Chapter 31
Immunizations

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Overview

Vaccines have played a vital role in preventing infections within our society. Because of immunizations, common life-threatening infections, such as polio, smallpox, measles, mumps, and rubella, are now rarely seen in modern society. For individuals with primary immunodeficiency diseases (PI), vaccination remains an important defense against infections. Most people with PI are able to make normal responses to vaccines, and immunizations will help to protect them against infections that could be dangerous in the setting of their PI.

Immunizations are designed to produce immunologic memory so that the immune system can respond rapidly and neutralize an infection before it becomes harmful. In this process, routine vaccines are generally categorized into two types: nonviable and viable (live).

Nonviable vaccines can contain either fragments of microbes or whole microbes that have been fully inactivated. These vaccines cannot directly cause an infection. Examples include the immunizations against tetanus, diphtheria, whooping cough, Haemophilus influenzae (Hib), pneumococcus, and influenza (the injectable form of the vaccine).

Viable vaccines, on the other hand, contain weakened microbes that do not usually cause disease in healthy people. In individuals with various types of PI, however, these weakened microbes can sometimes cause significant illness. Examples of viable immunizations include the measles-mumps-rubella (MMR), oral poliovirus (OPV), rotavirus, yellow fever, intranasal influenza, the older zoster vaccine and chickenpox vaccines. The Bacille Calmette-Guerin (BCG) vaccine is another viable immunization that is not routinely used in North America. It is important to note that the OPV and BCG vaccines are contraindicated in most, if not all, types of PI. A new non-viable vaccine (Shingrix) for preventing shingles and the painful complications, such as postherpetic neuralgia, is available. It is not known how effective this vaccine is in people with PI. However, if the T cell function is mostly intact and the antibody immune deficiency is variable, such as in mild Common Variable Immune Deficiency (CVID), IgG Subclass Deficiency, or Selective Antibody Deficiency, etc., this vaccine may be of benefit.

Guidelines for Immunizations in People with PI

Because various types of PI can differ so vastly in terms of what part of the immune system is not working properly, decisions regarding the administration or withholding of various immunizations should always be made at the discretion of the clinical immunologist who is caring for the affected individual. Nonetheless, broad guidelines concerning immunizations in PI offer insights regarding what may be safe and beneficial. For the purposes of guidelines for immunizations, PI can generally be categorized into five broad groups. (See Table 31:1)

The first category consists of individuals with primary T cell defects and is subdivided into severe deficiency and mild deficiency. Severe Combined Immunodeficiency (SCID) and complete DiGeorge Anomaly fall into the severe classification, and all immunizations are contraindicated in affected children prior to correction of the PI by hematopoietic stem cell or thymic transplantation. Persons with mild or partial T cell deficiency, on the other hand, should receive all nonviable immunizations, although some may not be fully effective. Viable immunizations can be given, depending upon the degree of T cell deficiency, and special care should be exercised concerning administration of the chickenpox, herpes zoster, and MMR vaccines.

The second category includes people with primary B cell defects. It is further divided into severe deficiency and mild deficiency. X-linked Agammaglobulinemia (XLA) and Common Variable Immune Deficiency (CVID) are examples

of conditions that fall into the severe category, whereas IgA Deficiency and Specific Antibody Deficiency and Specific Antibody Deficiency serve as examples of mild B cell deficiencies. Children and adults with severe B cell defects cannot make antibodies to vaccines and will usually be receiving immunoglobulin (Ig) replacement therapy. Use of nonviable immunizations is therefore safe but may not be helpful, unless induction of T cell immunity is desired. Annual nonviable influenza immunization is recommended for that reason. Very little data is available to guide decisions to administer or withhold viable vaccines despite overall recommendations to avoid them. **It should be noted that antibodies in Ig replacement therapy can neutralize any immunizations, rendering them less effective.** For mild B cell defects, all immunizations can usually be given safely, although some may be less effective. In some individuals, healthcare providers may measure antibody titers to determine whether certain vaccines are necessary or likely to be helpful. For people with concerns about infections by bacteria covered with polysaccharides, combined testing is recommended for protective levels of antibodies to both the nonviable 23-valent polysaccharide pneumococcal vaccine and the nonviable Salmonella typhi polysaccharide Vi vaccine. All parties should be aware that different laboratories may measure the pneumococcal antibody titers differently, and results must therefore be interpreted cautiously. Children and adults who have difficulty making antibodies to polysaccharide vaccines should be administered the corresponding protein-conjugated forms of the immunizations, if available. The safety of rotavirus immunization has not been studied in this population, and administration of the OPV and BCG vaccines is contraindicated.

The third category encompasses individuals with phagocytic cell defects. Examples include Chronic Granulomatous Disease (CGD), Leukocyte Adhesion Deficiency (LAD), and Chediak-Higashi syndrome (CHS). Nonviable vaccines can be given safely in these conditions. Immunizations containing viable bacteria are contraindicated. The decision to use viable viral vaccines will depend upon the specific disease. For instance, individuals with CGD should receive viable viral immunizations, but certain viable viral immunizations may not be safe for individuals with LAD or CHS.

The fourth category involves persons with complement deficiency. Nonviable immunizations are recommended and may need to be administered more frequently than usual (every 3 to 5 years). A few viable vaccines are not recommended, but most viable immunizations can be given safely.

The final category consists of individuals with other defects in innate immunity. Nonviable vaccines can be given safely, although in some of these conditions, they may not be effective. Meanwhile, the safety and efficacy of viable immunizations will depend upon the specific condition and must be approached on an individual basis.

Importance of Immunization of Close Contacts

Of utmost importance, all close contacts surrounding individuals with, including household members, family members, and caretakers, should be immunized fully and regularly. They should be given all of the nonviable immunizations, especially the injectable influenza vaccine, in accordance with recommended schedules. Even viable immunizations (with the exception of viable influenza in individuals close to someone with SCID and OPV in all PI situations) should be kept updated. If signs of infection, such as skin blisters following chickenpox vaccination, appear in a close contact after immunization, the individual with PI may need to be temporarily isolated away from the contact and assessed by a healthcare provider. Nevertheless, this practice of immunizing close contacts protects the child or adult who has PI by decreasing the likelihood that they will become exposed to the microbes that cause disease in the community which can cause severe illness in the individual with PI.

Summary

Immunizations are strongly recommended and encouraged for the protection of people with PI. Nonviable immunizations cannot directly cause infections in any person. With a proper understanding of the type of PI an individual has, viable vaccines can be appropriately administered or withheld, depending upon the situation. Thus, most affected children and adults can be safely vaccinated. Lastly, immunization of people surrounding individuals with PI must be promoted and practiced to minimize their risk for infections.

Expert Recommendations for Common Immunizations in Patients with PI

Table 31:1

Vaccine	Primary defect						
	T cell function		B cell function		Phagocytic function	Complement	Other innate immune function
	Severe	Mild	Severe	Mild			
Nonviable immunizations							
Hepatitis B (HepB)	N	Y	N	Y	Y	Y	Y
Diphtheria, tetanus, acellular pertussis (DTaP)	N	Y	N	Y	Y	Y	Y
Haemophilus influenzae, type B (Hib)	N	Y	N	Y	Y	Y	Y
Pneumococcal conjugate (PCV13)	N	Y	N	Y	Y	Y	Y
Inactivated poliovirus (IPV)	N	Y	N	Y	Y	Y	Y
Inactivated influenza (IIV)	N	Y	Y	Y	Y	Y	Y
Hepatitis A (HepA)	N	Y	N	Y	Y	Y	Y
Meningococcal (MenACWY)	N	Y	Y	Y	Y	Y	Y
Human papillomavirus (HPV)	N	Y	Y	Y	Y	Y	Y
Pneumococcal polysaccharide (PPSV23)	N	Y	N	Y	Y	Y	Y
Zoster recombinant (RZV)#	N	Y	N	Y	Y	Y	Y
Viable immunizations							
Rotavirus (RV)	N	N	N	Y	*	Y	*
Measles, mumps, rubella (MMR)	N	*	N	Y	*	Y	*
Varicella (VAR)	N	*	N	Y	*	Y	*
Attenuated influenza (LAIV)	N	N	N	N	N	N	*
Zoster live (ZVL)	N	*	N	Y	*	Y	*
Bacille Calmette-Guerin (BCG)	N	N	N	N	N	Y	*

Y = recommended, N (shaded boxes) = not recommended, * = recommendation depends upon the specific immunodeficiency, # - Shingrix zoster vaccine