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Vaccination in special populations

Are you really ”up to date”?

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CHEO

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Faculté de médecine
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Disclosure Statement

- I have no affiliation (financial or otherwise) with a pharmaceutical, medical device or communications organization.

Introduction

- Vaccine preventable infections continue to cause diseases across the world.
- Various special populations are at increased risk of complications from these vaccine-preventable diseases.
- There are vaccination strategies and programs that are in place for these groups.
- But many people remain **under vaccinated**.

Our patient population is increasingly complex

- Acute condition
- Underlying chronic medical conditions
- Immunosuppression

Questions

- Which vaccines are recommended specifically for my patient?
- Who should be vaccinating these patients?
- When should I be vaccinating these patients?
- How should I vaccinate my patients?
- How can I find resources or guidance to help me optimize immunization?

After this session, attendees will be able to:

- Describe general principles of immunization in immunocompromised or high-risk patients
- Distinguish between low-level and high-level immunosuppression
- Understand how to optimize vaccination in special populations and/or immunocompromised patients

Bonus objectives

- By the end of this session – all attendees will have:

1. Subscribed to the Canadian Immunization Guide updates
2. Downloaded the CanImmunize App

Each health care encounter is an opportunity to review the immunization status

Goal # 1

- Ensure patients are “**up to date**” with their immunization status, in order to optimize health and avoid vaccine preventable disease

- **Are you “up to date”?**
- As per provincial/territorial schedule for age

- **Are you “really up to date”?**
- As per potential risk factor

Risk factors

Medical/Health

- Pregnancy
- Prematurity
- Asplenia/splenic dysfunction
- Neurological condition
- Chronic lung disease (including asthma, COPD, CF)
- Chronic liver disease
- Chronic kidney disease
- Chronic heart disease
- Diabetes
- Malignancy
- Transplant recipients (SOT, HSCT)
- Primary immunodeficiency
- HIV
- Cochlear implants, chronic CSF leak
- Immunosuppressive therapies (including chemotherapy, biologics)
- Chronic inflammatory diseases (including IBD,
- > 65, elderly

Work/Lifestyle

- Smokers
- Health care workers
- Child care workers
- Laboratory workers
- Workers exposed to animals
- Refugee workers or humanitarian relief workers
- Emergency services workers
- Workers or inmates of correctional facilities
- Workers or clients of shelters
- International travelers
- Men who have sexual contact with men
- Persons new to Canada
- Household contacts of immunocompromised
- IV drug user

Immunocompromised patients are at risk for vaccine-preventable infections

Incidence of invasive pneumococcal disease in immunocompromised patients: A systematic review and meta-analysis

Mariëlle van Aalst[a], Felix Lötsch[a,b], René Spijker[c,d], Jan T.M. van der Meer[a], Miranda W. Langendam[e], Abraham Goorhuis[a], Martin P. Grobusch[a,f,*], Godelie

Disseminated Varicella Zoster Virus Infection in Adult Renal Transplant Recipients: Outcome and Risk Factors

M. Rommelaere, C. Maréchal, J.-C. Yombi, E. Goffin, and N. Kanaan

Epidemiol. Infect. (2017), **145**, 397–400. © Cambridge University Press 2016
doi:10.1017/S0950268816002405

SHORT REPORT
Overwhelming post-splenectomy sepsis in patients with asplenia and hyposplenia: a retrospective cohort study

J. CHONG[1,2], P. JONES[1], D. SPELMAN[1], K. LEDER[2] AND A. C. CHENG[1,2]*

Clinical Infectious Diseases
MAJOR ARTICLE

A 5-Year Prospective Multicenter Evaluation of Influenza Infection in Transplant Recipients

Deepali Kumar,[1] Victor H. Ferreira,[1] Emily Blumberg,[2] Fernanda Silveira,[3] Elisa Cordero,[4] Pilar Perez-Romero,[4] Teresa Aydillo,[4] Lara Danziger-Isakov,[5] Ajit P. Limaye,[6] Jordi Carratala,[7] Patricia Munoz,[8] Miguel Montejo,[9] Francisco Lopez-Medrano,[10] Maria Carmen Farinas,[11] Joan Gavalda,[12] Asuncion Moreno,[13] Marilyn Levi,[14] Jesus Fortun,[15] Julian Torre-Cisneros,[16] Janet A. Englund,[17] Yoichiro Natori,[1] Shahid Husain,[1] Gail Reid,[18] Tanvi S. Sharma,[19] and Atul Humar[1]

Undervaccinated!

Seasonal influenza vaccination rates and reasons for non-vaccination in children with gastrointestinal disorders

Noam Peleg[a], Noam Zevit[a,b], Raanan Shamir[a,b], Gabriel Chodick[a], Itzhak Levy[a,c,*]

[a] Sackler Faculty of Medicine, Tel.: Aviv University, Tel: Aviv, Petach Tikva, Israel
[b] Institute of Gastroenterology, Nutrition and Liver Diseases, Petach Tikva, Israel
[c] Unit of Pediatric Infectious Diseases, Schneider Children's Medical Center of Israel, Petach Tikva, Israel

Immunization Rates and Vaccine Beliefs among Inflammatory Bowel Disease Patients: An Opportunity for Improvement

Sharmeel K Wasan, MD*, Audrey H Calderwood, MD*, Millie D Long, MD, MPH**, Michael D Kappelman, MD**, Robert S. Sandler, MD, MPH, and Francis A Farraye, MD, MSc*

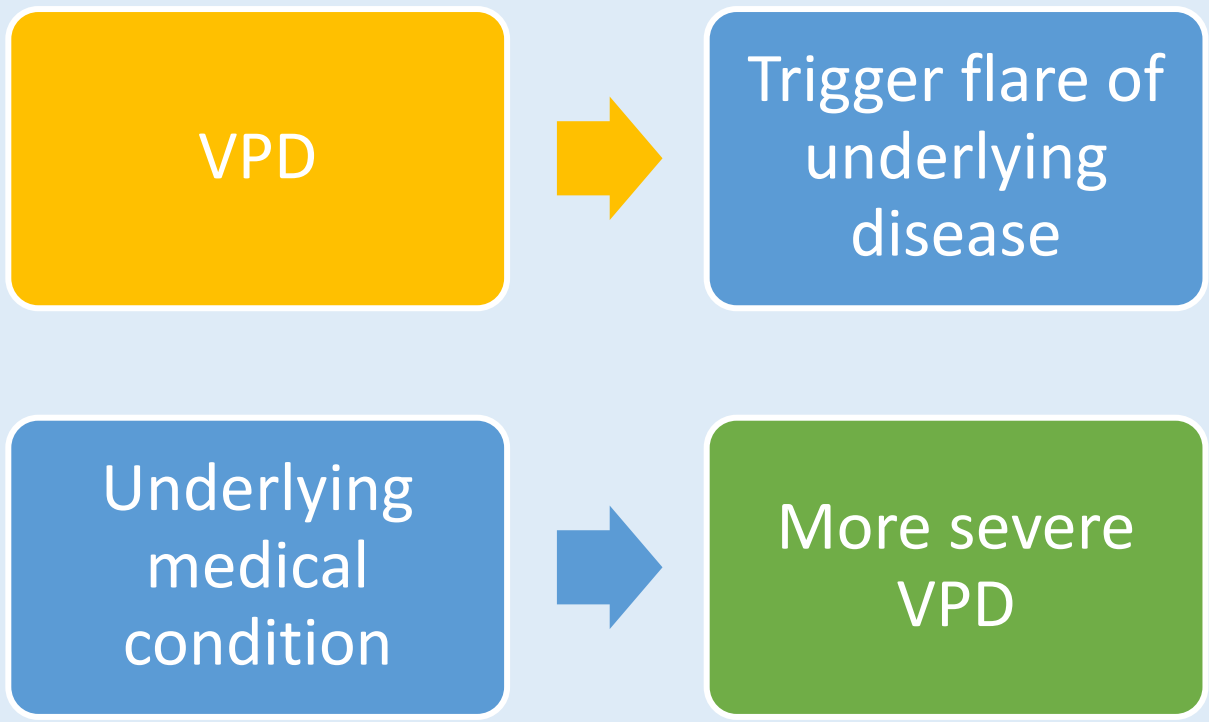
* Section of Gastroenterology, Department of Medicine, Boston Medical Center
** Medicine, Division of Gastroenterology and Hepatology, University of North

Short communication

Low rates of vaccination in listed kidney transplant candidates

Transplant Infectious Disease, ISSN 1398-2273

Chronic medical disease and VPD



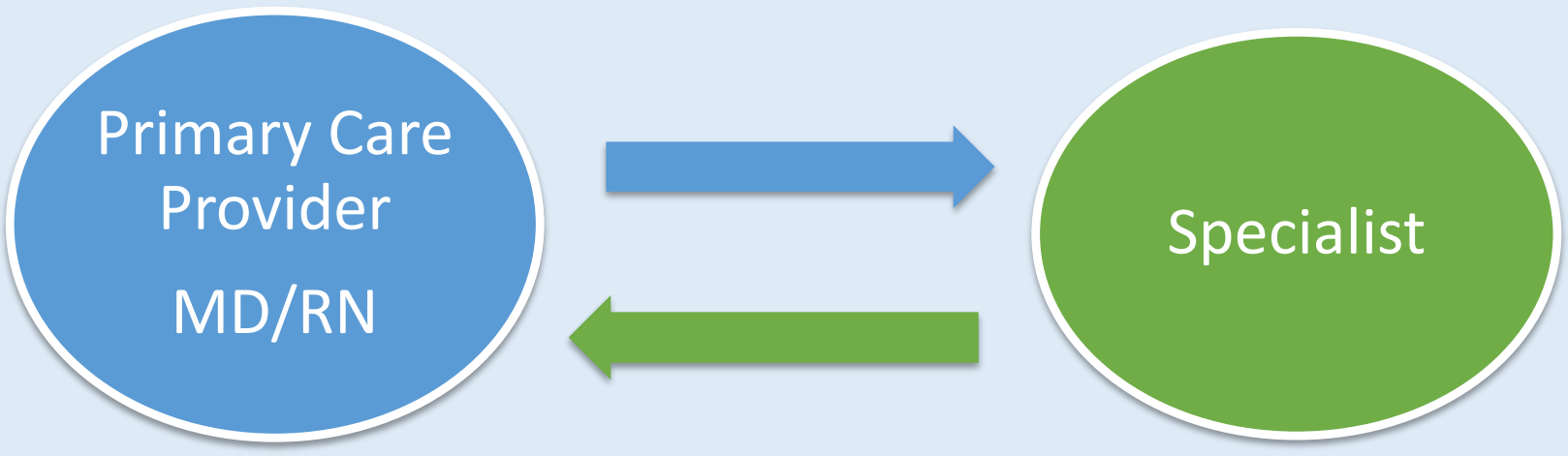
Goal # 2

Protection

General Principles
Vaccines in immunocompromised

Inactivated Vaccines	Live attenuated vaccines
• Safe - **Yes** • Immunogenic?	• Risk? • Immunogenic?

Whose responsibility is it?



How to protect your patient?

- **Routine vaccines**
  - Inactivated: Extra dose? Higher dose?
  - Live attenuated vs alternative
- **Additional vaccines for high-risk patient**
- **Indirect protection**
  - Vaccinate household

When should the patient be vaccinated?

- Prior to planned immunosuppression
- Early in course of disease

Review vaccines early

- Vaccination status should be assessed and documented at the **earliest time point** after diagnosis
- Recommended vaccinations should be administered as soon as possible

Timing is important

Inactivated:

- ≥ 2 weeks PRIOR to planned immunosuppression
- Give when patient is on the lowest anticipated dose of immunosuppressive agents.
- If feasible hold or reduce immunosuppression temporarily*

Timing is important

Live:

- ≥ 4 weeks PRIOR to immunosuppression
- ≥ 4 weeks AFTER stopping high dose steroid (> 2 mg/kg/day x > 14 days)
- > 3 months after completing chemotherapy (and T cell function normal)
- > 6 months after anti-B cell therapy
- ≥ 2 years after allo-HSCT **

Accelerated schedules

Table 1: Minimum age and minimum intervals between vaccine doses in healthy children less than 18 years of age [1] [2]

Vaccine	Minimum age at first dose	Minimum time until 2nd dose	Minimum time until 3rd dose	Minimum time until 4th dose	Comments
Diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated polio, Haemophilus influenzae type b (DTaP-HB-IPV-Hib) OR Diphtheria, tetanus, acellular pertussis, inactivated polio, Haemophilus influenzae type b (DTaP-IPV-Hib)	6 weeks	4 weeks	4 weeks	6 months after third dose [a]	Number of doses of Hib-containing vaccine varies by age. Refer to Haemophilus Influenzae Type B Vaccine in Part 4 for additional information. [a] The fourth dose may be given to children less than 12 months of age in certain situations such as travel, but must be re-administered at or after 12 months of age for sustained immunity. Refer to Diphtheria Toxoid in Part 4 for additional information.
Hepatitis A monovalent (HA)	6 months	24 weeks	N/A	N/A	Refer to Hepatitis A Vaccine in Part 4 for additional information.
Hepatitis B monovalent (HB)	Birth	4 weeks (3 dose schedule) OR 16-24 weeks (2 dose schedule [b])	8 weeks after second dose AND 16 weeks after first dose	N/A	[b] A 2 dose schedule may be used for adolescents 11 to less than 16 years of age; intervals between doses are product-specific. Refer to Hepatitis B Vaccine in Part 4 for additional information.

https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-10-timing-vaccine-administration.html#p1c9a3

Timing between blood products and live vaccines

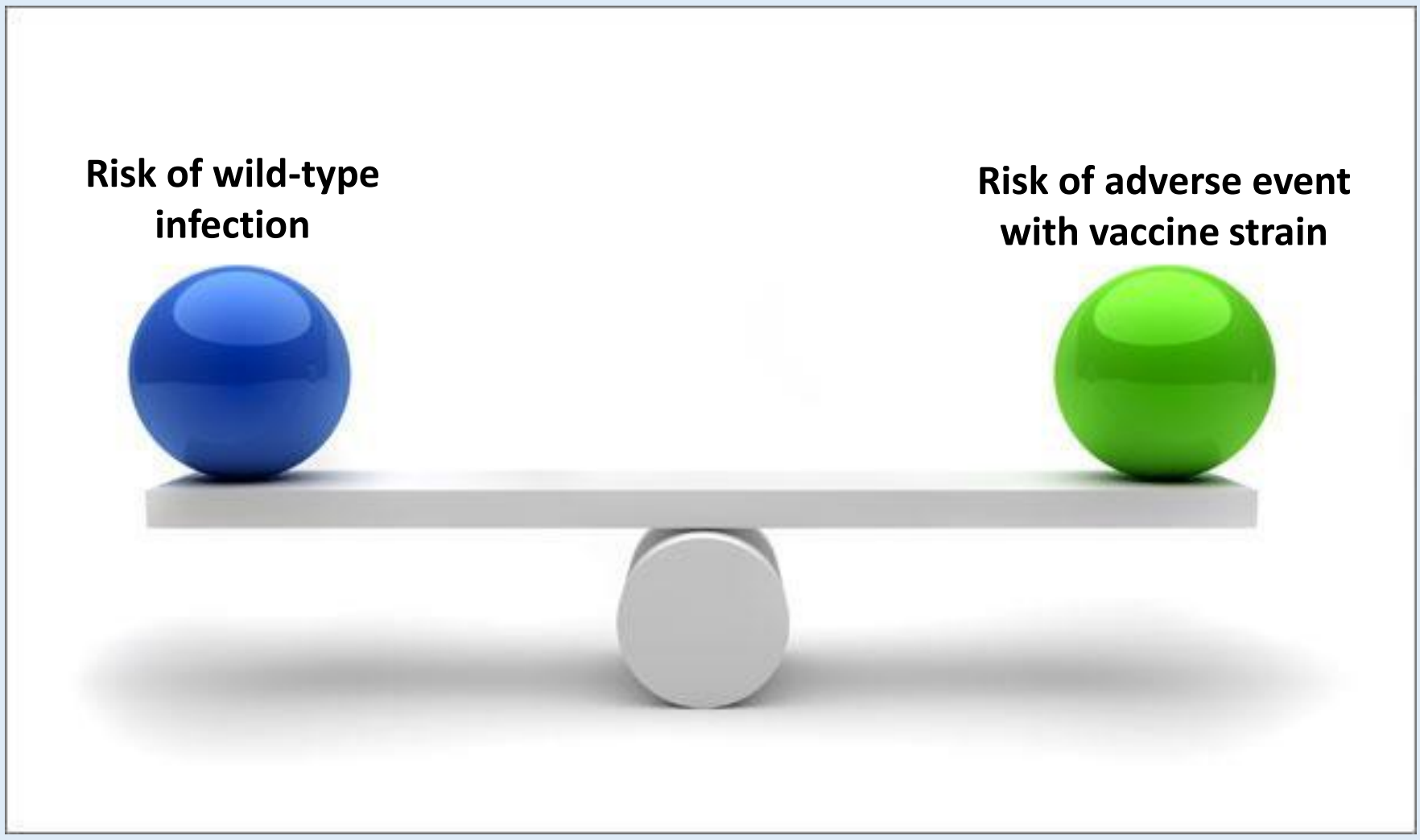
Immune globulin or blood product	Dose, route	Interval between receipt of Ig or blood product and subsequent administration of MMR, MMRV or univalent varicella vaccine (months)
Standard immune globulin (human) [1]		
Immune globulin (Ig)	0.02 - 0.06 mL/kg, IM	3
	0.25 mL/kg, IM	5
	0.50 mL/kg, IM	6
Intravenous immune globulin (IVIg)	300 - 400 mg/kg, IV	8
	1,000 mg/kg, IV	10
	2,000 mg/kg, IV	11
Blood transfusion products		
Plasma and platelet products	10 mL/kg, IV	7
Whole blood	10 mL/kg, IV	6
Packed red blood cells	10 mL/kg, IV	5
Reconstituted red blood cells	10 mL/kg, IV	3
Washed red blood cells [2]	10 mL/kg, IV	0

Can I vaccinate an immunosuppressed patient?

- **Yes…. BUT:**
- Each individual with an underlying acute or chronic condition is different
- Presents **unique** considerations regarding immunization.
- Guidance of patients with more than one chronic condition is an emerging area.

Relative degree of immunosuppression

- **Depends on:**
  - Underlying condition
  - Progression of disease
  - Immunosuppressive medication
  - Chronic co-morbidities
- **Can change over time**


Risk of wild-type infection
Risk of adverse event with vaccine strain

Immunosuppressive or immunomodulatory therapy

- **Glucocorticoids**
- **Immunophilin binding drugs:**
  - Calcineurin Inhibitors (Cyclosporine, tacrolimus)
  - mTOR inhibitors (Sirolimus)
- **Inhibition of new nucleotide synthesis:**
  - MMF, leflunomide
- **Anti-metabolites:**
  - Azathioprine, cyclophosphamide,
- **DMARDS:**
  - Methotrexate, Hydroxychloroquine, sulfazalazine
- **Monoclonal antibodies:**
  - anti-TNFα agents, anti-B cell agents, anti-cytokine

Degree of immunosuppression depends on agent, dose, duration

High Level Immunosuppression

- Combined primary immunodeficiency
- Chemotherapy for malignancy
- Within 2 months of SOT
- HIV
  - CD4 < 200 in adults or < 15% for infants/children
- Daily corticosteroids therapy
  - ≥ 20 mg (or > 2 mg/kg/day for patients < 10 kg) or prednisone or equivalent for ≥ 14 days
- Biologics immunomodulators
  - ex: anti-TNFα, rituximab

Low level immunosuppression

- Asymptomatic HIV
  - CD4 >200 (adults) or > 15% (infants and children)
- Low daily dose of systemic corticosteroids for ≥ 14 days or alternate-day corticosteroids
- Methotrexate ≤ 0.4 mg/kg/week
- Azathioprine ≤ 3 mg/kg/day
- 6-MP ≤ 1.5 mg/kg/day

Immunocompromised and live vaccines

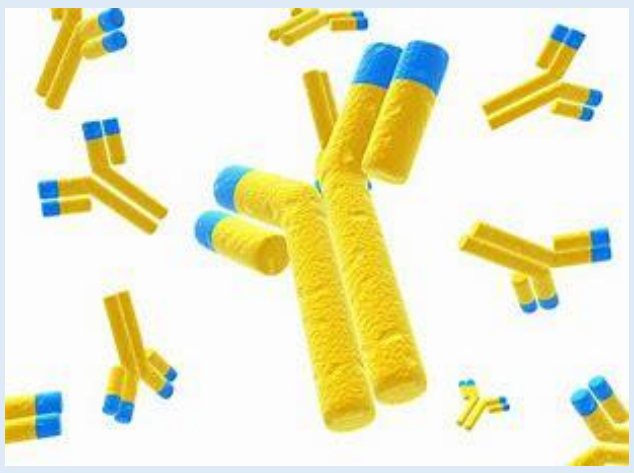
- ***In general*** – **AVOID**
- Except:
  - Var and MMR to asymptomatic HIV infected children with mild to moderate immune deficiency
  - Live zoster vaccine – low level immunosuppression

MMWR Recomm Rep 2008; 57:1–30.

- **If risks of wild-type disease > risk of attenuated viral vaccine**

Did it work?

- Check immune response
- Understand correlates of protection



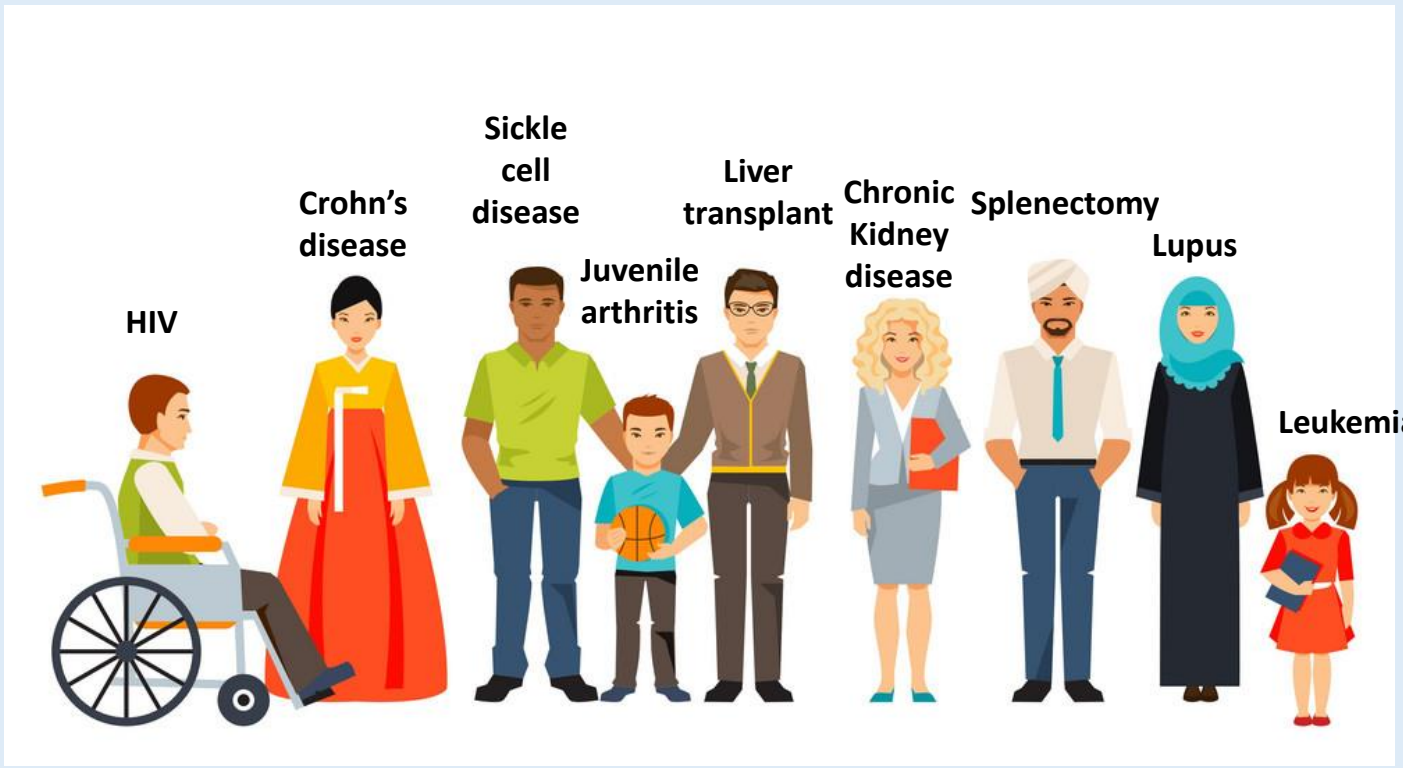
Correlates of protection

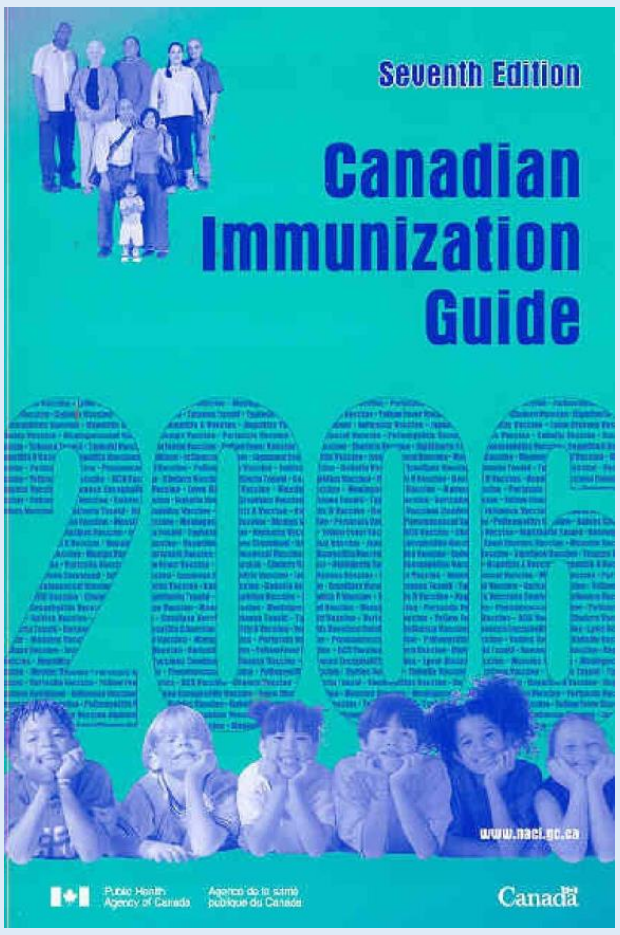
Vaccine	Level required for protection
Diphtheria	> 0.1 IU/mL
Tetanus	> 0.1 IU/mL
Hepatitis B	> 10 mIU/mL
Hib	> 0.15 ug/mL
Varicella	> 5 IU/mL (gp ELISA)
Measles	> 120 mIU/mL

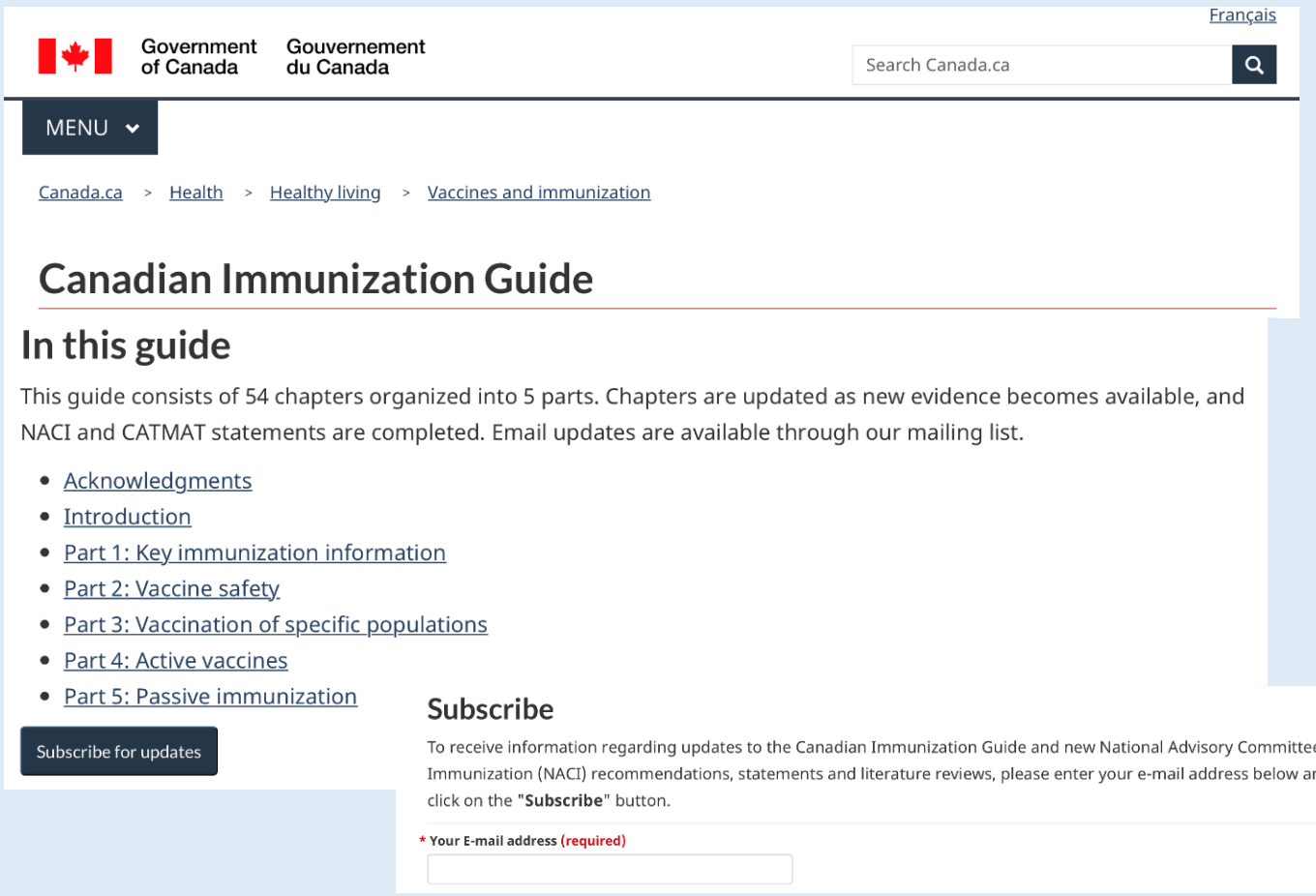
Adapted from Plotkin S. Clinical and Vaccine Immunology. July 2010

A FEW EXAMPLES

Special populations







https://www.canada.ca/en/public-health/services/canadian-immunization-guide.html

Provincial and Territorial Resources

- **BC**: http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/immunization
- **Alberta**: Immunization Program Standards Manual: https://www.albertahealthservices.ca/info/Page10802.aspx
- **Manitoba:** Immunization Program Manual for Immunization Providers in Manitoba https://www.gov.mb.ca/health/publichealth/cdc/div/manual/index.html
- **Saskatchewan:** Saskatchewan Immunization Manual https://www.ehealthsask.ca/services/Manuals/Pages/SIM.aspx
- **Nunavut:** Immunization Manual: https://www.gov.nu.ca/health/information/manuals-guidelines
- **Ontario**: https://www.publichealthontario.ca/en/health-topics/immunization
- **Quebec:** Protocole d'immunization du Quebec (PIQ): https://www.msss.gouv.qc.ca/professionnels/vaccination/protocole-d-immunisation-du-quebec-piq/
- **Nova Scotia**: Nova Scotia Immunization Manual: https://novascotia.ca/dhw/cdpc/documents/Immunization-Manual.pdf
- **Newfoundland/Labrador**: https://www.health.gov.nl.ca/health/publichealth/cdc/immunizations.html
- **New Brunswick**: Immunization Program Guide: https://www2.gnb.ca/content/gnb/en/departments/ocmoh/for_healthprofessionals/cdc/NBImmunizationGuide.html
- **NWT:** https://www.hss.gov.nt.ca/en/services/immunization-vaccination
- **Yukon:** Immunization Program Manual: http://www.hss.gov.yk.ca/yipm.php

28 yo M, sickle cell disease

- New to your practice
- No immunization record
- Got all his “routine” shots as a kid
- Does not recall any recent vaccines
- Oh… and getting an elective splenectomy in about 3 months

Asplenia or sickle cell disease

- High risk of disease from encapsulated organisms:
  - Pneumo, Hib, Meningo, Salmonella
  - **PCV13**, **PPSV23**, **Meningo** (**MCV4, MenB**), **Hib**, **influenza** +\- **S typhi** for travel
- Boost once with PPSV23 (@ 5 years post)
- Boost with meningo vaccines (q 5 years)
  - Men-C-ACYW and Men-B vaccines (many formulations)

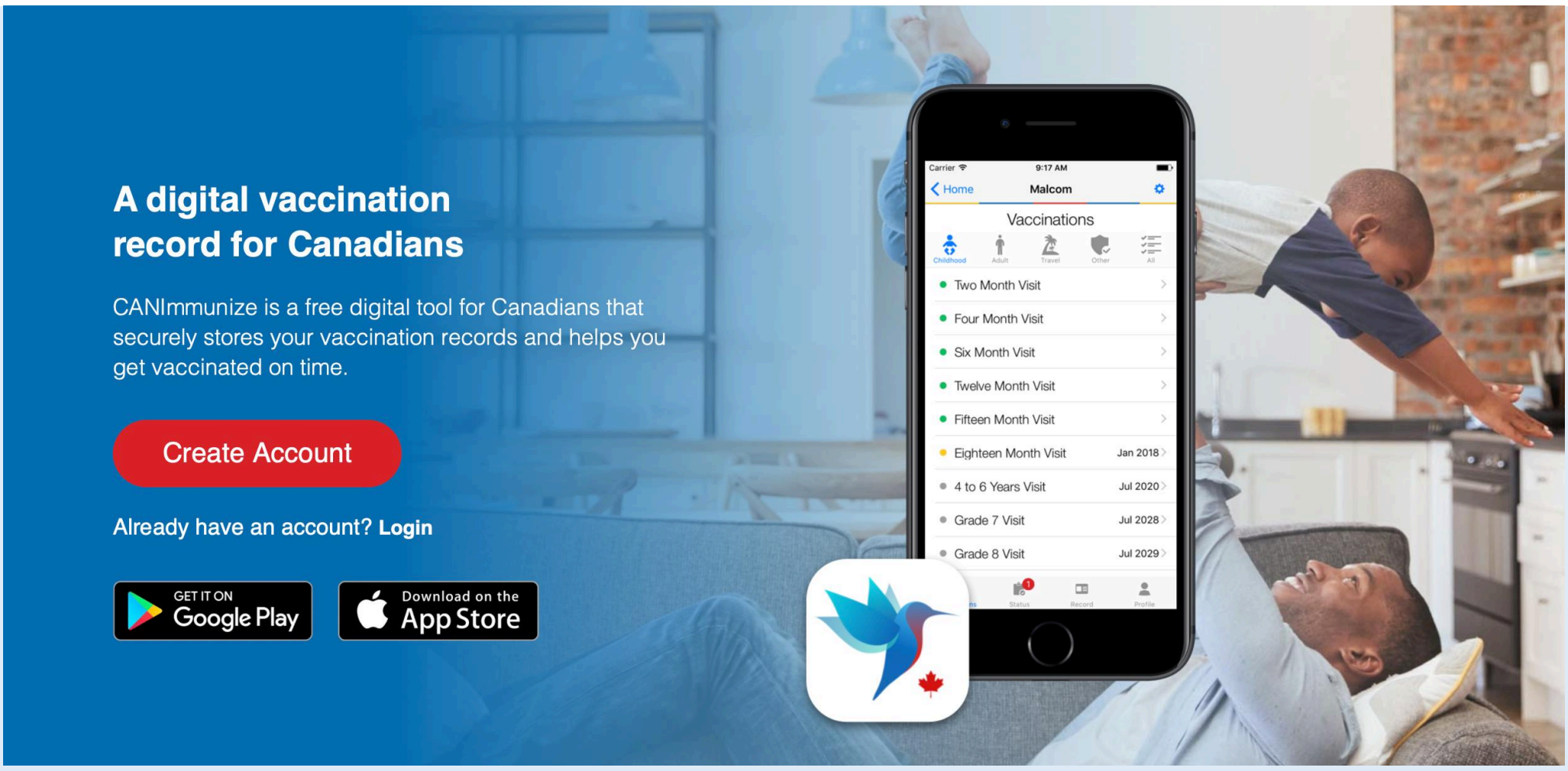
Splenectomy

- <u>Optimal time:</u>
  - > 2 weeks **prior** to splenectomy
- Otherwise:
  - Start 2 weeks **post** splenectomy

- *Increased risk of fulminant bacteremia/sepsis with high mortality rate is highest **<u>in the first 2 years</u>** following splenectomy but **<u>remains elevated for life</u>**.*

28 yo M, sickle cell disease

- Give Hib, MenB, MCV4, PCV13 on 1st visit
- Give MCV4 in 4 weeks (and Men B - depending on formulation)
- Give PPV23 in 8 weeks
- Ask patient to download **CanImmunize App** and have immunization record on mobile device



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

55 yo Type 2 diabetes

- Also chronic kidney disease
- On hemodialysis
- Oh… and awaiting kidney transplant

55 yo Type 2 diabetes

- Also **chronic kidney disease**
- On **hemodialysis**
- Oh… and awaiting **kidney transplant**

Chronic kidney disease

- Severe VPD and/or VPD may exacerbate disease or co-morbidities
- Immunological changes
- Change in immunogenicity/response to vaccines
- Health care associated risks
- Potential immunosuppression due to therapy or uremic state

- **<u>Pneumococcal</u>** and **<u>hepatitis B</u>** vaccines are the main (in addition to routine)
- Hep B: double the µg dose for healthy individual of same age (3 dose series)
- PCV13 then PPV23 8 weeks after
- Check anti-HBs titre 1-6 months after completion of vaccine series.

Diabetes mellitus

- Some patients with longstanding diabetes may have complications and co-morbitidies (cardiac, renal, etc) which can lead to complications with VPD
- Prevention of influenza and pneumococcus is recommended.

30 yo pregnant woman

- Also has IBD
- On infliximab – pre conception and during pregnancy

Pregnancy

- Altered host immunologica state
- Important VPD: **Influenza**, **pertussis**
  - Give Pertussis vaccine and seasonal influenza vaccine for **each** pregnancy
- Barriers:
  - failure of HCP to recommend vaccines, misconceptions of safety and benefits, logistics of providing vaccines at OB office

Chronic inflammatory diseases on immunosuppressive drugs

- Optimize pneumococcal and influenza vaccine coverage
- Varicella – risk/benefit
  - ok for low dose immunosuppression (but not during pregnancy!)
- **AVOID: other live vaccines** with high immunosuppression:
- Immune response likely decreased with rituximab
- Vaccine is not associated with disease exacerbation

Immunization of infants exposed to maternal immunosuppressants

- Certain immunosuppressive medications, which may be used in pregnancy can cross the placenta and impact infant.
- In general:
  - all inactivated vaccines ok
  - Caution with live vaccines for certain drug exposure
- Emerging population – suggest referral to expert consultation (Special Immunization Clinics).

15 yo with ALL

- On maintenance chemotherapy
- Central line
- Doesn’t know if received all routine childhood immunizations.
- Got first series of vaccines in Grade 7 (ON), then sick and missed the second doses (HPV4, HepB)

Malignancy on chemotherapy

- **Ok to give inactivated vaccines but immune response might be suboptimal.**
  - Delay if on intensive chemo or anti-B cell therapy
- **Optimize pneumococcal, influenza vaccines**
  - Doses during chemo may not be valid – may need additional doses
- **Wait 3 months after <u>completion</u> for other inactivated and live vaccines**
  - Wait 6 months for anti-B cell therapy
  - Delay between blood products (IVIG, etc) and live vaccines
  - Some experts recommend giving systematic revaccination postchemotherapy.

Immunization in adolescence

- Some studies report variable and often low vaccination coverage among adolescents with chronic medical conditions
- Variable reasons:
  - Missed school age vaccines due to illness/absenteeism
  - Misperceptions (prevention vs treatment)
  - Logistical reasons
  - lack of knowledge/awareness

OTHER GENERAL PRINCIPLES

Vaccinate Household

- Review immunization status of close-contact and household members
  - Pneumococcal, Pertussis, MMR, Varicella, influenza, etc
- In general all vaccines ok – because viral shedding is unlikely and pose little risk o infection to immunocompromised patient.
  - For rotavirus vaccine – wash hands well when handling diapers
- If varicella rash develops: cover blisters
- **AVOID:**
  - Oral polio vaccine

Everyone

- Should get influenza vaccine
- Inactivated influenza vaccine (IIV)
- Benefits > risk and potential decreased immunogenicity

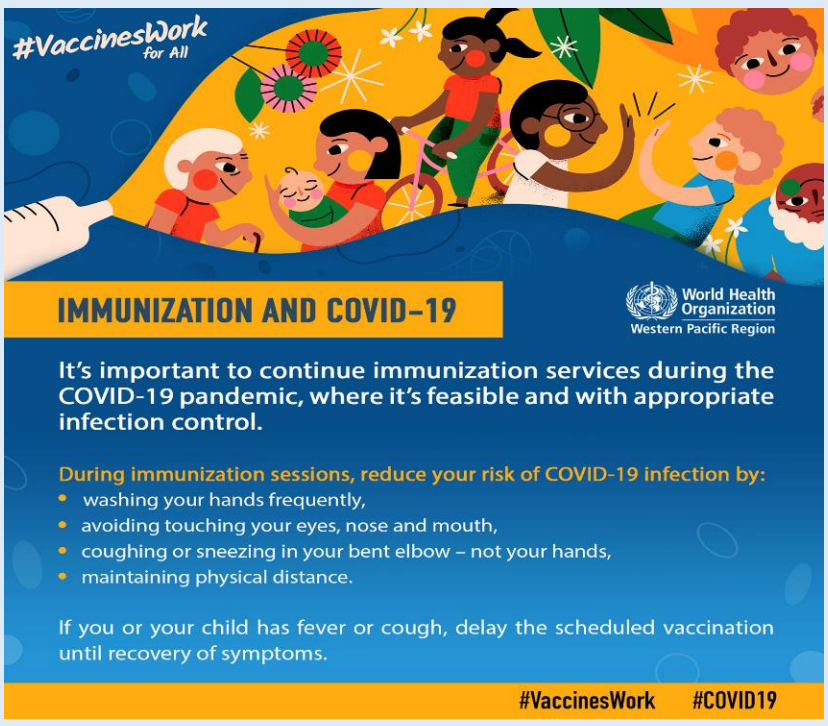
General Principles

1. Vaccinate at optimal time
2. Vaccinate broadly
3. Give boosters accordingly
4. Assess risk/benefit of live vaccines vs live disease
5. Monitor serologic response if indicated

Maintaining immunization during COVID-19 pandemic

- Many public health measures taken to limit transmission of COVID-19.
- In some cases, deferral of non-essential medical visits were recommended.
- But **immunizations**, particularly in infants and toddlers, are **essential**.

Questions?


#VaccinesWork for All
IMMUNIZATION AND COVID-19
World Health Organization
Western Pacific Region
It's important to continue immunization services during the COVID-19 pandemic, where it's feasible and with appropriate infection control.
During immunization sessions, reduce your risk of COVID-19 infection by:
• washing your hands frequently,
• avoiding touching your eyes, nose and mouth,
• coughing or sneezing in your bent elbow – not your hands,
• maintaining physical distance.
If you or your child has fever or cough, delay the scheduled vaccination until recovery of symptoms.
#VaccinesWork #COVID19


KEEP
CALM
AND
KEEP
UP TO DATE

References

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