Immunization of immunocompromised persons

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Introduction and general principles

- In general, immunocompromised persons are more susceptible to vaccine-preventable infections and may have severe infections.
- The safety and effectiveness of vaccines in immunocompromised persons are determined by the type of immunodeficiency and degree of immunosuppression.
- The relative degree of immunodeficiency is variable depending on the underlying condition, the progression of disease and use of immunosuppressive agents.

Non-live vaccines

- Non-live vaccines, including inactivated and recombinant, may generally be administered to immunocompromised people if indicated because the antigens in the vaccine cannot replicate and there is no increase in the risk of vaccine-associated adverse events; however, the magnitude and duration of vaccine-induced immunity are often reduced.

Live attenuated vaccines

- In general, people who are severely immunocompromised or in whom immune status is uncertain should not receive live vaccines because of the risk of disease caused by the vaccine strains.

General principles

- Maximize benefit while minimizing harm
- Susceptibility to infection and ability to respond to a vaccine vary according to degree of immune suppression
- Immunize at the time when maximum immune response can be anticipated
- Immunize prior to any planned immunosuppression, if possible

General principles

- Delay immunization if the immunodeficiency is transient
- Stop or reduce immunosuppression to permit better vaccine response, if appropriate.
- Vaccinate family members and other close contacts as appropriate

Immunocompromised patients

- Primary immunodeficiency
- Acquired (secondary) immunodeficiency

Acquired (secondary) immunodeficiency

- Malignant hematologic disorders
- Non-hematologic malignant solid tumours
- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic
- Solid organ transplantation
- Immunosuppressive therapy

Acquired (secondary) immunodeficiency

- Malignant hematologic disorders

- (e.g., leukemia, lymphomas, blood dyscrasias or other malignant neoplasms affecting the bone marrow or lymphatic systems)

Acquired (secondary) immunodeficiency

- Malignant hematologic disorders
- In general, non-live vaccines should be administered to people with malignant hematologic disorders according to routine immunization schedules, although response may be sub-optimal.
- Immunization should be given at least 2 weeks prior to the start of immunosuppressive therapy or when immunosuppressive therapy is at the lowest level unless the risk of imminent exposure to the pathogen is high.

Acquired (secondary) immunodeficiency

- Malignant hematologic disorders

Non-live vaccines:

- Hepatitis B vaccine
- HPV
- Pneumococcal vaccine
- Hib
- INFLUEENZA
- RSV
- SARS-COV-2

Acquired (secondary) immunodeficiency

- Malignant hematologic disorders

- **Live attenuated vaccines:**
- Live attenuated vaccines are contraindicated in individuals with severe immunodeficiency due to blood dyscrasias, lymphomas, leukemias of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems and in people undergoing immunosuppressive chemotherapy or radiotherapy treatment for these conditions.

Acquired (secondary) immunodeficiency

- Malignant hematologic disorders

- In general, if the cancer is in remission and chemotherapy and/or radiotherapy have been completed for at least 3 months, and T cell function is normal, the person is no longer considered immunocompromised and live vaccines may be given. Live vaccines should be deferred for at least 6 months after therapy with anti B-cell antibody.

Acquired (secondary) immunodeficiency

- Malignant hematologic disorders
- Non-hematologic malignant solid tumours
- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic
- Solid organ transplantation
- Immunosuppressive therapy

Acquired (secondary) immunodeficiency

- Non-hematologic malignant solid tumours

- Non-live vaccines should be administered to people with malignant solid tumours according to routine immunization schedules.
- Immunization should be given at least 2 weeks prior to the start of immunosuppressive therapy or when immunosuppressive therapy is at the lowest level unless the risk of imminent exposure to the pathogen is high.

Acquired (secondary) immunodeficiency

- Non-hematologic malignant solid tumours

Non-live vaccines:

- Hepatitis B vaccine
- HPV
- Pneumococcal vaccine
- Hib
- INFLUEENZA
- RSV
- SARS-COV-2

Acquired (secondary) immunodeficiency

- **Non-hematologic malignant solid tumours**

- Live attenuated vaccines are contraindicated in individuals with severe immunodeficiency due to blood dyscrasias, lymphomas, leukemias of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems and in people undergoing immunosuppressive chemotherapy or radiotherapy treatment for these conditions.
- In general, if the cancer is in remission and chemotherapy and/or radiotherapy have been completed for at least 3 months, and T cell function is normal, the person is no longer considered immunocompromised and live vaccines may be given. Live vaccines should be deferred for at least 6 months after therapy with anti B-cell antibody.

Acquired (secondary) immunodeficiency

- Non-hematologic malignant solid tumours

- Live vaccines are contraindicated in people undergoing immunosuppressive treatment for any malignant solid tumour. In general, if chemotherapy has been completed for at least 3 months and the cancer is in remission, the person is no longer considered immunocompromised.

Acquired (secondary) immunodeficiency

- Malignant hematologic disorders
- Non-hematologic malignant solid tumours
- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic
- Solid organ transplantation
- Immunosuppressive therapy

Acquired (secondary) immunodeficiency

- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic

- HSCT is the transplantation of hematopoietic stem cells following bone marrow ablation or non-ablative conditioning (chemotherapy and/or radiotherapy to deplete the hematopoietic system prior to transplant). HSCT recipients receive either their own cells (autologous HSCT) or cells from a donor (allogeneic HSCT). Stem cells are sourced from bone marrow, peripheral blood, or umbilical cord blood.

Acquired (secondary) immunodeficiency

- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic

- **Pre-HSCT immunization:**

- If time permits, careful consideration must be given to the pre-transplant immunization status of the HSCT candidate.
- All routine non-live vaccines should be given as appropriate for age.

Acquired (secondary) immunodeficiency

- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic

  - **Pre-HSCT immunization:**

Non-live vaccines:

- Pneumococcal vaccine
- INFLUEENZA
- RSV
- SARS-COV-2

Acquired (secondary) immunodeficiency

- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic

  - **Pre-HSCT immunization:**

- Donor vaccination may improve responses of the HSCT recipient to some vaccines.

Acquired (secondary) immunodeficiency

- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic

  - **Post-HSCT immunization**

- HSCT recipients should be viewed as "never immunized" and require re-immunization after transplant because the ablation of hematopoietic cells in the bone marrow pre-transplant eliminates most or all immune memory. In addition, certain vaccine preventable diseases pose increased risk for HSCT recipients of all ages (e.g., pneumococcus, Hib, measles, varicella, and influenza).

Acquired (secondary) immunodeficiency

- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic

  - **Post-HSCT immunization**

Non-live vaccines:

- All routine non-live vaccines should be given (or repeated) for HSCT recipients generally beginning 6 to 12 months post-transplant (Pneu-C-20 and COVID-19 vaccines may be given beginning at 3 months post-transplant; non-live influenza vaccine may be given beginning at 4 to 6 months post-transplant).

Acquired (secondary) immunodeficiency

- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic

  - **Post-HSCT immunization**

Live attenuated vaccines

- MMR and univalent varicella vaccines may be considered 24 months or more post-transplant provided there is no evidence of chronic GVHD, immunosuppression has been discontinued for at least 3 months and the underlying disease for which the transplant was done.
- Other live vaccines are contraindicated.

Acquired (secondary) immunodeficiency

- Malignant hematologic disorders
- Non-hematologic malignant solid tumours
- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic
- Solid organ transplantation
- Immunosuppressive therapy

Acquired (secondary) immunodeficiency

- Solid organ transplantation

Solid organ transplant recipients are at increased risk of severe illness with many vaccine preventable diseases, including invasive pneumococcal or Hib disease, influenza, varicella, and HPV-related diseases.

Acquired (secondary) immunodeficiency

- Solid organ transplantation

  - **Pre-solid organ transplantation**

Pre-transplant immunization is routine at most transplant centres. Candidates should be immunized prior to transplantation and as early in the course of disease as possible because vaccine response may be reduced in people with organ failure pre-transplant.

Acquired (secondary) immunodeficiency

- Solid organ transplantation
  - **Pre-solid organ transplantation**

    Non-live vaccines:
    - Hepatitis B vaccine
    - HPV
    - Pneumococcal vaccine
    - Hib
    - INFLUEENZA
    - HAV
    - Meningococal
    - RSV
    - SARS-COV-2

Acquired (secondary) immunodeficiency

- Solid organ transplantation
  - **Pre-solid organ transplantation**

Non-live vaccines should be given at least 2 weeks before transplantation and live attenuated vaccines (MMR, MMRV, varicella, rotavirus, LAIV) should be given at least 4 weeks prior to transplantation.

Acquired (secondary) immunodeficiency

- Solid organ transplantation
  - **Post-solid organ transplantation**

Solid organ recipients generally receive lifelong immunosuppression, which varies substantially depending on the organ transplanted.
Usually the degree of immune suppression is greatest in the first 3 to 6 months post-transplant.

Acquired (secondary) immunodeficiency

- Solid organ transplantation
  - **Post-solid organ transplantation**

Non-live vaccines:

In general, vaccination with non-live vaccines should not be re-initiated until maintenance immunosuppression is attained.

Acquired (secondary) immunodeficiency

- Solid organ transplantation
  - **Post-solid organ transplantation**

Non-live vaccines:

- Hepatitis B vaccine
- HPV
- INFLUEENZA
- RSV
- SARS-COV-2

Acquired (secondary) immunodeficiency

- Solid organ transplantation
  - **Post-solid organ transplantation**

Live attenuated vaccines:

Live vaccines are generally contraindicated after transplant. However, univalent varicella vaccine has been given to selected pediatric renal and liver transplant recipients without recent graft rejection.

Acquired (secondary) immunodeficiency

- Malignant hematologic disorders
- Non-hematologic malignant solid tumours
- Hematopoietic stem cell transplantation (HSCT): autologous or allogeneic
- Solid organ transplantation
- Immunosuppressive therapy

Acquired (secondary) immunodeficiency

- Immunosuppressive therapy

- Long-term immunosuppressive therapy is used for various disease conditions including cancer, organ transplantation, GVHD following HSCT, and chronic inflammatory conditions (e.g., inflammatory bowel disease, inflammatory arthritis, psoriasis, systemic lupus erythematosus).

Acquired (secondary) immunodeficiency

- Immunosuppressive therapy

- Therapies include cancer chemotherapy, radiation therapy, long term high-dose steroid treatment (prednisone equivalent of ≥ 2 mg/kg/day or 20 mg/day if weight > 10 kg, for ≥ 14 days), cytotoxic drugs, calcineurin inhibitors, chimeric antigen receptor (CAR) T cell therapy targeting lymphocytes, biological response modifiers and antibodies that target lymphocytes.

Acquired (secondary) immunodeficiency

- Immunosuppressive therapy

- In general, if a patient is 3 months post-chemotherapy and the cancer is in remission, or if immunosuppression has been discontinued for at least 3 months (6 months or more for anti-B cell antibodies or CAR T cells targeting lymphocytes), the person is no longer considered immunocompromised.

Acquired (secondary) immunodeficiency

- Immunosuppressive therapy

- **Prior to immunosuppressive therapy:**
- Ideally, all appropriate routine vaccines or boosters should be administered before the initiation of immunosuppressive therapy so that optimal immunogenicity is achieved.
- Although non-live vaccines can be safely administered at any time before, during or after immunosuppression, non-live vaccines should be administered at least 14 days before initiation of immunosuppressive therapy to optimize immunogenicity.
- Live vaccines should be administered at least 4 weeks before immunosuppressive therapy is started to reduce the risk of disease caused by the vaccine strain.

Acquired (secondary) immunodeficiency

- Immunosuppressive therapy

- **During or after immunosuppressive therapy:**
- If immunization cannot be completed prior to initiation of immunosuppressive therapy, generally a period of at least 3 months should elapse between therapy cessation and the administration of non-live vaccines or live vaccines.

Close contacts

- Annual influenza vaccine and up-to-date routine immunizations are recommended for household members and other close contacts of people with chronic diseases, as well as for their health care workers.
- Non-immunized close contacts of immunocompromised people should be immunized against pertussis, Hib, rotavirus, pneumococcus, measles, mumps, rubella, varicella, zoster and influenza as appropriate for age.
- Non-immune household or close contacts of immunocompromised people should be given hepatitis B vaccine.

Close contacts

- Vaccine viruses in MMR vaccine are not transmitted to contacts.
- Transmission of varicella vaccine virus from people with post-varicella vaccine rash occurs but is rare.
- Susceptible close contacts of immunocompromised people should receive MMR, MMRV, varicella or herpes zoster vaccine as appropriate for age.

Close contacts

- Infants living in households with persons who have or are suspected to have immunosuppressive conditions or who are receiving immunosuppressive medications can receive rotavirus vaccine.
- Following administration of rotavirus vaccine, viral antigen shedding in the stool may be detected in some vaccinees and may persist for up to 4 weeks.
- To minimize the risk of transmission of vaccine virus during the 4 weeks after immunization, careful hand washing should be performed after contact with the vaccinated infant, especially after handling feces (e.g., after changing a diaper), and before food preparation or direct contact with the immunocompromised person.

Close contacts

- Annual immunization with influenza vaccine is recommended for close contacts of immunocompromised persons.
- Because of the theoretical risk for transmission, recipients of live attenuated influenza vaccine should avoid close association with persons with severe immunocompromising conditions (e.g., HSCT) for at least 2 weeks following vaccination.

Close contacts

- Oral polio vaccine should not be administered to household contacts of an immunocompromised person. If there are household contacts who have received live, oral polio vaccine within the last 6 weeks, they should not have contact with immunocompromised persons.

Thanks