

VACCINATION GUIDE FOR IMMUNOSUPPRESSED PATIENTS WITH INFLAMMATORY BOWEL DISEASE

STANDARD CANADIAN VACCINATIONS

INACTIVATED VACCINES

- Inactivated vaccines are safe in immunosuppressed patients, but patients on immunosuppressive therapy may have a suboptimal response to vaccination
- Optimize vaccination status prior to initiating immunosuppression whenever possible
- Antibody and T-cell response to vaccine requires 2 - 4 weeks
- Suggested time intervals to allow for best response to vaccine:
 - Between vaccine and initiation of immunosuppression: at least 2 weeks, and preferably 3 - 4 weeks
 - Between discontinuing immunosuppression and vaccine: ≥ 3 months (this interval may vary with the type and intensity of treatment, underlying disease, or urgency of vaccination if vaccines are needed for post-exposure or outbreak management)
- If vaccines are administered during immunosuppression, attempt to give them when the next 2 weeks represent the least immunosuppression
- Additional doses of inactivated vaccines may cause an increase in sore arm, but are not associated with adverse effects. In patients whose immunosuppression may be temporary, it is acceptable to give a vaccine which is due during immunosuppression in order to provide some immediate protection, and then give another dose when the patient is no longer immunosuppressed and may respond more effectively.

VACCINE	CHECK TITER BEFORE VACCINATION?	RECOMMENDATIONS / COMMENTS
Tetanus diphtheria/ Tetanus diphtheria acellular pertussis/ Tetanus diphtheria acellular pertussis and inactivated polio (Td/Tdap/DTaP/DTaP-IPV-Hib)	No	Give according to routine schedule. Td booster every 10 years; with Tdap used at 14 - 16 years of age ¹ . Pregnant women should be offered Tdap vaccine to be given at 27 - 32 weeks gestation during every pregnancy, irrespective of previous immunization history.
Hemophilus influenza type B (Hib)	No	Give according to routine schedule.
Human papillomavirus (HPV)	No	Intended for males and females, ages 9 - 26 years old. 2 doses (0, then 6 - 12 months after) or 3 doses. Highly recommended for MSM**.
Influenza (inactivated/injectable form)	No	Annual vaccine. Timing of administration should balance nadir of immunosuppression and the need to deliver vaccine prior to the onset of influenza season (usually mid-December).
Pneumococcal (conjugate) [Pneu-C-13]	No	Give according to routine schedule ⁱⁱ . In adults, if no prior pneumococcal vaccine, give 1 dose Prevnar 13, wait 8 weeks minimum, and then give 1 dose Pneumovax 23.
Pneumococcal (polysaccharide) [Pneu-P-23]	No	As above, with one time booster after 5 years (if first vaccine was given at > 10 years of age) or 3 years (if first vaccine given at ≤ 10 years) and immunosuppressed.
Meningococcal (conjugate) [Men-C-ACYW]	No	Give according to routine schedule. Vaccinate at-risk patients if none previously.
Hepatitis A Vaccination (HAV)	No	2 doses required: Give at 0, 6 - 12 months; or 0, 6 - 18 months ⁱⁱⁱ . If vaccinated during an immunosuppressed period and patient is in an at-risk group, consider booster when no longer immunosuppressed. Recommended for at risk groups (e.g. Liver disease such as *PSC, travelers, **MSM).
Hepatitis B Vaccination (HBV)	Yes	Give according to routine schedule. Dosing schedule depends on particular vaccine. ⁱⁱⁱ ; check post-vaccine titers at 1 month after finishing last dose. Refer to Canadian immunization guide for non-responders.
Twinrix (Combination Hepatitis A/B)	Yes	May be given instead of HAV and HBV individually. Give according to routine schedule.
Herpes zoster vaccine, inactivated	No, but wait one year after episode of shingles	Two doses, given 2 - 6 months apart. Recommendations may change as further information becomes available.

*PSC – primary sclerosing cholangitis **MSM – males who have sex with males



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LIVE VACCINES

- Contraindicated in patients who are immunosuppressed due to the concern that vaccination may result in disease
- Patients considered to be immunosuppressed include, but are not limited to:
 - Immunomodulators: Azathioprine, 6-Mercaptopurine, Methotrexate^{iv}
 - Steroids: Patients on ≥ 2 mg/kg/day (patients < 10 kg) or ≥ 20 mg/day (patients ≥ 10 kg) for at least 2 weeks^{vi}
 - Biologics such as TNF antagonist (Infliximab, Adalimumab, Golimumab)^{vii}, IL 12/23 antagonist (Ustekinumab). (*EXCEPTION: Integrin Receptor Antagonist Vedolizumab^v*)
 - Significant Protein-Calorie Malnutrition
- Suggested time intervals to allow for immune system recovery:
 - Between last dose of vaccine and initiation of immune suppression: 4 - 6 weeks
 - From discontinuation of immunosuppression and vaccination: 3 months (1 month for high-dose steroids)
- Family members should be vaccinated to prevent transmission from family members to patients (see section on Vaccination of Family Members)

VACCINE	WHEN SHOULD TITRES BE CHECKED?	BEFORE INITIATION OF ANTI-TNF OR IMMUNOMODULATOR?	WHAT TO DO IF ALREADY IMMUNOSUPPRESSED? (ON ANTI-TNF OR IMMUNOMODULATOR?)
Measles, mumps, rubella (MMR)	Considered immune if 2 documented doses of vaccine or positive serology	Contraindicated if plan to start therapy in < 4 weeks. Contraindicated in pregnancy.	Contraindicated
Varicella	Considered immune if good history of natural infection, or two doses of vaccine, or born before 1970. Check serology prior to vaccination if > 25 years of age, or one dose of vaccine or child with history of chickenpox in the immediate family but not individual.	Contraindicated if plan to start therapy in < 4 weeks. Contraindicated in pregnancy.	Contraindicated
Herpes Zoster (for > 50 years old)	Persons who have had shingles in the last year are considered immune.	Not recommended. Use inactivated vaccine.	Not recommended. Use inactivated vaccine.
Live Attenuated Influenza (Flu Mist intranasal form)	Not applicable	Contraindicated (use inactivated vaccine)	Contraindicated
Rotavirus	Not applicable	Contraindicated	Contraindicated

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VACCINATION IN SPECIAL CIRCUMSTANCES

TRAVEL VACCINES

- The same principles apply as outlined above for inactivated and live vaccines but timing of travel may also play role in optimal timing for vaccination
- Ensure that all routine vaccinations are up-to-date (especially MMR, tetanus and pertussis)
- The following are vaccines that may be indicated for travel to specific areas^{viii}:

VACCINE	USE
INACTIVATED VACCINES	
Typhoid (injectable)	Considered safe. Indicated for travel to certain regions.
Japanese Encephalitis	Considered safe. Indicated for travel to certain parts of Asia.
Rabies	Considered safe. Pre-exposure prophylaxis can be considered if traveling to high-risk area. Given possible suboptimal response to vaccine if immunosuppressed, post-exposure prophylaxis with both vaccine and immunoglobulin should be considered in the event of exposure.
Hepatitis A and B	Considered safe.
Meningococcal Vaccine	Considered safe. Indicated for travel to certain areas.
LIVE VACCINES	
Yellow Fever	Contraindicated if immunosuppressed. If traveling to a yellow fever area consult Infectious Disease specialist.
Typhoid (Oral)	Contraindicated if immunosuppressed. Consider injectable inactivated form if indicated.
Bacillus Calmette-Guerin (BCG)	Contraindicated.

RECENT BLOOD TRANSFUSION / IMMUNE GLOBULIN

- Blood products of human origin can interfere with the immune response to live vaccines
- If vaccination with MMR or varicella is indicated and there are no contraindications as previously outlined, the recommended minimal intervals between blood products or immune globulin and vaccination are:
 - Reconstituted RBCs: 3 months
 - Washed RBCs: No delay necessary
 - Intravenous Immune Globulin (400 mg/kg): 8 months^{ix}

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VACCINATION OF FAMILY MEMBERS

- Family members in close contact with immunosuppressed patients should be vaccinated to help prevent disease transmission
- All inactivated vaccines can safely be administered to family members
- Live vaccines are also safe to give family members, with the possible exception of rotavirus and varicella (chickenpox) vaccines (see below):

VACCINE	SAFE TO GIVE FAMILY MEMBERS?	CONSIDERATIONS
MMR	Yes	Safe to give family members.
Varicella	Yes	Approximately 5% of vaccinated patients develop a vesicular rash. Immunosuppressed persons should avoid contact with the individual that has a rash present. Post-exposure prophylaxis (see below) is recommended, as it is not possible to differentiate between rash from vaccine and true varicella infection.
Rotavirus	Yes	Limited data on excretion of live rotavirus in stool after vaccination but the inoculum is likely less than with active infection. Need to consider risks and benefits. If vaccine given to family members, good hand hygiene to prevent theoretical transmission.
Oral Typhoid	Yes	Oral typhoid vaccine is not known to result in live vaccine-strain typhoid being shed in the stool of healthy subjects and there is no documented secondary transmission.
Yellow Fever	Yes	Safe to give family members.
Oral Polio	No	Vaccine not used in Canada.

POST-EXPOSURE PROPHYLAXIS FOR COMMON EXPOSURES (see Red Book² for significant exposure definitions)

Varicella: For immunosuppressed patients exposed to varicella, varicella immune globulin (VariZIG) should be administered as soon as possible within 10 days of exposure³. If VariZIG is not available or contraindicated, some experts recommend oral acyclovir (80 mg/kg/day divided 4 times/day; maximum 800 mg, 4 times/day) starting 7-10 days after exposure and continuing for 7 days².

Measles: Immunosuppressed patients exposed to measles should be given IM Immune Globulin (IVIG) within 6 days of exposure regardless of vaccination history. Vaccination is not an option in immunosuppressed patients (live vaccine).

Hepatitis A: Immunosuppressed patients exposed to hepatitis A should be given IM Immune Globulin (IVIG) within 2 weeks of exposure because response to vaccination may be suboptimal.

This is a reference only. You should discuss vaccination decisions with your health care provider.

For travel vaccinations, it is recommended that you consult a Travel Medicine Specialist about immunization questions specific to your destination. Please notify the travel medicine clinic of current medications prescribed.

For the most updated Canadian Immunization schedule, please visit <http://www.phac-aspc.gc.ca/im/is-cv/#a>

1. NACI. Update on the Use of Conjugate Pneumococcal Vaccines in Childhood; 2010.
2. Committee on Infectious Diseases AAoP. Red Book: 2015 Report of the Committee on Infectious Diseases. 30 ed: American Academy of Pediatrics; 2009.
3. Diseases AAoPCoI. Prevention of varicella: recommendations for use of varicella vaccines in children, including a recommendation for a routine 2-dose varicella immunization schedule. Pediatrics. 2007 Jul;120(1):221-31.

¹ CDC now recommends 2 doses of HPV vaccine for people starting the vaccination series before the 15th birthday. Three doses of HPV vaccine are recommended for people starting the vaccination series on or after the 15th birthday and for people with certain immunocompromising conditions (CDC October 2016)

² In patients ≥ 5 years where pneumococcal polysaccharide vaccine is indicated, some experts recommend the use of conjugate vaccine prior to administration of polysaccharide vaccine in immunosuppressed patients (regardless of age) to enhance immune response. In these cases, the polysaccharide vaccine should be given at least 8 weeks after the conjugate, wait 5 years then one time revaccination with Pneumovax 23 booster dose (NACI 2012). Prevnar 13 is currently not licensed in patients ≥ 5 years of age, although its use is still recommended in high-risk patients. NACI. Update on the Use of Conjugate Pneumococcal Vaccines in Childhood; 2010. NACI. Statement on the Use of Conjugate Pneumococcal Vaccine - 13 Valent in Adults (Pneu-C-13), 2013.

³ The dosage schedule for Hepatitis A and Hepatitis B vaccines depend on the vaccine used. See vaccine product monograph for instructions. Accelerated schedules are available for some vaccines.

⁴ As per NACI, ≤ methotrexate 0.4 mg/kg/week; ≤ azathioprine 3.0 mg/kg/day; ≤ 6-mercaptopurine 1.5 mg/kg/day.

⁵ Patients receiving treatment with Vedolizumab may continue to receive non-live vaccines. There are no data on the secondary transmission of infection by live vaccines in patients receiving Vedolizumab. Live vaccines may be administered concurrently with ENTYVIO[™] only if the benefits outweigh the risks.

⁶ For patients on high-dose steroids (≥ 2 mg/kg/day or ≥ 20 mg/day) for less than 2 weeks, some experts would consider having a two-week interval between discontinuing steroids and vaccination.

⁷ Immunodeficiency that follows the use of recombinant human proteins, including tumor necrosis factor alpha antagonists (i.e. adalimumab, infliximab and etanercept) or anti-B cell monoclonal antibodies (i.e. rituximab) may be prolonged. The interval until immune reconstitution varies with the specific treatment regimen and other factors. Recommendations may change as further data become available.

⁸ This list is not comprehensive. Vaccination requirements vary depending on the location of travel. Consult an infectious disease specialist for specific recommendations.

⁹ A longer interval is recommended for higher doses of immune globulin (see Red Book²).

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