ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Special Article

Hypersensitivity reactions to vaccines and immunization in patients with asthma: joint recommendations of the Brazilian Association of Allergy and Immunology and the Brazilian Immunization Society

Reações de hipersensibilidade a vacinas e imunização de pacientes com asma: recomendações conjuntas da Associação Brasileira de Alergia e Imunologia e da Sociedade Brasileira de Imunizações

Ana Karolina Barreto Berselli Marinho[1,2,3], Claudia França Cavalcante Valente[1,3,4], Ekaterini Simões Goudoris[5,6], Anete Sevciovic Grumach[6,7], Fátima Rodrigues Fernandes[1,8], Claudia Leiko Yonekura Anagusko[1,2], Clarissa Morais Busatto Gerhardt[1,2], Gisele Feitosa Zuvanov Casado[1,9], Angelica Varela Rondon[1,10], Monica Araujo Álvares Silva[1,4], Ronney Corrêa Mendes[1,11], Antonio Paulo Costa Penido[1,12], Lorena de Castro Diniz[1,13], Bianca Noleto Ayres Guimarães[1,14], Ana Paula Neves Burian[3,15], Renato de Ávila Kfouri[3,16], Mônica Levi[3,17], Fabio Chigres Kuschnir[18,19]

ABSTRACT

This article provides information and recommendations on hypersensitivity reactions to vaccines and the immunization of patients with asthma. We present an analysis of both immediate and delayed reactions, emphasizing the importance of a thorough assessment of the patient's allergy history and the use of specific diagnostic tests to identify sensitizations. We also discuss strategies such as fractionated-dose vaccination, with the goal of minimizing the risk of severe allergic reactions. Finally, we explore the safety and effectiveness of new vaccines, including those for dengue infection, COVID-19, respiratory syncytial virus, and pneumococcal diseases, in the setting of hypersensitivity reactions and immunization of patients with asthma. Ensuring safe immunization for this group of patients is essential not only for individual protection but also for public health, by preventing outbreaks of infectious diseases and increasing confidence in vaccination programs. The recommendations presented here were adapted to the Brazilian context and developed by consensus among allergy and immunology experts from the Brazilian Association of Allergy and Immunology (ASBAI) and the Brazilian Immunization Society (SBIm).

Keywords: Allergy, asthma, hypersensitivity, immunity, vaccines.

RESUMO

Este artigo oferece informações e recomendações sobre reações de hipersensibilidade a vacinas e imunização de pacientes com asma. Apresenta-se uma análise das reações de hipersensibilidade imediata e tardia às vacinas, enfatizando a importância da avaliação cuidadosa dos antecedentes alérgicos do paciente e do uso de testes diagnósticos específicos para identificar sensibilizações. Discute-se ainda a aplicação de estratégias como a vacinação em doses fracionadas, visando minimizar o risco de reações alérgicas graves. O artigo também explora a segurança e a eficácia de vacinas recentes, como as para dengue, COVID-19, vírus sincicial respiratório recombinante e doenças pneumocócicas no contexto dos pacientes alérgicos, incluindo aqueles com asma. A imunização segura desse grupo de pacientes é essencial não apenas para a proteção individual, mas também para a saúde coletiva, prevenindo surtos de doenças infecciosas e aumentando a confiança nas campanhas de vacinação. As recomendações apresentadas nesta publicação foram adaptadas ao contexto brasileiro e ajustadas por consenso entre especialistas membros da Associação Brasileira de Alergia e Imunologia (ASBAI) e da Sociedade Brasileira de Imunizações (SBIm).

Descritores: Alergia, asma, hipersensibilidade, imunidade, vacinas.

1. Associação Brasileira de Alergia e Imunologia (ASBAI), Scientific Department of Immunizations - São Paulo, SP, Brazil.
2. Hospital das Clínicas, School of Medicine, Universidade de São Paulo, Department of Clinical Immunology and Allergy - São Paulo, SP, Brazil.

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3. Technical Committee for Revision of Vaccination Schedules, Sociedade Brasileira de Imunizações (SBIm) - São Paulo, SP, Brazil.
4. Hospital da Criança de Brasília, Department of Allergy and Immunology - Brasília, DF, Brazil.
5. Department of Pediatrics, School of Medicine, UFRJ; Allergy and Immunology Department, IPPMG, UFRJ - Rio de Janeiro, RJ, Brazil.
6. ASBAI, Scientific Department of Inborn Errors of Immunity - São Paulo, SP, Brazil.
7. Centro Universitário Saúde ABC (CEUFMABC), School of Medicine, Reference Center for Rare Diseases and Clinical Immunology - Santo André, SP, Brazil.
8. Hospital Infantil Sabará, Fundação José Luiz Egydio Setúbal, Instituto PENSI - São Paulo, SP, Brazil.
9. Permanent Member, State Committee for Pharmacovigilance of Vaccines and Other Biologics (CEFAVI) - Maceió, AL, Brazil.
10. Fundação Oswaldo Cruz, Reference Center for Special Biologics (CRIE) - Rio de Janeiro, RJ, Brazil.
11. Alervac Clínica de Vacinação - São Luiz, MA, Brazil.
12. Hospital Felício Rocho, Coordinator of the Allergy and Immunology Center and the Immunization Center - Belo Horizonte, MG, Brazil.
13. CRIE - Goiânia, GO, Brazil.
14. Municipal Health Secretariat, Rocha Maia Municipal Hospital, CRIE - Rio de Janeiro, RJ, Brazil.
15. CRIE - Vitória, ES, Brazil.
16. Vice President, Sociedade Brasileira de Imunizações (SBIm) - São Paulo, SP, Brazil.
17. President, Sociedade Brasileira de Imunizações (SBIm) - São Paulo, SP, Brazil.
18. Universidade do Estado do Rio de Janeiro (UERJ), School of Medical Sciences, Department of Pediatrics - Rio de Janeiro, RJ, Brazil.
19. Chair, Associação Brasileira de Alergia e Imunologia (ASBAI) - 2023-2024.

Introduction

The establishment of national immunization programs during the 1960s transformed the reality of public health worldwide. Global immunization efforts are estimated to have saved approximately 154 million lives over the past 50 years, the majority (101 million) being children under 1 year of age.[1] This makes vaccination the main contributor to the decline in global rates of child mortality.[1]

Vaccination drastically reduces or even eliminates the risk of infection or severe manifestations of more than 20 diseases. In allergic individuals, however, immunization may require special considerations and individualized assessment, as this population may experience adverse reactions, including hypersensitivity reactions which, although rare, can be severe. This article presents recommendations for the immunization of allergic patients and proposes approaches for the investigation, prevention, and management of vaccine-related allergic reactions. It also reviews current indications for immunization in patients with asthma. The goal of this document is to provide clear and practical guidelines to ensure safe and effective immunization in this population.

Methods

The recommendations presented in this document were developed based on current, publicly available evidence and adapted to the Brazilian context. A nonsystematic literature review was conducted between June and July 2024. The MEDLINE database was searched for articles addressing different aspects of immunization in allergic patients.

Initially, we searched for studies investigating both immediate and delayed hypersensitivity reactions to vaccines, including vaccination in specific clinical settings such as asthma. Studies on new vaccines in the context of allergic patients or patients with asthma, particularly dengue, respiratory syncytial virus (RSV), COVID-19, and invasive pneumococcal disease (IPD) vaccines, were also reviewed.

The collected evidence was discussed during the 1st Immunization of Immunocompromised and Allergic Patients Forum, held on August 9, 2024, in the city of São Paulo, Brazil. Recommendations were adopted or refined by consensus among participating specialists, all members of the Scientific Department of the Brazilian Association of Allergy and Immunology (ASBAI) and/or the Brazilian Society of Immunization (SBIm).

Hypersensitivity reactions to vaccines

The global increase in the prevalence of allergic diseases[2] has also led to an increase in concerns regarding possible allergic reactions associated with vaccines and their components.

The World Allergy Organization recommends classifying immune reactions to vaccines based on the timing of symptom onset: reactions occurring within minutes to a few hours after vaccination are classified as immediate, whereas those occurring several hours or days after vaccination are classified as delayed.

This classification primarily helps distinguish between immunoglobulin (Ig) E-mediated reactions, known as type I hypersensitivity, from other types of reaction (Table 1).[3] Immediate reactions, which are typically IgE-mediated, are of particular concern because of the risk of anaphylaxis if the patient is re-exposed to the allergen.[4]

Hypersensitivity reactions to vaccines may be triggered by several components, including vaccine antigens, residual media used for organism culture, stabilizers, preservatives, or other excipients, as detailed in Table 2.

Immediate hypersensitivity reactions

Immediate allergic reactions, whether IgE-mediated or not, may involve a wide range of symptoms. The most common clinical manifestations are listed below.

– Cutaneous symptoms: flushing, pruritus, urticaria, and angioedema.

Table 1
Classification and characteristics of hypersensitivity reactions

Type of reaction	Immune response	Pathophysiology	Time to onset	Example of reaction
Type I	IgE	IgE-mediated immediate hypersensitivity	A few minutes to 6 hours	Anaphylaxis, urticaria, bronchospasm, angioedema, hypotension
Type II	IgG and complement	Antigen or hapten bound to a cell interacts with antibody, leading to cellular or tissue injury	5 to 15 days	Hemolytic anemia, thrombocytopenia, neutropenia
Type III	IgM or IgG, complement, Fc receptors	Immune complexes trigger omplement activation and/or neutrophil recruitment through interaction with IgG Fc receptors	4 to 12 hours 7 to 21 days	Arthus reaction Serum sickness, vasculitis
Type IVa	Th1 (IFN-γ, TNF-α)	Monocytic inflammation	1 to 2 days	Eczema
Type IVb	Th2 (IL-4, IL- 5)	Eosinophilic inflammation	1 to several days 2 to 6 weeks	Maculopapular exanthem DRESS or SHID
Type IVc	Cytolytic T cells (perforin, granzyme, Fas ligand)	CD4 and CD8 T-cell-mediated keratinocyte death through cytotoxicity	1 to days 4 to 28 days	Maculopapular exanthem Stevens-Johnson syndrome/toxic epidermal necrolysis
Type IVd	T cells (IL-8, CXCL-8, GM-CSF)	Neutrophilic inflammation	1 to 2 days	Acute exanthematous pustulosis

DRESS = drug reaction with eosinophilia and systemic symptoms; DIHS = drug-induced hypersensitivity syndrome.
Adapted from Demoly P et al.[5].

– Respiratory symptoms: runny nose, nasal congestion, voice changes, tightness in throat, stridor, cough, wheezing, and dyspnea.
– Cardiovascular symptoms: lightheadedness, syncope, altered mental status, palpitations, and hypotension.
– Gastrointestinal symptoms: abdominal pain, vomiting, and diarrhea.

The most severe manifestation of an immediate allergic reaction is anaphylaxis, defined as a rapidly evolving systemic allergic reaction that can be fatal.[7] Anaphylaxis to vaccines is rare, with an incidence of 0.3 to 2.9 cases per million vaccine doses.[8-11] Although anaphylaxis is a potentially life-threatening disease, in most cases it can be effectively treated with favorable outcomes and no long-term sequelae or fatalities. A review of reports submitted to the United States Vaccine Adverse Event Reporting System describes only eight deaths possibly attributable to anaphylaxis following vaccination over a 26-year period (1990 to 2016).[10]

When anaphylaxis occurs following vaccination, symptoms typically begin within 30 minutes of vaccine administration, although in rare cases they may arise only several hours later.[10] Delayed symptoms tend to be less severe and may result from the slow absorption of the allergen or exposure to another allergen after vaccination.[12] In this context, it is important to note that the occurrence of anaphylaxis or another adverse event may not have been necessarily caused by the vaccine. Many events are temporally associated or arise from unrelated underlying health conditions.

In addition, it is essential to distinguish anaphylaxis from other reactions, such as post-vaccination vasovagal events and anxiety-related symptoms.[13] Vasovagal reactions are characterized by hypotension, pallor, and fainting, in contrast to anaphylaxis, which

Table 2
Main causes of vaccine hypersensitivity

Cause of hypersensitivity	Description
Vaccine antigens	Components of organisms or toxoids present in the vaccine. Example: viral or bacterial proteins such as those in influenza vaccines or tetanus toxoid
Residual culture media	Substances used to grow organisms during vaccine production. Example: egg proteins (influenza vaccine) or yeast proteins (hepatitis B vaccine)
Stabilizers	Substances added to vaccines to maintain stability and potency. Example: gelatin
Preservatives	Compounds used to prevent contamination of vaccines. Example: thimerosal,a an ethylmercury-based preservative
Adjuvants	Substances that enhance the immune response to the vaccine. Example: aluminum salts
Antibiotics	Added in small amounts to prevent bacterial contamination during manufacturing. Example: neomycin
Latex	Material found in the rubber stoppers of some vaccine vials

[a] The use of thimerosal in vaccines has decreased substantially due to concerns about cumulative mercury exposure in children. It is now known that ethylmercury (the type present in some vaccines) is far less likely than methylmercury (an environmental contaminant) to accumulate in the body or cause harm.[6]

is commonly accompanied by flushing, pruritus, and tachycardia.[13] Post-vaccination anxiety symptoms may include vocal cord spasms, which may cause stridor and dyspnea, and panic attacks, which may cause a feeling of tightness in throat, hypertension, tachycardia, and dyspnea, among others.[14]

Individuals with egg allergy

Some vaccines are produced using embryonated eggs. In this process, the virus is inoculated into embryonated eggs, where it replicates. After replication, the virus is harvested and subsequently inactivated or attenuated for vaccine production.[15] As a result, some vaccines may contain small amounts of egg proteins, such as ovalbumin.[16] However, advances in manufacturing have significantly reduced residual protein content, making these vaccines increasingly safe for egg-allergic individuals.

The measles-mumps-rubella (MMR) and measles-mumps-rubella-varicella (MMRV) vaccines contain minimal amounts of ovalbumin.[17,18] These vaccines are considered safe for individuals with egg allergy, and there is no contraindication to their use or recommendation for prior skin testing.[17-19] Therefore, routine immunization is recommended. For patients with severe allergy and a very low threshold for reactions upon contact with egg, administration in a setting equipped to manage anaphylaxis should be considered.

The influenza vaccine, although containing traces of ovalbumin, is also safe for individuals with egg allergy.[20] A review of 28 studies involving 4,315 egg-allergic patients, of whom 656 had a history of anaphylaxis to egg, reported no severe vaccine-related reactions.[21] Therefore, influenza vaccination is recommended for egg-allergic individuals without restrictions. For patients with severe allergy and a very low threshold for reactions upon contact with egg, administration in a setting equipped to manage anaphylaxis should be considered.

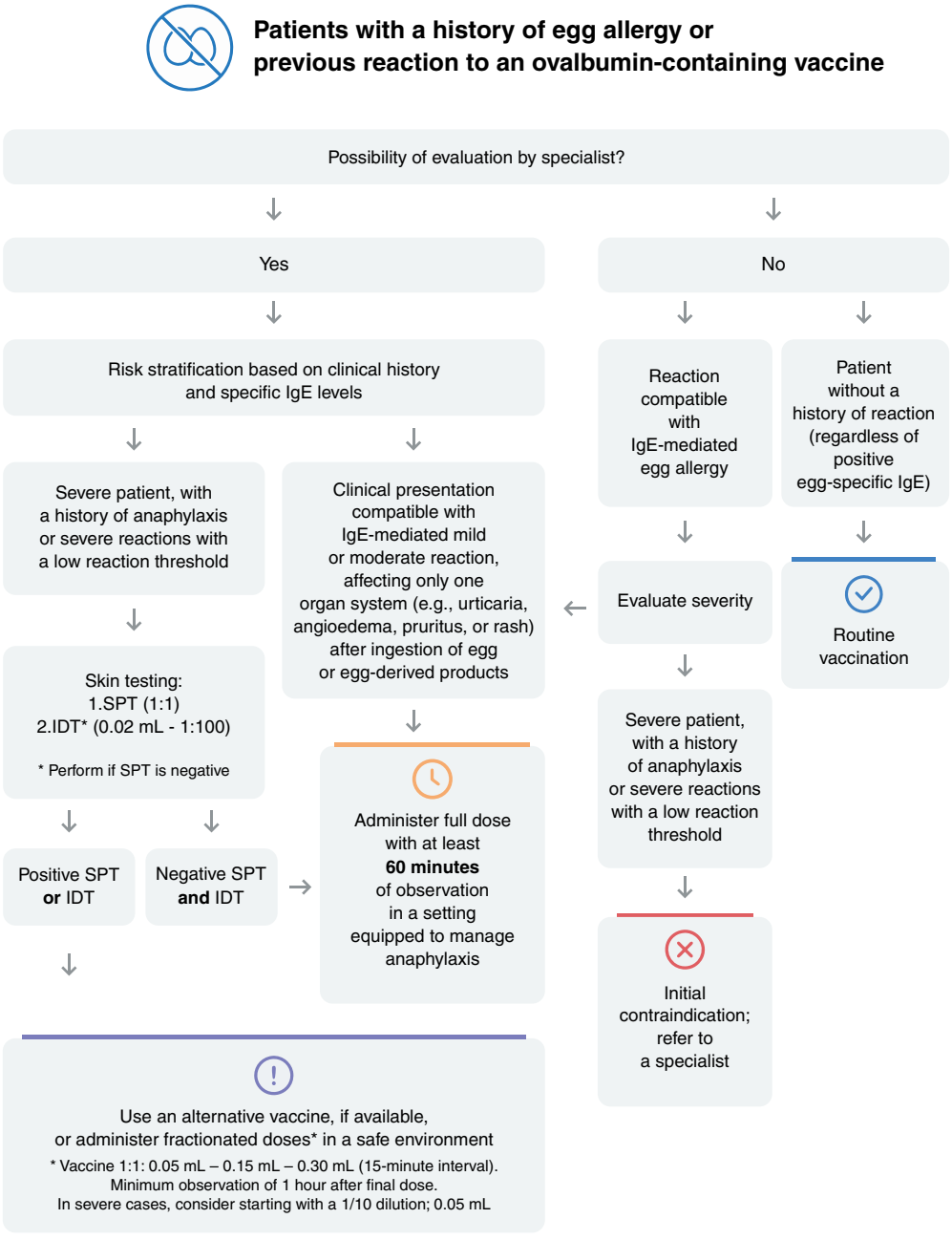
The yellow fever vaccine contains higher amounts of residual egg proteins compared to the MMR, MMRV, and influenza vaccines. While this vaccine is highly immunogenic and plays a crucial role in disease control in Brazil,[22] a structured risk stratification is required for patients with severe egg allergy to allow safe vaccination. This stratification should consider the patient's clinical history as well as specific tests, such as serum IgE to egg and its components, as shown in Figure 1. In addition, skin testing with the yellow fever vaccine (skin prick test [SPT] and intradermal testing [IDT]) may be necessary to determine the safest immunization strategy. For patients with mild to moderate allergy, vaccination in a setting equipped for anaphylaxis management is recommended. In severe cases, an SPT for immediate reactions may be helpful. If both SPT and IDT are negative, administration of the full dose in an appropriately equipped facility with 60 minutes of observation is recommended. If either test is positive, fractional dose vaccination or a desensitization protocol is recommended.[23]

Gerhardt et al.[24] evaluated yellow fever vaccination in egg-allergic patients at a quaternary-care hospital, stratifying risk based on skin testing results. Of the 43 patients evaluated, 37 had negative SPT and IDT and received the full vaccine dose without adverse reactions. Only six patients had positive IDT results and required desensitization; half of them (3/6) experienced mild hypersensitivity reactions, managed with antihistamines and/or oral corticosteroids. In another study by Cançado et al.,[25] 132 egg-allergic patients received the yellow fever vaccine without adverse events. Of these, 92 (70%) received the full dose, while 40 (30%; 17 with positive SPT and 23 with positive IDT) underwent desensitization. A separate Brazilian cohort evaluated at a reference center for special biologics[26] included 829 children with a history of egg allergy who received the yellow fever vaccine. Only 11 (1.3%) experienced immediate post-vaccination adverse events. In the same study, 25 children with a history of egg-induced anaphylaxis underwent skin testing. Fifteen had positive tests (six with positive SPT and nine with positive IDT) and underwent desensitization; only one developed urticaria. All children with negative skin tests (SPT and/or IDT) experienced no reactions following vaccination.

Individuals with cow's milk allergy

Some vaccines may contain milk-derived proteins, such as lactalbumin and casein, which are used during the manufacturing process. Among the vaccines that may include these components are the MMR vaccine produced by the Serum Institute of India, as well as the dTpa (diphtheria, tetanus, and pertussis for children under 7 years of age) and Tdap (tetanus, diphtheria, and pertussis for adolescents and adults) vaccines from specific manufacturers.

For patients with cow's milk allergy, it is recommended to use an MMR vaccine that does



Note: Consumption of egg before vaccination is not recommended, and measurement of egg-specific IgE should not be performed prior to yellow fever vaccination. If a patient has never ingested egg and an egg-specific IgE test was nonetheless obtained and yielded a positive result, the patient should preferably be referred to an allergist. This situation may lead to unnecessary delays in vaccination.

Figure 1

Algorithm for the evaluation and management of patients with a history of egg allergy or previous reaction to an ovalbumin-containing vaccine

IgE = immunoglobulin E, IDT = intradermal testing; SPT = skin prick test.

not contain milk proteins, such as the formulation produced by Fiocruz-Bio-Manguinhos. If this option is unavailable, postponing vaccination until a safe alternative becomes accessible is advisable.

dTpa and Tdap vaccines may also contain milk proteins used as a growth medium for antigen production. Although the residual quantities are very small and insufficient to trigger reactions in most patients, there have been reports of severe anaphylactic reactions in children with pronounced milk allergy, possibly due to the presence of casein derivatives.[27] For individuals with severe allergy and a very low threshold for reactions upon contact with milk, administration of these vaccines in a setting equipped to manage anaphylaxis should be considered. In all other cases, routine vaccination is recommended.

Finally, the rotavirus vaccine does not contain cow's milk protein in its formulation, and there is no scientific evidence that administration of this vaccine causes cow's milk allergy.[28] Therefore, routine rotavirus immunization is considered safe for individuals with cow's milk allergy.

Individuals with gelatin allergy

Gelatin is frequently added to vaccines as a stabilizer, particularly in live attenuated viral vaccines (depending on the manufacturer), such as MMR, varicella, and yellow fever vaccines. Studies have shown that gelatin is the main trigger of severe allergic reactions, including anaphylaxis, associated with some of these vaccines.[17,29,30]

Before administering vaccines that contain gelatin, it is essential to assess the patient's clinical history regarding previous reactions to gelatin, whether through ingestion or in response to earlier vaccinations. Patients with galactose-α-1,3-galactose (alpha-gal) allergy, a condition associated with delayed allergic reactions to red meat and related products, should also be evaluated with caution before receiving gelatin-containing vaccines.[16]

In cases where there is a history of gelatin allergy or prior reactions to gelatin-containing vaccines, the evaluation may include serum-specific IgE testing for gelatin, SPT with the undiluted vaccine, and, if the SPT is negative, IDT with the vaccine diluted 1:100.[17] If skin test results are negative, the vaccine may be administered in the usual manner as a single full dose, with the patient observed for at least 30 minutes to monitor for potential reactions.[17] If any skin test is positive, administering fractioned doses of the vaccine in a setting equipped for anaphylaxis management is recommended,[17] as shown in Figure 2. For patients with a history of severe hypersensitivity reaction after a gelatin-containing vaccine (severe anaphylaxis with respiratory failure requiring supplemental oxygen, refractoriness to bronchodilators or epinephrine, need for mechanical ventilation, or shock), administration of vaccines containing gelatin is contraindicated.

Individuals with latex allergy

Vaccines currently licensed in Brazil are supplied in vials and syringes that may contain latex. However, allergic reactions resulting from this type of exposure are extremely rare, and in most reported cases no specific investigations were conducted to determine whether latex was the actual cause of the reaction.[31]

To minimize risk in patients with latex allergy, it is recommended that vaccination be performed in a latex-free environment. In addition, for vaccines in multi-dose vials, it is recommended to administer the first dose withdrawn from the vial to latex-allergic patients. This recommendation is based on the rationale that the initial dose has a lower likelihood of contamination with latex particles.

Individuals with fungal allergy

In the manufacturing process of certain vaccines, such as hepatitis B, human papillomavirus (HPV), and some types of conjugate meningococcal vaccines (including MenB-4C and ACWY), the antigens are recombinant proteins expressed in Saccharomyces cerevisiae or other yeast species.[16] Although concerns have been raised about potential allergic reactions to these vaccines in individuals with fungal allergies, such reactions are extremely rare.

Given the rarity of yeast-associated allergic reactions, it is recommended that patients with a history of allergy to *S. cerevisiae* undergo specific skin testing. If the result is positive, supervised administration of the vaccine, preferably using fractionated doses, should be considered to minimize the risk of an adverse reaction.

Individuals with polyethylene glycol or polysorbate 80 allergy

Polyethylene glycol (PEG, or macrogol) is an ether polymer with a molecular weight ranging from 200 to

35,000 g/mol. It is used both in its pure form, such as in colonoscopy preparations and laxatives, and as an excipient in cosmetics, medications, and certain vaccines.[32] Polysorbate 80 (PS80, or Tween 80) is a nonionic surfactant whose poly(ethylene oxide) side chains share structural similarity with PEG.[32] Allergy to PEG or PS80 is considered extremely rare, although its true prevalence remains unknown.[33]

For patients with a history suggestive of PEG or PS80 allergy, a careful evaluation is recommended, including a detailed clinical history and skin testing, as outlined in Figure 3. The algorithm described in Figure 3 also applies to patients with a suspected history of allergic reaction to a vaccine, which is discussed in the section "Algorithm for the evaluation of patients with a suspected allergic reaction to a vaccine."

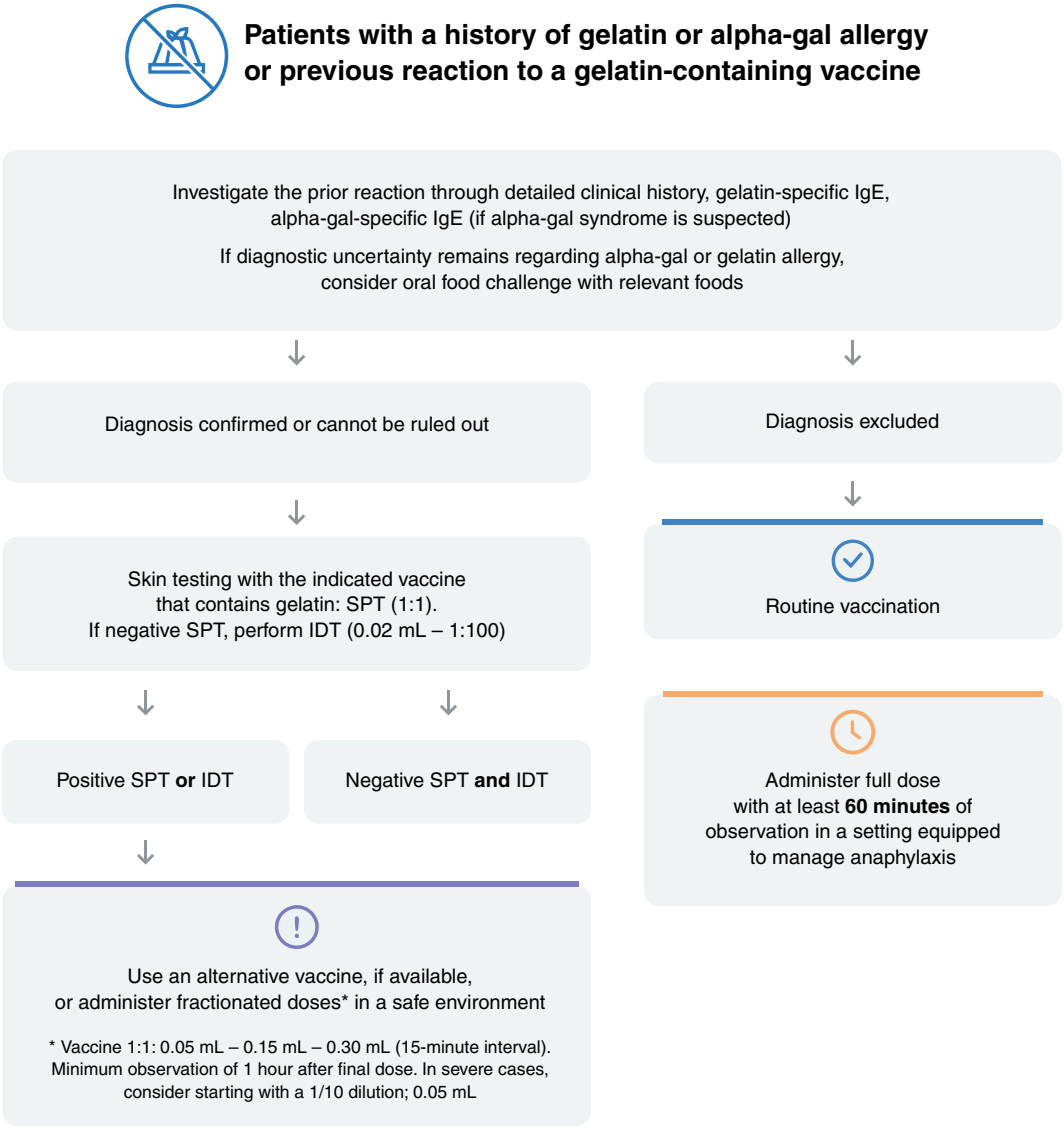


Figure 2
Algorithm for the evaluation and management of patients with a history of gelatin or alpha-gal allergy
Alpha-gal = galactose-α-1,3-galactose; IgE = immunoglobulin E, IDT = intradermal testing; SPT = skin prick test.

Summary of recommendations for the immunization of patients with a history of immediate hypersensitive reaction

Table 3 summarizes the recommendations for the immunization of patients with a history of immediate hypersensitive reaction.

Delayed hypersensitivity reactions

Local reactions, such as prolonged warmth, flushing, induration, and swelling at the injection site, are the most common delayed immunologic reactions following vaccination. These reactions may occur many hours to weeks after immunization, which can make causal assessment challenging.[34] Such local reactions generally do not progress in severity and do not contraindicate future vaccinations.[35]

In contrast, more severe reactions, such as Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN), do contraindicate subsequent doses of the associated vaccine. However, it should be noted these reactions are extremely rare.[36-38] Erythema multiforme major is primarily associated with viral (such as herpes simplex) and bacterial infections (such as *Mycoplasma pneumoniae*) and is only rarely linked to vaccines.[39,40]

Other rare cutaneous reactions reported in association with vaccines include acute generalized exanthematous pustulosis, erythema nodosum, granuloma annulare, bullous pemphigoid, Sweet syndrome, Gianotti-Crosti syndrome, lichenoid eruptions, cutaneous lupus, lupus vulgaris, and serum sickness-like reactions.[41] In many cases, there are reports of previous active infection prior to vaccination and the onset of these conditions.[41] Most cases do not recur after booster doses of the same vaccine.[41]

Delayed hypersensitivity reactions to vaccine excipients, such as antimicrobials, preservatives, and adjuvants, have also been described and may present as generalized eruptions or as contact-type reactions at the injection site.[41] Overall, these reactions tend to be mild and locally confined. If a vaccine excipient is suspected as the cause of delayed hypersensitivity, patch testing with the intact vaccine or with the isolated excipient may be performed,[42] as described in Figure 4. There is no contraindication to subsequent doses of the same vaccine, provided that adequate clinical monitoring is ensured.

Arthus reaction

An Arthus reaction is a type III hypersensitivity reaction characterized by the deposition of antigen–antibody (IgG) immune complexes and complement in local blood vessels.[43] It tends to present with pain, edema, and induration at the injection site and, in more severe cases, may progress to local ulceration or necrosis.[43]

The Arthus reaction usually begins between 2 and 12 hours after vaccine administration and is more common in individuals who have preexisting IgG antibodies against the vaccine antigen.[44] Vaccines that have been associated with Arthus reaction include tetanus-containing vaccines, hepatitis B vaccine, rabies vaccine, and the 23-valent pneumococcal polysaccharide vaccine.[43]

Management is predominantly symptomatic and may include antihistamines, application of cold compresses to the affected area, and analgesics for pain relief. It is important to reassure patients that this is a self-limited reaction with a short course, typically resolving within about 1 week. Despite the reaction, there is no contraindication to receiving future doses of the same vaccine.

Guillain-Barré Syndrome

Neurologic complications such as Guillain-Barré syndrome (GBS) are rare adverse events associated with vaccination.[41] GBS typically presents with progressive muscle weakness beginning in the extremities and ascending toward the trunk, and may lead to respiratory failure or cranial nerve weakness.[45] Symptom onset is considered potentially related to vaccination if it occurs within 6 weeks following administration of vaccines containing tetanus toxoid, poliovirus, rabies, or influenza antigens.[41] The pathophysiology involves a delayed, immune-mediated reaction with participation of CD4+ and CD8+ T lymphocytes that exhibit cross-reactivity with components of the nervous system.[45]

Given the delayed onset of symptoms, a comprehensive understanding of GBS-related events is essential for accurate diagnosis and assessment of potential causality. Other factors, such as previous infections with *Campylobacter jejuni*, cytomegalovirus, Epstein-Barr virus, influenza A, *Mycoplasma pneumoniae*, or *Haemophilus influenzae*, may also trigger the syndrome.[41]

There is no contraindication to vaccinating patients with a history of GBS, provided the previous episode was not associated with the vaccine to be administered. If the patient developed GBS less than 3 months earlier, postponing vaccination is advisable.[45] If a case of GBS is suspected to have been associated with a prior vaccination, subsequent doses of the same vaccine are contraindicated.

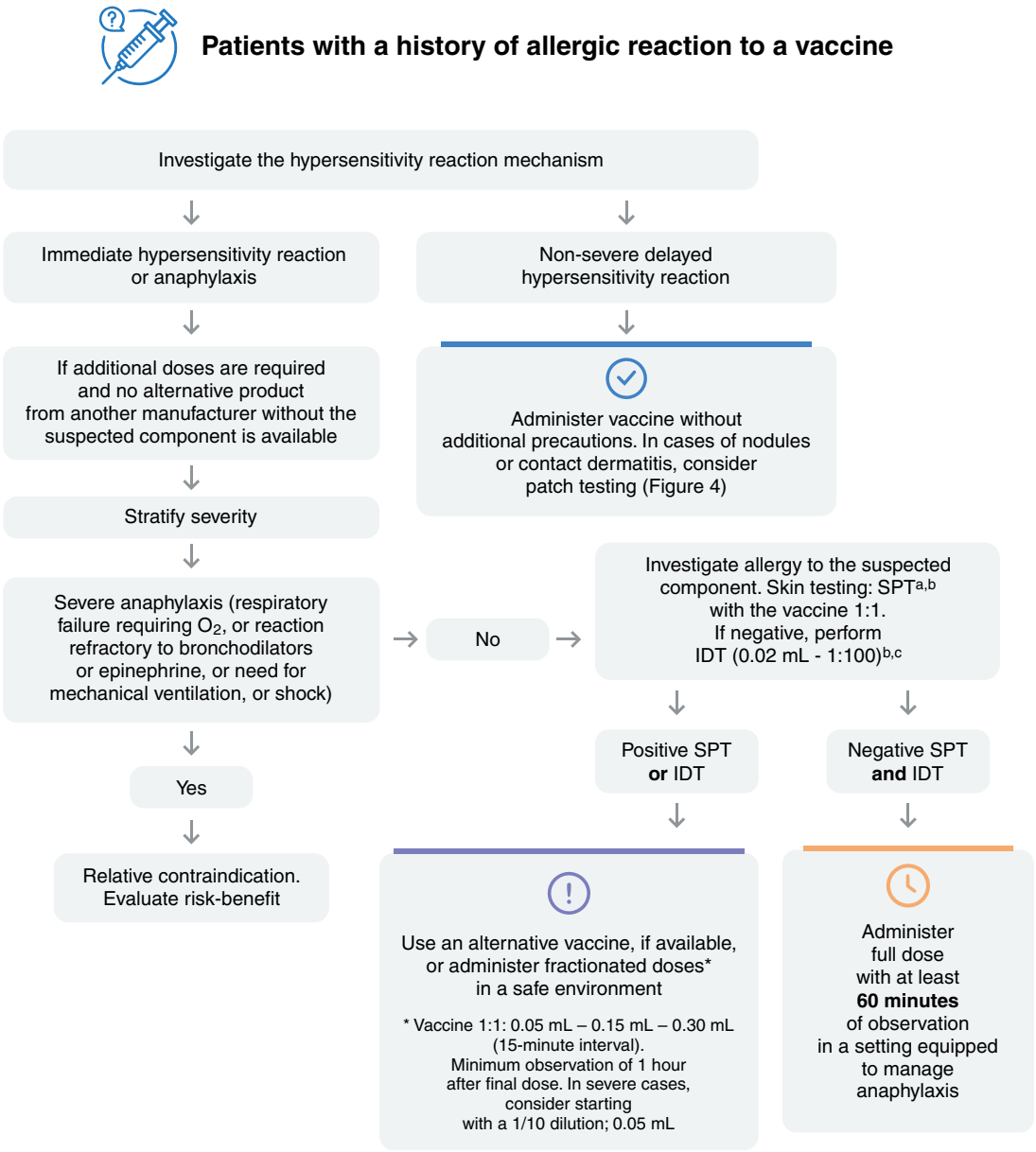


Figure 3

Algorithm for the evaluation and management of patients with a history of suspected allergic reaction to a vaccine

[a] In patients with a history of severe anaphylaxis, it is appropriate to dilute the vaccine 1:10 or even 1:100, as these concentrations are considered non-irritating.

[b] Whenever possible, perform testing with the same vaccine from the same manufacturer involved in the original reaction.

[c] Undiluted IDT is discouraged due to a high irritant rate. Whenever possible, perform testing with the same vaccine from the same manufacturer involved in the original reaction.

IDT = intradermal testing.

Table 3
Main types of allergy and recommendations for immunization in patients with a history of immediate hypersensitivity

Allergen	Vaccine	Recommendation
Egg	MMR, MMRV, and influenza	Routine vaccination. Preferably administer in a setting equipped to manage anaphylaxis, depending on medical assessment of previous reaction severity and reaction threshold
	Yellow fever	Perform risk stratification; consider skin testing and administer in a setting with anaphylaxis support if necessary (Figure 1)
Cow's milk	MMR	Do not use the formulation manufactured by the Serum Institute of India; choose an alternative without milk (eg, Fiocruz-Bio-Manguinhos).
	DTPa/Tdap	No contraindication. Individualized assessment for patients with severe cow's milk allergy and low reaction threshold; consider vaccination with at least 30 minutes of observation in a setting capable of managing anaphylaxis
Gelatin	MMR, MMRV, influenza, yellow fever, varicella, rabies	Evaluate history of gelatin allergy and perform skin testing if needed. If positive, administer fractionated doses in a setting prepared for anaphylaxis management (Figure 2)
Latex	Any vaccine in vials or syringes containing latex	Use latex-free gloves. For multidose vials, administer the first dose withdrawn from the vial to the latex-allergic patient.
Fungi *(Saccharomyces cerevisiae)*	Hepatitis B, HPV, meningococcal conjugate vaccines (MenB-4C and ACWY)	Consider skin testing; if positive, consider supervised administration with fractionated doses of the vaccine that may contain yeast
PEG and PS80	HPV DTPa/Tdap, Influenza (some formulations), hepatitis B (some formulations), COVID-19 (some formulations), RSV, pneumococcal conjugate vaccines, meningococcal conjugate vaccines	Consider skin testing with the vaccine. If positive, consider using alternative vaccines or administering fractionated doses in an anaphylaxis-prepared setting. If negative, administer the vaccine in a facility equipped to manage anaphylaxis (Figure 3)

COVID-19 = coronavirus disease 2019; DTPa = diphtheria, tetanus, and pertussis for children under 7 years of age; Fiocruz = Fundação Oswaldo Cruz; HPV = human papillomavirus; PEG = polyethylene glycol; PS80 = polysorbate 80; RSV = respiratory syncytial virus; Tdap = tetanus, diphtheria, and pertussis for adolescents and adults.

In such cases, evaluating the situation in alignment with the investigation and official response to the reported adverse event following immunization is essential.

Summary of recommendations for the immunization of patients with a history of non-immediate hypersensitive reaction

Figure 4 summarizes the recommendations for the immunization of patients with a history of non-immediate post-vaccination hypersensitivity.

Individuals with a personal or family history of atopy have no contraindications to immunization and should receive vaccines according to routine health guidelines. For those with a history of allergy to a specific vaccine component, a prior evaluation, preferably conducted by an Allergy and Immunology specialist, is recommended. In cases of local reactions such as contact dermatitis, nodules, flushing, pain, edema, or induration at the injection site, patch testing may be considered to confirm the causal agent. Testing may be performed using the intact vaccine or its individual components, alongside a negative control. These reactions generally do not contraindicate future doses of the same vaccine, and the patient may continue the immunization schedule as usual.

If a GBS episode is suspected to have been associated with a previous vaccination, subsequent

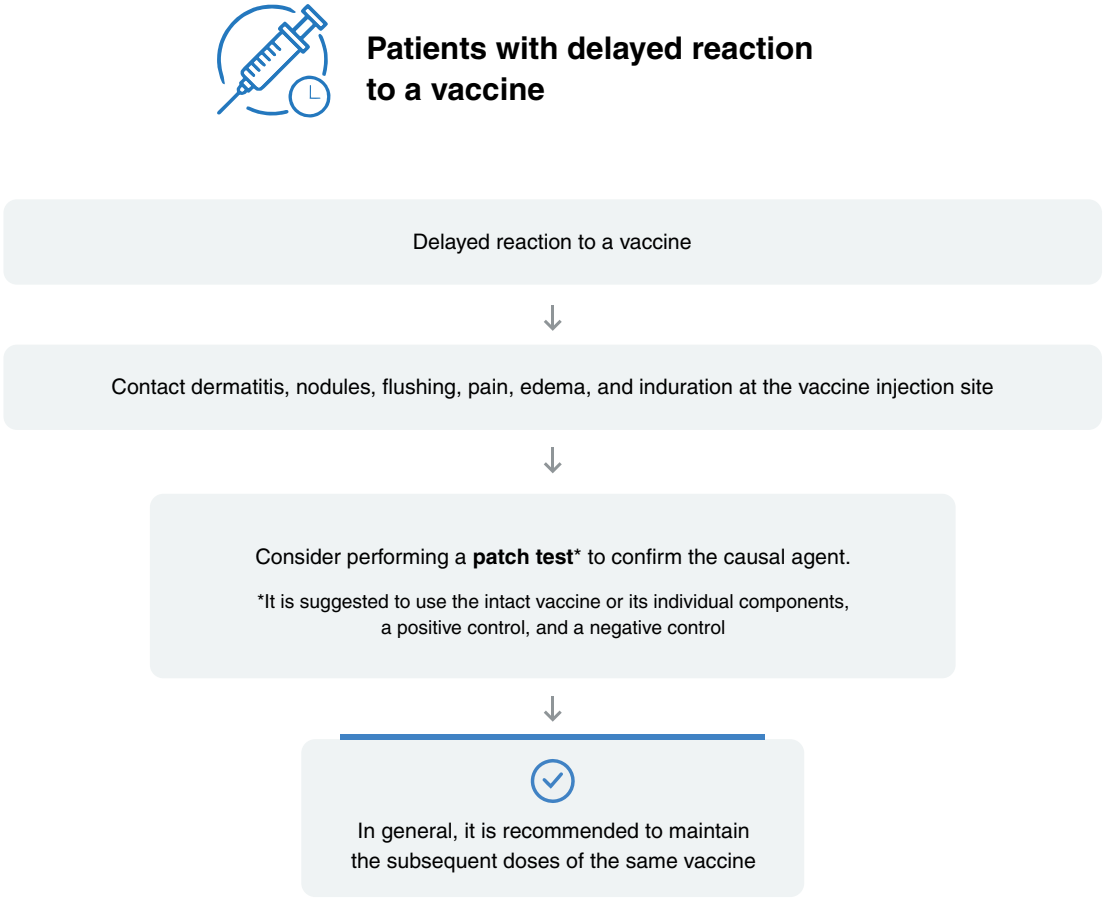


Figure 4
Algorithm for the evaluation and management of patients with a history of suspected delayed allergic reaction to a vaccine

doses of the implicated vaccine should be withheld. However, if the episode occurred more than 3 months prior and was not related to vaccination, routine immunization can be safely resumed.

Special considerations for patients with hypersensitivity reactions

Dengue vaccine (Qdenga®)

In 2023, Brazil recorded more than 1.6 million cases of dengue, with 1,179 deaths.46 By October 12, 2024 (epidemiological week 41), over 6.5 million suspected cases had been reported, with 6,613 confirmed dengue-related deaths and an additional 1,499 deaths under investigation.[46] These figures indicate a substantial worsening of the dengue epidemiological landscape in Brazil, with increases in both case numbers and mortality.

In the absence of specific treatment, dengue management relies on early identification of warning signs and severe manifestations, requiring organized healthcare systems and adequately trained personnel. Prevention efforts are challenged by the *Aedes aegypti* mosquito's resistance to insecticides.[47] Moreover, urbanization and climatic factors, such as prolonged periods of elevated temperatures, contribute to rising dengue incidence, even in areas with historically low transmission rates.[48]

Although the tetravalent dengue vaccine (CYD-TDV; Dengvaxia, Sanofi-Pasteur) is licensed in Brazil, it is recommended only for individuals with a laboratory-confirmed prior dengue infection. The approval of Qdenga® (Takeda) by Anvisa in 2022 introduced a new option for disease prevention. Qdenga® is a live-attenuated vaccine that protects against all four dengue virus serotypes: DENV-1, DENV-2, DENV-3, and DENV-4.

Considering both seronegative and seropositive individuals prior to vaccination, Qdenga® demonstrated an efficacy of approximately 61% against virologically confirmed symptomatic dengue of any severity and 84% against hospitalization up to 54 months after the second dose.[49] Throughout the vaccine's clinical development program, safety data were assessed in approximately 27,000 phase 2 and phase 3 participants from endemic and non-endemic regions.[45] An integrated safety analysis did not identify significant risks. The vaccine was well tolerated regardless of age, sex, or baseline dengue serostatus in individuals aged 4 to 60 years.[50] The most common adverse events following the first vaccine dose were injection-site pain (43% for Qdenga® vs. 26% for placebo) and headache (34% vs. 30%, respectively). Most adverse reactions at injection site were mild and resolved within 1 to 3 days.[50]

Qdenga® was incorporated into the Brazilian National Immunization Program (PNI) in December 2023, and vaccination of adolescents aged 10 to 14 years began in March 2024 across 521 municipalities selected based on epidemiological data.

Post-marketing safety data collected between March 2023 and March 2024 identified 70 hypersensitivity reactions associated with Qdenga® in Brazil, corresponding to an overall incidence of 19.15 per 100,000 administered doses.[51] Of these, 16 cases were classified as anaphylaxis, yielding an incidence of 4.38 per 100,000 doses. Most anaphylaxis cases involved cutaneous and mucosal manifestations, with a substantial proportion presenting respiratory, circulatory, or gastrointestinal involvement. No cases progressed to death.[51]

Pharmacovigilance monitoring identified 85 cases of immediate hypersensitivity reactions following Qdenga® vaccination, including 24 anaphylaxis cases (63.1 per million doses), three of which involved anaphylactic shock, among 380,358 administered doses between March 1, 2023, and March 11, 2024.[52] In 10 of these cases (41.7%), symptoms began within 15 minutes of vaccination. No deaths, sequelae, or complications related to anaphylaxis occurred. These data underscore the need for careful evaluation of allergic patients before and after vaccine administration.[8-11] It is therefore essential to assess any history of severe allergies to vaccine components or past vaccination before administering the vaccine.

Patients who, after the first dose, experienced isolated or subjective immediate symptoms, such as cough, nausea, vomiting, dizziness, or a sensation of throat tightness without objective evidence of airway compromise (e.g., edema, hoarseness, erythema, or pruritus), and who recovered quickly without medical intervention should receive the second dose and be observed for at least 30 minutes. It is also important to consider alternative diagnoses to ensure that symptoms were not attributable to other medical conditions.

For patients who developed urticaria and/or angioedema (localized or generalized) or other isolated symptoms not typical of anaphylaxis, the recommendation is also to proceed with the second

dose and monitor for at least 30 minutes for possible reactions. In addition, referral to an allergist should be considered to investigate other potential triggers of the initial reaction. For individuals who experienced urticaria or an Arthus reaction after the first dose, administration of antihistamines 30 minutes before the second dose may be considered. The duration of antihistamine use may vary depending on the severity and recurrence of allergic reactions. Importantly, the use of antihistamines before vaccination does not reduce the risk or severity of recurrent events in patients who experienced previous reactions, including anaphylaxis.

In cases of anaphylaxis involving two or more organ systems (e.g., cutaneous, respiratory, gastrointestinal, among others), patients should preferably be evaluated by an allergist. This assessment should consider the epidemiological risk and, in some cases, SPT or IDT may be required to identify the allergenic component responsible for the reaction. When administration of the second vaccine dose is considered necessary, it is recommended to follow the investigation algorithm described in Figure 3.

Finally, preparedness and response capacity are critical to minimizing risks and effectively managing any allergic reaction following dengue vaccination or other immunizations in allergic patients, whether vaccination occurs within healthcare facilities or in community settings (extramural vaccination).[53]

COVID-19 vaccine

The potential allergens contained in the COVID-19 vaccines currently available in Brazil are listed in Table 4.

Both mRNA vaccines (Comirnaty and Spikevax) share a similar structure: they contain no protein or adjuvant, only mRNA encapsulated within stabilizers inside a lipid nanoparticle coated with PEG to enhance water solubility. Although PEG was initially suspected as the primary trigger of allergic reactions to mRNA vaccines,[54] subsequent studies have indicated that the presence of PEG in the formulation does not impact the efficacy or safety of lipid nanoparticle-based COVID-19 vaccines.[55]

In addition to PEG, Moderna's mRNA-1273 vaccine (Spikevax) also contains tromethamine (trometamol), a widely used buffering agent. Some reports of anaphylaxis to injectable medications have been attributed to tromethamine.[56,57] In the second formulation of Comirnaty® (Pfizer, ready-to-use vials), tromethamine was also added. Although initial reports suggested an elevated risk of anaphylaxis with COVID-19 vaccines, more recent pharmacovigilance data indicate that the incidence of anaphylaxis with mRNA vaccines (8.96 cases per million administered doses) is comparable to rates observed with other vaccines (between 1 and 10 cases per million doses).[58,59] The incidence of anaphylactic shock was 1.46 per million doses, and fatal reactions were extremely rare, with rates of 0.04 per million doses for anaphylactic reactions and 0.02 per million doses for anaphylactic shock.[59] These findings reinforce the safety profile of these vaccines.

Some studies have described delayed local reactions following administration of mRNA COVID-19 vaccines. These reactions, characterized by erythema, induration, and tenderness at the injection site, typically occur 6 to 8 days after vaccination and may persist for up to 2 weeks.[60-63] Although uncomfortable, these reactions are not considered contraindications to subsequent doses. In most reported cases, individuals who experienced such reactions after the first dose received the second dose without recurrence or with less intense reactions.[60-63] In the phase 3 trial of Moderna's mRNA-1273 vaccine, delayed local reactions occurred in 0.8% of participants after the first dose and 0.2% after the second.[64]

For patients with a suspected history of allergic reaction to a COVID-19 vaccine, it is recommended to follow the investigation algorithm described in Figure 3.

Immunization of patients with asthma

Asthma is a chronic disease that affects approximately 300 million people worldwide.[65] In Brazil, 23.2% of the population is estimated to live with asthma,[66] which is one of the leading causes of hospitalization among children and adolescents and a common reason for emergency care visits.[67]

Vaccination against influenza

In patients with asthma, chronic airway inflammation and type II immune responses are believed to impair antiviral immunity in the respiratory tract,[68] causing greater susceptibility to severe influenza-related disease and associated bacterial infections. The mechanisms that increase susceptibility to influenza in patients with asthma include weaker innate immune responses, reduced type 1 helper T-cell activity, and

deficient interferon-α responses from plasmacytoid dendritic cells upon influenza exposure.[69] In addition, influenza infections may lead to asthma exacerbation, often requiring hospitalization.[70] During the 2009 influenza pandemic, patients with asthma were at significantly higher risk of hospitalization, with most seeking care due to exacerbation of respiratory symptoms rather than influenza infection alone.[71]

In addition to being safe, influenza vaccination is effective in individuals with asthma. A case-control study conducted in Scotland evaluated influenza vaccine effectiveness in patients with asthma during 6 seasons (from 2010/2011 to 2015/2016), using 5,910 swab samples. Vaccination was associated with a 55% reduction in laboratory-confirmed influenza infections over the 6 seasons.[72]

It is recommended that patients with asthma follow the Brazilian routine vaccination schedule, receiving annual doses of the trivalent or quadrivalent influenza vaccine starting at 6 months of age.

In 2023, a high-dose quadrivalent influenza vaccine became available in Brazil for individuals aged 60 years and older. Manufactured by Sanofi Pasteur and marketed as Efluelda®, the vaccine contains 4 times the antigen content of standard-dose quadrivalent influenza vaccines. Efluelda® demonstrated an incremental efficacy of 24.2% compared to the standard-dose vaccine. A meta-analysis evaluating data across 10 influenza seasons showed that the high-dose vaccine provides protective benefits beyond influenza prevention, including a 27% reduction in pneumonia-related hospitalizations and an 18% reduction in cardiorespiratory hospitalizations.[73-75] The vaccine is available in private vaccination clinics and offers enhanced protection for adults aged 60 years and older, whose vaccine responsiveness is lower due to immunosenescence and the frequent presence of comorbidities.

Strategies to improve adherence to influenza vaccination among patients with asthma are essential,

Table 4
Types of COVID-19 vaccines, active substances, and potential allergens

Type of vaccine	Vaccine name	Active substance	Potential allergens
mRNA vaccine encoding the SARS-CoV-2 spike glycoprotein	BNT162B2 Pfizer/BioNTech Comirnaty Herpes zoster	mRNA	PEG 2000; tromethamine and tromethamine hydrochloride (in ready-to-use vials only)
mRNA vaccine encoding the SARS-CoV-2 spike glycoprotein	mRNA-1273 Moderna Spikevax	mRNA	PEG 2000; tromethamine and tromethamine hydrochloride
Recombinant spike protein vaccine with adjuvant	NVX-CoV2373 Novavax Nuvaxovid/Covovax	Recombinant spike protein adjuvanted with Matrix-M, produced in Sf9 *Spodoptera frugiperda* insect cells	PS80

COVID-19 = coronavirus disease 2019; DTPa = diphtheria, tetanus, and pertussis for children under 7 years of age; Fiocruz = Fundação Oswaldo Cruz; HPV = human papillomavirus; PEG = polyethylene glycol; PS80 = polysorbate 80; RSV = respiratory syncytial virus; Tdap = tetanus, diphtheria, and pertussis for adolescents and adults.

as they can significantly reduce the risk of influenza-triggered exacerbations.

Vaccination against respiratory syncytial virus

RSV is the leading cause of bronchiolitis and pneumonia in children under 5 years of age.[76] Each year, RSV accounts for approximately 33 million infections, more than 3 million hospitalizations, and over 100,000 deaths among children aged 0 to 5 years worldwide, with the greatest impact occurring in economically disadvantaged regions.[76] In addition to affecting children, RSV-associated hospitalizations are also high among older adults, particularly those aged 65 years or more, and among individuals with chronic conditions,[77,78] underscoring the need to include these populations in RSV immunization strategies.

The association between severe RSV disease in infancy and the development of asthma is well established.[79,80] Although a causal link between RSV infection and asthma has not yet been proven, immunological evidence suggests skewing toward a Th2-type response, and reduction of interferon-γ antiviral immunity during RSV infection supports airway hyper-reactivity in a subset of susceptible children.[79] Bronchiolitis due to RSV has also been linked to more severe asthma, demonstrated by a 3-fold increase in asthma-related hospitalizations and medication use compared with age-matched controls without prior RSV-associated lower respiratory tract infection.[81]

In a study including approximately 25,000 adults aged 60 years or older, the adjuvanted RSV vaccine (RSVPreF3 OA, Arexvy, GlaxoSmithKline) was well tolerated and reduced the risk of RSV-associated lower respiratory tract disease by 82.6% and of RSV-associated acute respiratory infection (including mild infection) by 72%.[82] When evaluating participants with one or more chronic conditions, such as asthma, chronic lung disease, chronic heart failure, and diabetes, vaccine efficacy was even higher.[83] Among those with at least one chronic condition, the vaccine reduced the risk of RSV-associated lower respiratory tract disease by 95% and of RSV-associated acute respiratory infection by 81%.[83] In participants with two or more chronic conditions, the risk reduction for lower respiratory tract disease was 92% and for acute respiratory infection was 88%.[83] These findings indicate that the RSV vaccine may serve as an important tool for preventing severe RSV-related disease in adults aged 60 years and older with chronic health conditions, including asthma.

In Brazil, the National Health Surveillance Agency (Anvisa) recently authorized the registration of two RSV vaccines:

– Arexvy (adjuvanted), from GlaxoSmithKline, was the first RSV vaccine registered in the country (2023). Approved for use in adults aged 60 years or older, as well as adults aged 50-59 years at increased risk for RSV infection, the vaccine is administered intramuscularly as a single dose at any time of the year, regardless of viral seasonality. Current data demonstrate sustained protection across three RSV seasons (nearly 3 years).[84] Thus, booster doses are not currently recommended.
– Abrysvo, from Pfizer, was licensed by Anvisa for use in pregnant individuals between 24 and 36 weeks of gestation to protect newborns. It is administered intramuscularly as a single dose. The vaccine has demonstrated protection through two RSV seasons. It has also been authorized for administration in persons aged 60 years or older, and in adults aged 18-59 years at increased risk for RSV infection, with safety and efficacy data comparable to those of Arexvy.

The use of these vaccines in patients with asthma aged 60 years or older is recommended by both SBIm and ASBAI.

In addition to vaccines, palivizumab and nirsevimab are monoclonal antibodies indicated for the prevention of RSV infection in infants, particularly those at high risk. Palivizumab is a humanized monoclonal antibody that binds to the RSV fusion (F) protein, inhibiting viral entry into host cells.[85] Clinical studies have shown that palivizumab significantly reduces RSV-related hospitalizations in extremely premature infants (born at <28 weeks), as well as in those with bronchopulmonary dysplasia or hemodynamically significant congenital heart disease.[85,86] Prophylaxis with palivizumab requires monthly administration during the RSV season, for up to five doses.

Nirsevimab is a long-acting monoclonal antibody that also targets the RSV F protein but has an extended half-life, allowing protection with a single dose for the entire viral season.[87] Clinical trials have demonstrated that nirsevimab effectively reduces severe RSV infections and hospitalizations in healthy infants, preterm infants, and those with comorbidities.[87-89] Its efficacy was comparable to or greater than that of palivizumab, with the added benefit of a single-dose regimen.[88]

In summary, palivizumab and nirsevimab are effective for RSV prevention in infants, with nirsevimab offering the advantage of once-per-season dosing.

Vaccination against invasive pneumococcal disease

Pneumococcal disease refers to any infection caused by *Streptococcus pneumoniae* (pneumococcus),[90] which is the most common bacterial causative agent of a wide range of infections, including noninvasive (such as sinusitis, otitis media, and community-acquired pneumonia) and invasive disease, when pneumococcus enters previously sterile sites such as the bloodstream (bacteremia) or the tissues and fluids surrounding the brain and spinal cord (meningitis).[90,91] These conditions are severe, frequently require hospitalization, and may be fatal.[90]

Approximately 100 pneumococcal serotypes have been identified based on antigenic differences in their polysaccharide capsules. Polysaccharide capsules are the most important virulence factors of this bacterium and are responsible for inducing serotype-specific immunity in the host.[92] Consequently, these capsular antigens form the basis of current pneumococcal vaccine formulations used for disease prevention.

Asthma has been associated with an increased risk of pneumonia and IPD, particularly among children.[93,94] In addition, asthma may worsen pneumonia outcomes and increase mortality risk.[95] For this reason, health agencies, including the U.S. Centers for Disease Control and Prevention (CDC),[96] consider asthma an indication for pneumococcal vaccination. The GINA initiative notes that there are still limited data conclusively demonstrating pneumococcal vaccine efficacy specifically in the asthma population to recommend universal use, although it acknowledges that these patients, especially children and older adults, are at higher risk for pneumococcal infections.[65]

Pneumococcal vaccination is part of the childhood immunization schedule in about half of World Health Organization member states, including Brazil. Vaccination reduces pneumonia-related hospitalizations in children and adults and lowers the risk of invasive disease.[97,98] Two types of vaccines are available: the pneumococcal polysaccharide vaccine (PPSV) and pneumococcal conjugate vaccines (PCVs). PPSV induces serotype-specific immunity to the serotypes included in the formulation (as detailed in Figure 5), generating a short-term immune response by stimulating a subset of B cells that produce IgG2 antibodies. Conjugate vaccines, which link a polysaccharide to a carrier protein, stimulate a T-cell-dependent, serotype-specific immune response and activate memory B cells. PPSV23 has been available in Brazil since 1989, and the 7-valent PCV (PCV7) – licensed in 2000 – was the first conjugate vaccine introduced globally. It was later replaced by conjugate vaccines covering additional serotypes, and Brazil currently offers PCV10, PCV13, PCV15, and PCV20.

Routine immunization against *Streptococcus pneumoniae* is safe in patients with asthma and may help mitigate the gradual decline in lung function caused by recurrent infection-triggered exacerbations.[99] The recommended immunization schedules for the pneumococcal vaccines currently available in Brazil (PCV10, PCV13, PCV15, PCV20, and PPSV23), including guidelines for patients with asthma, are provided in Table 5. In summary, it is recommended that patients with asthma receive the PCV13, PCV15, or PCV20 vaccine. For those previously vaccinated with PCV7 or PCV10, additional protection with vaccines containing serotype 19A is important. PPSV23 is recommended from 2 years of age onward for individuals who have received PCV13 or PCV15. PPSV23 is not recommended for those vaccinated with PCV20. The number of doses will depend on the patient's age and immune status.

It is important to emphasize that serologic testing is not recommended before or after pneumococcal vaccination.

Vaccination against COVID-19

Individuals with mild to moderate asthma who contract COVID-19 are not at increased risk for severe disease.[65,100] However, those with uncontrolled asthma have a higher risk of hospitalization due to severe COVID-19 if infected.[101-103]

In Brazil, the National Immunization Program incorporated COVID-19 vaccination into the routine schedule for children from 6 months to under 5 years of age, including those with asthma. In this population, two or three doses of the most up-to-date vaccine formulation are administered, with an interval of 4 weeks between the first and second doses and 8 weeks between the second and third doses (primary immunization schedule).[104]

In 2024, booster doses were implemented for individuals aged 60 years and older and for priority groups. Patients aged 5 years or older with severe

asthma (defined as those requiring recurrent systemic corticosteroid use and/or hospitalization for asthma exacerbation in the previous year) are considered a priority group for COVID-19 vaccination and should receive annual booster doses. Immunocompromised individuals and those aged 60 years or older who meet these criteria should receive semiannual booster doses with the most up-to-date vaccine formulation available. According to Brazil's 2024 COVID-19 Vaccination Strategy, primary immunization schedules are no longer routinely recommended for individuals aged 5 years or older who are not part of priority groups. For those who have never been vaccinated, a single COVID-19 vaccine dose may be administered.[104]

Summary of recommendations for the immunization of patients with asthma

Table 6 shows the recommendations for vaccination in patients with asthma.

Algorithm for the evaluation of patients with a history of suspected allergic reaction to a vaccine

Patients with a history of hypersensitivity to vaccines should undergo evaluation whenever possible. The investigation begins with a detailed clinical history, including the clinical presentation, the extent of the reaction (local or systemic), the timing of onset and duration (immediate or delayed), and

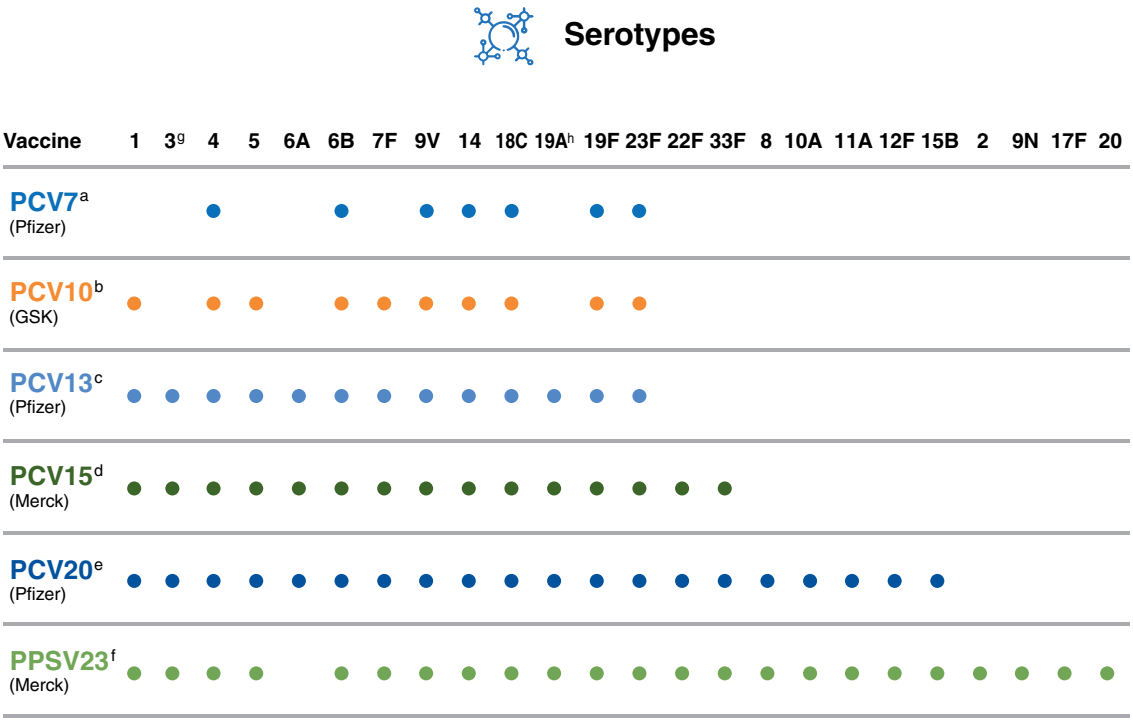


Figure 5
Pneumococcal vaccines licensed in Brazil

[a] No longer used in Brazil.
[b] Available at public primary healthcare units.
[c] Available in private clinics and at Reference Centers for Special Biologics (CRIE) for certain patient groups.
[d] Available in private clinics.
[e] Licensed for use in individuals aged ≥18 years; use in children is still under review.
[f] Licensed for use in individuals aged ≥2 years.
[g,h] Currently responsible for most cases of severe pneumococcal disease in Brazil.

Table 5
Recommended vaccination schedules for pneumococcal vaccines (PCV10, PCV13, PCV15, PCV20, and PPSV23)

Unvaccinated children up to 5 years of age

Age	Vaccine	Vaccination schedule	Notes
2-6 months	PCV10, PCV13, PCV15, or PCV20	Three doses in the first year of life, with a 2-month interval between doses, and a booster between 12 and 15 months of age	PCV10 is provided in public primary healthcare units and is part of Brazil's National Childhood Immunization Schedule
7-11 months	PCV10, PCV13, PCV15, or PCV20	Two doses in the first year of life, with a 2-month interval between doses, and a booster between 12 and 15 months of age	PCV15 and PCV20 are recommended as the preferred options when available. If not available, PCV13 should be used
12-24 months	PCV10, PCV13, PCV15, or PCV20	Two doses, 2 months apart	For children aged 2-5 years with chronic conditions that increase vulnerability to pneumococcal infections (including asthma), supplemental vaccination with the 23-valent pneumococcal polysaccharide vaccine (PPSV23) may be necessary for those who received PCV10, PCV13, or PCV15
2-5 years	PCV10, PCV13, PCV15, or PCV20	One dose	

Children aged 6 years or older, adolescents, and adults with chronic conditions that increase the risk for IPD (including asthma) who have not yet been vaccinated

A single dose of PCV13, PCV15, or PCV20 should be administered. For those who receive PCV13 or PCV15, vaccination should be supplemented with PPSV23

Adults

- Vaccination in individuals aged between 50 and 59 years of age with PCV20, PCV15, or PCV13 is at the discretion of the clinician.
- Pneumococcal vaccines are recommended for adults of any age with chronic lung diseases, such as asthma. In these cases, a single dose of PCV20 is indicated, or a sequential schedule beginning with PCV15 or, if unavailable, PCV13, followed by one dose of PPSV23 two months later, and a second dose of PPSV23 five years after the first.

Individuals aged 60 years or older

Status	Recommendation
General	A single dose of PCV20, or a sequential schedule starting with PCV15 or, if unavailable, PCV13, followed by one dose of PPSV23 two months later, and a second PPSV23 dose five years after the first. If PCV20 is chosen, no sequential PPSV23 doses are indicated
Individuals who have already received one dose of PPSV23	Administer PCV20, PCV15, or PCV13 after a 1-year interval from the PPSV23 dose. Those who receive PCV20 do not require an additional PPSV23 dose. Those who begin a sequential schedule with PCV15 or PCV13 should receive a second PPSV23 dose 5 years after the first, maintaining an interval of 6–12 months after PCV15 or PCV13
Individuals who have received two doses of PPSV23 and no PCV	Administer one dose of PCV20 or PCV15; if unavailable, PCV13 may be used. Any of these should be given at a minimum interval of 1 year after the last PPSV23 dose
Individuals with an incomplete schedule using PCV15 or PCV13 and/or PPSV23	Immunization can be completed with a single dose of PCV20, provided that at least 2 months have passed since the last PCV15 or PCV13 dose, or 1 year since PPSV23
Individuals with a complete sequential schedule of PCV15 or PCV13 + PPSV23	A single dose of PCV20 may be recommended at clinician discretion, respecting an interval of 1 year after PPSV23 and 2 months after PCV15 or PCV13

IPD = invasive pneumococcal disease; PCV10 = 10-valent pneumococcal conjugate vaccine; PCV13 = 13-valent pneumococcal conjugate vaccine; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

Table 5 *(continued)*
Recommended vaccination schedules for pneumococcal vaccines (PCV10, PCV13, PCV15, PCV20, and PPSV23)

Interchangeability of vaccines	
Vaccine	**Recommendation**
PCV13, PCV15, PCV20	PCV20, PCV15, and PCV13 are interchangeable, and switching between them at any point in the vaccination schedule is acceptable. Healthy children who have completed the schedule with PCV13 do not need revaccination with PCV20 or PCV15, unless they are at higher risk for IPD (including patients with asthma). In such cases, completion with PCV20 or a sequential schedule including PPSV23 is recommended
PCV10 to PCV13, PCV15, or PCV20	To ensure adequate protection against the main serotypes responsible for severe disease (19A and 3), the full age-appropriate schedule recommended for PCV13, PCV15, or PCV20 must be followed beginning at the time the first dose of the new vaccine is administered

IPD = invasive pneumococcal disease; PCV10 = 10-valent pneumococcal conjugate vaccine; PCV13 = 13-valent pneumococcal conjugate vaccine; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

the treatment required. For etiologic assessment, it is essential to record the manufacturer and lot number of the administered vaccine and to review the package insert to identify potential allergenic components, including aluminum, formaldehyde, thimerosal, 2-phenoxyethanol, lactose, gelatin, antibiotics, latex, ovalbumin, and yeasts.

If the clinical history suggests a hypersensitivity reaction to the vaccine, diagnostic evaluation should follow the mechanism of hypersensitivity involved, according to the algorithm illustrated in Figure 3. For immediate hypersensitivity reactions or anaphylaxis, skin testing (including SPT and IDT) with the vaccine and its components should be considered. If both tests are negative, the vaccine may be administered under supervision, with observation for at least 60 minutes, in a setting equipped to treat anaphylactic reactions.

When skin tests indicate sensitization, the specialist may choose an alternative vaccine that does not contain the suspected component. If this is not possible, vaccination may be performed using fractional dosing or a desensitization protocol in a setting prepared to manage potential adverse reactions.[105,106]

Non-allergic local reactions, such as erythema, pain, and edema, as well as fever do not contraindicate subsequent vaccine doses.[12] In all cases, it is essential that immunization is not delayed, in order to prevent increased susceptibility to infectious diseases, particularly in the current context of declining vaccination coverage in Brazil.

Although severe hypersensitivity reactions to vaccines are rare, vaccination settings must be prepared to manage such events. Facilities should be adequately equipped with epinephrine, antihistamines, corticosteroids, beta-2 agonists, and oxygen supply, have trained personnel, and follow clear emergency protocols to ensure rapid and effective response in cases of anaphylaxis. Importantly, a history of hypersensitivity to one vaccine does not contraindicate all others, since reactions are caused by specific components rather than by vaccines in general. An allergist can assist in this assessment and help ensure that subsequent vaccines are administered safely.

Reporting of adverse events following immunization

Adverse events following immunization (AEFI) must be reported and investigated in accordance with the 4th

Table 6
Summary of vaccination recommendations for patients with asthma

Vaccine	Recommendation
Influenza[a]	Annual vaccination with trivalent or quadrivalent influenza vaccine starting at 6 months of age. A high-dose influenza vaccine may be used for individuals aged 60 years or older
RSV	Arexvy (adjuvanted): recommended for adults aged ≥60 years and for adults aged 50–59 years at increased risk for RSV infection. Protection demonstrated through the third RSV season. Abrysvo: licensed by Anvisa for pregnant individuals ≥24 weeks' gestation and for adults aged ≥60 years, as well as adults aged 18–59 years at increased risk for RSV infection. Protection demonstrated through the second season
Pneumococcal vaccines	PCV13, PCV15, or PCV20. PCV13 and PCV15 should be complemented with PPSV23 in individuals ≥2 years old. Follow age- and risk-appropriate schedules (Table 5)
COVID-19[b]	Primary schedule of two or three doses (depending on the manufacturer) for children aged 6 months to <5 years. For patients aged ≥5 years with severe asthma, annual booster doses are recommended.
For others vaccines	Follow the routine vaccination schedule

[a,b] Influenza and COVID-19 vaccines may be administered on the same day.
COVID-19 = coronavirus disease 2019; PCV = pneumococcal conjugate vaccine; PPSV = pneumococcal polysaccharide vaccine; RSV = respiratory syncytial virus.

edition of the Manual of Epidemiological Surveillance of Adverse Events Following Immunization.[107] Adequate and timely reporting is essential to ensuring vaccine safety, allowing rapid responses to minimize risks, and informing adjustments to vaccination strategies when necessary. Reporting may be conducted by the institution that administered the vaccine or by the attending physician.

Conclusion

Early identification of allergic reactions, combined with adequate risk stratification based on clinical history and diagnostic testing, is essential to guide vaccine selection and the safe administration of immunizations in patients with a history of hypersensitivity reactions to vaccines. In addition, strategies such as fractional dose vaccination in controlled environments are effective in reducing the risk of hypersensitivity reactions, thereby supporting safe vaccination in this population.

Adequate management of patients who experience hypersensitivity reactions requires collaboration, whenever possible, between allergy and immunology specialists and other healthcare professionals. Continuous surveillance of AEFIs, together with transparent communication with patients about risks and benefits, is fundamental to strengthening trust in vaccination. Moreover, promoting immunization among allergic patients, particularly those with asthma, protects these individuals against preventable infections, improves underlying disease control, and reduces the risk of exacerbation.

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References

1. Shattock AJ, Johnson HC, Sim SY, Carter A, Lambach P, Hutubessy RCW, et al. Contribution of vaccination to improved survival and health: modelling 50 years of the Expanded Programme on Immunization. Lancet. 2024 May 25;403(10441):2307-16. doi: 10.1016/S0140-6736(24)00850-X.
2. Lötvall J, Pawankar R, Wallace DV, Akdis CA, Rosenwasser LJ, Weber RW, et al.; American Academy of Allergy, Asthma & Immunology (AAAAI); American College of Allergy, Asthma & Immunology (ACAAI); European Academy of Allergy and Clinical Immunology (EAACI); World Allergy Organization (WAO). We call for iCAALL: International Collaboration for Asthma, Allergy and Immunology. Ann Allergy Asthma Immunol. 2012 Apr;108(4):215-6. doi: 10.1016/j.anai.2012.02.025.
3. Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. J Allergy Clin Immunol. 2004 May;113(5):832-6. doi: 10.1016/j.jaci.2003.12.591.
4. Mahler V, Junker AC. Anaphylaxis to additives in vaccines. Allergo J Int. 2022;31(5):123-36. doi:10.1007/s40629-022-00215-8.
5. Demoly P, Adkinson NF, Brockow K, Castells M, Chiriac AM, Greenberger PA, et al. International Consensus on drug allergy. Allergy. 2014 Apr;69(4):420-37. doi: 10.1111/all.12350.
6. Clarkson TW, Magos L, Myers GJ. The toxicology of mercury-current exposures and clinical manifestations. N Engl J Med. 2003;349(18):1731-7. doi:10.1056/NEJMra022471.
7. Cardona V, Ansotegui IJ, Ebisawa M, El-Gamal Y, Fernandez Rivas M, Fineman S, et al. World allergy organization anaphylaxis guidance 2020. World Allergy Organ J. 2020 Oct 30;13(10):100472. doi: 10.1016/j.waojou.2020.100472.
8. Bohlke K, Davis RL, Marcy SM, Braun MM, DeStefano F, Black SB, et al.; Vaccine Safety Datalink Team. Risk of anaphylaxis after vaccination of children and adolescents. Pediatrics. 2003 Oct;112(4):815-20. doi: 10.1542/peds.112.4.815.
9. McNeil MM, Weintraub ES, Duffy J, Sukumaran L, Jacobsen SJ, Klein NP, et al. Risk of anaphylaxis after vaccination in children and adults. J Allergy Clin Immunol. 2016 Mar;137(3):868-78. doi: 10.1016/j.jaci.2015.07.048.
10. Su JR, Moro PL, Ng CS, Lewis PW, Said MA, Cano MV. Anaphylaxis after vaccination reported to the Vaccine Adverse Event Reporting System, 1990-2016. J Allergy Clin Immunol. 2019;143(4):1465-73. doi:10.1016/j.jaci.2018.12.1003.
11. Choe YJ, Lee H, Kim JH, Choi WS, Shin JY. Anaphylaxis following vaccination among children in Asia: A large-linked database study. Allergy. 2021;76(4):1246-9. doi:10.1111/all.14562.
12. Kelso JM, Greenhawt MJ, Li JT, Nicklas RA, Bernstein DI, Blessing-Moore J, et al. Adverse reactions to vaccines practice parameter 2012 update. J Allergy Clin Immunol. 2012 Jul;130(1):25-43. doi: 10.1016/j.jaci.2012.04.003.
13. Taylor S, Asmundson GJG. Immunization stress-related responses: implications for vaccination hesitancy and vaccination processes during the COVID-19 pandemic. J Anxiety Disord. 2021;84:102489. doi:10.1016/j.janxdis.2021.102489.
14. Gold MS, MacDonald NE, McMurtry CM, Balakrishnan MR, Heininger U, Menning L, et al. Immunization stress-related response - Redefining immunization anxiety-related reaction as an adverse event following immunization. Vaccine. 2020 Mar 23;38(14):3015-3020. doi: 10.1016/j.vaccine.2020.02.046.
15. Pérez Rubio A, Eiros JM. Cell culture-derived flu vaccine: Present and future. Human Vaccines & Immunotherapeutics. 2018;14(8): 1874-82. doi: 10.1080/21645515.2018.1460297.
16. McNeil MM, DeStefano F. Vaccine-associated hypersensitivity. J Allergy Clin Immunol. 2018;141(2):463-72. doi:10.1016/j.jaci.2017.12.971.
17. Dreskin SC, Halsey NA, Kelso JM, Wood RA, Hummell DS, Edwards KM, et al. International Consensus (ICON): allergic reactions to vaccines. World Allergy Organ J. 2016 Sep 16;9(1):32. doi: 10.1186/s40413-016-0120-5.
18. James JM, Burks AW, Roberson PK, Sampson HA. Safe administration of the measles vaccine to children allergic to eggs. N Engl J Med. 1995;332(19):1262-6. doi:10.1056/NEJM199505113321904.
19. Baxter DN. Measles immunization in children with a history of egg allergy. Vaccine. 1996;14(2):131-4. doi:10.1016/0264-410x(95)00154-s.
20. Kelso JM. Influenza vaccine and egg allergy: nearing the end of an evidence-based journey. J Allergy Clin Immunol Pract. 2015;3(1):140-1. doi:10.1016/j.jaip.2014.08.011.
21. Kelso JM. Administering influenza vaccine to egg-allergic persons. Expert Rev Vaccines. 2014;13(8):1049-57. doi:10.1586/14760584.2014.933079.
22. Takey PRG. Imunogenicidade e segurança da vacina contra a febre amarela: revisão sistemática e metanálise [tese]. Rio de Janeiro, RJ: Fundação Oswaldo Cruz, Instituto Nacional de Infectologia Evandro Chagas (INI) - Programa de Pós-graduação em Pesquisa Clínica em Doenças Infecciosas; 2020. Available from: https://sucupira-legado.capes.gov.br/sucupira/public/consultas/coleta/trabalhoConclusao/viewTrabalhoConclusao.jsf?popup=true&id_trabalho=10263752 .
23. Gerhardt CMB, Feitosa GSJ, Aquilante BP, Dorna MB, Santos CJN, Pastorino AC, et al. Segurança da vacina de febre amarela em pacientes comprovadamente alérgicos à proteína do ovo. Arq Asma Alerg Imunol. 2019;3(2):143-50. doi: 10.5935/2526-5393.20190025.
24. Gerhardt CMB, Castro APBM, Pastorino AC, Dorna MB, Nunes-Santos CJ, Aquilante BP, et al. Safety of yellow fever vaccine administration in confirmed egg-allergic patients. Vaccine. 2020 Sep 29;38(42):6539-44. doi: 10.1016/j.vaccine.2020.08.020.
25. Cancado B, Aranda C, Mallozi M, Weckx L, Sole D. Yellow fever vaccine and egg allergy. Lancet Infect Dis. 2019;19(8):812. doi:10.1016/S1473-3099(19)30355-X.
26. Guimarães BNA, Petraglia TCMB, Marinho AKBB, Barbosa ADM. Eventos adversos imediatos à vacina febre amarela em crianças alérgicas ao ovo. Arq Asma Alerg Imunol. 2022;6(4):519-26. doi: 10.5935/2526-5393.20220060.
27. Kattan JD, Konstantinou GN, Cox AL, Nowak-Wegrzyn A, Gimenez G, Sampson HA, et al. Anaphylaxis to diphtheria, tetanus, and pertussis vaccines among children with cow's milk allergy. J Allergy Clin Immunol. 2011 Jul;128(1):215-8. doi: 10.1016/j.jaci.2011.04.046.
28. SBIm, ASBAI, SBP. Nota técnica conjunta SBIm/ASBAI/SBP – 08/02/2017. Vacina rotavírus [Internet]. Available from: https://sbim.org.br/images/files/nota-sbim-asbai-sbp-rotavirus08022017-v2.pdf. Accessed on: Nov 01 2024.
29. Kumagai T, Yamanaka T, Wataya Y, Umetsu A, Kawamura N, Ikeda K, et al. Gelatin-specific humoral and cellular immune responses in children with immediate- and nonimmediate-type reactions to live measles, mumps, rubella, and varicella vaccines. J Allergy Clin Immunol. 1997 Jul;100(1):130-4. doi: 10.1016/s0091-6749(97)70204-5.
30. Pool V, Braun MM, Kelso JM, Mootrey G, Chen RT, Yunginger JW, et al.; VAERS Team. US Vaccine Adverse Event Reporting System. Prevalence of anti-gelatin IgE antibodies in people with anaphylaxis after measles-mumps rubella vaccine in the United States. Pediatrics. 2002 Dec;110(6):e71. doi: 10.1542/peds.110.6.e71.
31. Russell M, Pool V, Kelso JM, Tomazic-Jezic VJ. Vaccination of persons allergic to latex: a review of safety data in the Vaccine Adverse Event Reporting System (VAERS). Vaccine. 2004;23(5):664-7. doi:10.1016/j.vaccine.2004.06.042.
32. Nicaise-Roland P, Granger V, Soria A, Barbaud A, Pallardy M, Chollet-Martin S, et al. Immediate hypersensitivity to COVID-19 vaccines: Focus on biological diagnosis. Front Allergy. 2022 Sep 30;3:1007602. doi: 10.3389/falgy.2022.1007602.

33. Wenande E, Garvey LH. Immediate-type hypersensitivity to polyethylene glycols: a review. Clin Exp Allergy. 2016 Jul;46(7):907-22. doi: 10.1111/cea.12760.
34. Loughlin AM, Marchant CD, Adams W, Barnett E, Baxter R, Black S, et al. Causality assessment of adverse events reported to the Vaccine Adverse Event Reporting System (VAERS). Vaccine. 2012 Nov 26;30(50):7253-9. doi: 10.1016/j.vaccine.2012.09.074.
35. National Center for Immunization and Respiratory Diseases. General recommendations on immunization – Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2011;60(2):1-64.
36. Ma L, Du X, Dong Y, Peng L, Han X, Lyu J, et al. First case of Stevens-Johnson syndrome after rabies vaccination. Br J Clin Pharmacol. 2018 Apr;84(4):803-5. doi: 10.1111/bcp.13512.
37. Christou EM, Wargon O. Stevens-Johnson syndrome after varicella vaccination. Med J Aust. 2012;196(4):240-1. doi:10.5694/mja11.11484.
38. Chahal D, Aleshin M, Turegano M, Chiu M, Worswick S. Vaccine-induced toxic epidermal necrolysis: a case and systematic review. Dermatol Online J. 2018;24(1). doi:10.5070/D3241037941.
39. Keller N, Gilad O, Marom D, Marcus N, Garty BZ. Nonbullous Erythema Multiforme in Hospitalized Children: A 10-Year Survey. Pediatr Dermatol. 2015;32(5):701-3. doi:10.1111/pde.12659.
40. Canavan TN, Mathes EF, Frieden I, Shinkai K. Mycoplasma pneumoniae-induced rash and mucositis as a syndrome distinct from Stevens-Johnson syndrome and erythema multiforme: a systematic review. J Am Acad Dermatol. 2015;72(2):239-45. doi:10.1016/j.jaad.2014.06.026.
41. Stone Jr CA, Rukasin CRF, Beachkofsky TM, Phillips EJ. Immune-mediated adverse reactions to vaccines. Br J Clin Pharmacol. 2019;85(12):2694-706. doi:10.1111/bcp.14112.
42. Phillips EJ, Bigliardi P, Bircher AJ, Broyles A, Chang YS, Chung WH, et al. Controversies in drug allergy: Testing for delayed reactions. J Allergy Clin Immunol. 2019 Jan;143(1):66-73. doi: 10.1016/j.jaci.2018.10.030.
43. Peng B, Wei M, Zhu FC, Li JX. The vaccines-associated Arthus reaction. Hum Vaccines Immunother. 2019;15(11):2769-77. doi:10.1080/21645515.2019.1602435.
44. Pool V, Mege L, Abou-Ali A. Arthus Reaction as an Adverse Event Following Tdap Vaccination. Vaccines. 2020;8(3):385. doi:10.3390/vaccines8030385.
45. Willison HJ, Jacobs BC, Doorn PA van. Guillain-Barré syndrome. The Lancet. 2016;388(10045):717-27. doi:10.1016/S0140-6736(16)00339-1.
46. Brasil, Ministério da Saúde. Painel de Monitoramento das Arboviroses [Internet]. Available from: https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/a/aedes-aegypti/monitoramento-das-arboviroses/painel . Accessed on: Aug 28 2024.
47. Yang F, Schildhauer S, Billeter SA, Hardstone Yoshimizu M, Payne R, Pakingan MJ, et al. Insecticide Resistance Status of Aedes aegypti (Diptera: Culicidae) in California by Biochemical Assays. J Med Entomol. 2020 Jul 4;57(4):1176-83. doi: 10.1093/jme/tjaa031.
48. Barcellos C, Matos V, Lana RM, Lowe R. Climate change, thermal anomalies, and the recent progression of dengue in Brazil. Sci Rep. 2024;14(1):5948. doi:10.1038/s41598-024-56044-y
49. Tricou V, Yu D, Reynales H, Biswal S, Saez-Llorens X, Sirivichayakul C, et al. Long-term efficacy and safety of a tetravalent dengue vaccine (TAK-003): 4·5-year results from a phase 3, randomised, double-blind, placebo-controlled trial. Lancet Glob Health. 2024 Feb;12(2):e257-e270. doi: 10.1016/S2214-109X(23)00522-3.
50. Patel SS, Rauscher M, Kudela M, Pang H. Clinical safety experience of TAK-003 for dengue fever: a new tetravalent live attenuated vaccine candidate. Clin Infect Dis. 2023;76(3):e1350-e1359. doi:10.1093/cid/ciac418.
51. Anvisa - Agência Nacional de Vigilância Sanitária. Segurança da vacina Qdenga [Internet]. Available from: https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/seguranca-da-vacina-qdenga . Accessed on: Aug 29 2024.
52. Percio J, Kobayashi CD, Silva RMA, Marinho AKBB, Capovilla L, Andrade PHS, et al. Safety signal detected: Anaphylaxis after attenuated dengue vaccine (TAK-003) - Brazil, march 1, 2023-march 11, 2024. Vaccine. 2024 Dec 2;42(26):126407. doi: 10.1016/j.vaccine.2024.126407.
53. Brasil, Ministério da Saúde. Nota Técnica N° 7/2024-CGFAM/DPNI/SVSA/MS [Internet]. Available from: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/notas-tecnicas/2024/nota-tecnica-no-7-2024-cgfam-dpni-svsa-ms/view . Accessed on: Aug 29 2024.
54. Krantz MS, Liu Y, Phillips EJ, Stone CA. COVID-19 vaccine anaphylaxis: PEG or not? Allergy. 2021;76(6):1934-7. doi:10.1111/all.14722.
55. Guerrini G, Gioria S, Sauer AV, Lucchesi S, Montagnani F, Pastore G, et al. Monitoring Anti-PEG Antibodies Level upon Repeated Lipid Nanoparticle-Based COVID-19 Vaccine Administration. Int J Mol Sci. 2022 Aug 9;23(16):8838. doi: 10.3390/ijms23168838.
56. Lukawska J, Mandaliya D, Chan AWE, Foggitt A, Bidder T, Harvey J, et al. Anaphylaxis to trometamol excipient in gadolinium-based contrast agents for clinical imaging. J Allergy Clin Immunol Pract. 2019 Mar;7(3):1086-7. doi: 10.1016/j.jaip.2018.08.035.
57. Guler S, Ertok I, Sahin NY, Ramadan H, Katirci Y. Anaphylaxis after intravenous infusion of dexketoprofen trometamol. Turk J Emerg Med. 2016;16(3):132-3. doi:10.1016/j.tjem.2016.09.003.
58. Maltezou HC, Anastassopoulou C, Hatziantoniou S, Poland GA, Tsakris A. Anaphylaxis rates associated with COVID-19 vaccines are comparable to those of other vaccines. Vaccine. 2022;40(2):183-6. doi:10.1016/j.vaccine.2021.11.066.
59. Boufidou F, Hatziantoniou S, Theodoridou K, Maltezou HC, Vasileiou K, Anastassopoulou C, et al. Anaphylactic Reactions to COVID-19 Vaccines: An Updated Assessment Based on Pharmacovigilance Data. Vaccines (Basel). 2023 Mar 8;11(3):613. doi: 10.3390/vaccines11030613.
60. Baeck M, Marot L, Belkhir L. Delayed large local reactions to mRNA vaccines. N Engl J Med. 2021;384(24):e98. doi:10.1056/NEJMc2104751.
61. Blumenthal KG, Freeman EE, Saff RR, Robinson LB, Wolfson AR, Foreman RK, et al. Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS-CoV-2. N Engl J Med. 2021 Apr 1;384(13):1273-7. doi: 10.1056/NEJMc2102131.
62. Samarakoon U, Alvarez-Arango S, Blumenthal KG. Delayed Large Local Reactions to mRNA Covid-19 Vaccines in Blacks, Indigenous Persons, and People of Color. N Engl J Med. 2021 Aug 12;385(7):662-4. doi: 10.1056/NEJMc2108620.
63. Higashino T, Yamazaki Y, Senda S, Satou Y, Yonekura Y, Imai K, et al. Assessment of Delayed Large Local Reactions After the First Dose of the SARS-CoV-2 mRNA-1273 Vaccine in Japan. JAMA Dermatol. 2022 Aug 1;158(8):923-7. doi: 10.1001/jamadermatol.2022.2088.
64. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al.; COVE Study Group. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021 Feb 4;384(5):403-16. doi: 10.1056/NEJMoa2035389.
65. Global Initiative for Asthma. 2024 Global Initiative for Asthma (GINA) report: global strategy for asthma management and prevention [Internet]. Available from: https://ginasthma.org/wp-content/uploads/2024/05/GINA-2024-Strategy-Report-24_05_22_WMS.pdf. Accessed on: Aug 29 2024.
66. Brasil, Ministério da Saúde. Em 2021, SUS registrou 1,3 milhão de atendimentos a pacientes com asma na Atenção Primária à Saúde [Internet]. Available from: https://www.gov.br/saude/pt-br/assuntos/noticias/2022/maio/em-2021-sus-registrou-1-3-milhao-de-atendimentos-a-pacientes-com-asma-na-atencao-primaria-a-saude-1. Accessed on: Aug 26 2024.
67. Marques CPC, Bloise RF, Lopes LBM, Godói LF, Souza PRP, Santa Rosa IM, et al. Epidemiologia da asma no Brasil, no período de 2016 a 2020. Res Soc Dev. 2022;11(8):e5211828825-e5211828825. doi:10.33448/rsd-v11i8.28825.

68. Ritchie AI, Jackson DJ, Edwards MR, Johnston SL. Airway epithelial orchestration of innate immune function in response to virus infection. A focus on asthma. Ann Am Thorac Soc. 2016;13 Suppl 1:S55-63. doi:10.1513/AnnalsATS.201507-421MG.

69. Gill MA, Bajwa G, George TA, Dong CC, Dougherty II, Jiang N, et al. Counterregulation between the FcepsilonRI pathway and antiviral responses in human plasmacytoid dendritic cells. J Immunol. 2010 Jun 1;184(11):5999-6006. doi: 10.4049/jimmunol.0901194.

70. Papadopoulos NG, Christodoulou I, Rohde G, Agache I, Almqvist C, Bruno A, et al. Viruses and bacteria in acute asthma exacerbations – a GA² LEN-DARE systematic review. Allergy. 2011 Apr;66(4):458-68. doi: 10.1111/j.1398-9995.2010.02505.x.

71. Wark PAB. Why are people with asthma more susceptible to influenza? Eur Respir J. 2019;54(4). doi:10.1183/13993003.01748-2019.

72. Vasileiou E, Sheikh A, Butler CC, Robertson C, Kavanagh K, Englishby T, et al. Seasonal Influenza Vaccine Effectiveness in People With Asthma: A National Test-Negative Design Case-Control Study. Clin Infect Dis. 2020 Oct 23;71(7):e94-e104. doi: 10.1093/cid/ciz1086.

73. DiazGranados CA, Dunning AJ, Kimmel M, Kirby D, Treanor J, Collins A, et al. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. N Engl J Med. 2014 Aug 14;371(7):635-45. doi: 10.1056/NEJMoa1315727.

74. Chang LJ, Meng Y, Janosczyk H, Landolfi V, Talbot HK, QHD00013 Study Group. Safety and immunogenicity of high-dose quadrivalent influenza vaccine in adults ≥65 years of age: A phase 3 randomized clinical trial. Vaccine. 2019;37(39):5825-34. doi:10.1016/j.vaccine.2019.08.016

75. U.S. Food and Drug Administration (FDA). 2020. Package Insert – Fluzone High-Dose Quadrivalent. Sanofi Pasteur [Internet]. Available from: www.fda.gov/media/132238/download. Accessed on: Aug 26 2024.

76. Li Y, Wang X, Blau DM, Caballero MT, Feikin DR, Gill CJ, et al.; Respiratory Virus Global Epidemiology Network; Nair H; RESCEU investigators. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. Lancet. 2022 May 28;399(10340):2047-64. doi: 10.1016/S0140-6736(22)00478-0.

77. Shi T, Vennard S, Jasiewicz F, Brogden R, Nair H; RESCEU Investigators. Disease Burden Estimates of Respiratory Syncytial Virus related Acute Respiratory Infections in Adults With Comorbidity: A Systematic Review and Meta-Analysis. J Infect Dis. 2022 Aug 12;226(Suppl 1):S17-S21. doi: 10.1093/infdis/jiab040.

78. Zhou H, Thompson WW, Viboud CG, Ringholz CM, Cheng PY, Steiner C, et al. Hospitalizations associated with influenza and respiratory syncytial virus in the United States, 1993-2008. Clin Infect Dis. 2012 May;54(10):1427-36. doi: 10.1093/cid/cis211.

79. Binns E, Tuckerman J, Licciardi PV, Wurzel D. Respiratory syncytial virus, recurrent wheeze and asthma: A narrative review of pathophysiology, prevention and future directions. J Paediatr Child Health. 2022;58(10):1741-6. doi:10.1111/jpc.16197.

80. Rosas-Salazar C, Chirkova T, Gebretsadik T, Chappell JD, Peebles RS Jr, Dupont WD, et al. Respiratory syncytial virus infection during infancy and asthma during childhood in the USA (INSPIRE): a population-based, prospective birth cohort study. Lancet. 2023 May 20;401(10389):1669-80. doi: 10.1016/S0140-6736(23)00811-5.

81. Coutts J, Fullarton J, Morris C, Grubb E, Buchan S, Rodgers-Gray B, et al. Association between respiratory syncytial virus hospitalization in infancy and childhood asthma. Pediatr Pulmonol. 2020 May;55(5):1104-10. doi: 10.1002/ppul.24676.

82. Papi A, Ison MG, Langley JM, Lee DG, Leroux-Roels I, Martinon-Torres F, et al.; AReSVi-006 Study Group. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. N Engl J Med. 2023 Feb 16;388(7):595-608. doi: 10.1056/NEJMoa2209604.

83. Feldman RG, Antonelli-Incalzi R, Steenackers K, Lee DG, Papi A, Ison MG, et al.; AReSVi-006 Study Group. Respiratory Syncytial Virus Prefusion F Protein Vaccine Is Efficacious in Older Adults With Underlying Medical Conditions. Clin Infect Dis. 2024 Jan 25;78(1):202-9. doi: 10.1093/cid/ciad471.

84. Ison MG, Papi A, Langley JM, Lee DG, Leroux-Roels I, Martinon-Torres F, et al. 1936. Efficacy of One Dose of the Respiratory Syncytial Virus (RSV) Prefusion F Protein Vaccine (RSVPreF3 OA) in Adults > 60 Years of Age Persists for 2 RSV Seasons. Open Forum Infect Dis. 2023 Nov 27;10(Suppl 2):ofad500.2467. doi: 10.1093/ofid/ofad500.2467.

85. National Library of Medicine. DailyMed. SYNAGIS- palivizumab injection, solution [Internet]. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=3a0096c7-8139-44cd-bba4-520ab05c2cb2 . Accessed on: Oct 16 2024.

86. Gonzales T, Bergamasco A, Cristarella T, Goyer C, Wojdyla M, Oladapo A, et al. Effectiveness and Safety of Palivizumab for the Prevention of Serious Lower Respiratory Tract Infection Caused by Respiratory Syncytial Virus: A Systematic Review. Am J Perinatol. 2024 May;41(S 01):e1107-e1115. doi: 10.1055/a-1990-2633.

87. Griffin MP, Yuan Y, Takas T, Domachowske JB, Madhi SA, Manzoni P, et al.; Nirsevimab Study Group. Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants. N Engl J Med. 2020 Jul 30;383(5):415-25. doi: 10.1056/NEJMoa1913556.

88. Sun M, Lai H, Na F, Li S, Qiu X, Tian J, et al. Monoclonal Antibody for the Prevention of Respiratory Syncytial Virus in Infants and Children: A Systematic Review and Network Meta-analysis. JAMA Netw Open. 2023 Feb 1;6(2):e230023. doi: 10.1001/jamanetworkopen.2023.0023.

89. Hammitt LL, Dagan R, Yuan Y, Baca Cots M, Bosheva M, Madhi SA, et al.; MELODY Study Group. Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants. N Engl J Med. 2022 Mar 3;386(9):837-46. doi: 10.1056/NEJMoa2110275.

90. Scelfo C, Menzella F, Fontana M, Ghidoni G, Galeone C, Facciolongo NC. Pneumonia and invasive pneumococcal diseases: the role of pneumococcal conjugate vaccine in the era of multi-drug resistance. Vaccines. 2021;9(5):420. doi:10.3390/vaccines9050420.

91. O'Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, McCall N, et al.; Hib and Pneumococcal Global Burden of Disease Study Team. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. Lancet. 2009 Sep 12;374(9693):893-902. doi: 10.1016/S0140-6736(09)61204-6.

92. Song JY, Nahm MH, Moseley MA. Clinical implications of pneumococcal serotypes: invasive disease potential, clinical presentations, and antibiotic resistance. J Korean Med Sci. 2013;28(1):4-15. doi:10.3346/jkms.2013.28.1.4.

93. Li L, Cheng Y, Tu X, Yang J, Wang C, Zhang M, et al. Association between asthma and invasive pneumococcal disease risk: a systematic review and meta-analysis. Allergy Asthma Clin Immunol. 2020 Nov 10;16(1):94. doi: 10.1186/s13223-020-00492-4.

94. Castro-Rodriguez JA, Abarca K, Forno E. Asthma and the risk of invasive pneumococcal disease: a meta-analysis. Pediatrics. 2020;145(1):e20191200. doi:10.1542/peds.2019-1200.

95. Czaicki N, Bigaj J, Zielonka TM. Pneumococcal vaccine in adult asthma patients. Adv Exp Med Biol. 2021;1289:55-62. doi:10.1007/5584_2020_562.

96. CDC, Pneumococcal disease. Summary of risk-based pneumococcal vaccination recommendations [Internet]. Available from: https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/risk-indications.html. Accessed on: Aug 27 2024.

97. Moberley S, Holden J, Tatham DP, Andrews RM. Vaccines for preventing pneumococcal infection in adults. Cochrane Database Syst Rev. 2013;2013(1):CD000422. doi:10.1002/14651858.CD000422.pub3.

98. Gladstone RA, Jefferies JM, Tocheva AS, Beard KR, Garley D, Chong WW, et al. Five winters of pneumococcal serotype replacement in UK carriage following PCV introduction. Vaccine. 2015 Apr 21;33(17):2015-21. doi: 10.1016/j.vaccine.2015.03.012.

99. Torres A, Blasi F, Dartois N, Akova M. Which individuals are at increased risk of pneumococcal disease and why? Impact of COPD, asthma, smoking, diabetes, and/or chronic heart disease on community-acquired pneumonia and invasive pneumococcal disease. Thorax. 2015;70(10):984-9. doi:10.1136/thoraxjnl-2015-206780

100. Costa VC, Barreto MP, Andrade MCC, Lopes SMS, Nascimento MML, Carvalho FP, et al. Asma como fator de risco para infecção por COVID-19 em crianças: uma revisão integrativa. Enferm Bras. 2023;22(4):492-506. doi: 10.33233/eb.v22i4.5284.

101. Shi T, Pan J, Katikireddi SV, McCowan C, Kerr S, Agrawal U, et al.; Public Health Scotland and the EAVE II Collaborators. Risk of COVID-19 hospital admission among children aged 5-17 years with asthma in Scotland: a national incident cohort study. Lancet Respir Med. 2022 Feb;10(2):191-8. doi: 10.1016/S2213-2600(21)00491-4.

102. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020 Aug;584(7821):430-6. doi: 10.1038/s41586-020-2521-4.

103. Bloom CI, Drake TM, Docherty AB, Lipworth BJ, Johnston SL, Nguyen-Van-Tam JS, et al.; ISARIC investigators. Risk of adverse outcomes in patients with underlying respiratory conditions admitted to hospital with COVID-19: a national, multicentre prospective cohort study using the ISARIC WHO Clinical Characterization Protocol UK. Lancet Respir Med. 2021 Jul;9(7):699-711. doi: 10.1016/S2213-2600(21)00013-8.

104. Brasil, Ministério da Saúde. Esquema vacinal Covid-19 [Internet]. Available from: https://www.gov.br/saude/pt-br/assuntos/covid-19/esquemas-vacinais/esquema-vacinal-covid-19/view. Accessed on: Aug 27 2024.

105. Caubet JC, Rudzeviciene O, Gomes E, Terreehorst I, Brockow K, Eigenmann PA. Managing a child with possible allergy to vaccine. Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol. 2014;25(4):394-403. doi:10.1111/pai.12132.

106. Wood RA, Berger M, Dreskin SC, Setse R, Engler RJ, Dekker CL, et al.; Hypersensitivity Working Group of the Clinical Immunization Safety Assessment (CISA) Network. An algorithm for treatment of patients with hypersensitivity reactions after vaccines. Pediatrics. 2008 Sep;122(3):e771-7. doi: 10.1542/peds.2008-1002.

107. 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.

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Corresponding author:
Claudia França Cavalcante Valente
E-mail: claudiafcvalente@gmail.com