious can spread even in those who did get the vaccine. It's called herd immunity. And it's especially important for kids and adults who can't get vaccinated, like a kid that has leukemia.



6. Concern:

I know vaccines causes autism. My friend's child was diagnosed with autism after his last set of vaccinations.

Response:



Vaccines do not cause autism. No one really knows what causes autism yet. I would like to know too. Vaccines don't cause autism though. It just happens that autism is often diagnosed around the same age that vaccines are given. The person who tried to claim autism was caused by vaccines was proven to be a fraud and had his medical license taken away. There have been lots of other studies since then that have all concluded that vaccines do not cause autism.

10. Concern:

My child has a lot of allergies. I'm scared she will have a reaction to vaccines with all the stuff in them.

Response:

Even if your child has an allergy to eggs it is rare to have a life-threatening reaction to a vaccine that has little bits of egg products in it, like one in a million. You could double check with your family doctor.

<https://www.immunize.org/catg.d/p3094.pdf>

11. Concern:

There's just no way to know if vaccines are actually safe. I've heard too many stories from my friends. I just don't want to find out the hard way.

Response:

Nothing we do in life is without risk. I could get hit by a car crossing the street or struck by lightning. When it comes to vaccines it takes about 10 years from the time a vaccine is developed to being offered to the public. There are eight components to Canada's vaccine safety system that include all levels of government, the manufacturing companies, a reporting system after the vaccine has been approved, and an independent group that monitors vaccine safety. I'll give you a handout with all the website information before you go.

<https://www.canada.ca/en/public-health/services/publications/healthy-living/vaccine-safety-poster.html>

12. Concern:

Vaccines have too many side effects.

Response:

It's true that vaccines have some side effects. The most common things are that your child is fussier, gets a fever, or there's swelling near where he got poked. Sometimes someone will faint. Rarely there can be a seizure that's associated with a fever from the vaccine, but that's not epilepsy. It's scary, but it's actually okay. The worst thing is a really bad allergic reaction and that happens about as often as someone gets struck by lightning.

<https://immunizebc.ca/side-effects>

13. Concern:

I just can't put my baby through that kind of pain.

Response:

Vaccines do use needles and they do hurt. It hurt me when I saw my baby get vaccinated and cry. Breast-feeding them during the vaccination can help, or giving them some sugar on a soother, or some Tylenol before and after is okay. I'd rather my child got hurt by a needle than have to go through all the discomfort that getting measles or chicken pox would cause them, though.

Concern:

Vaccines are against my religion.

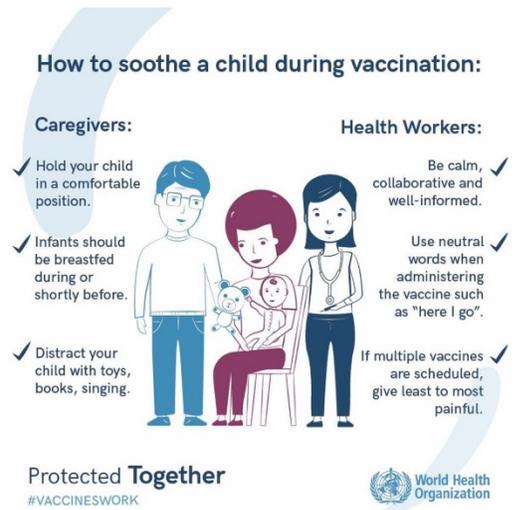
Response:

You are a good parent. It's ok to question vaccines and I respect your religious views. I want to help you become vaccine confident.

The main concerns from religious leaders have to do with some of the components of vaccines. The human cells (diploid and kidney fibroblasts) that the MMR vaccine originated from were harvested by 2 different aborted fetuses. Human albumin is used as part of a growth medium, although this is now recombinant and doesn't contain human blood products. There is gelatin in some vaccines to stabilize them and may be of pig or cow origin. For most faiths, including Judaism, Islam, Hinduism, Christianity, Amish, and Jehovah's witness the ultimate decision of whether to vaccinate is an individual one. Christian Scientists and the Dutch Reformed Church are the two religious groups that are openly opposed to vaccination. Most religious groups concerns are more about safety I suggest you discuss your concerns with your faith leader and your physician.

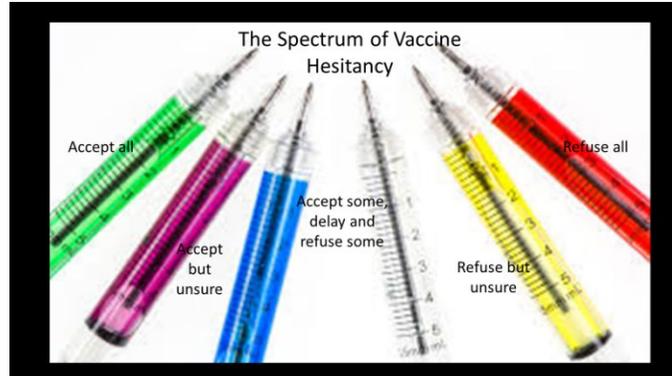
CONCLUSIONS AND TAKE-HOME POINTS:

1. We have a unique roll in the emergency department to address vaccine hesitancy, as we routinely ask about children's vaccination status. We serve as an interface between the community and the hospital.
2. Roughly 3% of the Canadian population fall into the category of vaccine "refusal". Those who refuse to accept vaccination have existed since the advent of vaccinations themselves. We cannot and will not change everyone's mind. We need to work to convince those in the vaccine "hesitant" category to encourage enough individuals to vaccinate to meet the 95% community immunity threshold.
3. Vaccine hesitancy is growing and was named a global health threat by the WHO in 2019. Roughly 35% of Canadians fall into the spectrum of vaccine hesitancy.



4. Vaccine hesitancy is defined as, “Vaccine hesitancy refers to a delay in acceptance or refusal of vaccination despite availability of vaccination services. Vaccine hesitancy is complex and context specific, carrying across time, place and vaccines. It is influenced by factors such as complacency, convenience and confidence” by the SAGE working group.

5. Vaccine hesitancy is a spectrum. Those who are vaccine hesitant have paramount concerns about vaccination safety, when and how frequently vaccines should be given, questions of individual freedom, and skepticism of both medical professionals and the pharmaceutical industry. It is not simply ignorance or stupidity.



6. Start a conversation about vaccination status by sitting down, acknowledging that the individual is a good parent, that you know they have their child’s best interest at heart, and that it’s ok to question vaccination. Tell them you want to help them become “vaccine confident”. Be “conversational and relatable.” Address their concerns directly and honestly, using facts and your own story.

7. Common myths include:

- Vaccinations cause autism
- Physicians are in “cahoots” with the pharmaceutical industry and that we make money by giving or recommending vaccinations
- Vaccinations are unnecessary
- Vaccinations are unsafe
- Vaccinations contain toxins
- An infant or child’s immune system is unable to handle having so many vaccinations at once

8. Offer parents a handout for reliable sources of information on common vaccination concerns.

INFORMATION RESOURCES FOR PARENTS & CAREGIVERS ABOUT VACCINATIONS:

1. A Parent's Guide to Vaccination

<https://www.canada.ca/en/public-health/services/publications/healthy-living/parent-guide-vaccination.html>

2. Vaccine safety: Canada's system

https://www.caringforkids.cps.ca/handouts/vaccine_safety

3. Vaccine Safety: Canada's eight-step vaccine safety program

<http://centerforvaccinology.ca/vaccine-safety/>

4. Vaccine Safety in Canada (video)

<https://www.canada.ca/en/public-health/services/video/vaccine-safety.html>

5. Vaccines: Common concerns

<https://www.caringforkids.cps.ca/handouts/vaccines-common-concerns>

6. Vaccines: Myths and facts

<https://www.caringforkids.cps.ca/handouts/vaccines-myths-and-facts>

<https://www.immunize.org/catg.d/p2068.pdf>

7. Vaccines and Autism

<https://www.immunize.org/catg.d/p4026.pdf>

8. CANImmunize app – Track your family's immunizations on your phone

<https://www.canimmunize.ca/en/home>

9. Choosing not to vaccinate you're your child? Know your risks and responsibilities

[https://www.caringforkids.cps.ca/uploads/handout_images/CFK_tearsheet-ENG\(post\).pdf](https://www.caringforkids.cps.ca/uploads/handout_images/CFK_tearsheet-ENG(post).pdf)

10. Your child's best shot: A Parent's Guide to Vaccination. 4th Ed. (Book)

<https://bookstore.cps.ca/stock/details/your-childs-best-shot-a-parents-guide-to-vaccination-4th-edition>

11. Interior Health Local Public Health Centres

<https://www.interiorhealth.ca/YourHealth/Documents/PublicHealthCentres.pdf>

12. Fraser Health Local Public Health Centres

<https://www.fraserhealth.ca/Service-Directory/Services/Public-Health-Services/public-health-unit#.XXGnsOhKiUk>

13. Vancouver Coastal Health

<http://www.vch.ca/public-health/communicable-diseases-immunizations/immunizations>

APPENDIX

BASIC CONCEPTS OF IMMUNITY AND VACCINOLOGY

Innate Immune System

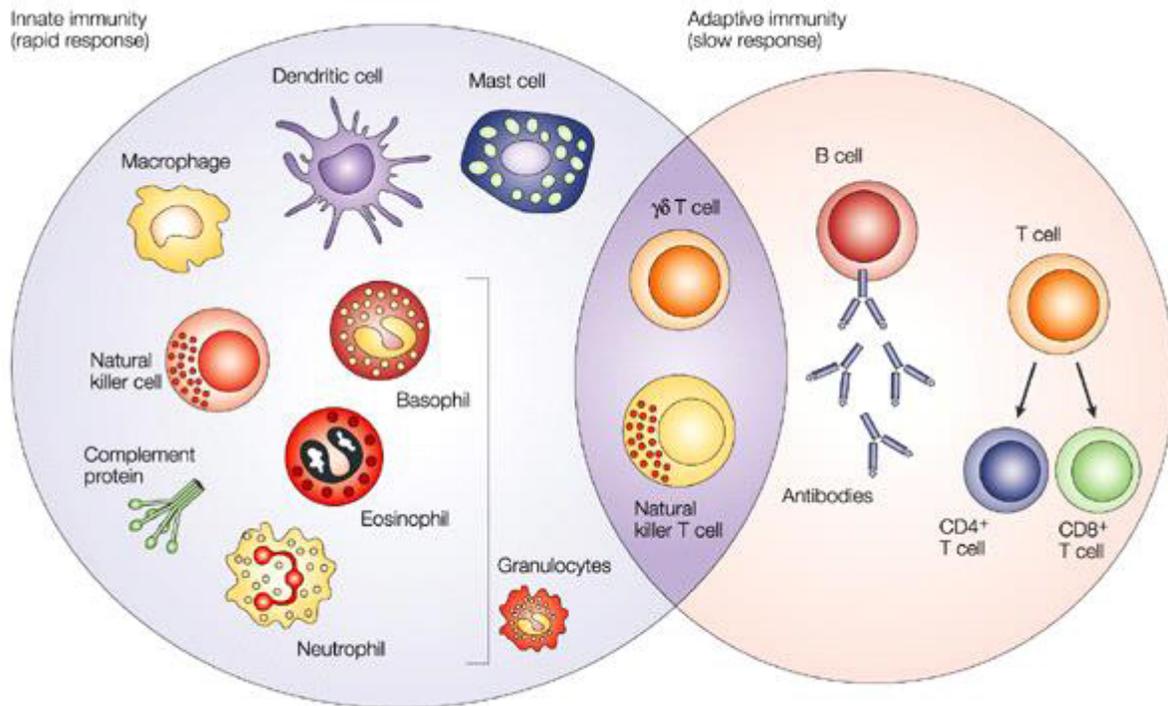
- Early detection of invading pathogens → activates adaptive immune response
- The innate immune systems job is to recognize, contain, and attempt to eliminate a pathogen.
- Cellular elements of the innate immune system include the mobilization of:
 - Tissue residing cells such as macrophages and dendritic cells
 - Mobile phagocytic cells (neutrophils, eosinophils, monocytes)
 - Natural killer cells
- Receptor molecules from these cells and/or damage to epithelial cells, vascular endothelial cells, and fibroblasts that secrete cytokines and chemokines to attract additional innate cells
- Phagocytosis may eliminate the pathogen alone
- Complement proteins may be activated to assist
- Non-specific response
- No immunologic memory → Insufficient for vaccine-related protective immune response

Adaptive Immune System

- Consists of B and T cell lymphocytes
- T cell receptor molecules are capable of recognizing trillions of antigen-specific receptor molecules with the assistance of Antigen Presenting Cells (APC)
 - Dendritic cells ingest and phagocytize antigens → peptide fragments on cell surface → embedded into major histocompatibility complex (MHC) molecules → activation of T cells
- Helper T cells secrete interferon and interleukins to help destroy pathogens and further activate innate immune cells
- Regulatory T cells kick in once there has been an effective protective response to downregulate the immune response
- B cell receptors (BCR) have a membrane bound copy of the antibody molecule that is secreted once activated
 - No need for antigen processing
 - Requires 10-14 days
 - Initial plasma cells response produces IgM antibodies
- Antigen binding to BCR → proliferation and differentiation into plasma cells → create and secrete antibodies into blood → phagocytosis or complement mediated killing of pathogens or toxins
- Antibodies have a constant fragment (Fc) that determines its class:
 - IgA, IgD, IgE, IgG, or IgM
 - Isotype determines the ability to localize to a particular body site and recruit effector cells
 - The initial IgM response changes to:
 - IgG → major isotype of B cell memory response
 - IgA → secreted to mucus membranes

OR

- IgE → defense for parasitic infections
- If there has been a previous exposure to the antigen the reaction time by memory T and B cells is shortened to 1-2 days

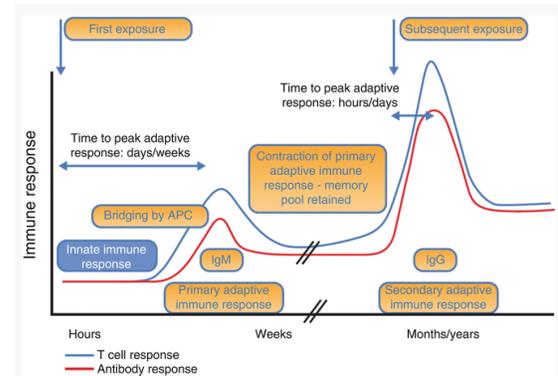
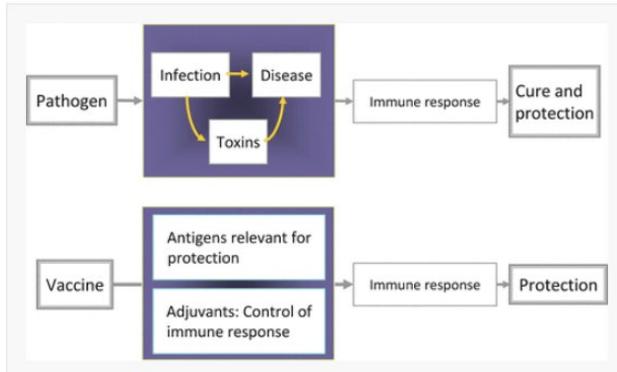


Nature Reviews | Cancer

Principles of Vaccination

- Vaccines are designed to create an immune response similar to that of the natural response from having the disease without experiencing its clinical symptoms and inherent risks on a population-based level
 - Focus traditionally on the role of the adaptive immune response to create immunological memory
- Both innate and adaptive immunity need to strongly interact to create a vigorous immune response
 - Need antigen processing and presentation by dendritic cells to have an efficient response → role of adjuvants
- Conventional vaccines use whole microbial pathogens → adequately stimulating activity for a heterogenous population
- Vaccines with more purified antigens have limited numbers of epitopes
 - Benefit → less vaccine related side effects
 - Risk → Insufficient interaction with the immune response of certain individuals in a population
- Need to balance having specific/pure antigens versus adequate antigen variety to ensure immune system of most individuals receiving the vaccine will have a robust response

- Protection of unvaccinated individuals occurs due to decreased person-to-person transmission
 - Requires 75-96% of the population to be vaccinated



Types of Vaccines:

Live Attenuated Vaccines

- Contain pathogens that have been weakened, altered, or selected to be less virulent than their natural infection therefore cannot cause or only slightly mimic the actual disease
- Contraindicated in immunocompromised or pregnant individuals (theoretical risk of fetal transmission)

Non-live Vaccines

- No living or infectious particles therefore cannot cause disease or reactivate
- Safe in immunocompromised
- Less immunogenicity and duration of protection than live vaccines
- Include
 - Inactivated vaccines → inactivation of whole pathogens using heat, radiation or chemicals such as formalin/formaldehyde
 - Destroys pathogens ability to replicate while maintaining immunogenicity

Sub-unit Vaccines

- Use fragments of pathogen to act as antigen
 - Proteins, polysaccharides or virus-like particles (VLP)
- Includes protein, toxoid, VLP, polysaccharide and polysaccharide conjugate vaccines

Polysaccharide Conjugate Vaccines

- Use polysaccharide antigen bonded to carrier protein such as inactivated tetanus or diphtheria toxoid
 - Polysaccharide antigen is in and of itself often inadequate (especially infants, young children, and elderly) to induce a memory-like immune response (i.e. innate response only)
 - Adding the carrier protein allows the polysaccharide component to be recognized and bound by the BCR → B cell acts as APC for T-helper cell → phagocytized →

presented with MHC → further activation of B cells including switch from IgM → IgG and generation of memory B cells

Vaccine Adjuvants

- Adjuvants are substances that can enhance and modulate the immunogenicity of an antigen
 - Potentiate vaccine-induced immune responses
- Include aluminum salts, emulsions, and liposomes
- Create proinflammatory and immunostimulatory effects
- Slowdown antigen degeneration → prolonging the persistence of vaccine antigens
- Allows vaccines to be tailored to the antigen and target population

REFERENCES:

1. Dhawan, S. et al. (2017). Conversations to build trust in vaccination: A training module for health workers. Powerpoint presentation. World Health Organization
2. Greenberg, J. et al. (2017). Vaccine Hesitancy: In Search of the Risk Communication Comfort Zone. PLoS Currents. March 3; 9.
3. <https://immunize.ca/immunization-mandatory-canada>
4. <https://globalnews.ca/news/5443023/b-c-student-immunization-registration/>
5. MacDonald, N. (2015) Vaccine hesitancy: Definition, scope, and determinants. Vaccine. 33: 4161-4164.
6. Gunaratne, K. et al. (2019) Temporal trends in anti-vaccine discourse on twitter. Vaccine. <http://doi.org/10.1016/j.vaccine.2019.06/086>
7. Doherty, M. et al. (2016) Vaccine impact: Benefits for human health. Vaccine. 34: 6707-6714.
8. Brewer, N.T. et al. Increasing vaccination: Putting psychological science into action. Psychological Science in the Public Interest. 18 (3): 149-207.
9. Immunology (Immune System Overview) Really Just the basics. <https://www.youtube.com/watch?v=LSYED-7riNY>
10. Vetter, V. et al. (2018) Understanding modern-day vaccines: what you need to know. Annals of Medicine: 50 (2): 110-120.
11. Zepp, F. (2016) principles of Vaccination. In: Thomas S. (Eds). Vaccine Design. Methods in Molecular Biology, vol 1403. Humana Press, New York, NY
12. <https://www.astro.org/Patient-Care-and-Research/Research/Professional-Development/Research-Primers/Innate-and-Adaptive-Immunity>
13. McIntosh, E.D.G et al (2016). Vaccine Hesitancy and Refusal. Journal of Pediatrics. 175:248-249.
14. Shixin, S. & Dubey, V. (2019) Addressing vaccine hesitancy: Clinical guidance for primary care physicians working with parents. Canadian Family Physician 65: 175-181
15. Edwards, K.M. et al. (2016) Countering vaccine hesitancy. Pediatrics 138(3): e2016-2146
16. Spencer, J.P. et al. (2017) Vaccine adverse events: Separating myth from reality. American Family Physician 95(12): 786-794.
17. Mina, M.J. (2017) Measles, immune suppression and vaccination: direct and indirect nonspecific vaccine benefits. Journal of Infection 74: 510-517.
18. <https://www.canada.ca/en/public-health/services/publications/diseases-conditions/measles-rubella-surveillance/2019/week-32.html>
19. <https://globalnews.ca/news/5443023/b-c-student-immunization-registration/>
20. Royal College of Physicians and Surgeons of Canada. (2018) Emergency Medicine Competencies. Version 1.0
21. <https://www.canada.ca/en/services/health/publications/vaccines-immunization/vaccine-uptake-canadian-children-preliminary-results-2017-childhood-national-immunization-coverage-survey.html>
22. Bastola, R. et al. (2017) Vaccine adjuvants: smart components to boost the immune system. Arch. Pharm. Res. 40: 1238-1248.
23. Principa, N. & Susanna, E. (2019) Vaccine-preventable diseases, vaccines and Guillain-Barre syndrome. Vaccine 37: 5544-5550.
24. Brown, A. Clear answers and smart advice about your baby's shots. www.immunize.org/catg.d/p2068.pdf

25. Wombwell, E. et al. (2014) Religious barriers to measles vaccination. *J. Community Health* 40:597-604.
26. Larson, H.J. et al. (2015) Measuring vaccine hesitancy: The development of a survey tool 33: 4165-4175.
27. Chu, D. & Abdurrahman, Z. (2019) Vaccine allergy. *CMAJ* 8(191): E395.
28. Goldenberg, M.J. (2019) Vaccines, values, and science. *CMAJ* 8(191): E397-8.
29. <https://www.astro.org/Patient-Care-and-Research/Research/Professional-Development/Research-Primers/Innate-and-Adaptive-Immunity>
30. <https://www.ctvnews.ca/vaccine-compensation-program-overdue-experts-1.641855>
31. <https://www.historyofvaccines.org/content/articles/misconceptions-about-vaccines>
32. <https://www.pbs.org/wgbh/nova/article/herd-immunity/>
33. <http://angusreid.org/mandatory-vaccination-canada/>
34. <http://angusreid.org/vaccination-infographic/>
35. <https://www.cbc.ca/radio/asithappens/as-it-happens-thursday-edition-1.4935124/this-formerly-vaccine-hesitant-mom-has-a-message-for-canadian-doctors-1.4935126>
36. <https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-3-benefits-immunization.html#p1c2a3>
37. <https://www.gavi.org/about/value/cost-effective/>
38. <https://www.historyofvaccines.org/content/articles/do-vaccines-cause-autism>
39. <https://www.immunize.org/catg.d/p4026.pdf>