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Survivorship: Immunizations and Prevention of Infections, Version 2.2014:

Clinical Practice Guidelines in Oncology

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Abstract

Cancer survivors are at an elevated risk for infection because of immune suppression associated with prior cancer treatments, and they are at increased risk of complications from vaccine-preventable diseases. This section of the NCCN Guidelines for Survivorship provides recommendations for the prevention of infections in survivors through education, antimicrobial prophylaxis, and the judicious use of vaccines. These guidelines provide information about travel and gardening precautions and safe pet care/avoidance of zoonosis, and include detailed recommendations regarding vaccinations that should be considered and encouraged in cancer and transplant survivors.

Cancer survivors are at elevated risk for infection because of immune suppression associated with previous cancer treatments, such as chemotherapy, radiation, corticosteroids, certain surgeries, and stem cell transplantation. In fact, antibody titers to vaccine-preventable diseases decrease after anticancer treatment.[1,2] In addition, survivors are at increased risk of complications from vaccine-preventable diseases, such as those caused by human papillomaviruses (HPV) and influenza viruses.[2,3]

Many infections in survivors can be prevented by the use of vaccines. However, a recent report of data from the Behavioral Risk Factor Surveillance System (BRFSS) found that 42% of survivors did not receive an influenza vaccination in 2009, and 52% reported never receiving a pneumococcal vaccination.[4] Analysis of the SEER-Medicare database showed that breast cancer survivors, aged 65 years or older, were less likely to receive an influenza vaccination than matched noncancer controls.[5] A separate analysis of the SEER-Medicare database by another group found similar results.[6]

Vaccines represent a unique challenge in cancer and transplant survivors because they may not trigger the desired protective immune responses because of possible residual immune

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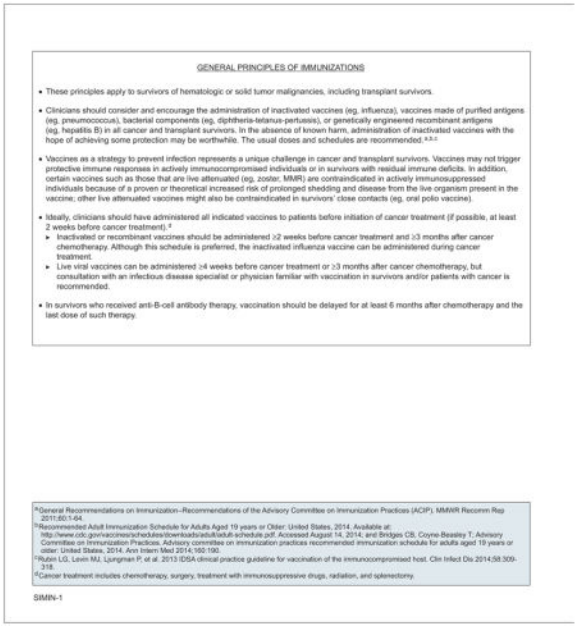
deficits.[7] In addition, certain vaccines, such as those that are live attenuated (eg, zoster;

measles, mumps, rubella [MMR]), are contraindicated in actively immunosuppressed survivors because of an increased risk of developing the disease and/or prolonged shedding from the live organism given in the vaccine.

Risk Assessment and Screening for Immunizations and Prevention of Infections

Survivors are at elevated risk for infections if their cancer treatment included chemotherapy, monoclonal antibodies, radiation, corticosteroids, splenectomy, and/or hematopoietic cell transplantation (HCT; which includes peripheral blood stem cell transplantation, bone marrow transplantation, and cord blood transplantation). Risk is also elevated if the survivor has prior or current exposure to endemic infections or epidemics, or has a history of blood transfusion.



GENERAL PRINCIPLES OF IMMUNIZATIONS

- These principles apply to survivors of hematologic or solid tumor malignancies, including transplant survivors.
- Clinicians should consider and encourage the administration of inactivated vaccines (eg, influenza), vaccines made of purified antigens (eg, pneumococcus), bacterial components (eg, diphtheria-tetanus-pertussis), or genetically engineered recombinant antigens (eg, hepatitis B) in all cancer and transplant survivors. In the absence of known harm, administration of inactivated vaccines with the hope of achieving some protection may be worthwhile. The usual doses and schedules are recommended.[a,b,c]
- Vaccines as a strategy to prevent infection represents a unique challenge in cancer and transplant survivors. Vaccines may not trigger protective immune responses in actively immunocompromised individuals or in survivors with residual immune deficits. In addition, certain vaccines such as those that are live attenuated (eg, zoster, MMR) are contraindicated in actively immunosuppressed individuals because of a proven or theoretical increased risk of prolonged shedding and disease from the live organism present in the vaccine; other live attenuated vaccines might also be contraindicated in survivors' close contacts (eg, oral polio vaccine).
- Ideally, clinicians should have administered all indicated vaccines to patients before initiation of cancer treatment (if possible, at least 2 weeks before cancer treatment).[a]
  - Inactivated or recombinant vaccines should be administered ≥2 weeks before cancer treatment and ≥3 months after cancer chemotherapy. Although this schedule is preferred, the inactivated influenza vaccine can be administered during cancer treatment.
  - Live viral vaccines can be administered ≥4 weeks before cancer treatment or ≥3 months after cancer chemotherapy, but consultation with an infectious disease specialist or physician familiar with vaccination in survivors and/or patients with cancer is recommended.
- In survivors who received anti-B-cell antibody therapy, vaccination should be delayed for at least 6 months after chemotherapy and the last dose of such therapy.

[a]General Recommendations on Immunization--Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2011;60:1-64.
[b]Recommended Adult Immunization Schedule for Adults Aged 19 years or Older: United States, 2014. Available at: http://www.cdc.gov/vaccines/schedules/downloads/adult/adult-schedule.pdf. Accessed August 14, 2014; and Bridges CB, Coyne-Beasley T; Advisory Committee on Immunization Practices. Advisory committee on immunization practices recommended immunization schedule for adults aged 19 years or older: United States, 2014. Ann Intern Med 2014;160:190.
[c]Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:309-318.
[d]Cancer treatment includes chemotherapy, surgery, treatment with immunosuppressive drugs, radiation, and splenectomy.

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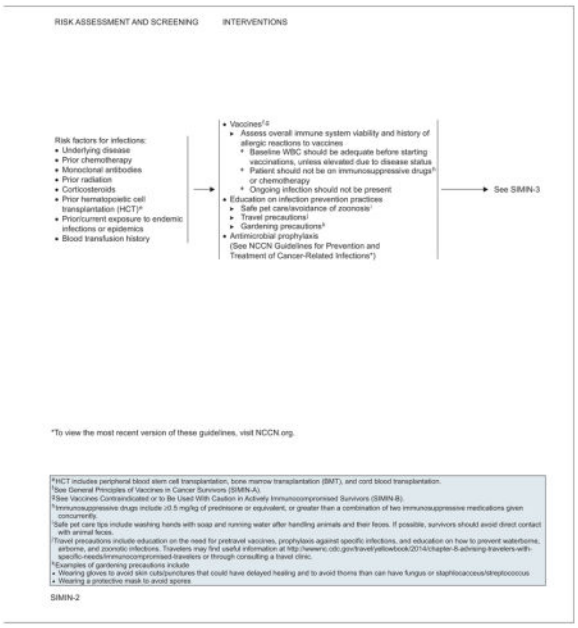

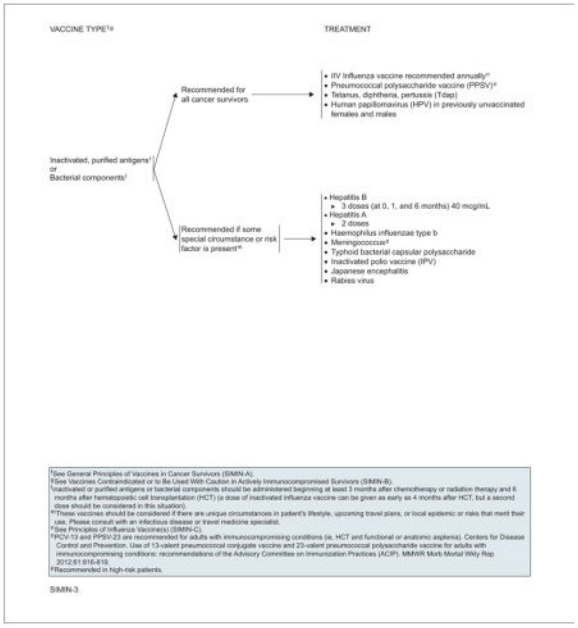

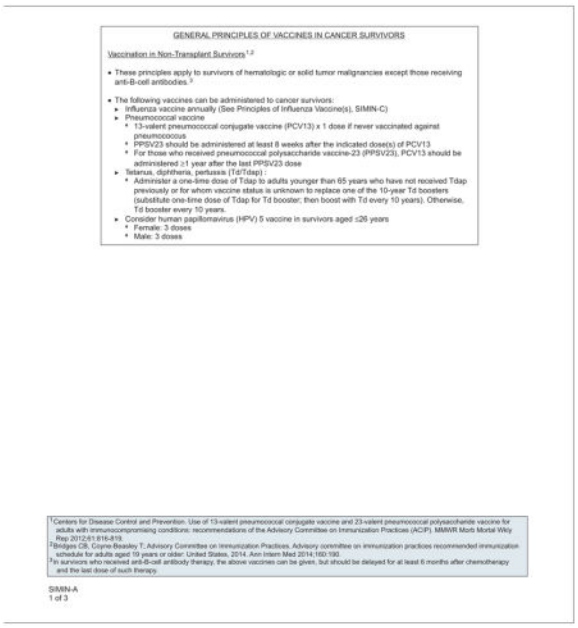

GENERAL PRINCIPLES OF VACCINES IN CANCER SURVIVORS

Vaccination in Non-Transplant Survivors[1,2]

- These principles apply to survivors of hematologic or solid tumor malignancies except those receiving anti-B-cell antibodies.[3]
- The following vaccines can be administered to cancer survivors:
  - Influenza vaccine annually (See Principles of Influenza Vaccine(s), SIMIN-C)
  - Pneumococcal vaccine
    - 13-valent pneumococcal conjugate vaccine (PCV13) x 1 dose if never vaccinated against pneumococcus
    - PPSV23 should be administered at least 8 weeks after the indicated dose(s) of PCV13
    - For those who received pneumococcal polysaccharide vaccine-23 (PPSV23), PCV13 should be administered ≥1 year after the last PPSV23 dose
  - Tetanus, diphtheria, pertussis (Td/Tdap) :
    - Administer a one-time dose of Tdap to adults younger than 65 years who have not received Tdap previously or for whom vaccine status is unknown to replace one of the 10-year Td boosters (substitute one-time dose of Tdap for Td booster; then boost with Td every 10 years). Otherwise, Td booster every 10 years.
  - Consider human papillomavirus (HPV) 5 vaccine in survivors aged ≤26 years
    - Female: 3 doses
    - Male: 3 doses

[1] Centers for Disease Control and Prevention. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2012;61:816-819.
[2] Bridges CB, Coyne-Beasley T; Advisory Committee on Immunization Practices. Advisory committee on immunization practices recommended immunization schedule for adults aged 19 years or older: United States, 2014. Ann Intern Med 2014;160:190.
[3] In survivors who received anti-B-cell antibody therapy, the above vaccines can be given, but should be delayed for at least 6 months after chemotherapy and the last dose of such therapy.

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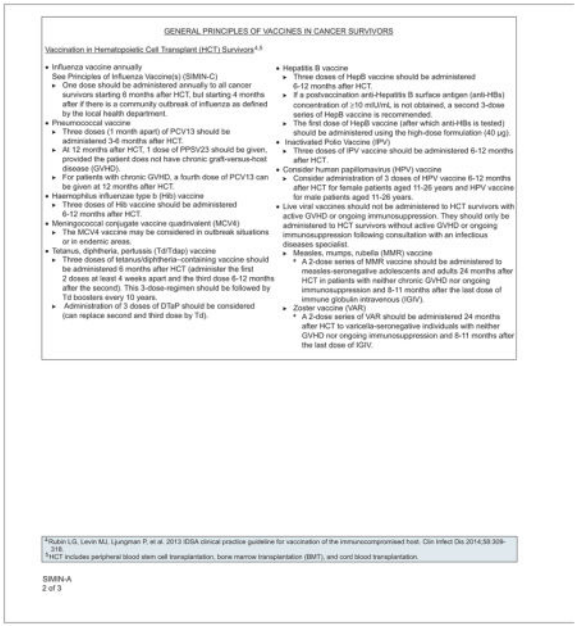

GENERAL PRINCIPLES OF VACCINES IN CANCER SURVIVORS

Vaccination in Hematopoietic Cell Transplant (HCT) Survivors[4,5]

- Influenza vaccine annually
  See Principles of Influenza Vaccine(s) (SIMIN-C)
  - One dose should be administered annually to all cancer survivors starting 6 months after HCT, but starting 4 months after if there is a community outbreak of influenza as defined by the local health department.
- Pneumococcal vaccine
  - Three doses (1 month apart) of PCV13 should be administered 3-6 months after HCT.
  - At 12 months after HCT, 1 dose of PPSV23 should be given, provided the patient does not have chronic graft-versus-host disease (GVHD).
  - For patients with chronic GVHD, a fourth dose of PCV13 can be given at 12 months after HCT.
- Haemophilus influenzae type b (Hib) vaccine
  - Three doses of Hib vaccine should be administered 6-12 months after HCT.
- Meningococcal conjugate vaccine quadrivalent (MCV4)
  - The MCV4 vaccine may be considered in outbreak situations or in endemic areas.
- Tetanus, diphtheria, pertussis (Td/Tdap) vaccine
  - Three doses of tetanus/diphtheria–containing vaccine should be administered 6 months after HCT (administer the first 2 doses at least 4 weeks apart and the third dose 6-12 months after the second). This 3-dose-regimen should be followed by Td boosters every 10 years.
  - Administration of 3 doses of DTaP should be considered (can replace second and third dose by Td).
- Hepatitis B vaccine
  - Three doses of HepB vaccine should be administered 6-12 months after HCT.
  - If a postvaccination anti-Hepatitis B surface antigen (anti-HBs) concentration of ≥10 mIU/mL is not obtained, a second 3-dose series of HepB vaccine is recommended.
  - The first dose of HepB vaccine (after which anti-HBs is tested) should be administered using the high-dose formulation (40 μg).
- Inactivated Polio Vaccine (IPV)
  - Three doses of IPV vaccine should be administered 6-12 months after HCT.
- Consider human papillomavirus (HPV) vaccine
  - Consider administration of 3 doses of HPV vaccine 6-12 months after HCT for female patients aged 11-26 years and HPV vaccine for male patients aged 11-26 years.
- Live viral vaccines should not be administered to HCT survivors with active GVHD or ongoing immunosuppression. They should only be administered to HCT survivors without active GVHD or ongoing immunosuppression following consultation with an infectious diseases specialist.
  - Measles, mumps, rubella (MMR) vaccine
    - A 2-dose series of MMR vaccine should be administered to measles-seronegative adolescents and adults 24 months after HCT in patients with neither chronic GVHD nor ongoing immunosuppression and 8-11 months after the last dose of immune globulin intravenous (IGIV).
  - Zoster vaccine (VAR)
    - A 2-dose series of VAR should be administered 24 months after HCT to varicella-seronegative individuals with neither GVHD nor ongoing immunosuppression and 5-11 months after the last dose of IGIV.

[4] Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:309-318.
[5] HCT includes peripheral blood stem cell transplantation, bone marrow transplantation (BMT), and cord blood transplantation.

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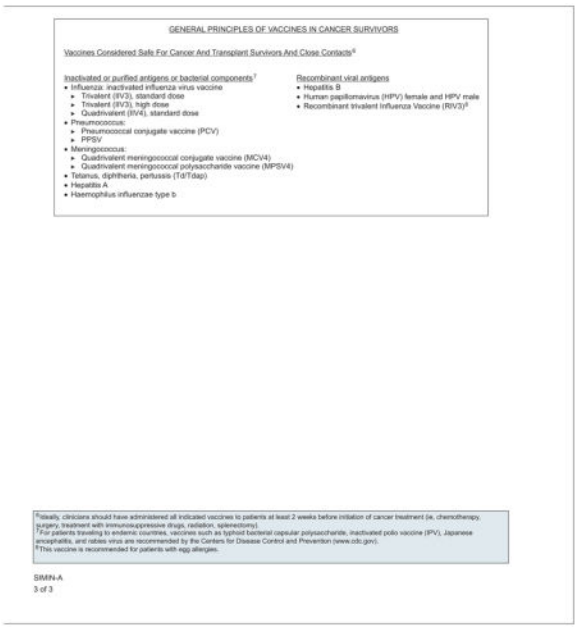

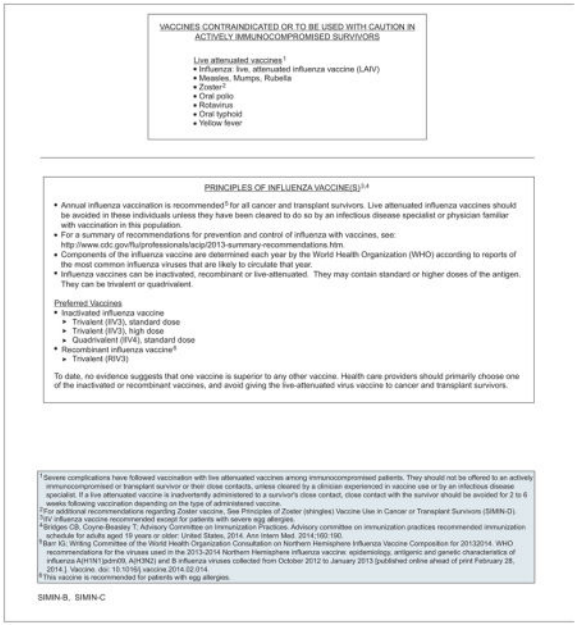

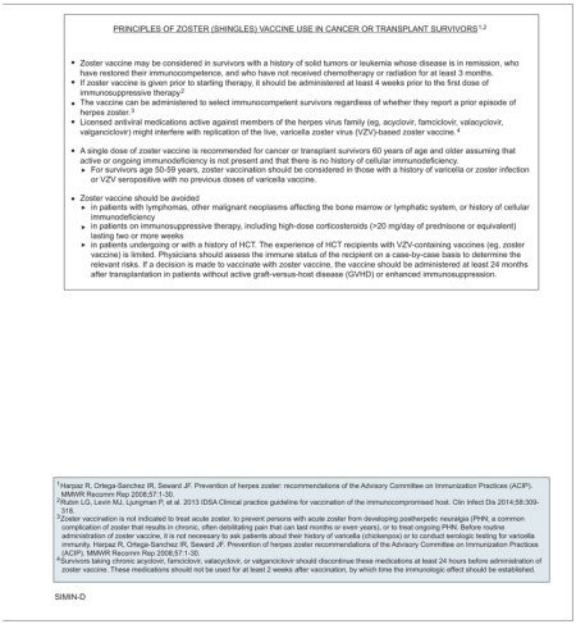

Interventions for Prevention of Infections

Infection in survivors can be prevented by education, antimicrobial prophylaxis, and the judicious use of vaccines.

Antimicrobial Prophylaxis and Education

Survivors should be educated about safe pet care/the avoidance of zoonosis, travel precautions, and gardening precautions.[8–13] Safe pet care tips include washing hands with soap and running water after handling animals and their feces. If possible, survivors should avoid direct contact with animal feces. Travel precautions include education on the need for pretravel vaccines, prophylaxis against specific infections, and education on how to prevent waterborne, airborne, and zoonotic infections. Travelers may find useful information at http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-8-advising-travelers-with-specific-needs/immunocompromised-travelers or through consulting a travel clinic. Gardening precautions include wearing gloves to avoid cuts and punctures that could be delayed in healing or could become infected with fungus or staphylococcus/streptococcus that may be present on thorns, and wearing a protective mask to avoid inhalation of spores.

For information regarding antimicrobial prophylaxis, please see the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Prevention and Treatment of Cancer-Related Infections (to view the most recent version of these guidelines, visit NCCN.org).

Immunizations

Vaccination, or “active immunization,” involves administration of all or part of a microorganism or a modified product of a microorganism (eg, a toxoid, a purified antigen, or an antigen produced by genetic engineering) to produce an immunologic response that mimics that of natural infection but usually presents little or no risk to the recipient. The use of vaccines that do not contain live organisms should be considered and encouraged in all

cancer and transplant survivors who have completed therapy at least 3 months before the planned vaccine administration. In general, the usual doses and schedules are recommended, as outlined by the Advisory Committee on Immunization Practices.[14,15] The Infectious Diseases Society of America has outlined guidance for vaccination in immunocompromised patients, including those with cancer and those post-HCT.[16] The NCCN Survivorship Panel outlined immunization guidelines specific to survivors of hematologic malignancies and solid tumors, with separate guidelines for survivors who received HCT. In survivors who received anti–B-cell antibody therapy, vaccination should be delayed for at least 6 months after chemotherapy or the last dose of such therapy to allow for reconstitution of the B-cell population. More details are available in the guidelines (NCCN.org).

Before vaccination, immune system viability and history of allergic reactions to vaccines should be assessed. Baseline WBC counts should be in the normal range or within reasonable limits before starting vaccinations, unless they are elevated because of disease status. The survivor should not be on immunosuppressive drugs or chemotherapy, and ongoing infection should not be present.

The following vaccines should be considered and encouraged for all survivors, administered according to the usual doses and schedules: influenza vaccine (only inactivated or recombinant); pneumococcal vaccine (PPSV-23/PCV-13); tetanus, diphtheria, pertussis (Tdap); and HPV (in survivors aged ≤26 years).[17–19] These vaccines do not contain live organisms; instead they contain inactivated organisms, purified antigens, bacterial components, or genetically engineered recombinant antigens. The effectiveness of these vaccinations might be suboptimal because of lingering immune suppression.[7] However, in the absence of known harm, their administration may be worthwhile with the hope of achieving some protection.

Other vaccines, as listed in the guidelines, should be considered in consultation with an infectious disease or travel medicine specialist if unique circumstances in the survivor's lifestyle, upcoming travel, or local epidemic/risks merit their use.

Influenza Vaccines—Annual influenza vaccination is recommended for all cancer and transplant survivors. Live attenuated influenza vaccines should generally be avoided in this population. Preferred vaccines include inactivated influenza vaccines (ie, trivalent [IIV3] standard-dose, trivalent [IIV3] high-dose, and quadrivalent [IIV4] standard-dose) or, for individuals with egg allergies, recombinant influenza vaccine (ie, trivalent [RIV3]).[15,20] To date, no evidence shows superiority of any one of these vaccines.

Live Viral Vaccines—Vaccines that contain live attenuated organisms (eg, live-attenuated influenza vaccine; MMR; oral polio vaccine [OPV]) are contraindicated in actively immunocompromised survivors because of a proven or theoretical increased risk of disease and prolonged shedding from the live organism present in the vaccine. They should not be offered to actively immunocompromised survivors unless cleared by a clinician experienced in vaccine use or by an infectious disease specialist. However, live viral vaccines can be administered to immunocompetent survivors 3 or more months after treatment, but consultation with an infectious disease specialist or clinician familiar with vaccination in

patients with cancer is recommended. An exception is the live-attenuated influenza vaccine, which should be avoided in survivors because safer alternatives exist (see earlier discussion).

Healthy immunocompetent individuals who live in a household with immunocompromised survivors can receive the following live vaccines: MMR, rotavirus vaccine in infants aged 2 to 7 months, varicella vaccine (VAR), and zoster vaccine. However, OPV should not be administered to individuals who live in a household with immunocompromised survivors. Highly immunocompromised survivors should avoid handling diapers of infants who have received the rotavirus vaccine for 4 weeks after vaccination. Immunocompromised survivors should avoid contact with persons who develop skin lesions after receipt of VAR or zoster vaccine until the lesions clear.

Zoster (Shingles) Vaccine—A single dose of zoster (shingles) vaccine is recommended for survivors aged 60 years or older without active or ongoing immunodeficiency, no history of cellular immunodeficiency or HCT, or who have not received chemotherapy or radiation within the past 3 months, and it can be given at least 4 weeks before initiation of chemotherapy or immunosuppressive drugs.[16,21,22] Zoster vaccination should also be considered for survivors aged 50 to 59 years with a history of varicella or zoster infection (VZV) or VZV seropositivity with no previous doses of varicella vaccine. The zoster vaccine should be avoided in immunocompromised survivors, but can be considered in transplant survivors without active graft-versus-host disease or enhanced immunosuppression 24 or more months after transplantation.

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