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Special Article

Vaccination in patients with inborn errors of immunity or receiving immunosuppressive or biologic therapy: joint recommendations of the Brazilian Association of Allergy and Immunology and the Brazilian Immunization Society

Vacinação em pacientes com erros inatos da imunidade ou em uso de imunossupressores ou imunobiológicos: recomendações conjuntas da Associação Brasileira de Alergia e Imunologia e da Sociedade Brasileira de Imunizações

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ABSTRACT

Patients with inborn errors of immunity or receiving immunosuppressive or biologic therapy are at high risk of developing severe infections, including those preventable by vaccines. Adequate immunization is an essential strategy to mitigate this risk and must be adapted according to the underlying condition and according to the patient's degree of immunosuppression. This article reviews the available scientific evidence and best practices regarding vaccination in immunocompromised patients, providing guidance to optimize immunization in this population, with a focus on recommendations adapted to the Brazilian context. The recommendations are organized according to the types of inborn errors of immunity and the immunosuppressive or biologic therapy used. Implementing these guidelines can significantly improve the quality of care for these patients and reduce the burden of preventable infectious diseases.

Keywords: Immunosuppression, immunodeficiency, immunity, immunocompromised host, vaccination, vaccines.

RESUMO

Pacientes com erros inatos da imunidade ou em uso de imunossupressores ou imunobiológicos estão sob maior risco de infecções graves, incluindo aquelas preveníveis por vacinas. A imunização adequada é uma estratégia essencial para mitigar esse risco, e deve ser adaptada conforme a doença subjacente e o grau de imunossupressão de cada paciente. Este artigo revisa as evidências científicas disponíveis e melhores práticas relacionadas à vacinação de pacientes imunocomprometidos, oferecendo orientações para otimizar a imunização nessa população, com foco em recomendações adaptadas ao contexto brasileiro. As recomendações são organizadas com base nos tipos de erros inatos da imunidade e tratamentos imunossupressores ou imunobiológicos utilizados. A implementação dessas orientações pode melhorar significativamente a qualidade do cuidado a esses pacientes, reduzindo a carga de doenças infecciosas preveníveis.

Descritores: Imunossupressão, imunodeficiência, imunidade, imunocomprometimento, vacinação, vacinas.

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Introduction

Patients with inborn errors of immunity or receiving immunosuppressive therapy are at increased risk of infections,[1] including vaccine-preventable ones. These individuals experience both higher attack rates and an elevated likelihood of developing complications or severe forms of various diseases.[2,3]

Preventing infections through vaccination against common pathogens is an essential strategy in the management of this patient population.[4] Therefore, enhanced vaccination approaches are required, involving not only the administration of additional booster doses1 but also, in some cases, caution with certain vaccines, particularly live attenuated vaccines.[5-8]

While immunocompromised individuals require vaccine recommendations tailored to their specific conditions, vaccination coverage in this group is generally lower than in the general population.[9,10] In this context, this article reviews the available evidence and provides recommendations that may increase vaccination coverage and mitigate the risk of severe infections in patients with inborn errors of immunity or receiving immunosuppressive or biologic therapy.

Methods

The evidence and recommendations presented in this study were based on published data available to date and adapted to the Brazilian context. A non-systematic literature review was conducted between June and July 2024 using the MEDLINE database to identify articles addressing different aspects of immunization in immunocompromised patients. These aspects included the immunization of individuals with inborn errors of immunity, such as predominantly antibody deficiencies, immune dysregulation, autoinflammatory diseases, combined immunodeficiencies, and conditions associated with defects in innate immunity. In addition, the review included studies on immunization in patients receiving biologic therapy, immunosuppressants, and small molecules.

The collected evidence was discussed during the "1st Immunization Forum for Allergic and Immunocompromised Patients," held on August 9, 2024, in São Paulo, Brazil. The recommendations were agreed on by consensus among participating experts, all of whom are members of the Brazilian Association of Allergy and Immunology (ASBAI) and the Brazilian Immunization Society (SBIm).

General principles

General principle No. 1: Vaccines are based on different platforms

There are 6 major vaccine platforms (Table 1): (1) inactivated vaccines; (2) live attenuated viral or bacterial vaccines; (3) vaccines based on pathogen components (such as subunit, recombinant, polysaccharide, conjugate, or virus-like particle vaccines); (4) toxoid vaccines; (5) viral vector vaccines; and (6) nucleic acid-based vaccines (DNA or messenger RNA).

Table 1
Vaccine platform technologies

Type of vaccine	Examples
Inactivated	Hepatitis A and inactivated poliovirus vaccine
Live attenuated viruses or bacteria	BCG, measles, mumps, rubella, rotavirus, chickenpox, yellow fever, and dengue
Subunit, recombinant, virus-like particle, polysaccharide, or conjugate	*Haemophilus influenzae* type b, hepatitis B, human papillomavirus (HPV), pertussis, respiratory syncytial virus, pneumococcal conjugate and polysaccharide vaccines, meningococcal, recombinant herpes zoster, and influenza vaccines
Toxoids	Diphtheria, tetanus, and pertussis (acellular)
Viral vector	COVID-19
DNA or messenger RNA (mRNA)	COVID-19

General principle No. 2: Inactivated vaccines can be safely administered to immunocompromised individuals

Inactivated vaccines can generally be administered to immunocompromised patients when indicated, as the antigens contained in these vaccines cannot replicate and do not increase the risk of vaccine-related adverse events. However, the magnitude and duration of vaccine-induced immunity are often reduced.[11]

In complex cases, referral to a clinician with expertise in immunization and/or immunodeficiency is recommended.

General principle No. 3: Live viral or bacterial vaccines are contraindicated for most patients with severe immunosuppression

Individuals with severe immunosuppression (Table 2) or uncertain immune status should generally not receive live viral or bacterial vaccines.[12,13] In less severely immunocompromised individuals or those with specific or limited immune impairment, the benefits of routinely recommended live vaccines may outweigh the risks, as detailed in the following sections.

A patient-centered assessment should consider the degree and type of immunosuppression, as well as comorbidities and personal factors that may influence vaccine responses. Local epidemiology and risk exposure should also be considered. For example, if a patient lives in an area with a high incidence of a vaccine-preventable disease, immunization may be strongly recommended, even in the presence of some immune impairment, provided that the potential benefits justify vaccination.

General principle No. 4: Passive immunization should be used to reduce post-exposure risk

Passive immunization should be used, whenever possible, to reduce the likelihood of illness and complications from infectious diseases in immunocompromised patients with significant exposure. Examples include hyperimmune globulins for tetanus, rabies, varicella-zoster, and hepatitis B.

The following sections discuss vaccination strategies for specific groups of immunocompromised patients.

Table 2
Classification of immunosuppression in relation to vaccination decision according to CD4+ T-lymphocyte counts and age[12,13]

Degree of alteration immunological	CD4+ T-lymphocyte counts (cells/mm^3)			
	Age < 12 months	Age 1 to 5 years	Age 6 to 12 years	Age ≥ 13 years
Absent	> 1500 (> 25%)	> 1000 (> 25%)	≥ 500 (≥ 25%)	≥ 350
Moderate	740–1499 (15%–24%)	500–999 (15%–24%)	200–499 (15%–24%)	Between 200 and 350
Severe	< 750 (15%)	< 500 (15%)	< 200 (15%)	< 200

Inborn errors of immunity

Inborn errors of immunity are classified according to the immune system component that is primarily compromised. For the purposes of this document, inborn errors of immunity were organized into 5 major groups, each addressed with specific vaccination recommendations:

– Predominantly antibody deficiencies;
– Immune dysregulation disorders;
– Autoinflammatory diseases;
– Combined T- and B-cell immunodeficiencies;
– Defects in innate immunity.

Beyond their essential role in protecting against infectious diseases, vaccine responses in these patients can serve as a diagnostic tool for inborn errors of immunity. Post-vaccination antibody responses, particularly to tetanus and diphtheria toxoids, *Haemophilus influenzae* type b, and *Streptococcus pneumoniae*, are frequently used to assess immune system function.[14,15] Additionally, detection of antibodies to hepatitis A, hepatitis B, influenza virus, and isohemagglutinins may help identify immunoglobulin disorders.[15] However, it is important to emphasize that the use of vaccines for diagnostic purposes is not the primary focus of immunization in immunocompromised individuals. Accordingly, this document does not address the use of vaccines for diagnostic purposes.

Predominantly antibody deficiencies

Patients with predominantly antibody (B-cell) deficiencies exhibit increased susceptibility to bacterial infections, which typically occur in early childhood or after the third decade of life. Most infections are caused by encapsulated bacteria, such as *S. pneumoniae*, *H. influenzae* type b, and *Neisseria meningitidis*.[16] Accordingly, vaccines targeting *S. pneumoniae*, *H. influenzae* type b, and *N. meningitidis* are indicated in this group. For patients with defects of specific antibody production, vaccination remains the only means of conferring protection against seasonal influenza. Therefore, annual influenza vaccination is recommended for these individuals, even when they are receiving immunoglobulin therapy.[17-19]

Severe predominantly antibody deficiencies

Severe predominantly antibody deficiencies include common variable immunodeficiency

and agammaglobulinemia. These conditions are associated with severely impaired antibody responses, and affected individuals almost always receive immunoglobulin replacement therapy, which passively provides protective antibodies against several pathogens.[20] Inactivated influenza vaccine is an exception because (1) immunoglobulin preparations may not contain antibodies to circulating strains, and (2) the vaccine may elicit some beneficial cellular immune responses.[17,18]

Live vaccines, such as measles, mumps, and rubella (MMR) or varicella, are contraindicated in patients with severe antibody deficiencies due to the increased risk of vaccine-related disease associated with deficient antibody responses, as well as the possibility of vaccine neutralization by immunoglobulin therapy.[21] However, in scenarios of high epidemiological risk, such as measles or varicella outbreaks, these vaccines may be considered even for patients with severe antibody deficiencies, provided that cellular immunity is evaluated. If cellular responses are preserved, MMR or measles, mumps, rubella, and varicella (MMRV) vaccines may be considered. Such decisions must be individualized, taking into account immune status and the likelihood of exposure to these infections.

Other live virus vaccines, including yellow fever and dengue vaccines, are contraindicated in patients with predominantly antibody deficiencies associated with severe phenotypes.

Mild predominantly antibody deficiencies

Predominantly antibody deficiencies associated with milder phenotypes include selective IgA deficiency, specific antibody deficiency with normal immunoglobulin, and IgG subclass deficiency. Although vaccine-induced antibody responses may be reduced in these individuals, they often retain some degree of protective response and can generally be safely vaccinated with both live and inactivated vaccines, with few exceptions.

In patients with mild antibody deficiencies or other disorders, such as ataxia-telangiectasia, the response to pure polysaccharide pneumococcal vaccine is poor; however, pneumococcal conjugate vaccines are immunogenic and should be administered.[22]

Immune dysregulation disorders

Patients with adaptive immune dysregulation, such as those with familial hemophagocytic lymphohistiocytosis, autoimmune lymphoproliferative syndrome (ALPS) and its variants, frequently present hematologic complications, including cytopenias and neutropenia. Patients with Epstein-Barr virus susceptibility, inflammatory bowel disease, or endocrinopathies (such as APECED, IPEX, and their variants) may develop hypogammaglobulinemia.[23]

Although evidence is limited for many conditions within this group, vaccination in these patients must be assessed individually, taking into account the diversity and severity of clinical manifestations. In the presence of neutropenia or hypogammaglobulinemia, adherence to disease-specific immunization guidelines is essential. Inactivated and recombinant vaccines, such as those against *S. pneumoniae*, *H. influenzae* type b, *N. meningitidis*, and influenza, are generally safe and strongly recommended to prevent severe infections in patients with APECED and IPEX,[24,25] conditions that may be associated with hypogammaglobulinemia.

Regarding live attenuated vaccines, available data are insufficient for a clear recommendation. Their use should be considered on a case-by-case basis, taking into account ongoing immunosuppressive therapy and patient immune status.

Vaccination of household contacts should be encouraged, as it provides indirect protection and helps reduce exposure to infectious agents.

Autoinflammatory diseases (monogenic)

Patients with monogenic autoinflammatory diseases generally do not exhibit significant immune deficiency. However, in rare conditions, such as adenosine deaminase 2 deficiency-related myelodysplasia and sideroblastic anemia with B-cell immunodeficiency, periodic fevers, and developmental delay (SIFD) syndrome, immune impairment may occur.[26,27]

Overall, there are no specific contraindications to vaccination in these patients, except when they are receiving immunosuppressive therapy. In such cases, administration of live attenuated vaccines should be carefully evaluated, and inactivated or recombinant vaccines should be preferred whenever possible.

Vaccines particularly recommended for this group include those against *S. pneumoniae*, *H. influenzae* type b, *N. meningitidis*, and influenza. Vaccination of household contacts is also strongly recommended to provide indirect protection for these patients.

Combined humoral and cellular immunodeficiencies

Patients with combined immunodeficiencies exhibit impairment of both cellular (T-cell) and humoral (B-cell) immunity.[28] Combined T- and B-cell immunodeficiencies can be grouped into two categories: complete defects and partial defects.

Combined T- and B-cell immunodeficiencies — complete defects

Combined immunodeficiencies with complete defects include severe combined immunodeficiency (SCID) and complete DiGeorge syndrome. All live attenuated vaccines (viral or bacterial) may cause severe complications in these patients; therefore, all live vaccines are contraindicated in these conditions.[29] Vaccination against *S. pneumoniae* and *H. influenzae* type b is strongly recommended for patients with complete combined immunodeficiencies, as is the indication of monoclonal antibody prophylaxis against respiratory syncytial virus.[28,29] Inactivated vaccines do not pose safety concerns; however, they are likely to be ineffective, and given their uncertain benefit, they are sometimes not administered to these patients.[29]

Combined T- and B-cell immunodeficiencies — partial defects

Partial combined immunodeficiencies include Wiskott-Aldrich syndrome, ataxia-telangiectasia, and partial DiGeorge syndrome. Live attenuated vaccines are often contraindicated in these disorders.[29] Vaccination in less severe cases (most patients) should be considered on an individual basis. Depending on the immune response, classification of immunosuppression according to age-adjusted CD4+ T-lymphocyte counts (Table 2), and the local epidemiologic risk, certain live attenuated vaccines may be considered in vaccination decision-making (Table 3).

In partial combined immunodeficiencies, inactivated vaccines may be effective in some cases and can be administered. Strongly recommended vaccines for this group include those against *H. influenzae* type b, *S. pneumoniae*, *N. meningitidis*, hepatitis A and B, DTaP or DTwP, inactivated poliovirus, influenza, HPV, recombinant herpes zoster, and COVID-19.[29]

Table 3 summarizes vaccination recommendations for patients with combined immunodeficiencies.

Defects in innate immunity

Defects in innate immunity encompass a heterogeneous group of genetic disorders that impair the ability of the immune system to respond appropriately to infection. Common conditions in this category include phagocytic disorders, complement deficiencies, toll-like receptor deficiency, and natural killer (NK) cell deficiencies.

These disorders vary widely in severity and in their impact on an individual's ability to respond appropriately to infection. Early diagnostic evaluation is essential to guide effective therapeutic interventions, which may include antimicrobial or antifungal prophylaxis and, in more severe cases, hematopoietic stem cell transplant for immune reconstitution. In general, no clinical trial has specifically evaluated vaccination practices in patients with defects in innate immunity. Therefore, recommendations are based on clinical complications observed in these populations.

Phagocytic disorders

Phagocytic disorders include congenital neutropenias, leukocyte adhesion deficiencies, and defective oxidative burst (chronic granulomatous disease and G6PD deficiency).

Neutropenia is classified as mild (absolute neutrophil count of 1000-1500/μL), moderate (500-1000/μL), and severe (< 500/μL).[30] Mild or moderate neutropenia is not associated with impaired vaccine responses or increased risk of adverse events. Unless additional relevant phenotypes or comorbidities are present, vaccination policies for these patients should not differ from those for the general population.[31]

All inactivated vaccines can be safely administered to patients with severe neutropenia. Certain specific vaccines are strongly recommended because of the elevated risk of infection in children with this condition, especially those against *S. pneumoniae* and *N. meningitidis*. Seasonal influenza and hepatitis B vaccines are also important to prevent nosocomial infections.[13,30,32,33]

Live bacterial vaccines, such as BCG, are contraindicated in severe neutropenia due to the risk of complications.[31] In many countries, however, newborns receive BCG vaccine in the first days of life, before severe neutropenia is even suspected. Although BCG-related complications are rarely reported in infants later diagnosed with severe neutropenia,

Table 3
Vaccination recommendations for patients with combined immunodeficiencies

Condition	Recommended	Benefit and efficacy unlikely Safe to administer	Consider according to cellular response	Not recommended
Combined T- and B-cell immunodeficiencies: complete defects	Palivizumab or Nirsevimab	Meningococcal conjugate Meningococcal B Hepatitis A and B DTaP or DTwP Inactivated polio Influenza HPV 23-valent pneumococcal Recombinant herpes zoster COVID-19		BCG Rotavirus Yellow fever MMR Varicella Dengue
Combined T- and B-cell immunodeficiencies: partial defects	*Haemophilus influenzae* B Pneumococcal conjugate Meningococcal conjugate Meningococcal B Hepatitis A and B DTaP or DTwP Inactivated polio Influenza HPV 23-valent pneumococcal Recombinant herpes zoster COVID-19 Palivizumab or Nirsevimab		MMR Varicella Dengue Yellow fever	BCG Rotavirus

BCG = Bacillus Calmette-Guérin (tuberculosis vaccine); DTaP = combined diphtheria, tetanus, and (acellular) pertussis vaccine; DTwP = combined diphtheria, tetanus, and (whole-cell) pertussis vaccine; HPV = human papillomavirus.

the contraindication is extrapolated from findings in patients with phagocytic cell defects, considering the limited efficacy of the vaccine.[13,30,32,33] BCG is also contraindicated in chronic granulomatous disease and in defects of the interleukin (IL)-12/interferon-gamma axis, as these conditions impair phagocyte function and significantly increase the risk of severe post-vaccination complications.

Live virus vaccines are not contraindicated in patients with severe neutropenia, but assessment of cellular and/or adaptive immunity is essential before administration. A safe practice is to formally exclude

significant cell and/or antibody immunodeficiency before administering live virus vaccines to these patients.[31]

Patients with leukocyte adhesion deficiency or cytotoxic granule defects may have impaired antiviral responses[32,34,35] and, therefore, should not receive live virus vaccines.

Complement deficiencies

Patients with complement deficiencies retain intact humoral and cellular immunity and may receive all live and inactivated vaccines. Vaccination against encapsulated organisms, such as *N. meningitidis*, *S. pneumoniae*, and *H. influenzae* type b, is especially critical, including for those with partial complement deficiencies.[33,36,37] Recommended meningococcal vaccination schedules are described below.

Meningococcal ACWY vaccine

- *Children < 1 year of age:* 2 doses at 3 and 5 months of age; booster at 12-15 months of age; booster at 5 years of age; additional boosters every 5 years.
- *Children ≥ 1 year of age, adolescents, and adults:* 2 doses 2 months apart; boosters every 5 years.

Meningococcal B vaccine

- *Children ≤ 23 months of age:* 2 doses + booster.
- *Children ≥ 24 months of age:* 2 doses.
- *Adolescents and adults:* 2 doses 1-6 months apart (depending on the vaccine used).
- *All individuals up to 50 years of age (use beyond age 50 is off-label):* a booster 1 year after the primary series and every 2-3 years thereafter.

In hereditary angioedema, a rare genetic disorder that involves the deficiency or dysfunction of C1 esterase inhibitor, a regulator of complement, fibrinolytic, coagulation, and kallikrein-kinin systems, vaccination against hepatitis A and B is also recommended for all patients.[38] For this group of patients, other vaccines should follow routine immunization schedules.

Toll-like receptor and natural killer cell deficiencies

Currently, there are no studies specifically guiding or contraindicating vaccination in patients with these deficiencies. Therefore, vaccines should follow routine immunization schedules.

Table 4 summarizes vaccination recommendations for patients with innate immune defects.

Patients who are candidates for or receiving immunosuppressive or biologic therapy

As part of the therapeutic arsenal against various immune-mediated diseases, an increasing number of individuals receive immunosuppressive agents, such as corticosteroids, 6-mercaptopurine, azathioprine, methotrexate, cyclosporine, tacrolimus, and mycophenolate mofetil. Small molecule drugs such as JAK inhibitors, as well as biologic agents including monoclonal antibodies, are also widely used in the management of immune-mediated conditions. While essential for disease control, these treatments can increase the risk of both common and opportunistic infections.[39-42] In addition, immunosuppressive drugs may negatively affect vaccine responses in certain populations.[43,44]

Non-biologic immunosuppressive agents

For patients who are candidates for or currently receiving non-biologic immunosuppressive therapy, vaccination should follow specific guidelines to ensure immunization efficacy and safety. The goal is to minimize the risk of vaccine-preventable infections while accounting for treatment-related immune impairment.

Inactivated vaccines are often safe and recommended for patients receiving immunosuppressive therapy. Ideally, they should be administered at least 2 weeks before initiating immunosuppression to allow for an adequate immune response.

When immunosuppressive therapy must be started urgently, completing the vaccination schedule beforehand may not be feasible. In such situations, inactivated vaccines may be administered during immunosuppression, provided that the first dose was given before therapy began. Studies show that, in patients receiving non-biologic immunosuppressants, the influenza vaccine remains effective, with 79% of patients achieving protective titers, compared with 98% in control groups.[45] Moreover, severe post-vaccination adverse events are not more common in patients receiving non-biologic immunosuppressive agents, supporting the safety of inactivated vaccines in this group of patients.[44] However, the optimal timing of vaccination may vary based on treatment planning. If a reduction in immunosuppressive dose is anticipated, it may be more effective to postpone

Table 4
Vaccination recommendations for patients with defects in innate immunity

Defect in innate immunity	Recommendation
Mild to moderate neutropenia	All vaccines can be safely administered
Severe neutropenia	Inactivated vaccines can be safely administered. Do not administer attenuated bacterial vaccines. Whenever possible, replace live attenuated virus vaccines with inactivated vaccines
Chronic granulomatous disease	Do not administer BCG or attenuated Salmonella typhi vaccines. All other vaccines can be safely administered
Defects of the interleukin-12/ interferon-gamma axis	Do not administer BCG or attenuated Salmonella typhi vaccines. All other vaccines can be safely administered
Leukocyte adhesion deficiency or cytotoxic granule defects	Do not administer live virus vaccines. All other vaccines can be safely administered
Complement deficiencies	Administer vaccines against encapsulated organisms for partial or complete deficiencies. In hereditary angioedema, vaccinate against hepatitis A and B. All other vaccines can be safely administered
Toll-like receptor deficiency	There are no known restrictions for vaccination; however, data on these cases are still limited
Natural killer cell deficiency	There are no known restrictions for vaccination; however, data on these cases are still limited

BCG = Bacillus Calmette-Guerin (tuberculosis vaccine).

vaccination to that period, when the immune response may be more robust.

Live attenuated vaccines, such as MMR, varicella, yellow fever, and dengue vaccines, should be used with caution. Ideally, these vaccines should be administered 4 weeks before the start of immunosuppression; if this is not possible, a minimum interval of 2 weeks may be considered, since vaccine-induced viremia typically occurs within this period. For patients already receiving immunosuppressive therapy, live attenuated vaccines are often contraindicated due to the risk of infection from the attenuated strain. In settings of high epidemiological risk, individualized risk-benefit assessment is warranted.

In planning vaccination, priority should be given to annual influenza vaccination (high-dose for adults > 60 years of age), respiratory syncytial virus vaccine, pneumococcal conjugate vaccine (PCV13, PCV15, or PCV20), followed by the 23-valent pneumococcal polysaccharide vaccine (if PCV13 or PCV15 was used), and recombinant herpes zoster vaccine for adults > 18 years of age (2 doses, 4 weeks apart). Live vaccines, such as yellow fever, MMR, and dengue vaccines (2 doses, 3 months apart), should be considered in light of the current epidemiological context. Table 5 provides minimum intervals between different vaccine administrations.

After discontinuation of immunosuppressive therapy, specific safety intervals must be observed before administering live attenuated vaccines, as described below.

– Cyclosporine: 3 months.
– Glucocorticoids > 2 mg/kg/day for > 2 weeks in children, or > 20 mg/day for > 2 weeks in adults: 1 month.
– Methotrexate > 20 mg/week or > 0.4 mg/kg/week: 4 weeks. Lower doses may not require a minimum interval.

For infants born to mothers who received immunomodulators or biologic agents during the last 2 trimesters of pregnancy, BCG vaccination should be deferred until 6-12 months after the mother's last dose, owing to potential effects on neonatal immune function. Rotavirus vaccine, however, is not contraindicated in this group. Regarding early measles vaccination (zero-dose MMR or MR) or yellow fever vaccination at 9 months of age, available evidence is insufficient to determine safety in infants born to mothers who received immunomodulators or biologic agents during the last 2 trimesters of pregnancy. Decisions should therefore be individualized, considering the infant's immune status and local epidemiological risk.

Both attenuated and inactivated vaccines can be safely administered to infants breastfed by mothers receiving immunosuppressive corticosteroid therapy with methotrexate and cyclosporine. However, caution is advised with live attenuated vaccines in infants breastfed by mothers receiving cyclophosphamide due to its greater immunosuppressive potential.[44]

Ensuring that household contacts of patients receiving immunosuppressive therapy are fully vaccinated is essential, particularly for influenza, COVID-19, varicella (for susceptible individuals), MMR, and Tdap.

Monoclonal antibodies

The use of monoclonal antibodies and the development of immunization strategies require an integrated assessment of clinical efficacy parameters and safety profiles. While monoclonal antibodies offer targeted therapeutic approaches for specific conditions, immunization remains essential for the prevention of infectious diseases. However, factors such as individual immune response, potential adverse effects, duration of protection, and associated risks should be carefully evaluated in each case (Table 6).

Monoclonal antibodies consist of an innovative class of biologic agents designed to interact specifically with precise immune targets. Some monoclonal antibodies modulate T-helper type 2 (Th2)-mediated immune responses, which play a key role in the pathophysiology of several allergic and inflammatory diseases.[46]

Th2 responses are amplified by cytokines such as IL-4, IL-5, and IL-13, which promote eosinophil activation, stimulate IgE production, and drive characteristic allergic inflammation. These medications, belonging to the IgG class, exert their therapeutic action by directly blocking these inflammatory cytokines and have demonstrated efficacy in conditions such as asthma, chronic obstructive pulmonary disease, chronic rhinosinusitis with nasal polyposis, atopic dermatitis, prurigo nodularis, eosinophilic esophagitis, eosinophilic granulomatosis with polyangiitis, and hypereosinophilic syndrome.[46,47]

Biologic agents have become essential in managing Th2-mediated inflammatory conditions by providing targeted and effective therapeutic interventions. Examples include anti-IL-4/IL-13 therapy (dupilumab), anti-IL-5 therapy (mepolizumab), anti-IL-5 receptor-α treatment (benralizumab), and anti-IgE therapy (omalizumab). In addition to Th2-targeted monoclonal antibodies, agents that block IL-1, such as canakinumab (anti-IL-1β), have been developed for the treatment of autoinflammatory and rheumatologic diseases, whose pathophysiological process involves IL-1 overproduction.[48]

Another important example includes monoclonal antibodies targeting thymic stromal lymphopoietin (TSLP), such as tezepelumab, which acts on early inflammatory responses and is particularly effective in the treatment of severe asthma.[49] Additional biologic agents, such as infliximab and adalimumab, block tumor necrosis factor (anti-TNF) and are widely used in rheumatoid arthritis and inflammatory bowel disease.[50,51] Rituximab, which binds to CD20 on B cells, induces cell lysis through immunological mechanisms such as antibody-dependent cytotoxicity and apoptosis. This B cell depletion reduces antibody production and is effective in the treatment of autoimmune and hematological conditions, such as rheumatoid arthritis and lymphomas.

Eculizumab is a monoclonal antibody used in the treatment of autoimmune conditions and rare complement-driven diseases. It inhibits protein C5 and prevents its activation, which avoids membrane attack complex formation, thereby reducing inflammation

and tissue damage. It is indicated for conditions such as paroxysmal nocturnal hemoglobinuria, reducing premature erythrocyte destruction, and atypical hemolytic uremic syndrome, which causes renal injury and anemia due to uncontrolled activation of the complement system.[52]

Inactivated vaccines

Inactivated vaccines, including mRNA vaccines, conjugate vaccines, toxoid vaccines, and non-replicating viral vector vaccines, can be administered safely and effectively to patients receiving anti-IL-4, anti-IL-5, anti-IL-13, and anti-IgE therapies.

For other inactivated vaccines, specific safety considerations apply. Pneumococcal vaccination in patients treated with canakinumab (anti-IL-1β) has produced conflicting data regarding disease exacerbation and adverse events. One study found that patients with cryopyrin-associated periodic syndromes treated with canakinumab exhibited more frequent and more severe reactions to pneumococcal vaccines than to other inactivated vaccines.[53] In this cohort, 12 of 18 patients developed vaccine reactions (fever, swelling, erythema, pain), often within hours, lasting up to 3 weeks; most importantly, pneumococcal vaccination exacerbated disease in 2 patients. Therefore, the potential benefits of

Table 5
Minimum intervals between different vaccine administrations

Types of vaccines	Intervals	Example / Note
Inactivated and conjugate	Simultaneous or no minimum interval	Meningococcal ACWY and Influenza
Inactivated and injected attenuated	Simultaneous or no minimum interval	Hepatitis A and MMR or varicella and pneumococcus
Inactivated and oral attenuated	Simultaneous or no minimum interval	Meningococcal C and rotavirus
Between injected attenuated	They can often be administered on the same day; if not, a 30-day interval is recommended	Varicella and yellow fever
Yellow fever and MMR	Do not administer on the same day to children under 2 years of age (minimum 30-day interval)	
Qdenga® and injected attenuated	They can be administered on the same day	Qdenga® and yellow fever, both routine vaccinations at age 4 according to the Brazilian Society of Pediatrics
Pneumococcal conjugate (13v or 15v) and 23v pneumococcal	Between conjugate and 23v pneumococcal: 2 months. Between 23v pneumococcal and a pneumococcal conjugate: 12 months. Use of the 20-valent conjugate vaccine eliminates the need for the PPSV23	Always begin with a conjugate vaccine, which provides superior and longer-lasting response

MMR = measles, mumps, and rubella; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

Table 6
Vaccination guidelines for patients receiving monoclonal antibodies

Monoclonal antibody	Inactivated vaccines	Attenuated vaccines	Notes
Omalizumab	Administration at any time	It is suggested that the vaccine be administered 7 days after the first dose of the monoclonal antibody to avoid confusion between adverse events of each biologic agent	x
Dupilumab	Administration at any time	It is suggested that the vaccine be administered 7 days after the first dose of the monoclonal antibody to avoid confusion between adverse events of each biologic agent	x
Mepolizumab	Administration at any time	It is suggested that the vaccine be administered 7 days after the first dose of the monoclonal antibody to avoid confusion between adverse events of each biologic agent	x
Benralizumab	Administration at any time	It is suggested that the vaccine be administered 7 days after the first dose of the monoclonal antibody to avoid confusion between adverse events of each biologic agent	x
Tezepelumab	Administration at any time	No evidence currently supports its safety or efficacy during therapy – vaccination schedule should be completed 4 weeks prior	x
Rituximab	Ideally, complete the vaccination schedule 4 weeks prior. If not possible, postpone vaccination until the next cycle and wait 2 weeks after immunization to administer the medication	Discontinue medication for 6 months before or 4 weeks after vaccine administration	Reduced efficacy: influenza, pneumococcal, hepatitis A, and COVID-19
Anti-TNF[a]	Ideally, complete the vaccination schedule 4 weeks prior. If not possible, postpone vaccination until the next cycle and wait 2 weeks after immunization to administer the medication	Discontinue immunosuppressant for one dosing interval before vaccination and for 4 weeks after vaccine administration	Reduced efficacy: influenza (this vaccine can be administered at any time) pneumococcal, hepatitis A, and COVID-19
Canakinumab	They are safe during medication use, but there is no evidence regarding their efficacy – Complete the vaccination schedule 4 weeks prior	Discontinue immunosuppressant for one dosing interval before vaccination and for 4 weeks after vaccine administration	Caution regarding pneumococcal vaccine and exacerbation of cryopyrin-associated periodic syndrome
Eculizumab	Caution regarding exacerbation of underlying disease due to complement activation – efficacy may be impaired in meningococcal vaccines	Discontinue immunosuppressant for one dosing interval before vaccination and for 4 weeks after vaccine administration[b]	Complete the vaccination schedule 2 weeks prior – priority to meningococcal, *Haemophilus influenzae* type b, and pneumococcal vaccines

[a] Infants exposed to anti-TNF therapy in utero should receive rotavirus vaccine, while the BCG vaccine should be postponed for 6 to 12 months after the last dose of the medication during pregnancy.
[b] No data available in the literature.

immunization with the pneumococcal vaccine must be balanced against safety concerns. The study suggests that pneumococcal conjugate vaccines should be prioritized over the 23-valent polysaccharide vaccine (PPSV23).[53]

Special attention is also warranted regarding inactivated vaccine efficacy in patients receiving rituximab or anti-TNF therapies. Patients treated with anti-TNF show reduced immune responses to certain vaccines, including influenza, pneumococcal, hepatitis A, and COVID-19 vaccines.[54-56] Thus, vaccination should ideally be updated at least 4 weeks prior to initiating rituximab or anti-TNF therapy. If this is not possible, vaccination should be postponed until the next treatment cycle and the medication delayed for 2 weeks after immunization to optimize vaccine efficacy. Influenza vaccination may be administered at any time in patients receiving anti-TNF therapy due to the seasonal nature of the disease.[57]

Patients receiving eculizumab have increased susceptibility to *N. meningitidis* infection due to the drug's mechanism of action. Therefore, vaccination against *N. meningitidis*, covering serogroups A, C, W, Y, and B, is recommended at least 2 weeks before therapy initiation.[58] If treatment is initiated earlier, prophylactic antibiotics should be administered until 2 weeks after vaccination.[58] Patients aged < 18 years should also be vaccinated against *H. influenzae* type b and *S. pneumoniae* and must adhere strictly to age-appropriate national vaccination schedules. In patients treated with eculizumab, vaccination may activate complement.[58] Therefore, patients should be carefully monitored for exacerbation of underlying disease (hemolysis in paroxysmal nocturnal hemoglobinuria or thrombotic microangiopathy in atypical hemolytic uremic syndrome). Because vaccination may not confer complete protection against *N. meningitidis*, close surveillance is essential for early detection of signs of infection, with prompt treatment if necessary.[58]

Live attenuated vaccines

Live attenuated vaccines may be administered safely to patients receiving monoclonal antibodies targeting Th2 immune responses.[59] Regarding safety and efficacy, there are no contraindications for immunization in patients treated with anti-IL-4, anti-IL-5, anti-IL-13, or anti-IgE therapies.[60-64] In this group, vaccination should preferably occur 4 weeks before starting treatment. If this is not feasible, the interval between vaccination and the first antibody dose should be as long as possible (with a minimum of 7 days) to allow the identification, through temporal correlation, of whether any adverse reaction was caused by the vaccine or the monoclonal antibody, noting that monoclonal antibody-related reactions are rare but most likely occur after the first dose.

Tezepelumab targets TSLP, a cytokine central to early inflammatory signaling and both activation and amplification of multiple immune pathways. By inhibiting this inflammatory signaling from the outset, tezepelumab impacts various cells and mediators involved in the immune response. As a consequence, the immunosuppressive effect of tezepelumab may affect the immune system's ability to respond to the vaccine antigen. This early blockade hinders the assessment of the risks and benefits of administering live attenuated vaccines to patients undergoing anti-TSLP treatment, owing to limited robust and conclusive data on the safety and efficacy of immunization in this situation. Therefore, administration of live attenuated vaccines is not recommended for patients receiving tezepelumab. Vaccination should instead be completed at least 4 weeks prior to initiation of monoclonal antibody treatment to ensure that the immune system has an adequate response to the vaccination.

For patients receiving canakinumab or anti-TNF therapy, the 2022 American College of Rheumatology Guideline for Vaccinations in Patients with Rheumatic and Musculoskeletal Diseases recommends, on an individual basis, temporary interruption of immunosuppressive therapy when live attenuated vaccines are required. The medication should be discontinued for one dosing interval before vaccination and for 4 weeks after the administration of live attenuated virus vaccines.[57] We suggest extending this precaution to eculizumab, despite limited supporting evidence.

In children receiving canakinumab for autoinflammatory diseases or systemic juvenile idiopathic arthritis, discontinuation of biologic therapy may pose substantial risk of disease worsening. In such cases, a shorter period of immunosuppressant discontinuation may be considered if live attenuated vaccination is essential.[57]

Infants exposed to anti-TNF therapy in utero should receive rotavirus vaccine within the first 6 months of life.[57]

For rituximab, treatment should be discontinued for 6 months before and 4 weeks after administration of live attenuated vaccines.[57]

Regarding revaccination after completion of monoclonal antibody therapy, there is no conclusive evidence to support this practice as a standard recommendation. Decisions on the need for revaccination should be individualized, considering each patient's clinical condition and the efficacy of immune responses after treatment.

Janus kinase inhibitors

The Janus kinase (JAK) family comprises 4 tyrosine kinase proteins (JAK1, JAK2, JAK3, and TYK2) that play key roles in the immune system, particularly in adaptive immunity and hematopoiesis. These kinases participate in inflammatory signaling, leukocyte maturation, pathogen recognition, and cytokine activation.[65] JAK inhibitors are orally administered synthetic small molecules that block cytokine-mediated signaling pathways in target cells, thereby modulating inflammatory responses in several diseases.[66] Some agents, such as tofacitinib, inhibit multiple JAKs, while others, such as upadacitinib, are selective.

Currently, no evidence indicates a risk of pathogen reactivation following administration of inactivated vaccines in patients receiving JAK inhibitors.[63] Therefore, individuals in this group may follow routine age-appropriate immunization schedules according to their clinical condition. Ideally, inactivated vaccines should be administered at least 14 days before initiation of JAK inhibitor therapy, although they may be given during treatment if necessary. Simultaneous vaccination is both feasible and recommended when indicated.

Live attenuated vaccines are contraindicated during treatment with JAK inhibitors due to the risk of complications.[63] If a live vaccine is required because of lack of prior immunization or absence of immunity, it should generally be administered 14-30 days before therapy initiation or at least 3 months after treatment is discontinued.[63,67] When administration of live attenuated vaccines is unavoidable during treatment, JAK inhibitors should be discontinued for 1-2 weeks prior to vaccination and restarted 4 weeks afterward.[57] In the context of rapidly progressive underlying disease, resuming therapy after 2 weeks may be considered.

Key vaccines to consider for this group of patients are listed below.

– *Recombinant herpes zoster vaccine:* For patients ≥ 18 years of age; 2 doses 1-2 months apart. Preferably administer before initiating JAK inhibitor therapy.
– *Pneumococcal vaccines:* Administer PCV13 or PCV15, followed 2 months later by PPSV23. PCV20 may be used as a single-dose alternative. In individuals who have already received PPSV23 but not PCV13 or PCV15, PCV13 or PCV15 should be administered after a 12-month interval, followed by a second PPSV23 dose 5 years later if indicated. Studies show that pneumococcal vaccine responses vary depending on the JAK inhibitor used. Patients receiving upadacitinib and baricitinib show satisfactory immune responses to both PCV13 and PPSV23,[68,69] whereas those receiving tofacitinib exhibit inadequate responses to PPSV23, even after a 2-week drug discontinuation. However, responses to conjugate vaccine PCV13 remain satisfactory.[70]
– *Influenza vaccine:* Recommended annually for individuals ≥ 6 months of age (high-dose formulations for adults aged > 60 years). A second dose of trivalent or quadrivalent vaccine may be considered beginning 3 months after the annual dose.
– *HPV vaccine:* Some JAK inhibitors have been associated with increased cancer risk.[71] Therefore, adolescents and immunocompromised adults aged < 45 years should receive the 3-dose HPV vaccine series. The 9-valent HPV vaccine (HPV9) is preferred due to its broader coverage, and revaccination should be considered in individuals previously immunized with HPV2 or HPV4.
– *COVID-19 vaccine:* A 3-dose primary series of monovalent vaccine is recommended, with 4 weeks between doses 1 and 2 and 8 weeks between doses 2 and 3 (primary schedule for immunocompromised patients). Adolescents and adults who have completed the primary series should receive mRNA booster doses every 6 months.
– *Hepatitis B vaccine:* Patients receiving JAK inhibitors require particular attention to hepatitis B immunization due to both potential hepatotoxicity of these medications and the increased risk of severe complications from hepatitis B during treatment. Ideally, the full 3-dose series should be completed before JAK inhibitor therapy is initiated.[72] If this is not possible, hepatitis B screening is essential, especially to identify active infection. Active hepatitis B constitutes a contraindication to JAK inhibitor therapy given the risk of hepatic deterioration and complications.

To ensure patient safety, household contacts of individuals receiving JAK inhibitors should be fully vaccinated according to their age-specific schedules.

Considerations on the use of BCG and herpes zoster vaccines in immunocompromised individuals

BCG vaccine

The BCG vaccine is used to prevent severe forms of tuberculosis, such as tuberculous meningitis and miliary tuberculosis. However, because it contains live attenuated *Mycobacterium bovis*, its administration in patients with inborn errors of immunity or other immunosuppressive conditions requires caution. Contraindications include primary or acquired immunodeficiencies, malignancies, prolonged use of high-dose systemic corticosteroids (for ≥ 2 weeks), newborns whose mothers received immunomodulators or biologic agents during the last 2 trimesters of pregnancy, and pregnancy.[73] In immunocompromised individuals, BCG may trigger serious adverse reactions, ranging from local manifestations to potentially fatal disseminated infections.[74]

Recent studies reinforce the need for a cautious approach to BCG vaccination in immunocompromised patients. In a systematic review, Fekrvand et al. identified 46 different inborn errors of immunity associated with adverse events following BCG vaccination, with SCID being the most common and carrying the highest mortality.[75] A Brazilian retrospective study reported complications in up to 65% of patients with SCID who were vaccinated with BCG before diagnosis, with high associated mortality.[76]

Patients with chronic granulomatous disease and Mendelian susceptibility to mycobacterial disease (MSMD) also face elevated risk of local and disseminated complications following BCG. In a retrospective study of 134 Chinese children with disseminated reactions to BCG, 48.6% were subsequently diagnosed with chronic granulomatous disease, 26.1% with MSMD, and 16% with SCID.[77] In Recife, state of Pernambuco, Brazil, a study of 53 patients with adverse reactions to BCG found that 16.8% had underlying inborn errors of immunity. While most cases (90%) involved locoregional reactions, all cases of disseminated reactions occurred in children later diagnosed with an inborn error of immunity, including 4 with chronic granulomatous disease, 3 with MSMD, and 2 with SCID.[78]

In patients with suspected inborn errors of immunity, it is currently recommended to delay BCG vaccination until specific diagnostic testing can confirm or exclude the disorder. Depending on age and resource availability, appropriate tests may include complete blood count, immunoglobulin measurement, lymphocyte immunophenotyping, TREC/KREC assay (if not performed during newborn screening), and dihydrorhodamine (DHR) assay.[75] Regional axillary lymphadenopathy should be regarded as a warning sign for inborn errors of immunity, as should any family history of adverse BCG reactions.[14]

For patients diagnosed with SCID who received BCG at birth, antimicrobial prophylaxis, such as isoniazid, may be used until hematopoietic stem cell transplant is possible. A triple-drug regimen (rifampicin, isoniazid, and ethambutol) may also be used, although toxicity is a potential concern.[76] In cases of disseminated BCG infection, the European Society for Immunodeficiencies recommends a therapeutic regimen with multiple antituberculosis drugs (rifampicin, ethambutol, isoniazid, and clarithromycin) until complete resolution of the infection. Thereafter, two antimycobacterial agents should be maintained until complete immune reconstitution after stem cell transplant. When toxicity occurs, agents such as levofloxacin are indicated.[79]

Recombinant herpes zoster vaccine

Immunocompromised individuals are at substantially increased risk of developing herpes zoster and its severe complications compared with immunocompetent adults of the same age group.[80-82] The recombinant herpes zoster vaccine is an inactivated, protein-based vaccine that uses the recombinant glycoprotein E antigen rather than a live virus. For this reason, it is considered safe for immunosuppressed populations.

In adults ≥ 50 years of age, pivotal trials demonstrated > 90% efficacy in preventing acute herpes zoster episodes.83 Among immunocompromised patients, reported efficacy includes 68.2% in hematopoietic stem cell transplant recipients[84] and 87.2% in patients with hematologic malignancies.[85]

The recombinant herpes zoster vaccine is recommended beginning at age 18 for immunocompromised individuals, administered as

2 doses spaced 2 months apart. When possible, the vaccine should be administered before starting immunosuppressive therapy, with a minimum interval of 1 month before immunosuppression. If this is not feasible, vaccination should occur at the most favorable clinical moment, ideally when the most intense phase of immunosuppression has subsided.

For individuals with prior herpes zoster infection, vaccination should be delayed for 6 months.

Herpes zoster vaccination recommendations for immunocompromised patients are provided in Table 7.

Summary of recommendations

Tables 8 and 9 outline the main vaccination recommendations for immunocompromised patients. Table 9 focuses on guidance regarding inactivated vaccines, which are often safe for this group of patients. Table 8 addresses live attenuated vaccines,

Table 7
Herpes zoster vaccination recommendations for immunocompromised patients

Clinical condition	Recommendation
Patients with severely compromised cellular immunity, untreated active tuberculosis, and pregnant women	Vaccination not recommended
Mild immunosuppression (patients receiving low doses of methotrexate, anti-TNF, systemic corticosteroids, or HIV+ patients with immune reconstitution [CD4 ≥ 200 cells/mm^3])	Vaccination may be considered
Bone marrow transplant	Administer the vaccine 6 to 12 months after transplant, preferably 2 months before discontinuing antiviral medication
Solid organ transplant	Vaccinate before transplant; if not possible, wait 6 to 12 months after the procedure, using low-dose immunosuppressants
Patients with cancer	Vaccinate before chemotherapy, radiation therapy, or immunosuppression, or after the most intense phase of immunosuppression has subsided
Immunosuppressive therapy	Non-biologic agents: administer at least 2 weeks before initiating treatment. They can be administered during immunosuppression, provided that the first dose was given before initiating treatment. Monoclonal antibodies: can be safely administered during treatment. JAK inhibitors: administer preferably before initiating treatment
Autoimmune diseases	Vaccinate before initiating aggressive immunosuppression, whenever possible

TNF = tumor necrosis factor; JAK = Janus kinase.

emphasizing contraindications and the specific situations in which they may be administered under strict monitoring, such as with yellow fever and varicella vaccines.

Conclusion

Immunization of immunocompromised patients requires a careful and structured approach to ensure adequate protection against infections. A key initial step is for health care professionals to assume responsibility for assessing and maintaining the vaccination status of both patients and their close contacts, since protecting the immediate household may be essential to preventing infections in this population.

A detailed understanding of the patient's medical history, including underlying immunosuppressive conditions and current treatments, is crucial to guide vaccine selection according to specific indications and contraindications. Immunocompromised patients should be referred to Referral Centers for Special Biologic Agents (CRIE), within the Brazilian Unified Health System (SUS), or to private immunization

Table 8
Summary of recommendations on the use of live attenuated vaccines in immunocompromised patients

Vaccine	Recommendation
BCG [a]	Contraindicated in patients with severe immunosuppression, such as those with combined immunodeficiencies, phagocytic disorders, or receiving immunosuppressive therapy
Measles-mumps-rubella	Generally contraindicated. It may be considered in patients with mild immunosuppression, depending on the patient's cellular response. Assess the epidemiological and immunological risk individually. Allowed in household contacts
Rotavirus	Contraindicated in patients with severe immunodeficiency or receiving immunosuppressive therapy. Allowed in household contacts
Yellow fever	Contraindicated in patients with severe immunosuppression. It may be considered in settings of high epidemiological risk, after careful assessment of the patient's immune status. Allowed in household contacts
Varicella	Contraindicated in patients with severe immunodeficiency and household contacts. It may be administered with caution in cases of mild immunosuppression after assessment of the patient's immune status.
Rabies	It should be administered even to individuals with inborn errors of immunity in situations of exposure to risk. The only exception is in cases of severe combined T- and B-cell immunodeficiencies
Dengue	Recommended with caution in endemic areas. It should be administered before initiating immunosuppression. Contraindicated in patients with severe immunosuppression. Assess the risk-benefit ratio in each case

[a] The BCG vaccine should be postponed in children undergoing newborn screening for immunodeficiency at birth. If the newborn screening results are normal, the child should be vaccinated as soon as possible.

Table 9
Summary of recommendations on the use of inactivated vaccines in immunocompromised patients

Vaccine	Recommendation
Influenza	Recommended annually for all immunocompromised patients. The vaccine is safe, but the immune response may be reduced
IPV	Recommended for immunocompromised patients, it is a safe alternative to OPV. Vaccination should occur before initiating immunosuppression, whenever possible
Pneumococcal	Highly recommended. It should be administered to all immunocompromised patients. Administer pneumococcal conjugate vaccine (PCV13/PCV15) followed by the polysaccharide vaccine (PPSV23) after 2 months, with a booster PPSV23 dose after 5 years, or the 20-valent vaccine (PCV20) alone. Vaccination should occur before initiating immunosuppression, whenever possible
Meningococcal (ACWY and B)	Recommended for most immunocompromised patients. Vaccination should be considered a priority in patients with immunodeficiencies that increase the risk of meningococcal infections, such as complement deficiencies, combined immunodeficiencies, chronic granulomatous disease, and severe neutropenia. Vaccination should occur before initiating immunosuppression, whenever possible
Haemophilus influenzae type b	Recommended for all immunocompromised patients. Vaccination should occur before initiating immunosuppression, whenever possible
Hepatitis B	Recommended. Immunocompromised patients usually receive a double dose and may require additional or booster doses. Vaccination should occur before initiating immunosuppression, whenever possible
Herpes zoster	Recommended for immunocompromised individuals aged 18 years and older. Administer 2 doses with a 2-month interval. Prioritize before initiating immunosuppression
HPV	Recommended for immunocompromised individuals using the 3-dose series
COVID-19	Highly recommended. Administer the 3-dose primary series and booster doses every 6 months. The vaccination schedule can be accelerated in immunocompromised individuals, and a 1-month interval between doses 1 and 2 can be considered. It can be administered during immunosuppression, but vaccination should be prioritized before initiating treatment, if possible
Respiratory syncytial virus	Recommended for patients at increased risk for RSV disease from 18 years of age (Abrysvo: 18 to 59 years and Arexvy: 50 to 59 years) and all adults aged 60 years and older

Note: Palivizumab or nirsevimab monoclonal antibodies should be used in immunocompromised children under 24 months of age.

units, accompanied by a report from their immunology specialist.

Optimizing the timing of vaccination is also important. In general, live attenuated vaccines should ideally be administered 4 weeks before the initiation of immunosuppression, whereas inactivated vaccines should be administered at least 2 weeks prior.

Finally, it is essential that health care professionals identify and overcome barriers that may hinder vaccine uptake. This includes addressing patients' concerns and hesitancy regarding vaccines, as well as eliminating health system obstacles that may limit access to immunization.

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References

1. See KC. Vaccination for the prevention of infection among immunocompromised patients: a concise review of recent systematic reviews. Vaccines. 2022;10(5):800. doi:10.3390/vaccines10050800.
2. Bin-Hussain I. Infections in the Immunocompromised Host. Textbook of Clinical Pediatrics. 2012:847-52. doi: 10.1007/978-3-642-02202-9_68.
3. Antinori A, Bausch-Jurken M. The Burden of COVID-19 in the immunocompromised patient: implications for vaccination and needs for the future. J Infect Dis. 2023;228(Suppl 1):S4. doi:10.1093/infdis/jiad181.
4. Lopez A, Mariette X, Bachelez H, Belot A, Bonnotte B, Hachulla E, et al. Vaccination recommendations for the adult immunosuppressed patient: A systematic review and comprehensive field synopsis. J Autoimmun. 2017 Jun;80:10-27. doi: 10.1016/j.jaut.2017.03.011.
5. Neven B, Pérot P, Bruneau J, Pasquet M, Ramirez M, Diana JS, et al. Cutaneous and Visceral Chronic Granulomatous Disease Triggered by a Rubella Virus Vaccine Strain in Children With Primary Immunodeficiencies. Clin Infect Dis. 2017 Jan 1;64(1):83-86. doi: 10.1093/cid/ciw675.
6. Perelygina L, Plotkin S, Russo P, Hautala T, Bonilla F, Ochs HD, et al. Rubella persistence in epidermal keratinocytes and granuloma M2 macrophages in patients with primary immunodeficiencies. J Allergy Clin Immunol. 2016 Nov;138(5):1436-9.e11. doi: 10.1016/j.jaci.2016.06.030.
7. Sarmiento JD, Villada F, Orrego JC, Franco JL, Trujillo-Vargas CM. Adverse events following immunization in patients with primary immunodeficiencies. Vaccine. 2016;34(13):1611-6. doi:10.1016/j.vaccine.2016.01.047.
8. Morillo-Gutierrez B, Worth A, Valappil M, Gaspar HB, Gennery AR. Chronic infection with rotavirus vaccine strains in UK children with severe combined immunodeficiency. Pediatr Infect Dis J. 2015;34(9):1040-1. doi:10.1097/INF.0000000000000788.
9. Loubet P, Kernéis S, Groh M, Loulergue P, Blanche P, Verger P, et al. Attitude, knowledge and factors associated with influenza and pneumococcal vaccine uptake in a large cohort of patients with secondary immune deficiency. Vaccine. 2015 Jul 17;33(31):3703-8. doi: 10.1016/j.vaccine.2015.06.012.
10. Furer V, Rondaan C, Heijstek MW, Agmon-Levin N, van Assen S, Bijl M, et al. 2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis. 2020 Jan;79(1):39-52. doi: 10.1136/annrheumdis-2019-215882.
11. Bemben NM, Berg ML. Efficacy of inactivated vaccines in patients treated with immunosuppressive drug therapy. Pharmacotherapy. 2022;42(4):334-42. doi:10.1002/phar.2671.
12. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde e Ambiente, Departamento de Imunizações e Doenças Imunopreveníveis. Manual dos Centros de Referência para Imunobiológicos Especiais. 6ª ed. Brasília: Ministério da Saúde; 2023.
13. Medical Advisory Committee of the Immune Deficiency Foundation; Shearer WT, Fleisher TA, Buckley RH, Ballas Z, Ballow M, Blaese RM, et al. Recommendations for live viral and bacterial vaccines in immunodeficient patients and their close contacts. J Allergy Clin Immunol. 2014 Apr;133(4):961-6. doi: 10.1016/j.jaci.2013.11.0.
14. Bonilla FA. Update: Vaccines in primary immunodeficiency. J Allergy Clin Immunol. 2018;141(2):474-81. doi:10.1016/j.jaci.2017.12.980.
15. Lee TK, Gereige JD, Maglione PJ. State-of-the-art diagnostic evaluation of common variable immunodeficiency. Ann Allergy Asthma Immunol. 2021 Jul;127(1):19-27. doi: 10.1016/j.anai.2021.03.005.
16. Conley ME, Dobbs AK, Farmer DM, Kilic S, Paris K, Grigoriadou S, et al. Primary B cell immunodeficiencies: comparisons and contrasts. Annu Rev Immunol. 2009;27:199-227. doi: 10.1146/annurev.immunol.021908.132649.
17. Hanitsch LG, Löbel M, Mieves JF, Bauer S, Babel N, Schweiger B, et al. Cellular and humoral influenza-specific immune response upon vaccination in patients with common variable immunodeficiency and unclassified antibody deficiency. Vaccine. 2016 May 5;34(21):2417-23. doi: 10.1016/j.vaccine.2016.03.091.
18. Junker AK, Bonilla FA, Sullivan KE. How to flee the flu. Clin Immunol. 2004 Sep;112(3):219-20. doi: 10.1016/j.clim.2004.03.013.
19. Mieves JF, Wittke K, Freitag H, Volk HD, Scheibenbogen C, Hanitsch LG. Influenza Vaccination in patients with common variable immunodeficiency (CVID). Curr Allergy Asthma Rep. 2017;17(11):78. doi:10.1007/s11882-017-0749-3.
20. Aguilar C, Malphettes M, Donadieu J, Chandesris O, Coignard-Biehler H, Catherinot E, et al. Prevention of infections during primary immunodeficiency. Clin Infect Dis. 2014 Nov 15;59(10):1462-70. doi: 10.1093/cid/ciu646.
21. Pavlov DN, Van Zyl WB, Kruger M, Blignaut L, Grabow WOK, Ehlers MM. Poliovirus vaccine strains detected in stool specimens of immunodeficient children in South Africa. Diagn Microbiol Infect Dis. 2006;54(1):23-30. doi:10.1016/j.diagmicrobio.2005.08.011.
22. Centers for Disease Control and Prevention. Licensure of a 13-valent pneumococcal conjugate vaccine (PCV13) and recommendations for use among children – Advisory Committee on Immunization Practices (ACIP), 2010. MMWR Morb Mortal Wkly Rep. 2010;59:258-61.
23. Azizi G, Pouyani MR, Abolhassani H, Sharifi L, Dizaji MZ, Mohammadi J, et al. Cellular and molecular mechanisms of immune dysregulation and autoimmunity. Cell Immunol. 2016 Dec;310:14-26. doi: 10.1016/j.cellimm.2016.08.012.
24. Jones A. Immunological disorders in infants and children. 5ª ed. Arch Dis Child. 2005;90(5):549. doi:10.1136/adc.2004.061770.

25. Associazione Italiana di Ematologia ed Oncologia Pediatrica (AIEOP). Sindrome IPEX (Immunodysregulation, Polyendocrinopathy, Enteropathy, X-linked). Raccomandazioni diagnostiche e terapeutiche [Internet]. 2009; p.9-10. Disponível em: https://www.aieop.org/web/wp-content/uploads/2018/02/IPEX-raccomandazioni-2009.pdf.
26. Jesus AA, Oliveira JB, Hilário MOE, Terreri MTRA, Fujihira E, WataseM, et al. Síndromes autoinflamatórias hereditárias na faixa etária pediátrica. J Pediatr (Rio J). 2010;86(5):353-66. doi:10.1590/S0021-75572010000500003.
27. Mendonça LO, Azzolini RK, Assis JP, Franco A, Kalil J, Castro FM, et al. Uma nova classe de doenças: doenças autoinflamatórias. Arq Asma Alerg Imunol. 2017;1(3):263-71. doi:10.5935/2526-5393.20170037.
28. Aranda CS, Guimarães RR, Pimentel MGP. Combined immunodeficiencies. J Pediatr (Rio J). 2021;97:39-48. doi:10.1016/j.jped.2020.10.014.
29. Sobh A, Bonilla FA. Vaccination in primary immunodeficiency disorders. J Allergy Clin Immunol Pract. 2016;4(6):1066-75. doi:10.1016/j.jaip.2016.09.012.
30. Donadieu J, Fenneteau O, Beaupain B, Mahlaoui N, Chantelot CB. Congenital neutropenia: diagnosis, molecular bases and patient management. Orphanet J Rare Dis. 2011;6:26. doi:10.1186/1750-1172-6-26.
31. Janczar S, Zalewska-Szewczyk B, Bąpol-Pokora K, Paąnik J, Zeman K, Młynarski W. Vaccination in children with chronic severe neutropenia – review of recommendations and a practical approach. Cent-Eur J Immunol. 2020;45(2):202-5. doi:10.5114/ceji.2020.97910.
32. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al.; Infectious Diseases Society of America. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis. 2014 Feb;58(3):309-18. doi: 10.1093/cid/cit816. doi:10.1093/cid/cit816.
33. Eibl MM, Wolf HM. Vaccination in patients with primary immune deficiency, secondary immune deficiency and autoimmunity with immune regulatory abnormalities. Immunotherapy. 2015;7(12):1273-92. doi:10.2217/IMT.15.74.
34. Anikeeva N, Somersalo K, Sims TN, Thomas VK, Dustin ML, Sykulev Y. Distinct role of lymphocyte function-associated antigen-1 in mediating effective cytolytic activity by cytotoxic T lymphocytes. Proc Natl Acad Sci USA. 2005;102(18):6437-42. doi:10.1073/pnas.0502467102.
35. Kohl S, Springer TA, Schmalstieg FC, Loo LS, Anderson DC. Defective natural killer cytotoxicity and polymorphonuclear leukocyte antibody-dependent cellular cytotoxicity in patients with LFA-1/OKM-1 deficiency. J Immunol. 1984 Dec;133(6):2972-8.
36. Blazina Š, Debeljak M, Košnik M, SimąąS, Stopinšek S, Markelj G, et al. Functional Complement Analysis Can Predict Genetic Testing Results and Long-Term Outcome in Patients With Complement Deficiencies. Front Immunol. 2018 Mar 21;9:500. doi: 10.3389/fimmu.2018.00500.
37. Brodszki N, Frazer-Abel A, Grumach AS, Kirschfink M, Litzman J, Perez E, et al. European Society for Immunodeficiencies (ESID) and European Reference Network on Rare Primary Immunodeficiency, Autoinflammatory and Autoimmune Diseases (ERN RITA) Complement Guideline: Deficiencies, Diagnosis, and Management. J Clin Immunol. 2020 May;40(4):576-91. doi: 10.1007/s10875-020-00754-1.
38. Maurer M, Magerl M, Betschel S, Aberer W, Ansotegui IJ, Aygören-Pürsün E, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2021 revision and update. Allergy. 2022 Jul;77(7):1961-90. doi: 10.1111/all.15214.
39. Dávila-Seijo P, Dauden E, Descalzo MA, Carretero G, Carrascosa JM, Vanaclocha F, et al.; BIOBADADERM Study Group. Infections in Moderate to Severe Psoriasis Patients Treated with Biological Drugs Compared to Classic Systemic Drugs: Findings from the BIOBADADERM Registry. J Invest Dermatol. 2017 Feb;137(2):313-21. doi: 10.1016/j.jid.2016.08.034.
40. Boerbooms AM, Kerstens PJ, van Loenhout JW, Mulder J, van de Putte LB. Infections during low-dose methotrexate treatment in rheumatoid arthritis. Semin Arthritis Rheum. 1995;24(6):411-21. doi:10.1016/s0049-0172(95)80009-3.
41. McLean-Tooke A, Aldridge C, Waugh S, Spickett GP, Kay L. Methotrexate, rheumatoid arthritis and infection risk: what is the evidence? Rheumatol Oxf Engl. 2009;48(8):867-71. doi:10.1093/rheumatology/kep101.
42. He J, Li Z. Dilemma of immunosuppression and infection risk in systemic lupus erythematosus. Rheumatol Oxf Engl. 2023;62(Suppl 1):i22-i29. doi:10.1093/rheumatology/keac678.
43. Agarwal N, Ollington K, Kaneshiro M, Frenck R, Melmed GY. Are immunosuppressive medications associated with decreased responses to routine immunizations? A systematic review. Vaccine. 2012 Feb 14;30(8):1413-24. doi: 10.1016/j.vaccine.2011.11.109.
44. Papp KA, Haraoui B, Kumar D, Marshall JK, Bissonnette R, Bitton A, et al. Vaccination Guidelines for Patients with Immune-Mediated Disorders on Immunosuppressive Therapies-Executive Summary. J Can Assoc Gastroenterol. 2019 Dec;2(4):149-52. doi: 10.1093/jcag/gwy069.
45. Adler S, Krivine A, Weix J, Rozenberg F, Launay O, Huesler J, et al. Protective effect of A/H1N1 vaccination in immune-mediated disease – a prospectively controlled vaccination study. Rheumatology (Oxford). 2012 Apr;51(4):695-700. doi: 10.1093/rheumatology/ker389.
46. Brasil. Agência Nacional de Vigilância Sanitária - Anvisa. Bula Nucala® [Internet]. Available from: https://consultas.anvisa.gov.br/#/medicamentos/1064523?numeroProcesso=25351486953201534. Accessed on: Nov 08 2024.
47. Brasil. Anvisa - Agência Nacional de Vigilância Sanitária. Bula Dupixent® [Internet]. Available from: https://consultas.anvisa.gov.br/#/medicamentos/1324521?numeroProcesso=25351189487201920. Accessed on: Nov 08 2024.
48. Imazio M, Lazaros G, Gattorno M, LeWinter M, Abbate A, Brucato A, et al. Anti-interleukin-1 agents for pericarditis: a primer for cardiologists. Eur Heart J. 2022 Aug 14;43(31):2946-57. doi: 10.1093/eurheartj/ehab452.
49. Panettieri R, Lugogo N, Corren J, Ambrose CS. Tezepelumab for severe asthma: one drug targeting multiple disease pathways and patient types. J Asthma Allergy. 2024;17:219-36. doi:10.2147/JAA.S342391.
50. Kamal ME, Werida RH, Radwan MA, Askar SR, Omran GA, El-Mohamdy MA, et al. Efficacy and safety of infliximab and adalimumab in inflammatory bowel disease patients. Inflammopharmacology. 2024 Oct;32(5):3259-69. doi: 10.1007/s10787-024-01508-w.
51. Fleischmann R, Goldman JA, Leirisalo-Repo M, Zanetakis E, El-Kadi H, Kellner H, et al. Infliximab efficacy in rheumatoid arthritis after an inadequate response to etanercept or adalimumab: results of a target-driven active switch study. Curr Med Res Opin. 2014 Nov;30(11):2139-49. doi: 10.1185/03007995.2014.942416.
52. Thomas TC, Rollins SA, Rother RP, Giannoni MA, Hartman SL, Elliott EA, et al. Inhibition of complement activity by humanized anti-C5 antibody and single-chain Fv. Mol Immunol. 1996 Dec;33(17-18):1389-401. doi: 10.1016/s0161-5890(96)00078-8.
53. Atagündüz P, Keser G, Soy M. Interleukin-1 inhibitors and vaccination including covid-19 in inflammatory rheumatic diseases: a nonsystematic review. Front Immunol. 2022;12:734279. doi:10.3389/fimmu.2021.734279.
54. Rabinowitz KM, Navon M, Edelman-Klapper H, Zittan E, Bar-Gil Shitrit A, Goren I, et al., On Behalf Of The Responses To Covid-Vaccine Israeli Ibd. Anti-TNFą Treatment Impairs Long-Term Immune Responses to COVID-19 mRNA Vaccine in Patients with Inflammatory Bowel Diseases. Vaccines (Basel). 2022 Jul 26;10(8):1186. doi: 10.3390/vaccines10081186.

55. Garcia Garrido HM, Veurink AM, Leeflang M, Spijker R, Goorhuis A, Grobusch MP. Hepatitis A vaccine immunogenicity in patients using immunosuppressive drugs: A systematic review and meta-analysis. Travel Med Infect Dis. 2019;32:101479. doi:10.1016/j.tmaid.2019.101479.

56. Müller KE, Dohos D, Sipos Z, Kiss S, Dembrovszky F, Kovács N, et al. Immune response to influenza and pneumococcal vaccines in adults with inflammatory bowel disease: A systematic review and meta-analysis of 1429 patients. Vaccine. 2022 Mar 18;40(13):2076-86. doi: 10.1016/j.vaccine.2022.02.027.

57. Bass AR, Chakravarty E, Akl EA, Bingham CO, Calabrese L, Cappelli LC, et al. 2022 American College of Rheumatology Guideline for Vaccinations in Patients With Rheumatic and Musculoskeletal Diseases. Arthritis Care Res (Hoboken). 2023 Mar;75(3):449-64. doi: 10.1002/acr.25045.

58. Bula de Soliris®: eculizumabe. Responsável técnica Luciana Maciel Zuicker Maziero. São Paulo. Alexion Serviços e Farmacêutica do Brasil Ltda., 2022.

59. Jaeger VK, Hoffman HM, van der Poll T, Tilson H, Seibert J, Speziale A, et al. Safety of vaccinations in patients with cryopyrin-associated periodic syndromes: a prospective registry based study. Rheumatology (Oxford). 2017 Sep 1;56(9):1484-91. doi: 10.1093/rheumatology/kex185.

60. Mari D, White K. Live vaccine administration in patients treated with biologics for allergic disease. J Allergy Clin Immunol Pract. 2024;12(10):2842-2843.e3. doi:10.1016/j.jaip.2024.06.032.

61. Blauvelt A, Simpson EL, Tyring SK, Purcell LA, Shumel B, Petro CD, et al. Dupilumab does not affect correlates of vaccine-induced immunity: A randomized, placebo-controlled trial in adults with moderate-to-severe atopic dermatitis. J Am Acad Dermatol. 2019 Jan;80(1):158-67.e1. doi: 10.1016/j.jaad.2018.07.048.

62. Wechsler ME, Souza-Machado A, Xu C, Mao X, Kapoor U, Khokhar FA, et al. Preclinical and clinical experience with dupilumab on the correlates of live attenuated vaccines. J Allergy Clin Immunol Glob. 2021 Dec 8;1(1):9-15. doi: 10.1016/j.jacig.2021.12.003.

63. Narbutt J, ąuber Z, Lesiak A, BieąN, Szepietowski JC. Vaccinations in selected immune-related diseases treated with biological drugs and JAK Inhibitors – literature review and statement of experts from Polish Dermatological Society. Vaccines. 2024;12(1):82. doi:10.3390/vaccines12010082.

64. Lieberman JA, Chu DK, Ahmed T, Dribin TE, Abrams EM, Anagnostou A, et al. A systematic review and expert Delphi Consensus recommendation on the use of vaccines in patients receiving dupilumab: A position paper of the American College of Allergy, Asthma and Immunology. Ann Allergy Asthma Immunol. 2024 Sep;133(3):286-94. doi: 10.1016/j.anai.2024.05.014.

65. Villarino AV, Kanno Y, Ferdinand JR, O'Shea JJ. Mechanisms of Jak/STAT signaling in immunity and disease. J Immunol. 2015 Jan 1;194(1):21-7. doi: 10.4049/jimmunol.1401867.

66. Schwartz DM, Kanno Y, Villarino A, Ward M, Gadina M, O'Shea JJ. JAK inhibition as a therapeutic strategy for immune and inflammatory diseases. Nat Rev Drug Discov. 2017;16(12):843-62. doi:10.1038/nrd.2017.201.

67. U.S. Centers for Disease Control and Prevention - CDC. Guidelines for Immunizations [Internet]. Available from: https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html. Accessed on: Oct 08 2024.

68. Winthrop KL, Bingham CO 3rd, Komocsar WJ, Bradley J, Issa M, Klar R, et al. Evaluation of pneumococcal and tetanus vaccine responses in patients with rheumatoid arthritis receiving baricitinib: results from a long-term extension trial substudy. Arthritis Res Ther. 2019 Apr 18;21(1):102. doi: 10.1186/s13075-019-1883-1.

69. Winthrop K, Vargas JI, Drescher E, Garcia C, Friedman A, Hendrickson B, et al. Evaluation of response to 13-valent conjugated pneumococcal vaccination in patients with rheumatoid arthritis receiving upadacitinib: results from a phase 2 open-label extension study. RMD Open. 2022 Mar;8(1):e002110. doi: 10.1136/rmdopen-2021-002110.

70. Winthrop KL, Silverfield J, Racewicz A, Neal J, Lee EB, Hrycaj P, et al. The effect of tofacitinib on pneumococcal and influenza vaccine responses in rheumatoid arthritis. Ann Rheum Dis. 2016 Apr;75(4):687-95. doi: 10.1136/annrheumdis-2014-207191.

71. Russell MD, Stovin C, Alveyn E, Adeyemi O, Chan CKD, Patel V, et al. JAK inhibitors and the risk of malignancy: a meta-analysis across disease indications. Ann Rheum Dis. 2023 Aug;82(8):1059-67. doi: 10.1136/ard-2023-224049.

72. Hong X, Xiao Y, Xu L, Liu L, Mo H, Mo H. Risk of hepatitis B reactivation in HBsAg-/HBcAb+ patients after biologic or JAK inhibitor therapy for rheumatoid arthritis: A meta-analysis. Immun Inflamm Dis. 2023 Feb;11(2):e780. doi: 10.1002/iid3.780.

73. Brasil. Ministério da Saúde. Manual de Vigilância Epidemiológica de Eventos Adversos Pós-Vacinação [Internet]. Available from: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/svsa/vacinacao-imunizacao-pni/manual_eventos-_adversos_pos_vacinacao_4ed_atualizada.pdf/view. Accessed on: Oct 16 2024.

74. Talbot EA, Perkins MD, Silva SF, Frothingham R. Disseminated bacille Calmette-Guérin disease after vaccination: case report and review. Clin Infect Dis Off Publ Infect Dis Soc Am. 1997;24(6):1139-46. doi:10.1086/513642.

75. Fekrvand S, Yazdani R, Olbrich P, Gennery A, Rosenzweig SD, Condino-Neto A, et al. Primary Immunodeficiency Diseases and Bacillus Calmette-Guérin (BCG)-Vaccine-Derived Complications: A Systematic Review. J Allergy Clin Immunol Pract. 2020 Apr;8(4):1371-86. doi: 10.1016/j.jaip.2020.01.038.

76. Mazzucchelli JT, Bonfim C, Castro GG, Condino-Neto AA, Costa NM, Cunha L,et al. Severe combined immunodeficiency in Brazil: management, prognosis, and BCG-associated complications. J Investig Allergol Clin Immunol. 2014;24(3):184-91.

77. Zeng Y, Ying W, Wang W, Hou J, Liu L, Sun B, et al. Clinical and Genetic Characteristics of BCG Disease in Chinese Children: a Retrospective Study. J Clin Immunol. 2023 May;43(4):756-68. doi: 10.1007/s10875-022-01422-2.

78. Lyra PT, Souza E, Moura ACA, Matta MC, Torres LC, Coelho AVC, et al. Inborn Errors of Immunity in Patients with Adverse Events Following BCG Vaccination in Brazil. J Clin Immunol. 2022 Nov;42(8):1708-1720. doi: 10.1007/s10875-022-01302-9.

79. Ong RYL, Chan SB, Chew SJ, Liew WK, Thoon KC, Chong CY, et al. Disseminated bacillus-Calmette-Guérin infections and primary immunodeficiency disorders in Singapore: A single center 15-year retrospective review. Int J Infect Dis. 2020 Aug;97:117-25. doi: 10.1016/j.ijid.2020.05.117.

80. McKay SL, Guo A, Pergam SA, Dooling K. Herpes zoster risk in immunocompromised adults in the United States: a systematic review. Clin Infect Dis Off Publ Infect Dis Soc Am. 2020;71(7):e125-e134. doi:10.1093/cid/ciz1090.

81. Whitley RJ. Herpesvirus infections in the immunocompromised host: diagnosis and management. Adv Exp Med Biol. 1986;202:95-118. doi:10.1007/978-1-4684-1259-8_7.

82. Muñoz-Quiles C, López-Lacort M, Díez-Domingo J, Orrico-Sánchez A. Herpes zoster risk and burden of disease in immunocompromised populations: a population-based study using health system integrated databases, 2009-2014. BMC Infect Dis. 2020 Nov 30;20(1):905. doi: 10.1186/s12879-020-05648-6.

83. Lal H, Cunningham AL, Godeaux O, Chlibek R, Diez-Domingo J, Hwang SJ, et al.; ZOE-50 Study Group. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med. 2015 May 28;372(22):2087-96. doi: 10.1056/NEJMoa1501184.

84. Bastidas A, de la Serna J, El Idrissi M, Oostvogels L, Quittet P, López-Jiménez J, et al.; ZOE-HSCT Study Group Collaborators. Effect of Recombinant Zoster Vaccine on Incidence of Herpes Zoster After Autologous Stem Cell Transplantation: A Randomized Clinical Trial. JAMA. 2019 Jul 9;322(2):123-33. doi: 10.1001/jama.2019.9053.

85. Dagnew AF, Ilhan O, Lee WS, Woszczyk D, Kwak JY, Bowcock S, et al.; Zoster-039 study group. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in adults with haematological malignancies: a phase 3, randomised, clinical trial and post-hoc efficacy analysis. Lancet Infect Dis. 2019 Sep;19(9):988-1000. doi: 10.1016/S1473-3099(19)30163-X.

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