- Infections in patients with primary immunodeficiency disorders (PID), which are now referred to as inborn errors of immunity (IEI), often result in excessive morbidity and mortality, and antimicrobial therapy may be less effective than in the unimpaired host.

- Therefore, prevention through vaccination is an important component of care for patients with these diseases.

- Vaccines containing killed micro-organisms, mRNA encoding proteins, or subcomponents of micro-organisms are safe for all immunocompromised patients and should be given if the patient has sufficient ability to generate an immune response.

- In contrast, vaccines containing live-attenuated viruses or bacteria may result in unchecked proliferation and disseminated disease and are contraindicated in many forms of IEI .

- **Combined immunodeficiencies**

- Patients with combined immunodeficiencies have impaired cellular (T cell) and humoral (B cell) immunity.

- All live vaccines (viral and bacterial) are contraindicated in severe and partial combined immunodeficiencies.

- Severe IEIs include severe combined immunodeficiency and complete DiGeorge syndrome (DGS).

- All live vaccines of any type are contraindicated in these disorders. Inactivated vaccines are unlikely to be effective and are largely irrelevant.

- Partial combined immunodeficiencies include Wiskott-Aldrich syndrome, ataxia-telangiectasia, and many others.

- All live vaccines are generally contraindicated in these disorders. Inactivated vaccines may be at least partially effective in some cases and can be administered.

- Vaccination in less severe DGS (most patients) is considered on a case-by-case basis.

- **Viral** - Live viral vaccines include:

- MMR
- Measles-mumps-rubella-varicella
- Oral poliovirus
- Live-attenuated influenza vaccine
- Yellow fever
- Varicella
- Herpes zoster
- Rotavirus
- Smallpox (vaccinia)
- Adenovirus (used predominantly in military personnel)

- **Bacterial —** Live bacterial vaccines include:
- BCG
- Oral Ty21a *Salmonella typhimurium*

- **Antibody deficiencies**
- Some live viral and bacterial vaccines are contraindicated in antibody deficiencies, depending upon the severity of antibody dysfunction.

- **Severe**
- Severe IEIs affecting B cell function (humoral immunity) include X-linked (or autosomal recessive) agammaglobulinemia and common variable immunodeficiency.
- These patients should not receive certain live vaccines, such as oral poliovirus (OPV), smallpox, live-attenuated influenza vaccine, yellow fever, or live oral typhoid vaccines.
- Other live vaccines, such as MMR or varicella, are not given, because patients on immune globulin therapy should have passive immunization.

- **Mild**
- Patients with milder antibody deficiencies, such as symptomatic immunoglobulin (Ig)A or IgG subclass deficiencies or specific antibody deficiency, should not receive the OPV, Bacille Calmette-Guérin (BCG), or yellow fever vaccines but can receive other live vaccines if they are not receiving IgG replacement.

- **Phagocyte defects**

- Phagocyte defects include congenital neutropenias, chronic granulomatous disease (CGD), leukocyte-adhesion deficiency, and myeloperoxidase deficiency.

- Patients with these disorders should not be given live **bacterial** vaccines .

- However, all can safely receive live viral vaccines with the exception of those with leukocyte-adhesion defects and cytotoxic granule defects, who may have some deficiency in viral responses as well.

- Influenza vaccine is strongly recommended for CGD, as influenza infection has an important association with severe secondary bacterial infections in these patients

- **Complement deficiencies and congenital asplenia**

- Patients with complement deficiencies have intact cellular and humoral immunity and can receive all live and inactivated vaccines.

- It is especially important to vaccinate these patients against *Neisseria meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*.

- Similarly, patients with congenital asplenia should be immunized against these encapsulated bacteria using protein-conjugated vaccines.

Innate immune defects

- In patients with defects in innate immunity, the specific susceptibilities seen with each disorder should guide vaccine use.

- Patients with innate immune defects that are associated with invasive bacterial infections should not be given live bacterial vaccines, such as the *Salmonella* vaccine.

- Examples of these disorders include defects in the interleukin (IL)-12-interferon (IFN)-gamma axis, nuclear factor (NF)-kappa-B essential modulator (NEMO) deficiency, and GATA2 deficiency.

- Patients with innate immune defects associated with severe viral infections (defects in type 1 interferon signaling, such as signal transducer and activator of transcription 1 deficiency) should not receive live viral vaccines.

- Patients who have increased susceptibility to mycobacterial infections (all the disorders mentioned above) should not be given the BCG vaccine.

- All live viral and bacterial vaccines are contraindicated in disorders of the NF-kappa-B pathway that present as a combined immunodeficiency.

Asplenic patients

- Vaccine recommendations for children with impaired splenic function vary with patient age and vaccine history.

Children ≥2 years old

- **Pneumococcal vaccination**

- Two types of pneumococcal vaccination are recommended for children ≥2 years old with impaired splenic function in the United States: PCV13 (Prevnar) and PPSV23 (Pneumovax).

- For children ≥2 years old who are up to date on age-appropriate pneumococcal vaccinations (have received the full four-dose series of PCV13 before age 2), we give a single dose of PPSV23.

- We revaccinate with PPSV23 every five to seven years thereafter.

- For children ≥2 to 5 who did not complete the PCV13 series, give an additional one or two doses of PCV13 depending on the number of PCV13 doses previously received .

- Following receipt of the appropriate number of doses, vaccinate with PPSV23 ≥8 weeks after the last PCV13 dose.
- revaccinate with PPSV23 every five years thereafter.

- For children ≥6 years old who have not completed the PCV13 series or never received PCV13, give one dose of PCV13 followed by PPSV23 ≥8 weeks later .

- revaccinate with PPSV23 every five to seven years thereafter.

- ***H. influenzae* type b vaccination**
- Vaccination against Hib is recommended prior to splenectomy or for patients with established asplenia or hyposplenism.

- For children who have completed the routinely recommended primary Hib vaccine series, additional vaccination is not needed.

- For children ≥2 years who have not been vaccinated against Hib or who have not completed the full vaccine series or if vaccination status is unknown, give one or two doses of Hib depending on the child's age and previous Hib vaccination history .

- Revaccination is not needed for Hib.

- **Meningococcal vaccination**

- Two types of meningococcal vaccinations are recommended for children with impaired splenic function:

- A quadrivalent meningococcal conjugate vaccine that protects against meningococcal serotypes A, C, W, and Y (MenACWY; Menactra, Menveo, or MenQuadfi) and a univalent serogroup B vaccine (MenB-4C [Bexsero] or MenB-FHbp [Trumenba]).

- For children ≥2 years old who have not been vaccinated against *N. meningitidis*, we give a quadrivalent MenACWY vaccine. These vaccines are given as a two-dose series spaced at least eight weeks apart.

- Menveo and MenQuadfi can be given at the same time as PCV13.

- By contrast, Menactra must be given four weeks after PCV13 because Menactra may interfere with the protection conferred by pneumococcal conjugate vaccines. Revaccination is required; revaccinations vary by age.

- For children ≥10 years old, we also give one of the serogroup B vaccines, either Bexsero (two doses spaced at least one month apart) or Trumenba (three doses at 0, 1 to 2, and 6 months). Revaccination is also required for the serogroup B vaccine.

- **Seasonal influenza vaccination**

- We recommend that all asplenic or hyposplenic children ≥6 months old be vaccinated against seasonal influenza annually.

- Although live attenuated vaccines can be safely given to patients with impaired splenic function, the inactivated influenza vaccine is preferred over the live formulation because it is equally effective and available.

- Children over age 9 require only one influenza vaccination regardless of their vaccination history.

- Younger children (over six months of age) require two doses of influenza vaccine at least four weeks apart when they initiate seasonal influenza immunization, with annual single doses thereafter.

- **Timing of vaccination**

- The optimal timing of vaccination varies with the cause of impaired splenic function, the urgency of splenectomy (when performed), and the need for concurrent immunosuppressive treatment.

- For patients with nonsurgical asplenia or hyposplenism (impaired splenic function due to sickle cell disease or other medical condition), vaccine series should be started as soon as impaired splenic function is recognized.

- For patients undergoing elective splenectomy, vaccinations should ideally be started approximately 10 to 12 weeks prior to surgery so that the recommended vaccine series can be completed at least 14 days prior to splenectomy.

- If all recommended vaccine series cannot be completed in this time period, vaccine series can be resumed 14 days after splenectomy for most patients.

- For patients who will be receiving chemotherapy or other immunosuppressive treatment following splenectomy, vaccinations are usually resumed approximately three months after that treatment .

- For patients undergoing emergency splenectomy, vaccine series should be started 14 days after splenectomy.
- If vaccinations were given prior to postoperative day 14, it is reasonable to repeat these vaccinations eight weeks after the initial doses were given.

- Several small studies illustrate that patients probably develop adequate antibody responses to vaccination when vaccines are given approximately 14 days following the removal of the spleen.

- In a small randomized trial, functional antibody responses appeared to be greatest in patients vaccinated at day 14 post-splenectomy when compared with those vaccinated at earlier time points.

- Functional antibody responses on day 14 neared those of healthy controls but were not equivalent.

- In a subsequent small randomized trial, no significant difference in antibody responses to PPSV23 were detected between patients vaccinated at day 14 post-splenectomy versus those vaccinated at day 28.