Vaccinating Immunocompromised Patients

full update September 2024

Concerns are raised when a potentially immunocompromised (i.e., immunosuppressed) patient presents for vaccination. The concern with live vaccines is that the patient might contract the disease from the vaccine. Inactivated vaccines cannot cause disease, and some inactivated vaccines are especially recommended for immunocompromised patients. However, depending on the patient's degree of immunocompromise, response to some vaccines may be suboptimal. For some disease states/vaccinations, titers could be used to assess response. It is important to assess the patient's degree of immunocompromise when making vaccine decisions, especially for live vaccines. When in doubt, consult the specialist caring for the patient's immunocompromising condition.[3] If possible, ensure that patients are vaccinated with routine adult vaccinations (plus any others that are specific to their condition) **before** immunocompromise. And keep in mind that several live vaccines have inactivated alternatives (influenza, typhoid, polio).

--Information in chart may differ from product labeling.--

For help **identifying** which vaccines are **LIVE** and which are **INACTIVATED**, see:

- *Vaccines Licensed for Use in the United States* at https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states.
- *Contents of Immunizing Agents Authorized for Use in Canada* at https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-15-contents-immunizing-agents-available-use-canada.html#p1c14t1.

Clinical Question	Pertinent Information of Resource
WHO is or might be immunocompromised in the context of vaccination?	• Patients with **cancer** affecting the bone marrow or lymphatics.[3] • Patients being treated with **chemo** (e.g., alkylating agents, antimetabolites) or **radiation**, and for three months afterward.[1,3] • Patients receiving immunosuppressive **biologics** (e.g., anti-TNF agents, lymphocyte-depleting agents).[1,3] • Patients with **complement** deficiency, or receiving complement inhibitors (e.g., eculizumab).[2.3] • **Transplant** patients.[2,3] • Patients with **congenital (primary) immunodeficiency**.[1,3] • Patients receiving large doses of **corticosteroids (see footnote a)**.[1] • HIV patients.[1] Degree of immunocompromise varies widely; consider CD4 count and CD4 precentage.[3] • Patients taking **immunosuppressants** (e.g., high-dose methotrexate, azathioprine, or 6-mercaptopurine doses [see footnote a]; calcineurin inhibitors).[3] • Asplenia (increased risk of fulminant bacteremia).[2,4] • Chronic renal disease.[2]

Clinical Question	Pertinent Information of Resource
Can patients with immunocompromise receive **non-live** vaccines?	--Also see separate section on **immunosuppressive MEDICATIONS**, below.— • Non-live vaccines include killed whole-organism, recombinant, subunit, split-virus, toxoid, polysaccharide, polysaccharide protein-conjugate, and mRNA vaccines.[2,15] • Because non-live vaccines cannot replicate, they are safe for immunocompromised patients.[1-3] However, these patients may not respond as well as immunocompetent patients.[1,3] Consider the following: o If risk of infectious exposure is low, consider delaying inactivated vaccines until the person is less immunosuppressed.[3] o Review vaccination history and administer any needed vaccines **at least two weeks** before planned immunosuppression to optimize response.[3] o All vaccines are likely effective in patients with chronic kidney disease, primary complement deficiency, certain phagocytic deficiencies, and nonsevere antibody deficiency (e.g., IgA, IgG subclass).[2] For information on efficacy in other disease states, see reference 2. • Some inactivated vaccines are especially **encouraged** in immunocompromised patients. o For recommendations for specific disease states or conditions (e.g., HCT, solid organ transplant, chronic renal disease, asplenia), see resources in **footnote b**.
Can patients with immunocompromise receive **LIVE** vaccines?	--Also see separate section on **immunosuppressive MEDICATIONS**, below.-- **General concepts**: Avoid live vaccines unless immunocompromise is mild, data supports use of the vaccine, and the risk of natural infection is greater than the risk of immunization.[3] Live vaccines should not be given to severely immunocompromised patients, or if immune status is uncertain.[1,3] The ultimate determination of severe immunocompromise should be made by the provider treating the patient's immunocompromising condition.[1,3] **Special disease-considerations (medications are discussed below)**: • Some patients with **B-cell deficiency** can receive certain live vaccines.[1,3] For details, see resources in **footnote b**. • Live vaccines are **not** contraindicated in patients with **complement deficiency**.[2,3] • **HCT**: Live vaccines should not be given within four weeks of the onset of the pre-transplant conditioning regimen.[3] BCG should never be given to any patient who might need an HCT.[3] MMR and varicella vaccines can be given to HCT recipients 24 months post-transplant, assuming immunocompetence.[1] • **Solid organ transplant**: live vaccines should be given at least four weeks prior to transplant.[3] Live vaccines are generally contraindicated post-transplant.[3] • **Asplenia**: only LAIV (e.g., *FluMist*) is contraindicated (U.S.).[2] • **HIV** patients who are **not** severely immunocompromised can get MMR, varicella, and rotavirus.[2,3] For help identifying these patients, see resources in **footnote b**.

Clinical Question	Pertinent Information of Resource
Can patients receiving immunosuppressive **MEDICATIONS** receive vaccines?	**General concepts** • Because **inactivated** vaccines cannot replicate, they are safe for immunocompromised patients.[1-3] However, these patients may not respond as well as immunocompetent patients.[1,3] Consider the following: o Review vaccination history and administer any needed **inactivated** vaccines **at least two weeks** before planned immunosuppressive therapy to optimize response.[3] In addition to vaccines recommended as for immunocompetent patients, other vaccines may be recommended: ▪ **Pneumococcal** vaccination.[2,3,19] For guidance, see reference 11 (Canada) or 12 (US). ▪ **Recombinant zoster vaccine** (*Shingrix*) is recommended for adults ≥19 years of age (US).[2,19] ▪ **Meningococcal** vaccination is recommended for patients who will receive eculizumab (*Solaris*) or ravulizumab (*Ultomiris*).[2] For guidance, see references 11 (Canada) or 12 (US). o For patients already on immunosuppressive therapy: ▪ Response varies depending on the vaccine, drug, and patient population, and is generally attenuated; nevertheless, patients receiving immunosuppressive therapy can benefit from vaccination.[5-9,16,17] ▪ If risk of infectious exposure is low, consider delaying inactivated vaccines until the person is less immunosuppressed.[3] ▪ In adults receiving immunosuppressants for rheumatic disease, consider using a high-dose or adjuvanted **influenza vaccine**, if available, instead of a standard influenza vaccine.[19] ▪ If the patient is vaccinated during immunosuppression, consider checking titers once the drug is discontinued to guide whether vaccination requires repeating.[3] ▪ In chemo patients, expect vaccines to be held during chemo, although an inactivated vaccine (e.g., influenza) might be given between cycles. Patients might be revaccinated with vaccines given during chemo when chemo is over.[2] Each center will have protocols. ▪ Canada: double the usual hepatitis B vaccine dose, and use a 3- or 4-dose schedule.[3] ▪ HPV vaccine (e.g., *Gardasil 9*) should be given using a 3-dose schedule.[3,12] • In general, **live vaccines** should be avoided in patients receiving high-level immunosuppressive therapy (see **footnote a**).[1,3] Give any needed **live** vaccines **at least four weeks before** planned immunosuppressive therapy to reduce risk of acquiring an infection from the vaccine.[2,3] o **Varicella** vaccination is recommended for susceptible patients before IBD immunosuppressive therapy is started.[8] **Specific medications**: • Consult prescribing information/product monographs for **MS therapies** for guidance. Also see below concerning use of alemtuzumab for cancer. • **Deucravacitinib** for **psoriasis**: discontinue two to three half-lives prior to **live** vaccination, and restart two to four weeks post-vaccination.[18] **Non-live** vaccines can be given without deucravacitinib interruption.[18] • **Cyclosporine** for **psoriasis**: hold for two to four weeks after **live** vaccination. **Non-live** vaccines can be given without cyclosporine interruption.[18]
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Clinical Question	Pertinent Information of Resource
Can patients receiving immunosuppressive **MEDICATIONS** receive vaccinations, continued	• **Tofacitinib** for **rheumatic disease** or **psoriasis**: hold for one week prior to **live** vaccination, and restart two to four weeks after live vaccination (ACR: hold for four weeks post-vaccination).[18,19] **Non-live** vaccines can be given without tofacitinib interruption.[18,19] • **Leflunamide**, **mycophenolate**, **calcineurin inhibitors (e.g., cyclosporine)**, or **oral cyclophosphamide** for rheumatic disease: hold for four weeks prior to **live** vaccination, and restart four weeks after live vaccination.[19] **Non-live** vaccines can be given without treatment interruption.[19] • **Low-level immunosuppression** (**see footnote a**): varicella can be given.[3] Other live vaccines can be given after a risk/benefit assessment (e.g., MMR before travel).[3,5] Consult an expert if immunosuppressants are used in combination.[3] o **Methotrexate** for **rheumatic disease** or **psoriasis**: consider holding for two to four weeks prior to **live** vaccination, and restarting two to four weeks after live vaccination (ACR: hold methotrexate for four weeks before and after live vaccination. Hold times can be shorter if live vaccination is critical and disease flare risk is high.).[18,19] Consider holding methotrexate for two weeks after **non-live** vaccines (including COVID-19), if disease activity allows.[18,20] (ACR: consider holding methotrexate for two weeks after non-live **influenza** vaccine, if disease activity allows, but other **non-live** vaccines can be given without methotrexate interruption [COVID-19 not addressed].[19]) o **Azathioprine** for **rheumatic disease**: hold for four weeks prior to **live** vaccination, and restart four weeks after live vaccination.[19] Hold times can be shorter if live vaccination is critical and disease flare risk is high.[19] **Non-live** vaccines can be given without azathioprine interruption.[19] • **High-level immunosuppression** (**see footnote a**): IBD guidelines recommend a three-month washout of immunosuppressive therapy before giving live vaccines (four months for the yellow fever vaccine).[8] o **Biologics**: **live** vaccines should be avoided in patients receiving biologics (e.g., therapeutic monoclonal antibodies, [e.g., adalimumab, etanercept, infliximab, etc], lymphocyte-depleting agents).[1] ▪ Some rheumatologic experts recommend a washout of two to three half-lives before giving **live** vaccines (at least four weeks) and restarting two to three half-lives after administration of live vaccines (at least one to two weeks).[14] IBD guidelines recommend a three-month washout from high-level immunosuppressive therapy (**see footnote a**) (four months for the yellow fever vaccine).[8] ▪ **Rituximab** or **alemtuzumab** may cause prolonged immunosuppression.[1] Some experts advise waiting at least six to 12 months after treatment to vaccinate.[3,5] B cell enumeration is generally performed during rituximab therapy and should be reviewed prior to immunization.[3] Although data is lacking, some experts would recommend waiting at least four weeks after vaccination to restart rituximab.[1,5] o **Rituximab** for **rheumatic disease**: consider giving **non-live influenza** vaccine when appropriate, but consider deferring other non-live vaccines until the next rituximab dose is due. Wait two weeks post-**non**-live vaccination to restart rituximab, if disease activity allows.[19] ▪ **TNF inhibitors**, **IL-12/IL-23 inhibitors**, **IL-23 inhibitors**, **IL-17 inhibitors, IL-6 inhibitors, IL-1 inhibitors, or belimumab** for **psoriasis** or **rheumatic disease**: discontinue two to three half-lives prior to **live** vaccination,

Clinical Question	Pertinent Information of Resource
	and restart two to four weeks post-vaccination (ACR: hold for one dosing interval[c] prior to live vaccination, and restart four weeks post-vaccination).[18,19] **Non-live** vaccines can be given without treatment interruption.[18,19] ▪ **Anifrolumab** for rheumatic disease: hold for one dosing interval[c] prior to **live** vaccination, and restart four weeks post-vaccination. **Non-live** vaccines can be given without anifrolumab interruption.[19] ▪ **Abatacept** for **rheumatic disease** or **psoriasis**: discontinue four weeks (intravenous) or one week (subcutaneous) prior to **live** vaccination, and restart two to four weeks post-vaccination (ACR: hold for one dosing interval[c] prior to live vaccination, and restart four weeks post-vaccination..[18,19] **Non-live** vaccines can be given without abatacept interruption.[18,19] o **Cyclophosphamide**, intravenous, for **rheumatic disease**: hold for one dosing intervalc prior to live vaccination, and restart four weeks post-vaccination. Non-live vaccines can be given without cyclophosphamide interruption.[19] o If a **cancer** patient is at least three months post-**chemo/radiation**,[1-3] cancer is in remission, and T cell function is normal, live vaccines can be given.[3] Rituximab and alemtuzumab are exceptions (see above).[1,3] o Immunosuppressive **corticosteroid** dose (see **footnote a**): **Live** vaccines should be deferred for at least four weeks after stopping an **immunosuppressive corticosteroid** dose.[3,19] IBD guidelines recommend a three-month washout.[8] MS guidelines recommend a three-month washout after high-dose, systemic corticosteroids taken for ≥2 weeks, or one month after a short-term, high-dose pulse.[9,10] Wait four weeks post-vaccination to restart.[19] Consider giving non-live **influenza** vaccine when appropriate, but consider deferring other non-live vaccines until the corticosteroid dose can be tapered to the equivalent of prednisone <20 mg/day.[19]
Can **HOUSEHOLD CONTACTS** of immunocompromised patients receive LIVE vaccines?	• Household contacts may receive MMR, varicella, rotavirus, and LAIV (e.g., *FluMist*).[1,3] See resources in **footnote b** for other vaccines recommended for contacts. o If a recipient of the varicella vaccine develops a rash, they should keep the rash covered and avoid direct contact with the immunocompromised person until the rash has cleared.[3,5] o LAIV (e.g., *FluMist*) is contraindicated in close contacts and caregivers of severely immunocompromised patients (e.g., HCT recipients requiring hospital isolation).[3,13] Healthcare workers and visitors who have received LAIV should avoid contact with severely immunocompromised patients for seven days after vaccination (Canda: two weeks).[3,13] o Immunocompromised patients should avoid handling diapers of infants within the first month of infant rotavirus vaccination.[5]

Abbreviations: ACR = American College of Rheumatology; BCG = bacilli Calmette-Guerin; HCT = hematopoietic cell transplant; HPV = human papilloma virus; Hib = *Haemophilus influenzae* type b; IBD = inflammatory bowel disease; IL = interleukin; LAIV = live attenuated influenza virus; MMR = measles, mumps, rubella; MS = multiple sclerosis; TNF = tumor necrosis factor

a. **Immunosuppressive steroid dose (i.e., high-level immunosuppression dose)**: prednisone ≥20 mg daily or ≥2 mg/kg daily (or equivalent) for ≥14 days.[1,3] This does **NOT** include alternate-day regimen; rapid tapers; short (<14 day) high-dose regimen; topicals; physiologic replacement doses; or intra-articular, bursal, or tendon injection.[1-3] Live vaccines can be given to patients receiving inhaled corticosteroids (Canada: with the exception of LAIV, which should not be given to patients with severe asthma receiving high-dose inhaled corticosteroids).[1,3]
Low-level immunosuppression examples: methotrexate ≤0.4 mg/kg/week, azathioprine ≤3 mg/kg/day, or 6-mercaptopurine ≤1.5 mg/kg/day).[3]
High-level immunosuppression examples: immunosuppressive corticosteroid dose (see above), methotrexate >0.4 mg/kg/week, azathioprine >3 mg/kg/day, or 6-mercaptopurine >1.5 mg/kg/day; adalimumab, certolizumab, etanercept, golimumab, infliximab, natalizumab, vedolizumab.[1,3,8] Consult prescribing information for MS treatments (e.g., fingolimod).

b. **Additional resources**:
   - **US**: Altered immunocompetence. General best practice guidelines for immunization: best practices guidance of the Advisory Committee on Immunization Practices (ACIP). (https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html).
   - **US**: CDC Recommended Adult Immunization Schedule (https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf).
   - **Canada**: Canadian Immunization Guide, Immunization of Immunocompromised Persons (https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#t5).

c. If the drug has more than one approved dosing frequency, hold for the longest approved dosing interval; however, for IL-6 or IL-1 inhibitors, in children with systemic juvenile rheumatoid arthritis or other autoinflammatory disorder, shorter hold times can be considered if live vaccination is critical and the risk of disease flare is high.[19]

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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