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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Strengthening science and the specialty of Allergy and Immunology: the AAAI legacy for the future

Fortalecendo a ciência e a especialidade de Alergia e Imunologia: o legado dos AAAI para o futuro

Fábio Kuschnir[1]

As my term as Chair of the Brazilian Association of Allergy and Immunology (ASBAI) concludes, we are very pleased to highlight the relevance of the journal Arquivos de Asma, Alergia e Imunologia (AAAI) as an important tool in the dissemination of high-quality science and promotion of our specialty.

As the official publication of ASBAI and the Latin American Society of Asthma, Allergy, and Immunology, AAAI has received contributions from researchers not only from Brazil but also from other countries, further expanding its impact and scope. Over these 2 years, AAAI has become a cornerstone for expanding access to the latest knowledge, contributing to the improvement of clinical practice and the advancement of research in the field.

We extend our sincere appreciation to everyone who has contributed to this successful trajectory over the past term. We are grateful to the authors for sharing their research and clinical insights, to the reviewers for their diligent work in ensuring scientific excellence, and to the scientific departments and committees for the development of guidelines that are essential for the practice of our specialty. We are particularly grateful to the Editor-in-Chief, Dr. Pedro Bianchi, whose commitment was pivotal in achieving the indexing of AAAI in several scientific databases, a milestone that has already increased the journal's visibility and credibility. We remain dedicated to pursuing further indexing opportunities and strengthening the journal's relevance within the scientific community.

In this final issue of 2023-2024, we are pleased to share high-impact contributions that reflect the diversity and quality of Allergy and Immunology research conducted in our country. The three articles on "Starting an Allergy and Immunology Practice" offer a practical and detailed guide, beginning with office organization (Part 1), progressing through the implementation of Standard Operating Procedures (Part 2), and concluding with the basic concepts of compliance with the GDPR (Part 3). This collection is an indispensable resource for professionals aiming to structure a modern, efficient practice that adheres to current legal regulations.[1-3]

Among the review articles, we highlight a study on type 2 inflammatory diseases, which explores the safety profile of biologics during pregnancy, a critical issue for clinical practice.[4]

1. Chair of the Brazilian Association of Allergy and Immunology (ASBAI), 2023-2024.

Arq Asma Alerg Imunol. 2024;8(4):285-6.

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Among the original articles, we highlight a study on the prevalence of anaphylaxis in patients with allergic diseases in the state of São Paulo, which provides relevant data obtained via an online questionnaire, offering a new research tool and an updated perspective on the frequency of this condition in a specific population, and a study on sensitization to contact allergens in Brazil, which underscores the need for continuous monitoring of these factors in our population.[5,6]

Finally, we reaffirm our commitment to promoting high-quality science and thank everyone who, directly or indirectly, has contributed to the progress achieved. May we continue our collaborative efforts to strengthen our specialty and expand the horizons of knowledge.

With best wishes for much success, achievement, and advancement in our specialty to the incoming Chair, Dr. Fátima Rodrigues Fernandes, and the ASBAI Board of Directors for the 2025-2026 term.

We extend our gratitude and best wishes for success to all of you.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Special Article

A practical guide to Allergy and Immunology practice. Starting an Allergy and Immunology practice – Part 1: What do I need?

Guia prático da especialidade em Alergia e Imunologia. Construindo o consultório do Alergista e Imunologista – Parte 1: o que é preciso?

Eduardo Magalhães de Souza Lima[1], Adriana Aragão Craveiro Leite[1], Celso Taques Saldanha[1], Fátima Rodrigues Fernandes[1], Gustavo Falbo Wandalsen[1], Luís Felipe Chiaverini Ensina[1], Fábio Chigres Kuschnir[2], Dirceu Solé[3]

ABSTRACT

What do I need to start an Allergy and Immunology practice? This is a common concern among young specialists, yet it often goes unanswered. The Statute, Regulations, and Standards Committee of the Brazilian Association of Allergy and Immunology (CERN-ASBAI) proposes the publication of a series of articles aimed at providing guidance on the essential steps for establishing good practices in the clinical care of allergic patients.

Keywords: Allergy, immunology, practice guidelines.

RESUMO

O que é preciso para abrir o consultório do especialista em Alergia e Imunologia? Esta é uma preocupação frequente dos jovens especialistas que muitas vezes fica sem resposta. A Comissão de Estatuto, Regulamentos e Normas da Associação Brasileira de Alergia e Imunologia (CERN-ASBAI) propõe a publicação de uma série de artigos com o objetivo de orientar sobre os passos essenciais para o questionamento de boas práticas no atendimento clínico de pacientes alérgicos.

Descritores: Alergia, imunologia, guia de prática clínica.

Introduction

The Statute, Regulations, and Standards Committee of the Brazilian Association of Allergy and Immunology (CERN-ASBAI) has developed a practical guide on how to start an Allergy and Immunology practice. This guide is primarily based on the regulations of the Brazilian Federal Board of Medicine (Conselho Federal de Medicina, CFM) and includes updated rules for the inspection of medical offices,[1] which are already in effect. Additionally, several other principles of the ASBAI bylaws, as well as of organizations more directly involved with medicine – such as the Brazilian Medical Association (AMB), the National Sanitary Surveillance Agency (Anvisa), and other Brazilian public bodies[1-3] – should be observed.

According to CFM Resolution 2214/18, medical office inspections are conducted by the Inspection Departments of Regional Medical Boards (Conselhos Regionais de Medicina, CRMs), either *ex officio* or in response to complaints from the public or the Public Prosecutor's Office. The Inspection Department

1. Statute, Regulations, and Standards Committee of the Brazilian Association of Allergy and Immunology (ASBAI) – 2023/2024 Term.
2. President of ASBAI – 2023-2024 Term.
3. Research Director at ASBAI – 2023-2024 Term.

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plays a crucial role in regulating the quality of health care provided to the population. Under the updated regulation, medical offices and clinics are categorized into three groups based on the complexity and type of services and procedures they perform,[1] as described below.

– *Group 1:* Medical offices or services limited to providing basic care only – general procedures and those requiring local anesthesia or sedation are not permitted.
– *Group 2:* Medical offices authorized to perform consultations and simple allergy tests, such as the skin prick test and patch test.
– *Group 3:* Medical offices or services equipped to perform procedures that involve local anesthesia (without sedation), as well as desensitization and provocation tests with antigens.

After completing medical school and typically receiving training through the AMB/medical specialty societies or Medical Residency programs accredited by the Ministry of Education,[4] physicians often remain unaware of certain legal and ethical standards necessary for the adequate execution of their professional activities in private practices.

As a result, they may be caught off guard by different guidelines, fees, and inspections that periodically arise from both the CFM[1] – through the CRMs – and Anvisa[2] in each state. Therefore, having prior knowledge of these requirements is essential for physicians to respond adequately and effectively to such demands.

Opening and operating an Allergy and Immunology practice

A common question often arises: "What are the essential legal requirements established by regulatory bodies for opening and operating a private practice?".

Public documentation

In private practice, a physician who performs professional activities in a specific location must hold an active business license, which is mandatory documentation for this purpose. This documentation consists of different permits issued by several government agencies, as specified below.[2,5]

– Location and operating license: Issued by the Municipal Government.
– Health permit (may vary according to the rules of each state): Issued by the Municipal Government.
– Environmental license and Fire Department operational permit: Issued by the Municipal Fire Department.
– National Registry of Health Establishments6: Issued by the Municipal or State Health Department.
– Self-Employed Registration: Issued by the Municipal Government.

Taxes – Individual

There are specific taxes that physicians must be aware of, including the 1) Municipal Service Tax (Imposto Sobre Serviços, ISS), paid annually; 2) contribution to social security (Instituto Nacional do Seguro Social, INSS), paid monthly; and the 3) Individual Income Tax (Imposto de Renda de Pessoa Física, IRPF), paid monthly. The IRPF corresponds to the income tax originating from earnings received directly from individuals/private patients.

Taxes – Legal entity

If the medical office is registered as a legal entity (company),[3,4,6] it may opt for the "Simples Nacional," a simplified taxation system. It includes the following monthly taxes: 1) Social Integration Program (Programa de Integração Social, PIS); 2) Contribution to Social Security Financing (Contribuição para o Financiamento da Seguridade Social, COFINS); Company Income Tax (Imposto sobre a Renda das Pessoas Jurídicas, IRPJ); Social Contribution on Profits (Contribuição Social sobre o Lucro Líquido, CSLL); and the ISS.

Board certification

Individual

Board certification is the process by which physicians demonstrate their expertise in a specific medical specialty. In Brazil, this certification is a legal requirement issued by the CRMs.[7] Physicians board-certified in Allergy and Immunology are granted the authority to treat both adults and children with immune disorders and allergic diseases. To obtain the specialist title, physicians must successfully complete and pass an examination process, which is conducted annually by ASBAI in collaboration with the AMB.[4]

Technical Supervisor/Director in Allergy and Immunology

Specialized services that provide care for allergic diseases must not only have a designated Technical or Clinical Director, but it is also mandatory that this individual be board-certified in Allergy and Immunology.[8] Therefore, it is recommended that ASBAI-certified specialists, when operating as legal entities, avoid acting as directors in services not directly linked to their specialty. This preserves the integrity of the profession and ensures their actions adhere to the ethical principles outlined in ASBAI's bylaws.[9]

Handling allergen extracts in the medical office

The indication, guidance, supervision, and interpretation of skin tests with allergens (such as the skin prick test and patch test), as well as the prescription, planning, and supervision of allergen-specific immunotherapy – whether subcutaneous or sublingual – are acts restricted to licensed physicians.[10]

The CFM, its regional branches (the CRMs), the AMB, and the National Medical Residency Committee (CNRM), through CNRM Resolution 12/2019, acknowledge that handling allergen extracts is a common and standard practice for trained physicians, particularly those specialized in Allergy and Immunology. Therefore, the allergist/immunologist is considered the most qualified professional to handle such materials and administer immunotherapy.[10-14]

The CFM recognizes that the conditions established for Group 2 and Group 3 offices are appropriate for the performance of immediate-reading (prick) and delayed-reading (patch) allergy tests, dilution of allergen extracts, and administration of subcutaneous allergen-specific immunotherapy. These offices are also suitable for performing provocation tests and desensitization with medications and food, specifically within the scope of Allergy and Immunology.[10]

Of note, the *Arquivos de Asma, Alergia e Imunologia* (AAAI), a scientific journal published by ASBAI, recently published a letter highlighting the need for proficiency testing for the performance of skin prick tests. This requirement aims to protect the health of allergic patients and ensure that professionals maintain a high standard of care.[13]

Professional fees charged for activities performed in the medical office

When issuing a receipt or invoice for a procedure performed in the medical office, such as the handling/application of allergen extracts, it is necessary to specify that the fees correspond to the planning and/or monitoring associated with the administration of allergen-specific immunotherapy, as outlined in CFM Resolution 2215/2018.

Informed consent

In recent years, there has been a significant increase in lawsuits in the health care sector, including those related to medical malpractice. This underscores the importance of the Informed Consent Form as a fundamental component of ethical and legally sound medical practice. According to the CFM, informed consent is a decision-making process in which the patient, or their legal representative, freely agrees to and authorizes the proposed diagnostic or therapeutic procedures after receiving all necessary information and explanations, under the physician's responsibility. Therefore, physicians should provide and obtain the Informed Consent Form (available as an attachment to CFM Recommendation 1/2016[14]) when performing procedures in their office. This practice demonstrates ethical diligence and significantly contributes to the quality and safety of patient care.

Hiring additional health care professionals

Allergy and Immunology clinics and private practices are not obligated to hire additional health care professionals to supervise the physician assistant during procedures.

In fact, the CFM has determined that medical offices and other medical services in general are not subject to the regulations of the Nursing Board. The scope of these regulations applies only to nursing professionals. Conversely, it is the CFM's responsibility to oversee and regulate registered medical services.[15]

On the specialty's title

Several terms are commonly used to refer to the specialty of Allergy and Immunology on stamps, prescription forms, office signs, and other materials. Some of these include Allergology, Clinical Allergy, Allergy and Immunopathology, and Clinical

Immunology. However, according to CFM Resolution 1092/1983, the specialty is officially recognized in Brazil under the title "Allergy and Immunology."

It is important to note that the name of the scientific association – Brazilian Association of Allergy and Immunology – is defined in its bylaws and regarded as one of the institution's core assets. Therefore, to help strengthen and unify the identity of the specialty in Brazil, ASBAI encourages the standardized use of the title "Allergy and Immunology" across all professional materials, including office signs and any form of public or professional advertising. This is especially important given the specialty's broad scope of care, which encompasses patients of all age groups. An example of this standardization is provided in Figure 1.[19]

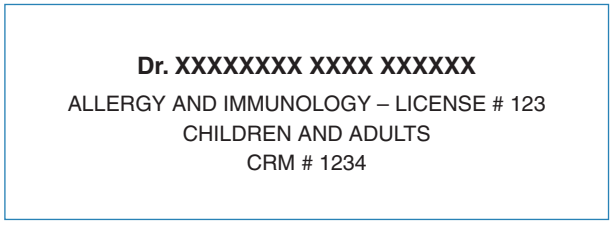

Figure 1
Standardization of the specialty's title in medical offices and other advertisements

Scope of practice in medical offices according to age group

According to CFM Resolution 1627/2001, Allergy and Immunology is not, and cannot be, a fragmented specialty restricted to only part of the human immune system. Specialists in this area are fully trained physicians qualified to manage allergic and immune disorders across all age groups. Therefore, the specialty is not restricted by age group, as recognized in Article 5, item 9, of ASBAI's bylaws; in Official Letter 123/2021 from the AMB Secretariat, supported by the Brazilian Society of Pediatrics; and in CFM Resolution 2215/2018, published in the Federal Official Gazette of Brazil on December 3, 2018 (Section 1, page 231). The latter states that when care is provided exclusively to pediatric patients, technical responsibility must be assumed by a physician board-certified in Allergy and Immunology or in Pediatric Allergy and Immunology.

There is no legal justification for health insurance providers to limit the practice of allergists/immunologists based on patient age.

Return appointments (per CFM Resolution 1958/2010)

During a consultation, the physician obtains the patient's medical history (focusing on specific conditions when applicable), performs a physical examination, formulates diagnostic hypotheses or conclusions, requests additional tests if necessary, and provides a therapeutic prescription. It is the physician's prerogative to determine the appropriate timeline for follow-up appointments.

If test results cannot be reviewed during the initial visit, a follow-up appointment should be scheduled and considered a continuation of the original consultation. In such cases, no additional fees should be charged.

However, if the patient presents with new symptoms or signs that require the physician to retake the medical history, perform a new physical exam, or develop a new diagnostic evaluation or treatment plan, the consultation is considered a new appointment and should be charged accordingly.

In cases of patients requiring long-term treatment, including reassessments and therapeutic adjustments, consultations may be charged at the physician's discretion. The follow-up schedule is also determined exclusively by the physician.

The time needed to evaluate the patient and interpret test results is determined solely by medical and technical criteria, not administrative ones.

Health insurance providers are not permitted to interfere with the physician's autonomy or the patient-physician relationship, nor can they impose mandatory intervals between consultations. If these regulations are violated, the technical directors of such institutions will be held ethically accountable, in accordance with CFM Resolution 1958/2010.[20]

How to proceed when receiving a patient referred from another physician

According to the Medical Code of Ethics, a physician "must not fail to refer the patient who was sent for a specialized procedure back to the attending physician, and must also provide appropriate information regarding the care provided during the period for which they were responsible."[21]

Thus, with the patient's best interest in mind, the allergist/immunologist, when receiving a patient referred from another physician, should act in accordance with ethical standards by providing a report to the referring physician. This should be done through appropriate documentation that clearly describes the actions taken.

Professional advertising

Clear communication is increasingly important in modern society – and medicine is no exception. To ensure that accurate and ethically sound information is shared in their practice, physicians must comply with medical advertising regulations and stay up to date with the specific rules governing public communication in health care. Compliance with these standards helps prevent ethical violations and potential disciplinary actions.[22]

Each CRM has a Commission for the Dissemination of Medical Information (*Comissão de Divulgação de Assuntos Médicos*, CODAME), which is responsible for guiding, educating, and overseeing physicians on matters related to professional advertising.

This body evaluates whether physicians – through social media posts or other communication channels such as interviews – are engaging in actions that violate patient confidentiality, inappropriately expose patient images, promise specific outcomes, engage in unfair competition, sensationalism, or other unethical practices.

Requirements for each type of office according to type of medical procedure

The requirements for establishing an Allergy and Immunology practice vary according to the classifications set by the CFM. Regardless of classification, patient privacy and confidentiality must be upheld in all circumstances. Offices are categorized into three groups based on the complexity of services provided: Group 1, Group 2, and Group 3.[1,20]

Group 1

Group 1 refers to medical offices or services limited to providing basic care only – general procedures and those requiring local anesthesia or sedation are not permitted. These offices are designated for consultations only and cannot administer immunotherapy or other medical interventions.

According to the SomaSUS Manual from the Brazilian Ministry of Health, the following items (unless explicitly marked as optional) are deemed essential and must be present in the office to meet regulatory and clinical standards.

Furniture:

– Two chairs or armchairs – one for the patient and one for the accompanying person.
– One chair or armchair for the physician and one desk.
– One simple cushioned examination table with a waterproof cover.
– One two- or three-step stool to assist patients in accessing the examination table.

If the office stores controlled substances:

– A locked storage area (mandatory; Ministry of Health Ordinance MS/SVS 344/1998, Article 67).

Clinical materials:

– Paper towels.
– Liquid soap for hand hygiene.
– Pedal bins.
– Disposable sheets for the examination table.
– One sphygmomanometer.
– One clinical stethoscope.
– One clinical thermometer.
– One battery-powered flashlight.
– Disposable tongue depressors.
– Disposable gloves.
– One X-ray viewer (negatoscope) or a digital alternative.
– One otoscope (optional).
– One anthropometric scale suitable for the patient's age (optional).
– One flexible, non-stretch plastic measuring tape (optional).
– One ophthalmoscope (optional).
– One reflex hammer (optional).
– Peak flow meter (optional).
– Pulse oximeter.
– Nasal speculum.
– One sink or washbasin (with a hospital faucet as recommended by CERN-ASBAI).

– Hand sanitizer (gel or spray).
– Derma alcohol.

Group 2

Group 2 refers to medical offices or services that can perform procedures that do not require local anesthesia or sedation. In addition to the basic diagnostic equipment listed for Group 1, these offices must also be equipped with the necessary tools for performing therapeutic procedures.

These are offices where consultations and simple allergy tests, such as the skin prick test and patch test, are performed.[1] They must comply with the following requirements:

If the office stores controlled substances[1]:

– A locked storage area (mandatory; Ministry of Health Ordinance MS/SVS 344/1998, Article 67).
– All items listed for Group 1 offices, as well as materials for asepsis and sterilization in accordance with sanitary regulations and a rigid container for the disposal of sharps and cutting instruments.

If allergy skin tests are performed, including for both immediate (eg, skin prick test) and delayed (eg, patch tests) reactions[1]:

– A room with walls covered in tile or other impermeable material (e.g., epoxy or ceramic finishes).
– Cold floor to facilitate cleaning.
– Sink or washbasin (with hospital faucet as recommended by CERN-ASBAI).
– Refrigerator with a minimum/maximum thermometer, exclusively for storing tests and vaccines (antigens registered with Anvisa).
– Straight counters and cabinets to facilitate cleaning.

If allergen immunotherapy is administered (inhalants and/or insects)[1]:

– A room with walls covered in tile or other impermeable material (e.g., epoxy or ceramic finishes).
– Cold floor to facilitate cleaning.
– Sink or washbasin (with hospital faucet as recommended by CERN-ASBAI).
– Refrigerator with a minimum/maximum thermometer, exclusively for storing allergen extracts for skin allergy tests and immunotherapy, registered with Anvisa.
– Straight counters and cabinets to facilitate cleaning.

Medications[1]:

– Adrenaline (epinephrine) 1 mg/mL (1:1000).
– Parenteral antihistamines (diphenhydramine or promethazine).
– Short-acting β2-agonists bronchodilators, inhalation aerosol with a spacer (eg, salbutamol 100 µg); (CERN-ASBAI recommendation: salbutamol nebulizer solution or unit dose vials [1.25 mg/mL] and a nebulizer).
– Parenteral glucocorticoids (hydrocortisone or methylprednisolone).
– Parenteral H2 antihistamines (ranitidine).
– Prednisolone (1 mL/3 mg).
– Second-generation oral antihistamines.

Group 3

Group 3 refers to medical offices authorized to administer immunotherapy and perform desensitization, provocation, and intradermal allergy tests, in addition to all procedures permitted for Groups 1 and 2.[1]

In addition to all equipment listed for Groups 1 and 2, the following materials are also required:

– Allergen extracts registered with Anvisa.
– Materials for minor surgical procedures (optional).
– Materials for dressings/stitch removal (optional).
– Materials for local anesthesia (optional).
– Materials for asepsis/sterilization in accordance with sanitary regulations.
– Rigid container for the disposal of sharps and cutting materials.

Safety requirements for treating complications[1]:

– Emergency care must be provided in the medical office or through referral to an appropriate service within 4 minutes.
– CERN-ASBAI recommends taking the Advanced Life Support in Anaphylaxis and Asthma course by ASBAI, for proper training on the medications and materials to be used in case of complications.

As outlined in the Medical Code of Ethics: It is forbidden for a physician to (...) "Article 2 – Delegate to other providers acts or duties restricted to the medical profession."

If intradermal allergy tests are performed[1]:

– A room with walls covered in tile or other impermeable material (eg, epoxy or ceramic finishes).
– Cold floor to facilitate cleaning.
– Sink or washbasin (with hospital faucet as recommended by CERN-ASBAI).
– Refrigerator with a minimum/maximum thermometer, exclusively for storing tests and vaccine concentrates.
– Allergen extracts registered with Anvisa.
– Counter.
– Straight cabinets to facilitate cleaning.

If desensitization and provocation tests are performed[1]:

– A room with walls covered in tile or other impermeable material (eg, epoxy or ceramic finishes).
– Cold floor to facilitate cleaning.
– Refrigerator with a minimum/maximum thermometer, exclusively for storing tests and vaccines.
– Antigen registered with Anvisa.
– Straight counters and cabinets to facilitate cleaning.

Medications (per Ministry of Health Ordinance MS/GM 2048/02, Annex, Item 1.31)[1]:

– Adrenaline (epinephrine) 1 mg/mL (1:1000).
– Parenteral antihistamines (diphenhydramine or promethazine).
– Short-acting β2-agonist bronchodilators (salbutamol 100 µg) with spacer.
– Salbutamol solution for nebulization or unit-dose vials (1.25 mg/mL) and nebulizer (CERN-ASBAI recommendation).
– Glucagon (CERN-ASBAI recommendation).
– Parenteral glucocorticoids (hydrocortisone or methylprednisolone).
– Prednisolone (1 mL/3 mg).
– Parenteral H2 antihistamines (ranitidine – note: see Anvisa notice on discontinuation of this medication).
– Oropharyngeal airways (Guedel).
– Automated external defibrillator.
– Medications for cardiac arrest and anaphylaxis management.
– Distilled water (ampoule or vial).
– Diazepam.
– Dipyrone, or alternative if the patient is allergic.
– 50% and 5% dextrose (CERN-ASBAI recommendation).
– 0.9% saline solution.
– Lactated Ringer's solution (CERN-ASBAI recommendation).
– Oxygen supply (fixed or portable cylinder) with applicator mask and humidifier (essential).
– Pulse oximeter.
– Manual resuscitator (self-inflating bag) with reservoir and mask (essential).
– Syringes, needles, and IV infusion sets (essential).
– Scalp vein set.
– Butterfly needles and intravenous cannulas, with all insertion materials.
– Gauze.
– Cotton pads.
– Crepe bandages.
– Disposable gloves.
– Rigid container for the disposal of sharps and cutting materials.

Conclusion

With the objective of guiding and standardizing the practice of Allergy and Immunology, while also facilitating adaptations in existing medical offices, this initial publication seeks to provide technical guidance according to the requirements of regulatory authorities for the ethical and professional practice of the specialty. It presents a structured operational framework for each classification group of medical offices, thereby promoting a model of care that is safe, ethical, and grounded in scientific principles.

This guide underscores that the use of allergen extracts registered with Anvisa is a routine and recognized practice within the specialty, endorsed

by leading medical institutions. Furthermore, it reaffirms that the scope of Allergy and Immunology is comprehensive, not fragmented, and not limited by patient age group, thereby increasing the specialty's reach and relevance across the continuum of care.

Finally, the recommendations presented in this guide are intended to address common questions within the field and to support the delivery of high-quality, standardized care in the practice of Allergy and Immunology. By doing so, this guide aims to foster greater safety, uphold ethical standards, and increase patient confidence in all clinical settings dedicated to the specialty.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Special Article

Starting an Allergy and Immunology practice. Part 2 – Standard Operating Procedure (SOP): What is it?

Construindo o consultório do Alergista e Imunologista. Parte 2 – Procedimento Operacional Padrão (POP): o que é?

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ABSTRACT

A standard operating procedure (SOP) is a structured organizational document that standardizes processes to ensure task planning and consistent quality in procedures. It provides a detailed description of a set of measures aimed at ensuring the quality and safety of care in medical offices through a descriptive manual. The SOP must be regularly reviewed, including all routine procedures, and updated whenever changes or alterations occur. Additionally, SOPs are subject to oversight by the Municipal Health Surveillance. This special article aimed to guide allergists on the necessary SOPs for their practice, according to the type of office, based on groups 1 to 3 as standardized by the Brazilian Federal Board of Medicine.

Keywords: Allergy, immunology, good practices, standard operating procedure.

RESUMO

O chamado POP (sigla para Procedimento Operacional Padrão) é um documento organizacional, padronizado, que uniformiza processos. O seu objetivo é garantir o planejamento de tarefa, assegurando uma qualidade consistente nos procedimentos a serem executados. Ele oferece uma descrição detalhada de um conjunto de medidas que visam à qualidade e segurança dos atendimentos prestados nos consultórios médicos, através de um manual descritivo, como está sendo proposto. O POP tem a necessidade de ser revisto constantemente, com toda a lista de rotina e, se necessário, atualizar o documento, diante de qualquer mudança ou alteração. Sendo assim, os POPs serão sempre cobrados pela Vigilância Sanitária Municipal. A proposta desse artigo especial é oferecer ao consultório do Alergologista um roteiro para ter orientação de quais POPS são necessários, conforme o tipo de consultório, baseado nos grupos 1 a 3, conforme padronização definida pelo Conselho Federal de Medicina.

Descritores: Alergia, imunologia, boas práticas, padrão operacional de procedimentos.

Introduction

The Statute, Regulations, and Standards Committee of the Brazilian Association of Allergy and Immunology (CERN-ASBAI) presents the second part of the practical guide on how to start an Allergy and Immunology practice, this time with a focus on Standard Operating Procedures (SOPs).

SOPs are standard sets of instructions of Good Medical Practices, which are strongly recommended

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by the Brazilian Federal Board of Medicine (Conselho Federal de Medicina, CFM) and especially by the National Sanitary Surveillance Agency (Anvisa). These are subject to oversight by state or municipal health surveillance authorities, with municipal inspections being the most common. This guide includes recent updates regarding inspection requirements for private practices,[1] which are already in effect, as outlined in RDC Resolution No. 50, of February 21, 2002, issued by the Brazilian Ministry of Health. Other principles established in the ASBAI bylaws should also be considered.

Once an Allergy and Immunology practice is established, SOPs must be developed. But what are they, and why are they important?

An SOP is a document that describes, in detail, the steps necessary to adequately plan an activity, ensuring consistent quality in all tasks performed in the medical office. It serves as a standardized protocol that allows any trained individual to perform tasks efficiently and correctly. Such procedures may range from basic activities, such as adequate hand-washing techniques, to more complex ones, such as patient care and the performance of food or drug challenge tests.

With that in mind, CERN-ASBAI developed this second publication with the goal of guiding allergists on the key steps for establishing good clinical practices in the care of patients with allergic and/or immunological diseases in their office.

Standard Operating Procedure

"SOP" is the most widely recognized and used term in health care organizations. It refers to detailed instructions outlined to achieve uniformity in the execution of tasks for a specific function.[1,2] SOPs are the final and fundamental document in the standardization process, describing the step-by-step sequence of a specific health care activity or procedure.

In the health care setting, the goal of an SOP is to maintain and ensure the smooth operation of a process through standardization and by minimizing deviations during the execution of a task. This guarantees that actions are performed as planned, correctly, and with the expected outcome.[1,3] SOPs regulate professional conduct and promote improvements that enhance the performance of the medical office by standardizing the tools and materials to be used, defining the individuals responsible for executing a task, outlining the correct way to perform a procedure, and establishing a schedule for periodic inspections of processes and equipment.

SOPs also aim to reduce the need for constant training, contributing to saving time and resources. Standardized processes can help reduce the time required for completing a task, resulting in greater productivity and reduced waste of resources.

SOPs can cover everything from cleaning protocols to patient care workflows. They include detailed instructions on how to consistently and safely perform specific tasks, helping ensure efficiency, safety, and regulatory compliance.[4] SOPs also serve as practical guides for new physicians or staff members, making it easier for them to understand how the office operates and helping resolve common day-to-day questions.

ISO 9001 does not mandate a specific format for SOPs, recognizing that each private practice has its own unique procedures. Nonetheless, SOPs should be concise, written in clear language, and based on technical and scientific knowledge. The sequence of steps must be logical and chronological, with prioritization based on the order in which each task should be performed.

State and municipal inspections of Allergy & Immunology offices[6] are conducted according to specific protocols developed for the specialty.

When drafting an SOP, the following elements should be considered[4,5]:

1. SOP number.
2. Date of creation.
3. Revision history.
4. Validation.
5. Implementation.
6. Title.
7. Names of individuals responsible for creating and validating the document.
8. Expected outcomes of the procedure.
9. List of required materials.
10. Description of main activities.
11. Description of how to manage the risks associated with the procedure and actions to be taken in case of noncompliance.

An SOP is considered valid when an individual is able to perform an activity using only the instructions provided. For this reason, SOPs should be simple, clear, and contain all necessary information for proper execution of the tasks.

Examples of SOPs include:

– SOP for hand hygiene.
– SOP for the use of Personal Protective Equipment (PPE).
– SOP for labeling disposable dispensing bottles.
– SOP for performing spirometry.
– SOP for cleaning office cabinets.
– SOP for cleaning office countertops, armchairs, and chairs.
– SOP for cleaning office windows, doors, and light switches.
– SOP for disinfecting the anthropometric scale.
– SOP for cleaning the office floor.

These SOPs are required for obtaining authorization to open a private practice or health care facility, for the issuance and/or renewal of a health permit, and even for affiliation with a health insurance provider, every 1 or 2 years.

As an example, Figure 1 illustrates the Municipal Health Surveillance Inspection Checklist used in city of Belo Horizonte, Brazil, for Allergy & Immunology offices.6 It includes several items that will be verified during the on-site inspection and must be supported by documentation proving compliance. Inspectors may even request a live demonstration of certain procedures. Items on the checklist are marked as: performed (Y), not performed (N), or not applicable (NA).

Figure 2 presents a standard SOP template, followed by instructions on how to properly complete each section of an SOP.

1.1 Company identification

Enter the name of the company as it appears on the National Registry of Legal Entities (Cadastro Nacional de Pessoas Jurídicas, CNPJ) or, in the case of an individual, the full legal name. If applicable, the company logo may also be included.

1.2 SOP number

Enter SOP number. For example: SOP No. 1, SOP No. 2, SOP No. 3, SOP No. 4.

Note: A separate SOP must be created for each work process.

1.3 Date of issuance/Effective date

Enter the date the document was issued and its effective date.

Note: Set a review deadline for the SOP. If a new procedure is added, the SOP should be reviewed before the scheduled deadline.

1.4 Revision number

Enter the current revision number of the document.

1.5 Procedure to be performed

Enter the name of the procedure.

For example: Cleaning of materials, sterilization of instruments, cleaning of the procedure room, cleaning of bathrooms, etc.

1.6 Person(s) responsible

Identify the employee(s) or team responsible for carrying out the activity.

1.7 Necessary materials and resources

List all materials and supplies needed to perform the activity (eg, tools, soap/detergent, disinfectant, PPE).

1.8 Procedure description

Provide a step-by-step description of the tasks required for performing the procedure, with prioritization based on the order in which they should be performed.

For example:

1. Hand washing as described in the Hand Hygiene SOP.
2. Donning PPE, according to the procedure's specific requirements (which should also be listed in the Materials section).
3. Gathering the materials and tools required for the procedure.
4. Executing each step of the procedure in the described order.

Note: Specify how often the procedure should be performed (frequency), taking into account its associated sanitary risks.

1.9 Observation

List any precautions that should be taken when performing an activity to ensure the effectiveness of the process.

For example:

– In the presence of visible dirt, wash with soap and water to remove residues.
– Cleaning should always be performed from the cleanest area to the dirtiest.

MUNICIPAL HEALTH DEPARTMENT
DIRECTORATE OF HEALTH SURVEILLANCE – DVSA/SMSA

INSPECTION CHECKLIST FOR ALLERGY & IMMUNOLOGY AND/OR PULMONOLOGY PRACTICES – Health Surveillance **REVISION DATE: 03/03/2021**

ID 390 **RVF_DVSA_73_VS** **EFFECTIVE DATE: 03/03/20**

CBO/CNAE #	OCCUPATION NAME
8640-2/99	DIAGNOSTIC SUPPORT SERVICES
2251/10	ALLERGIST AND IMMUNOLOGIST
2251/27	PULMONOLOGIST

ITEM	DESCRIPTION	Y	N	NA	LAW[a]
	INFRASTRUCTURE				
1065	IS THERE A WAITING ROOM FOR PATIENTS/ACCOMPANYING PERSONS?				LM 7031/96, ART. 97, SECTION II C/C RDC 50/02, PART II, 3, UNID. FUNC. 1 - ATEND. AMB. AMB. APOIO
7986	IS THERE A RECEPTION AREA FOR PATIENT REGISTRATION?				LM 7031/96, ART. 97, SECTION II C/C RDC 50/02, PART II, 3 - DIMENS. QUANT. E INST. PRED. UNID. FUNC. 1 - ATEND. AMB. AMB. APOIO
11862	IF DESENSITIZATION, INTRADERMAL, AND PROVOCATION TESTS ARE PERFORMED, DOES THE OFFICE HAVE: * A ROOM COVERED WITH WATERPROOFING MATERIAL/PAINT OR TILE? * A SINK WITH A COUNTER AND CABINET MADE OF SMOOTH, EASY-TO-CLEAN MATERIAL? * A REFRIGERATOR WITH A MINIMUM / MAXIMUM THERMOMETER?				LM 7031/96 ART. 97, SECTION II C/C RESOLUÇÃO 2153/2016 AND PORTARIA MS/GM 2048/02, ANNEX, ITEM 1.3
6573	IS THERE A UTILITY/DISPOSAL ROOM?				LM 7031/96, ART. 97, SECTION II C/C RDC 50/02, ART. 1, RT, PART II, 3 - DIMENS., QUANTIF. E INSTALAÇÕES PREDIAIS
1068	IF SO, IS THE UTILITY/DISPOSAL ROOM EQUIPPED WITH: * TORNEIRA SOB PRESSÃO * BRUSHES OF VARIOUS SIZES * ILLUMINATED MAGNIFIER * NEUTRAL OR ENZYMATIC DETERGENT * COMPRESSED AIR * HOT RUNNING WATER * PLASTIC CONTAINERS FOR IMMERSION OF MEDICAL INSTRUMENTS				LM 7031/96, ART. 97, SECTION II C/C REPUB. NOTIF. GER. COLEG. SUPERINT. VISA 202/2008 + LE nº 13317/99, ART. 81, SECTION I
35	DO THE TRASH CANS MEET THE FOLLOWING CRITERIA? * MADE OF WASHABLE MATERIAL * EQUIPPED WITH PLASTIC BAGS IN THE APPROPRIATE COLOR * TOUCH-FREE * CLEARLY LABELED WITH DESCRIPTIONS AND SYMBOLS * SUFFICIENT IN QUANTITY * IN GOOD CONDITION				LM 7031/96 art. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM.3.2.1.1.7 + RDC 222/2018, ART. 11
11508	ARE THE FLOOR, WALLS, AND CEILING EASY TO CLEAN, WITH MINIMAL GROOVES OR GAPS, AND IN GOOD CONDITION?				LM 7031/96, ART. 69 C/C RDC 50/02, ART. 1, RT, PART 6.2, C.1 + RDC 063/2011, ART. 36

[a] This table lists specific Brazilian laws.
DF = Federal Decree; LE = State Law; LM = Municipal Law; NA = Accessibility Act; NTE = Technical Note; RT = Technical Standard.

Figure 1
Municipal Health Surveillance Inspection Checklist for Allergy & Immunology Offices – City of Belo Horizonte, state of Minas Gerais, Brazil.

ITEM	DESCRIPTION	Y	N	NA	LAW[a]
	INFRASTRUCTURE				
11861	IS PREVENTIVE AND CORRECTIVE MAINTENANCE OF THE BUILDING INFRASTRUCTURE PERFORMED (IN-HOUSE OR OUTSOURCED)?				LM 7031/96, ART. 97, SECTION II C/C RDC 063/2011, ART. 23, INCISO VII AND IX + ART. 42
3084	ARE VISIBLE ELECTRICAL INSTALLATIONS IN GOOD CONDITION?				LM 7031/96, ART. 69 C/C PM 015/01, ART. 1, NTE 001/01, ANEX I, ITEM 3.12.6 C/C RDC 50/02, ART. 1, RT, PART III, 7 E RDC 63/2011, ART. 36
11316	ARE LIGHTING AND VENTILATION ADEQUATE FOR THE ACTIVITIES PERFORMED?				LM 7031/96, ART. 69 C/C RDC 063/2011, ART. 38
XXXX	ARE ALL AREAS WELL-MAINTAINED, SAFE, ORGANIZED, AND CLEAN?				LM 7031/96, ART. 69 C/C RDC 063/2011, ART. 56
9179	ARE RESTROOMS AVAILABLE FOR STAFF AND PATIENTS/ ACCOMPANYING PERSONS?				LM 7031/96, ART. 97, SECTION C/C RDC 50/02, ART. 1, RT, PART II, 3 - DIMENS., QUANT. E INST. PRED.
1071	ARE THERE APPROPRIATE RESTROOM FACILITIES FOR INDIVIDUALS WITH PHYSICAL DISABILITIES, ALLOWING WHEELCHAIR CIRCULATION, WITH OUTWARD-OPENING DOORS AND GRAB BARS POSITIONED 90 CM FROM THE FLOOR?				RDC 50/02, ART. 1° RT, PART III, 4; ITEM 4.1 C/C PM 015/01 ART. 1, NTE 001/01, NA. III IT. 3 SUBIT. 3.1.10 + 3.1.11 AND NBR 9050/94
1512	DO ALL DRAINS (EXCEPT THOSE CONNECTED TO THE STORM WATER SYSTEM) HAVE TRAPS AND FLIP-TOP COVERS?				LM 7031/96, ART. 97, II C/C RDC 50/02, ART. 1, RT, PART III, ITEM 6.2, B.5
1195	REGARDING OFFICE DIMENSIONS: * DO CONSULTATION ROOMS HAVE A MINIMUM OF 7.5 m^2? * ARE OFFICE DIMENSIONS COMPATIBLE WITH THE ACTIVITIES PERFORMED? * DO THEY ALLOW FOR A RATIONAL WORKFLOW?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01, ART. 1°, NTE 001/01, ANEXO III, ITEM 3.1.6 OR RDC 050/02, PART II, 3, ATIVIDADE
3625	IS THERE A CLEANING SUPPLY STORAGE ROOM CONTAINING AT LEAST: * A SINK OR BASIN * ADEQUATE LOCATION (CABINET/SHELF) FOR STORING SUPPLIES * A LIDDED PEDAL BIN WITH PLASTIC BAG * DISPOSABLE HAND TOWELS * LIQUID SOAP				LM 7031/96 ART. 97, SECTION II C/C RDC 050/02 ART. 1°, RT, C/C PM 015/01 ART. 1, NTE 001/01, NA. ITEM 3 SUBIT. 3.1.12
7771	IF THERE IS NO DESIGNATED CLEANING SUPPLY STORAGE ROOM, IS THERE ANOTHER APPROPRIATE PLACE FOR STORING CLEANING PRODUCTS AND EQUIPMENT?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART, 1°, NTE 001/01, ANEX III, ITEM 3.1.12
9330	IS DRINKING WATER EASILY ACCESSIBLE TO PATIENTS AND STAFF, WITH NO RISK OF CONTAMINATION?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1°, NTE 001/01, ANEX III, ITEM 3.1.3
2858	DO EXAMINATION ROOMS HAVE A WASHBASIN WITH SINK, RUNNING WATER, LIQUID SOAP AND/OR ANTISEPTIC SOLUTION, AND PAPER TOWELS?				LM 7031, ART. 97, SECTION II C/C RDC 48/2000, ART. 1, ANEX, ROTEIRO B, ITEM 25, PM 015/2001 NTE 001/01 ANEX IV ITEM 3.28 + RDC 063/2011, ART.

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Figure 1 *(continued)*
Municipal Health Surveillance Inspection Checklist for Allergy & Immunology Offices – City of Belo Horizonte, state of Minas Gerais, Brazil.

ITEM	DESCRIPTION	Y	N	NA	LAW[a]
	EQUIPMENT / MEDICATIONS AND MATERIALS				
3013	ARE ONLY MEDICATIONS, ANTIGENS, SOLUTIONS, DISINFECTANTS, AND GERMICIDES USED THAT ARE: * REGISTERED WITH THE APPROPRIATE REGULATORY AUTHORITY * WITHIN BEYOND-USE DATE				LM 7031/96 ART. 97. SECTION X C/C RDC 063/2011, ART. 17
3566	ARE MEDICATIONS AND MEDICAL SUPPLIES STORED: * IN AN EXCLUSIVE AREA * IN AN APPROPRIATE LOCATION * IN A PLACE FREE FROM HUMIDITY * IN A PLACE THAT IS EASY TO CLEAN * IN A PLACE THAT IS EASY TO DISINFECT				LM 7031/96, Art 97, SECTION II C/C RDC 050/2002, PART II 3 UM. FUNC. 4 - AP. DIAG.TER. ITEM 4.6 E RDC 063/2011, ART. 36
5326	ARE CONTROLLED SUBSTANCES KEPT IN A LOCKED CABINET/ROOM OR SECURED WITH ANOTHER SAFETY MECHANISM?				LM 7031/96, Art 97, SECTION II C/C Portaria MS/SVS 344/1998, ART. 67
11863 11826	IF DESENSITIZATION, PROVOCATION TESTS, OR IMMUNOTHERAPY FOR INHALANT/INSECT ALLERGY ARE PERFORMED, IS THE FOLLOWING AVAILABLE: H2 ANTIHISTAMINE FOR IV USE (RANITIDINE)				LM 7031/96 ART. 97, SECTION II C/C RESOLUÇÃO 2153/2016 AND PORTARIA MS/GM 2048/02, ANEX, ITEM 1.3
11864	IF SENSITIZATION AND PROVOCATION TESTS WITH ANTIGENS AND LOCAL ANESTHESIA (WITHOUT SEDATION) ARE PERFORMED, PIS THE OFFICE EQUIPPED FOR EMERGENCY SITUATIONS WITH: * ADRENALINE (EPINEPHRINE) * DISTILLED WATER * DEXAMETHASONE * DIAZEPAM * DIPYRONE * DEXTROSE * HYDROCORTISONE * PROMETHAZINE * SALINE SOLUTION				LM 7031/96 art. 97, SECTION II C/C RESOLUÇÃO 2153/2016 AND PORTARIA MS/GM 2048/02, ANEX, ITEM 1.3
11865	IF SENSITIZATION AND PROVOCATION TESTS WITH ANTIGENS AND LOCAL ANESTHESIA (WITHOUT SEDATION) ARE PERFORMED, IS THE OFFICE EQUIPPED FOR EMERGENCY SITUATIONS WITH: * AUTOMATED EXTERNAL DEFIBRILLATOR * OROPHARYNGEAL AIRWAYS (GUEDEL) * OXYGEN SUPPLY WITH APPLICATOR MASK AND HUMIDIFIER * PULSE OXIMETER * AMBU BAG WITH RESERVOIR AND MASK *SYRINGES, NEEDLES, AND IV INFUSION EQUIPMENT * SCALP VEIN SETS/BUTTERFLY NEEDLES AND INTRAVENOUS CANNULAS (WITH ALL INSERTION MATERIALS) * GAUZE, COTTON, CREPE BANDAGES, AND STERILE GLOVES				LM 7031/96 ART. 97, SECTION II C/C RESOLUÇÃO 2153/2016 AND PORTARIA MS/GM 2048/02, ANEX, ITEM 1.3
2138	IS THERE A DAILY LOG FOR TEMPERATURE CONTROL OF THE REFRIGERATOR USED FOR THERMOLABILE PRODUCTS AND IS THE TEMPERATURE MAINTAINED BETWEEN 2 °C AND 8 °C (MINIMUM AND MAXIMUM)?				7031/96 ART. 97 SECTION II C/C LM RDC 36/2013, ANEX III - PROTOCOLO DE SEGURANÇA NA PRESCRIÇÃO, USO E ADMINISTRAÇÃO DE MEDICAMENTOS - ITENS 6.1.1 E

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Figure 1 *(continued)*
Municipal Health Surveillance Inspection Checklist for Allergy & Immunology Offices – City of Belo Horizonte, state of Minas Gerais, Brazil.

ITEM	DESCRIPTION	Y	N	NA	LAW[a]
EQUIPMENT / MEDICATIONS AND MATERIALS					
1098	ARE THE DISPENSING BOTTLES: * SANITIZED * LABELED * MARKED WITH THE BOTTLING DATE * WITHIN THE EXPIRATION DATE				LM 7031/96 ART. 97 SECTION II C/C RDC 63/2011 ART. 57
10432	ARE ALL PADDED FURNITURE, INCLUDING MATTRESSES AND CUSHIONS, COVERED IN WASHABLE, WATERPROOF MATERIAL, AND FREE OF HOLES, TEARS, GROOVES, OR INDENTATIONS?				LM 7031/96, ART. 69 C/C RDC 063/2011, ART. 56
7532	ARE ONLY SAFETY SYRINGES WITH RETRACTABLE NEEDLES USED IN PROCEDURES?				LM 7031/96 ART. 97 SECTION II C/C LE 18797/10 ART. 1º
2692	ARE THERE SUFFICIENT QUANTITIES OF EQUIPMENT, MATERIALS, AND TOOLS FOR THE PROCEDURES PERFORMED, AND ARE THEY IN GOOD WORKING AND HYGIENIC CONDITIONS?				LM 7031/96 ART. 97. SECTION X C/C RDC 063/2011, ART. 53 AND LM 7031/96, ART. 32, § ÚNICO
1093	IS THERE ENOUGH SUPPLY OF REUSABLE ITEMS?				LM 7031/96 ART. 97. SECTION X C/C RDC 063/2011, ART. 53 + LM 7031/96, ART. 32, § ÚNICO
2616	IS THERE AN ADULT AND/OR PEDIATRIC STETHOSCOPE?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 3.2.1.1.1
4303	IS THERE A DIGITAL THERMOMETER?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 3.2.1.1.2 AND RDC 145/2017, ART. 1º
2617	IS THERE AN EXAMINATION TABLE?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 3.2.1.1.3
1203	IS THERE A SCALE FOR ADULTS AND/OR CHILDREN?				LM 7031/96 ART 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 3.2.1.1.5
1204	IS THERE A TABLE OR STAND FOR KEEPING MEDICAL DEVICES?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 3.2.1.1.8
1205	IS THERE A SPHYGMOMANOMETER WITH CUFFS FOR BOTH ADULTS AND CHILDREN?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 3.2.1.10
1206	IS THERE A NEGATOSCOPE?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 art. 1º, NTE 001/01, ANEX III, ITEM 3.2.1.10
1207	ARE TONGUE DEPRESSORS DISPOSABLE?				PM 015/01 ART. 1, NTE 001/01, ANEX III ITEM 3 SUBITEM 3.2.1.1.11
1198	DO ALL APPLICABLE MEDICAL DEVICES HAVE REGISTRATION WITH ANVISA OR THE MINISTRY OF HEALTH, WHEN REQUIRED?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 3.2.2

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Figure 1 *(continued)*
Municipal Health Surveillance Inspection Checklist for Allergy & Immunology Offices – City of Belo Horizonte, state of Minas Gerais, Brazil.

ITEM	DESCRIPTION	Y	N	NA	LAW[a]
	PROCEDURES				
1753	ARE THERE ILLUSTRATIVE HAND HYGIENE INSTRUCTIONS, POSTED PREFERABLY IN A VISIBLE LOCATION NEAR WASHBASINS?				LM 7031/96, ART. 97, II C/C RDC 63/2011, ART. 8º, II
11507	ARE THE NECESSARY SUPPLIES, PRODUCTS, AND EQUIPMENT MADE AVAILABLE TO ENSURE ADEQUATE HAND HYGIENE FOR WORKERS, PATIENTS, ACCOMPANYING PERSONS, AND VISITORS?				LM 7031/96 ART 97 SECTION II C/C RDC 063/2011, ART. 59
6923	ARE DISPENSERS FILLED WITH 70% ALCOHOL AVAILABLE IN ALL AREAS?				LM 7031/96, ART. 97, SECTION II C/C RDC 042/2010, ART. 1º, ITEM X 063/2011, ART. 59
572	IS 70% ETHYL ALCOHOL OR ANOTHER PROVEN DISINFECTANT USED TO DISINFECT EQUIPMENT, SURFACES, AND RECREATIONAL MATERIALS AFTER CLEANING?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 4.7.4
2673	IS 1% SODIUM HYPOCHLORITE OR AN EQUIVALENT DISINFECTANT USED TO DISINFECT SURFACES?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART 1º, NTE 001/01, ANEX III, ITEM 4.7.3
1089	FOR AREAS CONTAMINATED WITH BLOOD, SECRETIONS, OR EXCRETIONS, ARE THE FOLLOWING PROCEDURES FOLLOWED: * WASHING WITH WATER AND SOAP * DISINFECTION WITH 1% SODIUM HYPOCHLORITE OR ANOTHER PROVEN DISINFECTANT				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 4.7.2
1090	REGARDING LINENS (SHEETS, GOWNS, PILLOWCASES, TOWELS, ETC.), WHEN NOT DISPOSABLE: * ARE THEY REPLACED AFTER EACH PATIENT? * ARE THEY PROPERLY LAUNDERED?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 4.7.7
8508	ARE ALL CRITICAL ITEMS IN THE FACILITY STERILIZED?				LM 7031/96, ART. 97, II C/C RDC 63/2011, ART. 57
1092	ARE ALL MEDICAL DEVICES THAT COME INTO CONTACT WITH BODY FLUIDS, WHEN NOT DISPOSABLE, PROPERLY PROCESSED?				LM 7031/96 ART. 32
11360	DOES THE SERVICE ENSURE THE QUALITY OF DISINFECTION AND STERILIZATION PROCESSES FOR EQUIPMENT AND MATERIALS/ITEMS?				LM 7031/96, ART. 97, II C/C RDC 63/2011, ART. 57
11535	ARE THE SOLUTIONS USED FOR DISINFECTING MEDICAL DEVICES STORED IN SEALED AND LABELED PLASTIC CONTAINERS OR DISPENSERS WITH THE PRODUCT NAME, BOTTLING DATE, AND EXPIRATION DATE CLEARLY INDICATED?				LM 7031/96 ART 34, ART. 97, SECTION II, C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 4.10
1199	ARE DISINFECTED, STERILIZED, AND DISPOSABLE EQUIPMENT AND MATERIALS STORED IN CLEAN, CLOSED CABINETS OR DRAWERS?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART 1º, NTE 001/01, ANEX III, ITEM 4.11
9944	IS THE PROHIBITION AGAINST EATING OR STORING FOOD IN PATIENT CARE AND TREATMENT AREAS STRICTLY OBSERVED?				LM 7031/96, ART. 97, II C/C RDC 63/2011, ART. 64
4852	ARE SUSPECTED CASES OF NOTIFIABLE DISEASES PROPERLY REPORTED TO THE RELEVANT HEALTH AUTHORITIES?				LM 7031/96 ART. 97 SECTION II C/C RDC 063/2011, ART. 61
8502	IF INVASIVE PROCEDURES ARE PERFORMED, DOES THE OFFICE HAVE AN INFECTION CONTROL TEAM?				LM 7031/96, ART. 30 C/C LM 7031/96, ART. 97, SECTION II C/C RDC 063/2011, ART. 23, SECTION XV

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Figure 1 *(continued)*
Municipal Health Surveillance Inspection Checklist for Allergy & Immunology Offices – City of Belo Horizonte, state of Minas Gerais, Brazil.

ITEM	DESCRIPTION	Y	N	NA	LAW[a]
	HUMAN RESOURCES				
11890	IS THE OFFICE'S TECHNICAL SUPERVISOR BOARD-CERTIFIED IN ALLERGY AND IMMUNOLOGY BY THE REGIONAL MEDICAL BOARD (CRM) OF THEIR JURISDICTION?				LM 7031/96, ART. 97, SECTION II C/C ANEX RESOLUTION CFM nº2.147/2016, ART. 9º, § 1º
6403	ARE COLLECTIVE PROTECTIVE EQUIPMENT (CPE) AND PERSONAL PROTECTIVE EQUIPMENT (PPE) AVAILABLE, AND IS THERE DOCUMENTATION CONFIRMING THEIR DISTRIBUTION TO STAFF?				LM 7031/96, ART. 38, § ÚN. C/C PM 485/05, ART. 1, ANEX I - NR-32, ITEM 32.2.4.7 C/C RDC 63/11, ART. 47 C/C PM015/01 ART.1, NTE 001/01, ANEX III,4.12 E
543	DO STAFF MEMBERS RESPONSIBLE FOR CLEANING AND PROCESSING CONSISTENTLY AND UNDER SUPERVISION USE THE APPROPRIATE PPE WHEN NECESSARY, INCLUDING: * LONG-CUFF RUBBER GLOVES * WATERPROOF CLOSED-TOE SHOES * WATERPROOF GOWN * LONG-SLEEVED GOWN (FOR PROCESSING) * PROTECTIVE GOGGLES (FOR PROCESSING)				LM 7031/96, ART. 38, § ÚNICO C/C PM 485/05, ART.1, NA 1-NR- 32, ITEM 32.2.4.7 C/C RDC 63/11, ART. 47, NTE 001/01, ANEX III, 4.12 AND 4.15
656	ARE THE PPE IN GOOD HYGIENIC CONDITION AND PROPERLY MAINTAINED?				LM 7031/96 ART. 97 SECTION II C/C RDC 63/2011 ARTS. 17 AND 46
	DOCUMENTATION				
6955	DO THE ACTIVITIES LISTED ON THE OPERATING LICENSE AND REGISTRATION FORM MATCH THE ACTIVITIES ACTUALLY CARRIED OUT OR INTENDED TO BE CARRIED OUT AT THE SITE?				LM 7031/96, ART. 20 C/C RDC 63/11 ART. 10
6549	IS THERE A MANUAL OF POLICIES & PROCEDURES COVERING ALL WORK PROCESSES, INCLUDING TECHNICAL, ADMINISTRATIVE, AND HEALTH CARE ACTIVITIES, AS WELL AS RESPONSIBILITIES AND COMPETENCIES??				LM 7031/96, ART. 97, SECTION II C/C RDC 063/2011, ART. 51
9998	DOES THE HEALTH SERVICE MAKE THE FOLLOWING AVAILABLE TO ALL STAFF: * STANDARDS AND SAFETY PROTOCOLS RELATED TO BIOLOGICAL, CHEMICAL, PHYSICAL, OCCUPATIONAL, AND ENVIRONMENTAL HAZARDS? * INSTRUCTIONS FOR THE USE OF PPE? * INSTRUCTIONS IN CASE OF FIRE OR ACCIDENTS?				LM 7031/96, ART. 97, II C/C RDC 63/2011, ART. 50, ITENS I - IV
8254	ARE THERE TRAINING RECORDS FOR STAFF MEMBERS, BOTH PRIOR TO BEGINNING THEIR DUTIES AND ON AN ONGOING BASIS, INCLUDING DATE, DURATION (HOURS), CONTENT, NAME AND CREDENTIALS OF THE INSTRUCTOR, AND NAMES AND ROLES OF PARTICIPANTS?				LM 7031/96, ART. 97, II C/C RDC 63/2011, ART. 32
11509	ARE THERE RECORDS CONFIRMING THAT THE TRAINING AND QUALIFICATIONS OF PROFESSIONALS ARE COMPATIBLE WITH THE FUNCTIONS PERFORMED?				LM 7031/96, ART. 97, SECTION II C/C RDC 063/2011, ART. 31, § ÚNICO

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Figure 1 *(continued)*
Municipal Health Surveillance Inspection Checklist for Allergy & Immunology Offices – City of Belo Horizonte, state of Minas Gerais, Brazil.

ITEM	DESCRIPTION	Y	N	NA	LAW[a]
	D O C U M E N T A T I O N				
531	IS THERE PROOF OF WATER TANK CLEANING EVERY 6 MONTHS OR LESS?				LM 7031/96, ART. 97, II C/C RDC 63/2011, ART. 39, § 1° C/C LM 6673/94, ART. 1, II
7614	ARE THERE RECORDS OF MICROBIOLOGICAL AND PHYSICOCHEMICAL ANALYSES OF POTABLE WATER QUALITY?				LM 7031/96, ART. 97, II C/C RDC 63/2011, ART. 23, VI
4200	IF PEST CONTROL IS INCLUDED IN THE CLINIC'S INTEGRATED VECTOR CONTROL MANAGEMENT PLAN, IS THERE A VALID DISINFESTATION AND RODENT CONTROL CERTIFICATE ISSUED BY A SPECIALIZED COMPANY AND APPROVED BY THE MUNICIPAL HEALTH DEPARTMENT? * DID THE MUNICIPAL HEALTH DEPARTMENT ISSUE A HEALTH PERMIT FOR THE COMPANY? * IS THE CERTIFICATE WITHIN ITS VALIDITY PERIOD? * DOES THE SERVICE COMPLY WITH INTEGRATED VECTOR CONTROL AND PEST MANAGEMENT STANDARDS?				LM 7031/96 ART. 97, SECTION II C/C RDC 222/2018, ART. 1, ANEXO, ITEM 4.1.3 + RDC 63/11, ART. 63, § ÚNICO
9322	IS PREVENTIVE AND CORRECTIVE MAINTENANCE OF EQUIPMENT PERFORMED AND DOCUMENTED?				LM 7031/96, ART. 97, SECTION II C/C RDC 063/2011, ART. 23, SECTION IX
10237	ARE OUTSOURCED SERVICES AND ACTIVITIES GOVERNED BY FORMAL SERVICE CONTRACTS PROPERLY REGISTERED WITH THE RELEVANT HEALTH AUTHORITY?				LM 7031/96, ART. 97, SECTION II C/C RDC 063/2011, ART. 11
10010	IS THERE A VACCINATION PROGRAM THAT INCLUDES GUIDANCE AND MECHANISMS FOR IMMUNIZATION AGAINST TETANUS, DIPHTHERIA, HEPATITIS B, AND OTHER BIOLOGICAL AGENTS TO WHICH WORKERS MAY BE EXPOSED?				LM 7031/96, ART. 97, SECTION II C/C RDC 063/2011, ART. 43 AND PF 485/2005, NR 32, ITEM 32.3.1, ITEM e
10387	ARE MEDICAL RECORDS LEGIBLY COMPLETED, WITH SIGNATURE AND STAMP OF THE HEALTH CARE PROFESSIONAL DIRECTLY INVOLVED?				LM 7031/96, ART. 97, SECTION II C/C RDC 063/2011, ART. 41 AND LM 7031/96, ART. 27
11704	DO MEDICAL RECORDS INCLUDE DATA REGARDING PATIENT IDENTIFICATION AND ALL PROCEDURES PERFORMED?				LM 7031/96, ART. 97, SECTION II C/C RDC 063/2011, ART. 41 AND LM 7031/96, ART. 26
9128	ARE ALL MEDICAL RECORDS RELATED TO EACH PATIENT CONSOLIDATED INTO A SINGLE, UNIFIED RECORD, WITH LEGIBLE ENTRIES COMPLETED BY ALL PROFESSIONALS DIRECTLY INVOLVED IN THE PATIENT'S CARE, INCLUDING CLEAR IDENTIFICATION AND, FOR PHYSICAL RECORDS, THE PROFESSIONAL'S SIGNATURE AND STAMP?				LM 7031/96, ART. 97, SECTION II C/C RDC 63/2011 ART. 26
3021	DO MEDICAL RECORDS CONTAIN THE FOLLOWING INFORMATION: * CLINICAL HISTORY? * DIAGNOSIS? * TEST RESULTS?				LM 7031/96, ART. 97, SECTION II C/C RDC 63/2011 ART. 26 AND PM 015/01, ART. 1, NTE 001/01, ANEX I, ITEM 3.21.2
1283	DO PRESCRIPTION FORMS INCLUDE THE PHYSICIAN'S NAME, LICENSE NUMBER, AND OFFICE ADDRESS?				LM 7031/96 ART. 97, SECTION II C/C PM 015/01 ART. 1º, NTE 001/01, ANEX III, ITEM 4.3
1284	ARE PRESCRIPTION FORMS AND MEDICAL DOCUMENTS WRITTEN LEGIBLY?				LM 7031/96, ART. 97, II C/C RCFM 1246/88 CAPITULO III ART. 39

[a] This table lists specific Brazilian laws.
DF = Federal Decree; LE = State Law; LM = Municipal Law; NA = Accessibility Act; NTE = Technical Note; RT = Technical Standard.

Figure 1 *(continued)*
Municipal Health Surveillance Inspection Checklist for Allergy & Immunology Offices – City of Belo Horizonte, state of Minas Gerais, Brazil.

ITEM	DESCRIPTION	Y	N	NA	LAW[a]
	D O C U M E N T A T I O N				
1282	ARE PRESCRIPTION FORMS FOR CONTROLLED SUBSTANCES COMPLIANT WITH REGULATORY REQUIREMENTS, AS DESCRIBED: TYPE “A” FORMS FOR A1, A2, AND A3 MEDICATIONS (ANNEX IX), TYPE “B” FORMS FOR B1 AND B2 MEDICATIONS (ANNEX X), SPECIFIC FORMS FOR SYSTEMIC RETINOIDS (C2 MEDICATIONS, ANNEX XII), AND SPECIFIC FORMS FOR THALIDOMIDE (C3 MEDICATIONS, ANNEX).				LM 7031/96 ART. 97, SECTION II C/C PF 344/98, ART. 36, PARAGRAPH "a" to "m", ART. 52
10011	ARE WORKERS REGULARLY ASSESSED FOR OCCUPATIONAL HEALTH, WITH THE APPROPRIATE RECORDS MAINTAINED?				LM 7031/96, ART. 97, II C/C RDC 63/2011, ART. 44
	H C W M P				
2925	DOES THE CLINIC HAVE A HEALTH CARE WASTE MANAGEMENT PLAN (HCWMP)? * IS THE HCWMP FILED WITH THE COMPETENT AUTHORITIES? * IS THE HCWMP APPROVED BY THE COMPETENT AUTHORITIES? * OR IS THERE A STATEMENT OF ZERO WASTE?				LM 7031/96, ART. 97, SECTION II C/C RDC 063/2011, ART. 23, ITEM X
9264	IS THERE A CONTRACT OR PROOF OF SERVICE FOR EXTERNAL COLLECTION AND TRANSPORTATION OF WASTE BY A LEGALLY LICENSED COMPANY FOR THE TRANSPORT AND FINAL DISPOSAL OF HEALTH CARE WASTE?				Law 7031/96 ART 22 C/C DM 16509/16 ART.1, NA 1 ITEM 2.6.2
2530	IS THERE A RIGID CONTAINER FOR THE DISPOSAL OF SHARPS (NEEDLES, SCALPELS, ETC.), WITH ADEQUATE SUPPORT AND PLACED IN AN ADEQUATE LOCATION?				LM 7031/96, ART. 97, SECTION II C/C RDC 222/2018, ART. 11
11336	IS WASTE SEGREGATION CONDUCTED AT THE PLACE AND TIME OF ITS GENERATION?				Law 7031/96 ART. 97 SECTION II C/C RDC 222/2018 ART. 11
	S M O K I N G				
7055	DOES THE OFFICE COMPLY WITH THE REQUIREMENT TO POST AND MAINTAIN SIGNS, POSTERS, OR NOTICES REGARDING THE PROHIBITION OF SMOKING, PLACED IN CLEARLY VISIBLE AREAS?				LE 12.903/98 ART. 4
8503	DOES THE OFFICE RESPECT THE PROHIBITION ON THE USE OF CIGARETTES, CIGARS, CIGARILLOS, PIPES, OR ANY SMOKING PRODUCT, WHETHER TOBACCO-DERIVED OR NOT, IN PUBLIC OR PRIVATE ENCLOSED SPACES THAT ARE ACCESSIBLE TO THE GENERAL PUBLIC OR DESIGNATED FOR COLLECTIVE USE, WHETHER FULLY OR PARTIALLY ENCLOSED?				DF 8.262/14 ART. 3

[a] This table lists specific Brazilian laws.
DF = Federal Decree; LE = State Law; LM = Municipal Law; NA = Accessibility Act; NTE = Technical Note; RT = Technical Standard.

Figure 1 *(continued)*
Municipal Health Surveillance Inspection Checklist for Allergy & Immunology Offices – City of Belo Horizonte, state of Minas Gerais, Brazil.

SOP TEMPLATE

<table>
<tr><td>(1.1) COMPANY IDENTIFICATION (Logo/Name)</td><td colspan="3">STANDARD OPERATING PROCEDURE – SOP</td></tr>
<tr><td>(1.2) SOP No.: _____</td><td>(1.3) Date of Issuance:
___ / ___ / ___</td><td colspan="2">(1.3) Effective Date:
___ / ___ / ___</td></tr>
<tr><td>(1.4) REV.: _____</td><td colspan="3">(1.5) PROCEDURE TO BE PERFORMED:</td></tr>
<tr><td colspan="4">(1.6) PERSON(S) RESPONSIBLE:</td></tr>
<tr><td colspan="4">(1.7) NECESSARY MATERIALS AND RESOURCES:</td></tr>
<tr><td colspan="4">(1.8) STEP-BY-STEP DESCRIPTION OF THE PROCEDURE:</td></tr>
<tr><td colspan="4">(1.9) OBSERVATIONS:</td></tr>
<tr><td colspan="4">(1.10) REFERENCES:</td></tr>
<tr><td>(1.11) PREPARED BY:</td><td>(1.11) REVIEWED BY:</td><td colspan="2">(1.11) APPROVED BY:</td></tr>
</table>

Figure 2
Standard SOP template

– Do not mix different cleaning or disinfectant products in the same solution.
– Follow the correct direction when cleaning.

1.10 References

List the references consulted.

For example:

– BRAZIL. Agência Nacional de Vigilância Sanitária. Segurança do Paciente em Serviços de Saúde – Higienização das mãos. Brasília, 2009. Available from: www.gov.br. Accessed on May 21 2021.
– BRAZIL. Agência Nacional de Vigilância Sanitária. Segurança do Paciente em Serviços de Saúde – Limpeza e Desinfecção de Superfícies. Brasília, 2010. Available from: www.gov.br. Accessed on May 21 2021.
– Práticas Recomendadas SOBECC/Sociedade Brasileira de Enfermagem de Centro Cirúrgico, Recuperação Anestésica e Centro de Material e Esterilização. 5th ed. São Paulo: SOBECC; 2009.

1.11 Prepared by/Reviewed by/Approved by

Enter the full name and signature of the professional(s) responsible for the preparation, review, and approval of the SOP.

Below are several SOPs approved by the Municipal Health Surveillance Agency of Belo Horizonte, provided as templates for the development of your practice's SOPs. It is important to note that each health care facility has its own procedures and protocols. These examples are meant to serve only as suggestions. Health inspectors will verify the accuracy of each SOP based on the practice's actual activities.

SOP samples for CFM/ASBAI Group 3 Allergy & Immunology offices, drafted by the Coordinator of the Statute, Regulations, and Standards Commission of ASBAI in the city of Belo Horizonte, Minas Gerais, Brazil

SOP No. 1 – Date: __/__/__ – Revision: __/__/__

Procedure

Hand hygiene.

Person(s) responsible

All staff members.

Objectives

– "Hand hygiene" refers to any action taken to clean the hands with the purpose of preventing the transmission of microorganisms and thereby reducing the risk of acute respiratory infections (ARIs) among patients and health care workers.

Indications for hand hygiene

Hands must be cleaned at key points during patient care, in order to prevent ARIs caused by cross-transmission through hands.

– Before and after touching a patient, contaminated item, or surface.
– Before and after exposure to body fluids (eg, blood, secretions, or excretions).
– After contact between patients, between procedures, or whenever there is a risk of pathogen transfer.
– Between procedures on the same patient when there is a risk of cross-infection between different anatomical sites.
– Before and after using gloves.

Necessary materials

– Sink suitable for hand hygiene.
– Liquid soap dispenser.
– Paper towel.
– Trash bin.

Main activities

– Remove jewelry from hands and forearms, if worn.
– Turn on the tap and wet hands without touching the sink.
– Apply a sufficient amount of liquid soap to the palm.
– Lather hands by rubbing them together with the soap.
– Lather the back of each hand with the opposite palm.
– Lather between fingers.
– Rub back of fingers back and forth against the opposite palms.
– Rub each thumb clasped in opposite hand in a circular motion.
– Rub tips of fingers and nails in opposite palm in a circular motion.
– Rub each wrist with opposite hand in a circular motion.
– Rinse hands thoroughly to remove soap residue.
– Avoid direct hand contact with the faucet. Use a paper towel to turn it off.
– If the tap needs to be reopened, use a paper towel to do so.
– Dry hands with a paper towel, starting from the hands and moving to the wrists.
– Discard the paper towel in a trash bin for general waste.

Observations

Use liquid soap and water when:

– Hands are visibly dirty, stained with blood or other body fluids, and after using the bathroom.
– When exposure to spore-forming pathogens is suspected or confirmed, including *C. difficile* outbreaks.
– In situations where alcohol-based hand sanitizer is unavailable.

The use of gloves does not replace hand hygiene. The hand-washing procedure must be performed both before and after glove use.

References

– Brazil. Ministério da Saúde. Protocolo para prática de higiene das mãos em serviços de saúde [Internet]. Elaborado pela Equipe técnica da ANVISA. Brasília, 2013. Available from: www.gov.br. Accessed on May 21 2021.

– Stacciarini TSG. Procedimentos Operacionais Padrão em Enfermagem. Uberaba: Universidade Federal do Triângulo Mineiro; 2011.

– Brazil. Ministério do Trabalho e Emprego. Portaria n° 485 de 11 de novembro de 2005. Norma Regulamentadora nº 32 (NR32): Segurança e Saúde no Trabalho em Estabelecimentos de Saúde. Available from: www.gov.br. Accessed on May 21 2021.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified)

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 2 – Date: __/__/__ – Revision: __/__/__

Procedure

Hand rubbing with 70% alcohol gel.

Person(s) responsible

All staff members.

Objective

– Remove transient skin flora, ensuring safe health care delivery for all patients.

Necessary materials

– 70% alcohol-based hand rub (ABHR) dispenser.

– A bottle of 70% alcohol (INPM).

Indications for hand rubbing

– Before touching a patient.

– Before an aseptic procedure.

– After body fluid exposure risk.

– After touching a patient.

– After touching a patient's surroundings.

Main activities

– Remove jewelry from wrists and forearms, if worn.

– Apply enough ABHR to cover all hand surfaces.

– Rub hands palm to palm.

– Rub back of each hand with palm of other hand with fingers interlaced.

– Rub palm to palm with fingers interlaced.

– Rub back of fingers with opposing palms with fingers interlocked.

– Rub each thumb clasped in opposite hand in a circular motion.

– Rub tips of fingers and nails in opposite palm in a circular motion.

– Rub each wrist with opposite hand in a circular motion.

– Rub until hands feel dry. Do not use paper towels.

Observations

– Hand rubbing should last 20 to 30 seconds for maximum effectiveness.

– Hand rubbing with 70% alcohol gel or ABHR may replace hand hygiene with soap and water when hands are not visibly dirty, when the procedure has a low risk of infection, and in emergency situations or when physical infrastructure is limited.

– All 70% alcohol containers must be labeled with the date of opening and expiration date according to the manufacturer.

References

– Brazil. Ministério da Saúde. Protocolo para prática de higiene das mãos em serviços de saúde. Elaborado pela Equipe técnica da ANVISA. Brasília, 2013. Available from: www.gov.br. Accessed on May 21 2021.

– Brazil. Ministério do Trabalho e Emprego. Portaria n° 485 de 11 de novembro de 2005. Norma Regulamentadora nº 32 (NR32): Segurança e Saúde no Trabalho em Estabelecimentos de Saúde. Available from: www.gov.br. Accessed on May 21 2021.
– Brazilian National Health Surveillance Agency – Anvisa. Medidas de Prevenção de Infecção Relacionada à Assistência à Saúde/Agência Nacional de Vigilância Sanitária – Brasília: Anvisa, 2017. Available from: www.gov.br. Accessed on May 21 2021.
– Higienização das Mãos em Serviços de Saúde (inclui preparação alcoólica). Portal Anvisa, 2017. Available from: www.portal.avisa.gov.br. Accessed on May 21 2021.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 3 – Date: __/__/__ – Revision: __/__/__

Procedure

Use of Personal Protective Equipment (PPE).

Person(s) responsible

Administrative assistant, general services assistant, receptionist, nurse, and physician.

Objective

– Ensure that all staff are adequately protected from workplace-related environmental and occupational hazards in situations where it is not possible to completely eliminate or reduce exposure.

Necessary materials

– Gown: protects clothing and skin.
– Cap: prevents hair and scalp exposure to organic matter and chemicals; also limits shedding into the environment.
– Surgical mask: protects the oronasal mucosa and prevents respiratory secretion contamination of the environment.
– Disposable or long-cuff gloves: protect skin from biological and chemical exposure. Long cuffs are required when forearm exposure is expected.
– Safety goggles: protect the ocular mucosa. Must be made of acrylic material that does not impair vision, fits well to the face, and provides lateral protection. Its use is recommended during mechanical cleaning of instruments and materials (disinfection).
– Closed-toe shoes: protect the skin in environments with moisture or significant amounts of infectious material (eg, operating rooms, waste disposal areas, sterilization centers, autopsy areas, and during environmental cleaning).

Training and education

Frequency:

– Every 6 months or when regulatory updates occur regarding PPE use.

The employer must:

– Train and educate staff in cleaning and disinfecting environments and instruments.
– Train and educate staff on appropriate PPE use based on needs and tasks.
– Promote employee awareness of the occupational risks to which they are exposed daily through accessible theoretical and practical training.

The employee must:

– Follow all training and instructions.

Responsibilities

Employer

– Provide employees only with PPE approved by the Ministry of Labor (PPE with Certificate of Approval).

– Instruct and train employees on the adequate use, storage, and maintenance of PPE.
– Maintain a sufficient stock of PPE to meet demand.
– Immediately replace PPE when damaged or missing.
– Provide and enforce the mandatory use of PPE during work activities.

Employees

– Use PPE only for its intended purpose.
– Take responsibility for the care, storage, and cleaning of their PPE.
– Notify the Technical Supervisor if the PPE becomes damaged or unsafe for use.
– Comply with all employer instructions on adequate PPE use.

References

– NR 6 - Equipamentos de proteção individual. Available from: www.gov.br. Accessed on October 2022.
– Oliveira AC. Infecções Hospitalares: epidemiologia, prevenção e controle. 1st ed. Rio de Janeiro: Guanabara Koogan; 2005. p.70-5.
– Posso MBS. Semiologia e Semiotécnica de Enfermagem. 2nd ed. São Paulo: Atheneu; 2005. p. 18-28.

Actions in case of noncompliance

– Report to the clinic's Technical Supervisor in case of inadequate use, damage, or need for replacement of PPE.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Technical Supervisor (Physician).

SOP No. 4 – Date: __/__/__ – Revision: __/__/__

Procedure

Labeling of disposable dispensing bottles.

Person(s) responsible

Administrative assistant and nurse.

Objective

– Prevent contamination of fractionated solutions and ensure safe, harm-free care.

Necessary materials

– Alcohol dispensers.
– Labels for filling/expiration dates.
– Ballpoint pen.

Main activities

– Wash hands.
– Gather the alcohol dispensers to be used.
– Upon opening or refilling disposable dispensers:
– Label the dispenser with the substance name (70% alcohol) and the filling/opening date, using a ballpoint pen.
– The expiration period is 7 (seven) days from the date of filling or opening.
– Inspect all dispensers every Monday, checking expiration dates.
– If dispensers are expired and disposable, they must be discarded.

Special measures

– At the start of each workday, check all dispensers.
– The expiration period is 7 (seven) days from the date of filling or opening.

Actions in case of noncompliance

– If noncompliance is identified, immediately notify the clinic's Technical Supervisor.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Technical Supervisor (Physician).

SOP No. 5 – Date: __/__/__ – Revision: __/__/__

Procedure

Spirometry.

Person(s) responsible

Nurse and physician.

Definition

Spirometry, also known as pulmonary function test or ventilatory function test, is a diagnostic test used to assess the volume and speed of airflow that a person can inhale and exhale using a spirometer.

Objective

– Spirometry is used to diagnose or monitor the progression of pulmonary diseases and evaluate the patient's lung capacity, indicating whether their air intake is sufficient to meet their physiological needs.

Necessary materials

– 70% ethyl alcohol (INPM).
– PPE (disposable gown, N95 mask, gloves).
– Disposable mouthpiece.
– Disposable pulmonary function filter.
– Paper towel.
– Bronchodilator (per medical prescription).
– Calibrated scale.
– Sphygmomanometer and stethoscope.
– Computer with spirometry software.
– Spirometer.
– Blue pen.
– Letterhead A4 paper.
– Printer.

Procedure description

1. Call the patient, confirm their name, and introduce and explain the procedure.
2. Check medical prescription.
3. Confirm that pretest instructions were followed.
4. Prepare and calibrate the spirometer (computer) and check parameters against technical standards (Brazilian Society of Pulmonology and Phthisiology).
5. Take anthropometric measurements.
6. Perform hand hygiene (per SOP No. 1).
7. Don gloves, disposable gown, and N95 mask.
8. Prepare and instruct the patient.
9. Have the patient sit for 5-10 minutes, then breathe into the mouthpiece attached to the spirometer.
10. Instruct the patient to breathe calmly for a short period.
11. Instruct the patient to breath in completely and exhale as forcefully and quickly as possible, then repeat the maneuver 3 times.
12. Administer the prescribed bronchodilator inhaler and have the patient wait 15 minutes at rest.
13. Repeat the spirometry test.
14. Deliver test results to the patient.
15. Dispose of used materials in the appropriate trash cans; reusable items should be sent for decontamination with enzymatic detergent.
16. Doff gloves and wash hands (per SOP No. 1)
17. Document the nursing notes and make a record of the procedure.
18. Keep the workspace clean and organized.

Observations

– The patient should rest for 5 to 10 minutes before the test.
– Fasting is not required.
– The patient must not drink tea or coffee during the 6 hours before the test.
– The patient must not drink alcohol during the 4 hours before the test.
– The patient must suspend use of short-acting (eg, salbutamol) and long-acting (eg, tiotropium) bronchodilators for 4 hours and 10 hours before the test, respectively.
– The patient must not smoke for at least 2 hours before the test.
– The patient should refrain from eating a large meal at least 1 hour before the test.

References

- Conselho Federal de Enfermagem. Resolução n° 545/2017. Anotação de Enfermagem e Mudança nas Siglas das Categorias Profissionais. Available from: http://www.cofen.gov.br/wp-content/uploads/2017/05/Resolu%C3%A7%C3%A3o-545-17.pdf. Accessed on Oct 5 2020.
- Conselho Federal de Enfermagem. Resolução n° 429/2012. Dispõe Sobre o Registro das Ações Profissionais no Prontuário do Paciente, e em Outros Documentos Próprios da Enfermagem, Independente do Meio de Suporte - Tradicional ou Eletrônico. Available from: https://www.legisweb.com.br/legislacao/?id=242097. Accessed on Oct 5 2020.
- Jardim JRB, Romaldini H, Ratto OR. Proposta para Unificação dos Termos e Símbolos Pneumológicos no Brasil. J Pneumol. 1983;9:45-51.
- Sociedade Brasileira de Pneumologia e Tisiologia. Espirômetros: Requisitos. J Pneumol. 1996;25:1-9.
- Pereira CAC, Neder JÁ, Sociedade de Pneumologia e Tisiologia (SBPT). Diretrizes para Testes de Função Pulmonar. J Pneumol. 2002;28(3): S1-S238.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 6 – Date: __/__/__ – Revision: __/__/__

Procedure

Cleaning of office cabinets.

Person(s) responsible

General services assistant.

Objective

- Standardize the cleaning procedure for office cabinets, in order to prevent dirt accumulation and the proliferation of microorganisms.

Necessary materials

- PPE (gloves, mask, safety goggles, gown, neutral soap).
- Water.
- Quaternary ammonium solution.
- Procedure gloves.
- Bucket.
- 70% ethyl alcohol (INPM).
- Clean cloth.

Procedure description

- Wash hands.
- Don procedure gloves.
- Gather all required materials.
- Remove all items from inside the cabinet before starting.
- Wipe the cabinets with a damp cloth beforehand to make cleaning with water and neutral soap easier.
- Scrub the entire cabinet with a cloth soaked in quaternary ammonium solution.
- Use a clean cloth to remove excess disinfectant.
- Dry the entire cabinet with a clean cloth.
- Scrub the entire cabinet with 70% alcohol.
- Allow to air dry.
- Dispose of used cleaning cloths appropriately.
- Return items to the cabinet in an organized manner after drying.
- Doff gloves.
- Wash hands.
- Complete the cleaning log for record keeping.

Special measures

- Cleaning should be conducted once a week, or whenever necessary.
- All items must be removed from inside the cabinet before cleaning and only returned after completion.

Actions in case of noncompliance

- If the cleaning log is nearly full, notify the clinic's secretary to request more copies.
- For other instances of noncompliance, notify the clinic's Technical Supervisor so appropriate action can be taken.

References

– Brazil. Agência Nacional de Vigilância Sanitária. Segurança do paciente em serviços de saúde: limpeza e desinfecção de superfícies/Agência Nacional de Vigilância Sanitária. Brasília: Anvisa, 2010. Available from: www.gov.br. Accessed on May 21 2021.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Technical Supervisor (Physician).

SOP No. 7 – Date: __/__/__ – Revision: __/__/__

Procedure

Cleaning of office counters, armchairs, and chairs.

Person(s) responsible

Receptionist, assistant, and general services assistant.

Objective

– Standardize the cleaning procedure for office counters, armchairs, and chairs, in order to prevent the proliferation of microorganisms.

Necessary materials

– Water.
– Liquid soap.
– Procedure gloves.
– Bucket.
– 70% ethyl alcohol (INPM).
– Disposable cleaning cloth.

Main activities

– Wash hands.
– Don procedure gloves.
– Gather all required materials.
– Remove all items from the counters before starting.
– Wipe down counters with a damp cloth to make cleaning easier.
– Rub all counters with a cloth dampened with liquid soap.
– Use a clean cloth to remove soap residue.
– Dry all counters with a clean cloth.
– Rub all counters with 70% alcohol in a unidirectional manner.
– Allow to air dry.
– Rub armchairs and chairs with 70% alcohol.
– Allow to air dry.
– Dispose of used cleaning cloths appropriately.
– Doff gloves.
– Wash hands.
– Complete the cleaning log for record keeping.

Special measures

– Cleaning should be performed at the end of each day, or whenever necessary.
– All items must be removed from the counters before cleaning and only returned after completion.

Actions in case of noncompliance

– Notify the clinic's Technical Supervisor.

References

– Brazil. Agência Nacional de Vigilância Sanitária. Segurança do paciente em serviços de saúde: limpeza e desinfecção de superfícies. Brasília: Anvisa, 2012.
– Fernandes AT. Infecção hospitalar e suas interfaces na área da saúde. São Paulo: Atheneu; 2000.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Technical Supervisor (Physician).

SOP No. 8 – Date: __/__/__ – Revision: __/__/__

Procedure

Cleaning of office windows, doors, and light switches.

Person(s) responsible

General services assistant.

Objective

– Standardize the cleaning procedure for office windows, doors, and light switches, in order to prevent the proliferation of microorganisms.

Necessary materials

– Water.
– Neutral soap.
– Dedicated cleaning sponge.
– Two buckets.
– PPE (gloves, safety goggles, closed-toe shoes).
– Cleaning cloth.
– Quaternary ammonium solution.

Main activities

– Wash hands.
– Don PPE.
– Gather all required materials.
– Prepare the environment by moving furniture and equipment away from windows and walls.
– Fill both buckets halfway – one with clean water and the other with water and soap.
– Dampen a cloth with clean water, wring it out, and remove dust from surfaces using top-to-bottom and left-to-right motions.
– Dampen another cloth with soapy water, wring it, and clean glass surfaces, window and door frames, windowsills, and doorknobs.
– Use a third cloth dampened with clean water to remove any quaternary ammonium solution residue from windows and doors.
– Check if windows and doors are clean; if needed, repeat the process.
– Always dry windows and doors using a dry cleaning cloth.
– Remove any cloth placed beneath doors and windows.
– Return all furniture and equipment to their original positions.
– Clean all materials used and store them appropriately.

Special measures

– Cleaning should be conducted once a day, preferably at the end of the workday, or whenever necessary.
– All items must be moved before cleaning and only returned to their original place after completion.

Actions in case of noncompliance

– In case of noncompliance, notify the clinic's Technical Supervisor so appropriate action can be taken.

References

– Brazil. Agência Nacional de Vigilância Sanitária. Segurança do paciente em serviços de saúde: limpeza e desinfecção de superfícies. Brasília: Anvisa, 2012. Available from: www.gov.br. Accessed on May 21 2021.
– Fernandes AT. Infecção hospitalar e suas interfaces na área da saúde. 1st ed. São Paulo: Atheneu; 2000. 1706-21.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Technical Supervisor (Physician).

SOP No. 9 – Date: __/__/__ Revision: __/__/__

Procedure

Disinfection of the anthropometric scale.

Person(s) responsible

Receptionist, assistant, and general services assistant.

Objective

– Disinfect anthropometric scales to help prevent the spread of disease.

Necessary materials

– PPE (gloves, cap, safety goggles, and safety mask).
– 70% alcohol.
– Cleaning cloth.

Main activities

– Perform hand hygiene.
– Don listed PPE.
– Wipe the entire surface of the scale using a cloth soaked in 70% alcohol, using unidirectional movements.
– Allow to air dry.

Observations

– Disinfection of the anthropometric scale should be performed daily, or whenever necessary.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Technical Supervisor (Physician).

SOP No. 10 – Date: __/__/__ – Revision: __/__/__

Procedure

Cleaning of office floors.

Person(s) responsible

Receptionist, assistant, and general services assistant.

Objective

– Standardize the cleaning procedure for office floors in order to prevent the proliferation of microorganisms.

Necessary materials

– Water.
– Neutral soap.
– Quaternary ammonium solution.
– Broom.
– Squeegee.
– Bucket.
– PPE (gloves, safety goggles, closed-toe shoes).
– Cleaning cloth.

Main activities

– Wash hands.
– Don PPE.
– Gather all required materials.
– Wash ceramic floors with water and neutral soap, using a broom to scrub the entire floor.
– Remove excess water and soap using a squeegee and damp cloth.
– Dry the floor using a clean cloth.
– Afterwards, use a cloth dampened with quaternary ammonium solution to clean the entire floor again to remove remaining dirt.
– Dry the floor using a dry cloth.
– Rinse the cloth in a bucket with clean water and reapply quaternary ammonium solution.

Special measures

– Cleaning should be performed once a day, preferably at the end of the workday, or whenever necessary.
– All items must be removed before cleaning and only returned after completion.

Actions in case of noncompliance

– In case of noncompliance, notify the clinic's Technical Supervisor so appropriate action can be taken.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Technical Supervisor (Physician).

SOP No. 11 – Date: __/__/__ – Revision: __/__/__

Procedure

Cleaning of waste bins.

Person(s) responsible

Receptionist, assistant, and general services assistant.

Objective

– Standardize the cleaning procedure for waste bins in order to prevent the proliferation of microorganisms and maintain a safe work environment.

Necessary materials

– Water.
– Neutral soap.
– Cleaning sponge.
– PPE (gloves, safety goggles, gown, cap, and mask).
– Cleaning cloth.
– Quaternary ammonium solution.

Main activities

General waste bin

– Wash hands.
– Don PPE.
– Gather all required materials
– Begin cleaning with neutral soap, rubbing in a back-and-forth motion until the entire surface is clean.
– Rinse with water to remove all soap residue from the bin's surface.
– Disinfect the entire surface using quaternary ammonium solution, then wipe off the solution with a damp cloth.
– Rinse with a dry cloth and, once completely dry, insert a waste bag labeled for general waste.

Biohazard waste bin

– Wash hands.
– Don PPE.
– Gather all required materials.
– Pour quaternary ammonium solution into the interior of the bin and let it sit for 10 minutes.
– Begin cleaning with neutral soap, rubbing in a back-and-forth motion until the entire surface is clean.
– Rinse with water to remove all soap residue from the bin's surface.
– Disinfect the entire surface using quaternary ammonium solution, then wipe off the solution with a damp cloth.
– Rinse with a clean cloth and, once the bin is completely dry, insert a waste bag labeled for biological waste.

Special measures

– Cleaning should be conducted once a week, or whenever necessary.
– Waste must be removed before cleaning the bins.

Actions in case of noncompliance

– In case of noncompliance, notify the clinic's Technical Supervisor so appropriate action can be taken.

References

– Brazil. Agência Nacional de Vigilância Sanitária. Segurança do paciente em serviços de saúde: limpeza e desinfecção de superfícies. Brasília: Anvisa, 2012. Available from: www.gov.br. Accessed on May 21 2020.
– Fernandes AT. Infecção hospitalar e suas interfaces na área da saúde. 1st ed. São Paulo: Atheneu; 2000. p. 1706-21.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Technical Supervisor (Physician).

SOP No. 12 – Date: __/__/__ – Revision: __/__/__

Procedure

Cleaning of the refrigerator and cold box.

Person(s) responsible

Receptionist.

Objective

– Standardize the cleaning procedure for the refrigerator and cold box, in order to prevent microbial proliferation and avoid potential contamination of biologics.

Necessary materials

– PPE (gloves, safety goggles, and mask).
– Neutral soap.
– 70% alcohol.
– Disposable cleaning cloth.
– Neutral detergent.
– Water.

Main activities

– Perform hand hygiene.
– Don listed PPE.

Internal cleaning of the refrigerator

– Turn off the equipment and unplug it.
– Remove gel packs and biologics from the refrigerator and place them in a cold box (as outlined in the specific SOP) until cleaning is complete.
– Carefully remove each drawer and place them in a clean, dry area.
– Use a dry, clean cloth only. No cleaning products should be used inside the refrigerator, as per the manufacturer's recommendations.
– Begin cleaning from the top to the bottom, using slow movements.
– Once complete, return the drawers, plug the refrigerator back in, and wait 30 minutes before returning the contents.
– Perform internal cleaning every 3 months, or whenever necessary.

External cleaning of the refrigerator

– Turn off the equipment and unplug it.
– Use a solution of water and neutral detergent only (do not use solvents or chemical products).
– Wipe down the exterior with a soft cloth dampened with the detergent solution, followed by a dry cloth to remove moisture.
– Remove drawers and shelves and clean them in the same manner.
– External cleaning should be performed every 3 months, or whenever necessary.

Refrigerator disinfection

– Switch off the main circuit and unplug the refrigerator.
– Follow the standard cleaning procedure as described above.
– Wipe all internal and external surfaces with a soft cloth dampened with 70% alcohol.
– Disinfection should be performed every 3 months, or whenever a spill of contaminated material occurs.

Cleaning the cold box

– Clean the cold box with neutral detergent.
– Rub the entire internal surface and remove detergent residue with a damp cloth, then dry using a clean disposable cloth.
– Always clean before and after each use.

Observations

– The refrigerator must be used exclusively for storing vaccines. It is strictly prohibited to store food, beverages, or any materials other than biologics.
– Vaccine vials and ampoules should preferably be placed in vial trays on shelves to allow for adequate cold air circulation.
– Store vaccines in their original packaging, leaving two-finger spacing between them and maintaining distance from the refrigerator wall to ensure airflow.
– Vaccines nearing expiration should be placed at the front to be used first.
– If a power failure occurs, take the necessary measures as quickly as possible to restore normal operation:
– Check the temperature immediately.
– If necessary, place biologics and gel packs in a cold box at +2 °C to +8 °C.
– Determine how long the refrigerator was off.
– If changes in temperature are found or vaccine integrity is compromised, segregate the affected vaccines and contact the regional health authority for guidance.
– In all the situations described above, notify the clinic's Technical Supervisor for adequate action.

Note

Refrigerator maintenance is performed every 3 months by a third-party service provider.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 13 – Date: __/__/__ Revision: __/__/__

Procedure

Disinfection of shared toys.

Person(s) responsible

Receptionist, assistant, general services assistant.

Objective

– Disinfect shared toys to help prevent the spread of microorganisms.

Necessary materials

– PPE (gloves).
– Paper towel.
– 70% ethyl alcohol.
– Hair cap.
– Water and neutral soap.

Main activities

– Wash hands.
– Don listed PPE.
– If toys are visibly dirty, wash them with water and neutral soap.
– Soak a paper towel in 70% alcohol and rub the entire surface of each toy, repeating the motion 3 times over the entire area.
– Allow toys to air dry naturally.

Observations

– Toy disinfection should be performed at the end of each day, or whenever necessary.
– If the toy is visibly dirty, clean thoroughly with water and neutral soap, using a soft-bristle brush to scrub all surfaces.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 14 – Date: __/__/__ Revision: __/__/__

Procedure

Cleaning and disinfecting the peak flow meter.

Person(s) responsible

Receptionist or assistant.

Objective

– Standardize the procedure for cleaning and disinfecting peak flow meters used in clinical examinations.

Necessary materials

– PPE (cap, mask, safety goggles, gloves, and gown).
– Diluted enzymatic detergent solution (per SOP No. 5).
– Cleaning brushes.
– Clean disposable cloth.
– Immersion container.
– 70% alcohol.

Main activities

– Wash hands.
– Don listed PPE.
– Collect the used peak flow meters from the examination rooms.

- Immerse the devices in the enzymatic detergent solution for 5 minutes, as per the manufacturer's recommendations.
- After soaking, manually clean the peak flow meters by brushing the lumen and the internal and external surfaces 3 times with a cleaning brush.
- Afterwards, rinse thoroughly under running water until all enzymatic detergent and visible dirt are removed.
- Use a clean cloth to assist with drying.
- Check if the peak flow meters are functioning and fully clean using a magnifying glass.
- Wipe the entire internal and external surfaces with a disposable cloth soaked in alcohol and allow to air dry naturally.
- After disinfection, place the cleaned peak flow meters in a labeled container with a lid marked "Clean material" and return them to the appropriate rooms.
- It is recommended to clean all peak flow meters once a week, even if they have not been used.

Special measures

- Used peak flow meters should be stored in lidded containers and collected twice daily (at 12:00 PM and 4:00 PM) for cleaning and disinfection.
- Before using in a patient, the physician should disinfect the cleaned device again with 70% ethyl alcohol across all surfaces.
- After use, the physician must place the peak flow meter into a transparent, lidded container labeled "Contaminated material."

Actions in case of noncompliance

- In case of noncompliance, immediately notify the clinic's Technical Supervisor.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 15 – Date: __/__/__ Revision: __/__/__

Procedure

Cleaning of air conditioning units.

Person(s) responsible

General services assistant.

Objective

- Ensure compliance with occupational safety standards.
- Maintain the workspace clean and well-organized.

Necessary materials

- PPE (rubber gloves).
- Bucket with clean water.
- Bucket with water and neutral detergent.
- Clean cloths.
- Ladder.

Main activities

- Wash hands.
- Don listed PPE.
- Gather all required materials.
- Fully turn off the air conditioning unit and unplug it, if applicable.
- Remove the air filter. If the filter is torn or damaged, it must be replaced by the contracted maintenance company.
- Clean the air filter in the cleaning supply storage room by immersing it in water with detergent and performing manual cleaning, according to the manufacturer's recommendations (person responsible: contracted maintenance company).
- Clean the plastic front panel and visible external surfaces using a soft cloth lightly dampened with detergent solution (person responsible: general services assistant).

Special measures

- Cleaning should be performed once every 2 months, or whenever necessary.
- Never apply detergent, alcohol, or water directly onto the plastic front panel of the unit.
- Wait for the air filter to be completely dry before reinserting it into the unit.

– Do not plug the unit back in with wet or damp hands.
– This procedure does not replace preventive maintenance, which must be performed strictly according to the manufacturer's recommendations.

Actions in case of noncompliance

– In case of noncompliance, notify the clinic's Technical Supervisor so appropriate action can be taken.

For example:

Air conditioning company _____

Address: _____

Phone: _____

E-mail: _____

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 16 – Date: __/__/__ Revision: __/__/__

Procedure

Cleaning and disinfecting otoscope specula.

Person(s) responsible

Physician, receptionist, and assistant.

Objective

– Standardize the procedure for cleaning and disinfecting otoscope specula used in clinical examinations.

Necessary materials

– PPE (cap, mask, safety goggles, gloves, and gown).
– Prime Clear Spray.
– Clean disposable cloth.
– Immersion container.
– Enzymatic detergent.
– 70% ethyl alcohol (INPM).
– Small brush suitable for internal cleaning of the specula.

Main activities

Physician

– Wash hands before and after the procedure.
– Don gloves.
– Spray Prime Clear on otoscope specula immediately after use and place them into the designated container.

Receptionist and assistant

– Wash hands.
– Don listed PPE.
– Collect used otoscope specula from the examination rooms.
– Immerse the specula in the enzymatic detergent solution for 5 minutes, according to the manufacturer's recommendations.
– After soaking, manually clean the specula by brushing the lumen and the internal and external surfaces 3 times with a cleaning brush.
– Afterwards, rinse thoroughly under running water until all enzymatic detergent and visible dirt are removed.
– Use a clean cloth to assist with drying.
– Check if the specula are functioning and fully clean.
– Wipe the entire internal and external surfaces with a disposable cloth soaked in alcohol and allow to air dry.
– After disinfection, place the cleaned specula in a labeled container with a lid marked "Clean material" and return them to the appropriate medical rooms.
– Specula should be cleaned once a week, even if they have not been used.

Special measures

– Used specula should be sprayed with Prime Clear immediately after use to prevent biofilm formation.
– Avoid prolonged skin contact with Prime Clear. Always wash and dry hands after use.

– Before using a clean speculum on a patient, the physician should disinfect it again with 70% ethyl alcohol over the entire surface.

Actions in case of noncompliance

– In case of noncompliance, immediately notify the clinic's Technical Supervisor.

References

– Brazil. Agência Nacional de Vigilância Sanitária. Segurança do paciente em serviços de saúde: limpeza e desinfecção de superfícies. Brasília: Anvisa, 2012. Available from: www.gov.br. Accessed on May 21 2021.
– Fernandes AT. Infecção hospitalar e suas interfaces na área da saúde. 1st ed. São Paulo: Atheneu; 2000. p.1706-21.
– Ficha Técnica do PRIME CLEAR. Solução pré-limpeza. Produto cadastrado na ANVISA: Processo: 25351.542696/2014-00. Empresa Indalabor Indaiá Laboratório Farmacêutico Ltda. Available from: www.indalabor.com.br. Accessed on May 23 2021.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 17 – Date: __/__/__ Revision: __/__/__

Procedure

Cleaning and disinfecting nasal specula.

Person(s) responsible

Receptionist and assistant.

Objective

– Standardize the procedure for cleaning and disinfecting nasal specula used during clinical examinations.

Necessary materials

– PPE (cap, mask, safety goggles, gloves, and gown).
– Nasal speculum.
– Prime Clear Spray.
– Cleaning brushes.
– Enzymatic detergent.
– Clean disposable cloth.
– 70% ethyl alcohol.
– Immersion container.

Main activities

Physician

– Wash hands before and after the procedure.
– Don gloves.
– Spray Prime Clear on the nasal speculum immediately after use and place it into the designated container.

Receptionist and assistant

– Wash hands.
– Don listed PPE.
– Collect used nasal specula from the examination rooms.
– Immerse the specula in the enzymatic detergent solution for 5 minutes, according to the manufacturer's recommendations.
– After soaking, manually clean the specula by brushing the handle and internal and external surfaces 3 times with a cleaning brush.
– Afterwards, rinse thoroughly under running water until all enzymatic detergent and visible dirt are removed.
– Use a clean cloth to assist with drying.
– Check if the specula are functioning and fully clean.
– Wipe the entire internal and external surfaces and the handle with a disposable cloth soaked in alcohol and allow to air dry.
– After disinfection, place the cleaned specula in a labeled container with a lid marked "Clean material" and return them to the appropriate medical offices.
– Specula should be cleaned once a week, even if they have not been used.

Actions in case of noncompliance

– In case of noncompliance, immediately notify the clinic's Technical Supervisor.

References

– Brazil. Agência Nacional de Vigilância Sanitária. Segurança do paciente em serviços de saúde: limpeza e desinfecção de superfícies. Brasília: Anvisa, 2012. Available from: www.gov.br. Accessed on May 21 2021.
– Fernandes AT. Infecção hospitalar e suas interfaces na área da saúde. 1st ed. São Paulo: Atheneu; 2000. p.70-75.
– Ficha Técnica do Prime Clear. Solução pré-limpeza. Produto cadastrado na ANVISA: Processo: 25351.542696/2014-00. Empresa Indalabor Indaiá Laboratório Farmacêutico Ltda. Available from: www.indalabor.com.br. Accessed on May 23 2021.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 18 – Date: __/__/__ Revision: __/__/__

Procedure

Organize the cold box.

Person(s) responsible

Nurse and physician.

Objective

– Maintain stable temperatures between +2 °C and +8 °C, ensuring the quality of stored products.

Necessary materials

– Digital thermometer.
– Cold box.
– Gel ice packs.
– Allergen extracts and biologics.
– Disposable cups.
– PPE (disposable gloves and mask).

Main activities

– Wash hands (per SOP No. 1).
– Don listed PPE.
– Remove gel packs from the freezer and place them at the bottom of the cold box.
– Insert the thermometer, or its probe, into the cold box, depending on the type used.
– Close the lid of the cold box.
– Wait until the internal temperature reaches between +2 °C and +8 °C.
– Place allergen extracts and biologics into new disposable cups and arrange the cups on top of the gel packs.
– Check the cold box's temperature every 4 hours.
– If variations in temperature occur, remove biologics and extracts immediately.

Observations

– Ensure consistent temperature monitoring and adhere strictly to the reading schedule.
– Significant temperature variations must be reported to the clinic's Technical Supervisor for immediate corrective action.
– Avoid leaving the cold box open for extended periods to prevent fluctuations in temperature.
– The cold box should only be used in case of refrigerator temperature fluctuations or during refrigerator cleaning.
– Disinfect the cold box with 70% alcohol before and after each use.

References

– Brazil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Available from: www.gov.br. Accessed on May 21 2021.
– Brazil. Ministério da Saúde, Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Manual de rede de frio. 4th ed. Brasília: Ministério da Saúde; 2013. Available from: https://bvsms.saude.gov.br. Accessed on May 21 2021.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 19 – Date: __/__/__ – Revision: __/__/__

Procedure

Immediate-reading skin test (prick test).

Person(s) responsible

Board-certified physician (AMB- and ASBAI-certified).

Objective

– The prick test is performed to assess whether a patient has an allergic reaction to a specific substance by applying it to the skin and then puncturing it.

Necessary materials

– Tray.
– Allergen extracts.
– Sharps disposal container.
– Disposable pointed instrument (needle, plastic or stainless steel lancet).
– Cotton ball.
– 70% alcohol.

Main activities

– Perform hand hygiene.
– Choose the appropriate application site.
– Clean the site with 70% alcohol and apply one drop of each allergen extract to be tested.
– Maintain a minimum distance of 2 cm between drops and then gently puncture the drops with a pointed instrument (needle or lancet).
– The number of extracts tested depends on the patient's clinical needs and forearm size; both forearms may be used if necessary.
– Always include one positive control and one negative control.
– After 15 to 20 minutes, read results and evaluate for the presence of wheal formation indicative of an allergic reaction.
– Document the procedure in the patient's medical record.

Special measures

– Allergens tested may include dust mites, fungi, insects, animal dander, feathers, foods, and latex.
– It is important to inform patients that antihistamines, topical corticosteroids, and other medications can suppress allergic responses, possibly leading to false-negative results. These medications should ideally be discontinued 1 week before the test.

Actions in case of noncompliance

– In case of noncompliance, immediately notify the clinic's Technical Supervisor.

References

– Heinzerling LM, Burbach GJ, Edenharter G, Bachert C, Bindslev-Jensen C, Bonini S, et al. GA(2)LEN skin test study I: GA(2)LEN harmonization of skin prick testing: novel sensitization patterns for inhalant allergens in Europe. Allergy. 2009;64(10):1498-506.
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– Dreborg S. The skin prick test in the diagnosis of atopic allergy. J Am Acad Dermatol. 1989,21(4 Pt 2):820-1.
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Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 20 – Date: __/__/__ – Revision: __/__/__

Procedure

Skin contact allergy test (patch test).

Person(s) responsible

Physician or nurse.

Objective

– The patch test is used to assess allergic responses to certain allergens (substances that may trigger allergies). The test aims to reproduce a mild allergic reaction by deliberately exposing the patient to a minimal amount of allergens.

Necessary materials

– Hypoallergenic tape.
– Pen.
– Paper filter or plastic chambers.
– Allergen extracts.
– Cotton balls.
– Alcohol-ether solution.

Main activities

– Perform hand hygiene.
– Cut a 30-cm strip of hypoallergenic tape – enough to accommodate the 30 allergens to be tested.
– Number each allergen to be tested.
– Attach paper filters opposite each number on the strip.
– Once the patch test is prepared, apply one drop of each allergen onto its respective paper filter.
– Choose the application site (external side of the arm or upper back).
– Clean the site with alcohol-ether solution and let it air dry.
– Afterwards, apply the patch, ensuring full contact between the paper panel and the skin.
– The patch test must remain in place for 48 to 72 hours before the reading.
– Provide the patient with all test instructions.
– The number of allergens tested varies according to each case.
– Document the procedure in the patient's medical record before and after reading the results.

On the day of reading

– After 48 to 72 hours, instruct the patient to remove the patch test and place it in a plastic bag without folding it, to be returned to the physician.
– After removal, the patient should expose the tested area to sunlight for 15 minutes (back or outer arm).

Special measures

– The patient must not wet the patch test area during the test.
– Shortly before returning to the clinic, the patient should remove the patch test and expose the tested area to sunlight for 15 minutes. If sunlight is not available, instruct the patient to stand 10 cm from a television screen for the same amount of time.
– Instruct the patient not to wash the test site until the physician has completed the reading.
– If the patient experiences intense itching, they must inform the physician. If the discomfort is tolerable, they may wait until the scheduled consultation; otherwise, contact the clinic for guidance.
– It is important to inform patients that antihistamines, topical corticosteroids, and other medications can suppress allergic responses, possibly leading to false-negative results.

Actions in case of noncompliance

– In case of noncompliance, immediately notify the clinic's Technical Supervisor.

References

– Nettina SM. Brunner: prática de enfermagem. Vol. II. 7th ed. Rio de Janeiro: Guanabara Koogan; 2003.
– Smeltzer SC, Bare BG. Brunner & Suddarth: tratado de enfermagem médico-cirúrgica. Vol. III. 9th ed. Rio de Janeiro: Guanabara Koogan; 2002.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 21 – Date: __/__/__ – Revision: __/__/__

Procedure

Monitoring of refrigerator temperature.

Person(s) responsible

Receptionist and nurse.

Objective

– Maintain a stable temperature and ensure the quality and safety of stored products.

Necessary materials

– Digital refrigerator thermometer.
– Temperature monitoring spreadsheet (USB/digital format).

Main activities

– Review the temperature monitoring spreadsheet monthly.
– Check and record the refrigerator's temperature daily at 8:00 AM and 5:00 PM.
– Avoid keeping the refrigerator door open for extended or unnecessary periods.
– Maintain an internal temperature between +2 °C and +8 °C.

Observations

– **Significant temperature fluctuations must be reported to the clinic's Technical Supervisor for immediate corrective action.**
– Avoid leaving the refrigerator open for extended periods to avoid fluctuations in temperature.
– The refrigerator is equipped with an audible alarm that activates during temperature fluctuations. It also sends automatic alerts to the Clinic Administrator.
– The refrigerator has internal backup batteries with extended autonomy in case of power outages. In such situations, avoid opening the refrigerator and keep a cold box prepared with gel packs and a digital thermometer (+2 °C to +8 °C) for emergency use if needed.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 22 – Date: __/__/__ – Revision: __/__/__

Procedure

Preventive and corrective maintenance of the refrigerator and automated external defibrillator (AED).

Person(s) responsible

Nurse, clinic administrator, and/or physician.

Objectives

– Ensure adequate functioning of critical clinic equipment (refrigerator and AED).
– Establish a maintenance schedule in partnership with equipment suppliers (attached).
– Maintain direct communication channels with the maintenance team for immediate support.

Necessary materials

– Maintenance service agreement.
– Maintenance scheduling calendar.
– Communication channels with maintenance teams (email, phone, messaging apps).
– Maintenance checklist.

Main activities

– Conduct scheduled preventive maintenance and corrective maintenance as needed.
– Contact the service provider for corrective maintenance if any functional issues arise.
– Complete the maintenance checklist.

Procedure description

– Welcome the technician upon arrival.
– Check if the visit is aligned with the scheduled date.
– Accompany the technician during the procedure.
– Request that the technician completes the maintenance form.
– Request preventive and/or corrective maintenance, including repairs or replacement of parts if necessary, ensuring prior quotation of both service and materials is provided.
– Request that the technician affix a maintenance label to the equipment (including the date of service, the technician's name, and the next scheduled maintenance date) and provide the invoice for the service performed.

References

– Brazil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância das Doenças Transmissíveis. Manual de Rede de Frio do Programa Nacional de Imunizações / Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Vigilância das Doenças Transmissíveis. 5th ed. Brasília: Ministério da Saúde, 2017. Available from: www.gov.br. Accessed on May 21 2021.

– Brazil. Agência Nacional de Vigilância Sanitária - Anvisa. Resolução RDC nº 44, de 17 de agosto de 2009. Aprova o "Regulamento técnico sobre Boas Práticas Farmacêuticas para o controle sanitário do funcionamento, da dispensação e da comercialização de produtos e da prestação de serviços farmacêuticos em farmácias e drogarias e dá outras providências". Available from: www.gov.br. Accessed on May 21 2021.

Observations: examples of contact information.

1) Refrigerator manufacturer/maintenance:

_____

a) Address: _____

b) Telephone: _____

c) E-mail: _____

2) AED manufacturer/maintenance:

_____

a) Address: _____

b) Telephone: _____

c) E-mail: _____

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 23 – Date: __/__/__ – Revision: __/__/__

Procedure

Crash cart and automated external defibrillator (AED) check.

Person(s) responsible

Nurse and/or physician.

Objectives

– Organize medications, medical supplies, and the AED in the crash cart.
– Check all medications, supplies, and AED pads and properly discard any expired items.
– Check AED battery status weekly.
– Ensure patient safety during urgent and emergency situations.

Necessary materials

– Crash cart.
– Medications and medical supplies.
– AED and pads.
– Crash cart checklist.
– Ballpoint pen.

Main activities

– Organize medications, medical supplies, and the AED in the crash cart.
– Write down all medications on the checklist, including the beyond-use date and quantity.
– Highlight on the checklist any medications nearing expiration.
– Perform a full check monthly.

Procedure description

– Perform hand hygiene.
– Clean the crash cart and related equipment using nonsterile gauze soaked in 70% alcohol.
– Test laryngoscope and blades.
– Test the AED.
– Check all items against the checklist.
– Organize all supplies inside the crash cart according to clinic standards.

- Seal the crash cart after inspection.
- Label the seal with the date, time, seal number, and name of the inspector.
- Perform hand hygiene.
- Keep the workspace well-organized.
- Ensure the AED battery charger remains plugged into a power outlet, according to the manufacturer's recommendations.
- Recheck the checklist anytime the seal is broken.
- Open the crash cart and conduct a comprehensive check of the expiration dates and batch numbers of all materials and medications, either when a medication is to be used or during routine inspections.

General observations (per Resolution RDC 44/2009)

- All medications must be stored in an organized manner, according to the manufacturer's recommendations, and under conditions that maintain their identity, integrity, quality, safety, efficacy, and traceability.
- The storage area must be spacious enough to allow organized storage of different medication categories.
- The storage area must be kept clean and protected from direct sunlight, humidity, and heat to preserve the chemical, physical, and microbiological integrity of the products, ensuring their quality and safety.
- Products should be stored on shelves, in drawers, or equivalent supports, kept off the floor, walls, and ceiling to allow for proper cleaning and inspection.
- Disposal of such products must follow specific health care waste management legislation, including any applicable state or municipal regulations.
- Medications must be stored in areas with restricted access to staff. Public access to these areas is strictly prohibited.

AED observations

- The AED battery has a shelf life of five (5) years and must be kept charged.
- When the low battery indicator is triggered, the battery still holds enough charge for approximately 15 shocks or 30 minutes of monitoring.
- To replace the battery:
  1. Turn off the AED.
  2. Flip the AED upside down.
  3. Press the battery latch and remove the old battery pack.
  4. Insert the new battery until a "click" is heard.
  5. Turn the device back on and wait for the voice and display instructions until the message "Place the electrodes on the patient's chest" appears.
  6. Check the battery status on the bar graph indicator.
  7. Turn off the AED.
  8. Keep the charger connected to the AED and plugged into a power source until the AED is needed for use.

Corrective maintenance

- The AED performs routine self-checks and alerts the operator if maintenance is required by displaying a warning and emitting voice prompts, as shown in Figure 3.

Message	Required action
"Maintenance required. **Low battery**."	**Recharge** or **replace** the battery.
"Maintenance required. **Hardware failure**."	**Restart** the system. If the problem persists, **contact authorized technical support**.

Figure 3
Warning messages for maintenance of the crash cart and AED

Preventive maintenance

- The AED performs periodic self-checks, even when powered off. If the battery charge falls below 20% of its maximum capacity, the device emits an audible beep and visual warning, accompanied by voice and text prompts indicating the need for maintenance.

AED cleaning

- The AED and all its accessories must be cleaned after each use or when visibly dirty. All cleaning procedures should be performed at room temperature.
- Disconnect the battery charger from the power outlet.
- Gather the device and battery charger for cleaning.
- Use one cloth slightly dampened with neutral liquid soap and water, and another with 70% ethanol.
- Do not use abrasive agents, organic solvents, chlorine, or hydrocarbon-based products.
- Do not remove or damage the labels on the AED, accessories, or charger – they are essential for identification and safety.
- Wipe the external surface of the device and charger using the soapy cloth.
- Disinfect the same surfaces with the ethanol-soaked cloth.
- Use a dry washcloth to clean the display or, if necessary, a lightly dampened cloth to remove dust and debris.

AED testing

- Turn on the AED.
- Check the battery level on the display. If it is low, recharge immediately.
- Wait for the voice and display instructions until the message “Place the electrodes on the patient’s chest” appears.
- Turn off the AED.
- Keep the charger connected to the AED and plugged into a power source.

AED calibration

- The AED must be sent to an authorized technical service every 12 months for preventive maintenance and calibration.

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Prepared by: Registered Nurse (COREN-certified).

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Approved by: Clinic’s Technical Supervisor (Physician).

SOP No. 24 – Date: __/__/__ – Revision: __/__/__

Procedure

Inventory check of medications and disposal of expired medications.

Person(s) responsible

Receptionist or assistant.

Objectives

- Organize medication samples and other clinic medications.
- Check medication inventory and adequately discard expired items.

Necessary materials

- Medication samples and other clinic medications.
- Locked cabinet used exclusively for medication storage.
- Medication inventory checklist.
- Ballpoint pen.

Main activities

- Gather all sample medications.

– Write down all medications on the checklist, including the medication name, manufacturer (lab), lot number, beyond-use date, and box quantity.
– Store medications in a restricted-access cabinet, preferably in alphabetical order or according to the physician's preferences, ensuring easy visibility.
– Place medications nearing expiration at the front of the cabinet.
– Perform a full check every month.
– Separate expired medications by laboratory and return them to the respective representative upon their next visit. Alternatively, send them for incineration or dispose of them in a designated facility. Do not dispose of medications in regular trash, infectious waste, or via the sewage system.

Observation

– Until collection by the lab representative or appropriate disposal, expired medications must be stored in a clearly labeled bag or box ("Expired medication – Awaiting disposal") and kept in a separate area from active medical supplies.

General observations (per Resolution RDC 44/2009)

– All medications must be stored in an organized manner, according to the manufacturer's recommendations, and under conditions that maintain their identity, integrity, quality, safety, efficacy, and traceability.
– The storage area must be spacious enough to allow organized storage of different medication categories.
– The storage area must be kept clean and protected from direct sunlight, humidity, and heat to preserve the chemical, physical, and microbiological integrity of the products, ensuring their quality and safety.
– For medications requiring refrigeration or specific temperature conditions, follow the storage instructions on the package. The temperature must be monitored and logged daily.
– Medications should be stored on shelves, in drawers, or equivalent supports, kept off the floor, walls, and ceiling to allow for proper cleaning and inspection.
– Clinics dispensing controlled substances must use a secure cabinet or designated locked room under the supervision of a licensed health care professional (pharmacist, nurse, or physician).
– Medications that are expired, tampered with, suspected of being counterfeit, adulterated, or altered must be stored securely away from active inventory, clearly labeled, and segregated to prevent dispensing.
– Disposal of such products must follow specific health care waste management legislation, including any applicable state or municipal regulations.
– Medications must be stored in areas with restricted access to clinic staff. Public access to these areas is strictly prohibited.
– Do not store medications in cardboard boxes, shoeboxes, or any container other than the original packaging.

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Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 25 – Date: __/__/__ – Revision: __/__/__

Procedure

Inventory check of vaccines and biologics and disposal of expired medications.

Person(s) responsible

Physician and nurse.

Objectives

– Ensure the safe administration of vaccines and biologics according to the manufacturer's recommendations.

Necessary materials

– Tray.
– Vaccine.
– Sharps disposal container.

- Prefilled syringe or immunization device.
- Needle (13 × 4.5 or 25 × 7).
- Cotton ball.
- 70% ethyl alcohol (INPM).

Main activities

- Correctly and courteously identify the patient to receive the vaccine.
- Record the date of administration, dose, batch number, and vaccinator's name in the vaccination record card and the clinic's online control system (NetVacinas).
- Document the applied dose in the daily log (according to standard procedures) and enter vaccination information into the internal electronic system and the National Immunization Program Information System (SI-PNI).
- Review the patient's current vaccination status. Schedule the next dose (written in pencil) on the vaccination record card and in the clinic's online control system (NetVacinas), considering the recommended intervals between doses and additional vaccines, according to the national immunization schedule.
- Provide guidance by informing the patient about the importance of vaccination, next appointments, and how to manage possible adverse events.
- Verify the vaccine/biologic to be administered against the vaccination record card and/or medical prescription. Observe its appearance, integrity, and beyond-use date.

Administration of vaccines/biologics

- Perform hand hygiene before the procedure.
- Select the appropriate syringe and needle; if necessary, attach the needle to the syringe, keeping it capped. Use single-dose devices containing the vaccine, as recommended by the manufacturer.
- Follow the manufacturer's recommendations for route and dosage.
- Inspect the vaccine/biologic for appearance, packaging condition, batch number, and beyond-use date.
- Prepare the product according to the manufacturer's recommendations.
- Keep the needle capped until administration.
- Immediately return multi-dose vials to the refrigerator after drawing the dose.
- Administer according to specific techniques for each product.
- Do not recap the needle.
- Discard syringes/needles and ampoules in the sharps disposal container.
- Dispose of glass vials in rigid, clearly labeled toxic waste containers.
- Perform hand hygiene after the procedure.
- Document the procedure.

Special measures

- Antisepsis of the patient's skin is not routinely recommended unless it is visibly dirty. In such cases, clean with soap and water or 70% alcohol. Wait 30 seconds for drying if alcohol is used.
- When the sharps disposal container is full, it should be sealed, labeled "Biological waste," and disposed of properly.
- For administration of monoclonal antibodies (Xolair®, Fasenra®, Nucala®, etc.):
  a) Properly identify the patient and check the medical prescription.
  b) Wash hands before and after the procedure.
  c) Prepare the monoclonal antibody according to the manufacturer's recommendations: dilute and gently homogenize using rotational movements, then allow it to rest for approximately 15 minutes before administration.
  d) Inform the patient about the procedure and instruct them to report any adverse symptoms following administration.
  e) Don PPE (gloves and lab coat).
  f) Administer the monoclonal antibody subcutaneously using a 13 × 4.5-mm needle and a 3-mL syringe, following the prescribed number of doses according to the medical prescription and the manufacturer's recommendations.
  g) Monitor vital signs for 1 hour after the injection and report any changes.

h) Discharge the patient after observation and make all relevant notes and documentation.

i) Wash hands.

Receiving vaccines

– Wash hands and clean the workspace.

– Upon delivery, check packaging and record box temperature on the delivery note. Do not accept if the temperature is not within the +2 °C to +8 °C range.

– Check quantity and beyond-use date of each package.

– Store as instructed.

– Sign the delivery receipt and retain the invoice for entry in NetVacinas and the SI-PNI system.

Records

– Log doses daily in NetVacinas, the patient's electronic medical record, and the vaccination record card.

– Report applied doses and monthly inventory in the Ministry of Health's National Immunization Program Information System (SI-PNI) as instructed by the State Health Department.

Actions in case of noncompliance

– Do not accept vaccines that are outside the recommended temperature range or whose integrity is compromised.

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Prepared by: Registered Nurse (COREN-certified).

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SOP No. 26 – Date: __/__/__ – Revision: __/__/__

Procedure

Activities in the vaccination room.

Person(s) responsible

Physician and nurse.

Objectives

– Standardize the procedure for administering biologics in the vaccination room.

– Properly complete the vaccination record card and update the SI-PNI system.

– Organize the vaccination room.

Necessary materials

– Tray or emesis basin.

– Vaccines

– Sharps disposal container.

– Pedal-operated bin.

– Disposable syringe.

– Disposable needle.

– Cotton balls.

– PPE (gloves, lab coat, and mask).

– Liquid soap and 70% ethyl alcohol.

– Vaccination record card.

– Computer with Internet access.

Main activities

Procedure steps

– Check beyond-use date after opening a multi-dose vial, according to the National Immunization Program recommendations.

– Surround the interior of the daily-use cold box with gel packs after the "fog" disappears and temperature stabilization is confirmed (approximately +1 °C).

– Measure the internal temperature of the cold box with a long-probe thermometer, ensuring it is between +2 °C and +8 °C (ideally +5 °C) before placing vaccines inside. Position the thermometer probe in the center of the box.

– Place vaccines and diluents in the cold box once the recommended temperature is reached.

– Remove the vaccines from the refrigerator and separate the corresponding diluents in quantities required for the day's scheduled appointments and walk-in demand.

– Remove gel packs from the refrigerator and leave them on the sink or counter until the surface "fog" dissipates.

– Perform hand hygiene.

– Note: When cold box use is necessary (eg, high volume of administrations, power outage, refrigerator malfunction, or during refrigerator cleaning):

– Arrange forms and office supplies neatly on the worktable.

– Check that refrigerator temperature is between +2 °C and +8 °C.

– Ensure the vaccination room is clean and organized.

Room organization

– The vaccination room must be organized and visibly clean for patients.

– It must always be ready to receive patients.

Patient care

– Greet the patient courteously.

– Check the patient's current vaccination status.

– Gather health information to assess indications, precautions, and contraindications for vaccine administration.

– Educate the patient about the importance of vaccination and completing the immunization schedule according to their target group, based on the current schedule of the National Immunization Program and the Brazilian Society of Immunizations.

– Open all vaccination record documents (vaccination record card, SI-PNI, NetVacinas, and electronic medical record). If the immunization system is computerized, register the patient in both the clinic's and the Ministry of Health's electronic system.

– Keep the environment clean and instruct accompanying persons not to place personal items (eg, bags, cell phones, or vaccination record cards) on the preparation counter.

Documentation

– Review the patient's vaccination history to identify vaccines to be administered if returning.

– Record the date of application, dose, batch number, health care facility where the vaccine was administered, and the vaccinator's name in the vaccination record card and online control system (NetVacinas).

– Document the applied dose in the daily log (according to standard procedures) and enter vaccination information into the electronic system (both SI-PNI and NetVacinas).

– Schedule the next dose (written in pencil) on the vaccination record card and in the online control system (NetVacinas), considering the recommended intervals between doses and additional vaccines, according to the national immunization schedule and Brazilian Society of Immunizations guidelines.

– Provide guidance by informing the patient about the importance of vaccination, next appointments, and how to manage possible adverse events.

– Verify the vaccine to be administered against the vaccination record card and/or the medical prescription.

Vaccine administration

– Perform hand hygiene before the procedure.

– Select the appropriate syringe and needle; if necessary, attach the needle to the syringe, keeping it capped.
– Confirm the correct administration route and dosage.
– Inspect the vaccine for appearance, packaging condition, batch number, and beyond-use date.
– Prepare the vaccine.
– Keep the needle capped until administration.
– Immediately return multi-dose vials to the cold box after drawing the dose.
– Administer the vaccine according to specific techniques.
– Discard syringes/needles in the sharps disposal container.
– Perform hand hygiene after the procedure.
– Recommendations: After opening, the vaccine solution should be kept in the original vial.
– Only draw the dose immediately before administration.
– Never store prefilled syringes in the daily-use cold box.
– Observation: Antisepsis of the patient's skin is not routinely recommended unless it is visibly dirty. In such cases, clean with soap and water or 70% alcohol and wait 30 seconds for the skin to dry.
– Attention: For BCG vaccine, do not disinfect the skin with alcohol or any product – use only a dry cotton ball.
– Wearing gloves does not exempt from hand washing before and after the procedures.
– Special attire is not required for parenteral vaccine administration.
– Fill out the vaccination record card, provide guidance to the patient, and discharge them.

End of day

– Record the number of discarded vials (expired, broken, etc.) in the SI-PNI registration form to support the assessment of biologic stock movement and losses.
– Clean the cold box after use and wait for it dry before storing it.
– Complete all digital vaccine administration documents (SI-PNI, NetVacinas, and internal Excel® spreadsheets).
– Ensure refrigeration equipment is functioning properly.
– Leave the vaccination room clean and organized.

Disposing of the sharps container

– When full, the sharps disposal container must be replaced and collected by an authorized waste management company.

Vaccine orders

– Check vaccine stock.
– Notify the clinic administration to restock when necessary.

Receiving vaccines

– Wash hands and clean the workspace.
– Upon delivery, check packaging and record box temperature on the delivery note. Do not accept if the temperature is not within the +2 °C to +8 °C range.
– Fill out a noncompliance report if needed and refuse the vaccines.
– Quickly check quantity and beyond-use dates.
– Store vaccines immediately in the appropriate refrigerated space.
– Sign and keep the delivery receipt.

Special measures

– During vaccine administration, request the assistance of the child's guardian to help immobilize the child if necessary. The success of the procedure depends on this support and not solely on the vaccinator. If the guardian is uncomfortable doing so, reschedule the appointment for safety reasons.
– In case of an adverse event following immunization (AEFI), complete the appropriate online form and notify the Health Department. Correctly identify the patient and the vaccine, completing the AEFI form in full. Provide clinical support to the patient.
– The AEFI form is available from: http://pni.datasus.gov.br/Download/Eapv/Ficha_EAPV_ PNI070411.pdf.

Actions in case of noncompliance

– In case of noncompliance, immediately notify the clinic's Technical Supervisor.
– In case of refrigerator malfunction or power outage, follow the Contingency Plan.

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Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 27 – Date: __/__/__ – Revision: __/__/__

Procedure

Urgent and emergency care.

Person(s) responsible

Physician and nurse.

Objectives

– Provide immediate care to patients in urgent and emergency situations.

Necessary materials

– Crash cart.
– Automated external defibrillator (AED).
– Pulse oximeter.
– Rigid spine board.
– PPE (lab coat, glove, and mask).

Main activities

– Ensure the scene is safe.
– Check patient's responsiveness.
– Call for help.
– Simultaneously check for a central pulse and breathing or gasping.
– Bring the crash cart near the patient.
– Don PPE (lab coat, glove, and mask).
– Start cardiopulmonary resuscitation (CPR) with chest compressions if there is no pulse.
– Begin positive pressure ventilation using a bag valve mask (Ambu bag) connected to oxygen. For patients with no advanced airway, use a compression-to-ventilation ratio of 30:2. For patients with an advanced airway, provide continuous compressions with ventilations at a rate of 1 breath every 6 seconds (10 breaths per minute).
– Monitor the patient using pulse oximetry.
– Connect the AED as quickly as possible and check rhythm. If a shockable rhythm is detected (ventricular fibrillation/pulseless ventricular tachycardia), follow the AED's instructions, ensure everyone is clear, deliver a shock, and immediately resume CPR (5 cycles or 2 minutes).
– In the case of a refractory shockable rhythm: administer 300 mg of amiodarone IV as a bolus, followed by 150 mg if necessary.
– If the rhythm is non-shockable (asystole/PEA), immediately resume CPR (5 cycles or 2 minutes).
– Establish venous access.
– Administer medications as ordered by the physician, flush with 20 mL of normal saline, and elevate the venous access limb.
– Keep syringes with medications clearly labeled.
– Track the timing of medication administration (eg, adrenaline) every 3 to 5 minutes and notify the physician/team leader.

– Rotate professionals performing compressions and ventilation every 2 minutes.
– Continue CPR while indicated, reassessing rhythm and carotid or femoral pulse every 2 minutes.
– Maintain chest compressions.
– Minimize the frequency and duration of interruptions in chest compressions.
– Prepare orotracheal intubation equipment (laryngoscope with blades, endotracheal tube appropriate for patient's age); proceed with intubation, verify placement, and secure the tube.
– Perform post-resuscitation care.
– Discard used materials properly.
– Doff gloves.
– Perform hand hygiene.
– Call EMS and notify the patient's health insurance provider.
– Maintain patient support and monitoring until transfer.
– Document the incident in detail in the patient's medical record.

Special measures

– Ensure high-quality CPR, avoiding interruptions.
– Perform chest compressions in the lower half of the sternum, at a depth of 5–6 cm, allowing complete recoil of the chest after each compression, at a rate of 100 compressions per minute.
– Seal the bag-mask tightly around the patient's face. Deliver 2 breaths every 30 compressions. If using an advanced airway, deliver 1 breath every 6 seconds and perform continuous compressions for 2 minutes.
– Check for a central pulse for no more than 10 seconds every cycle or every 2 minutes.
– Emergencies related to severe allergies, anaphylaxis, or other conditions require the presence of a physician, immediate use of crash cart medications, and, if needed, transfer to a hospital facility.
– In case of an acute reaction following vaccination, provide initial support, identify the vaccine administered, fill out the AEFI report, and send it to the Health Department.

Documentation

– Document all actions in detail in the patient's electronic medical record.
– Complete the crash cart medication control form and restock medications.
– Complete the AEFI report form, if applicable.

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Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 28 – Date: __/__/__ – Revision: __/__/__

Procedure

Administration of allergen-specific sublingual immunotherapy.

Person(s) responsible

Physician and nurse.

Objectives

– Establish standardized procedures for the administration of the first dose of allergen-specific sublingual immunotherapy. Standardizing the administration method and prescription improves the safety of allergen immunotherapy practices.

Necessary materials

– Informed Consent Form for immunotherapy administration.
– Necessary resources and prior preparation.
– Immunotherapy administration record sheet.
– Evaluation before and after immunotherapy administration; and dispensing of immunotherapy vial for home treatment.

Activities

– The administration schedule for sublingual immunotherapy is described in Figure 4.

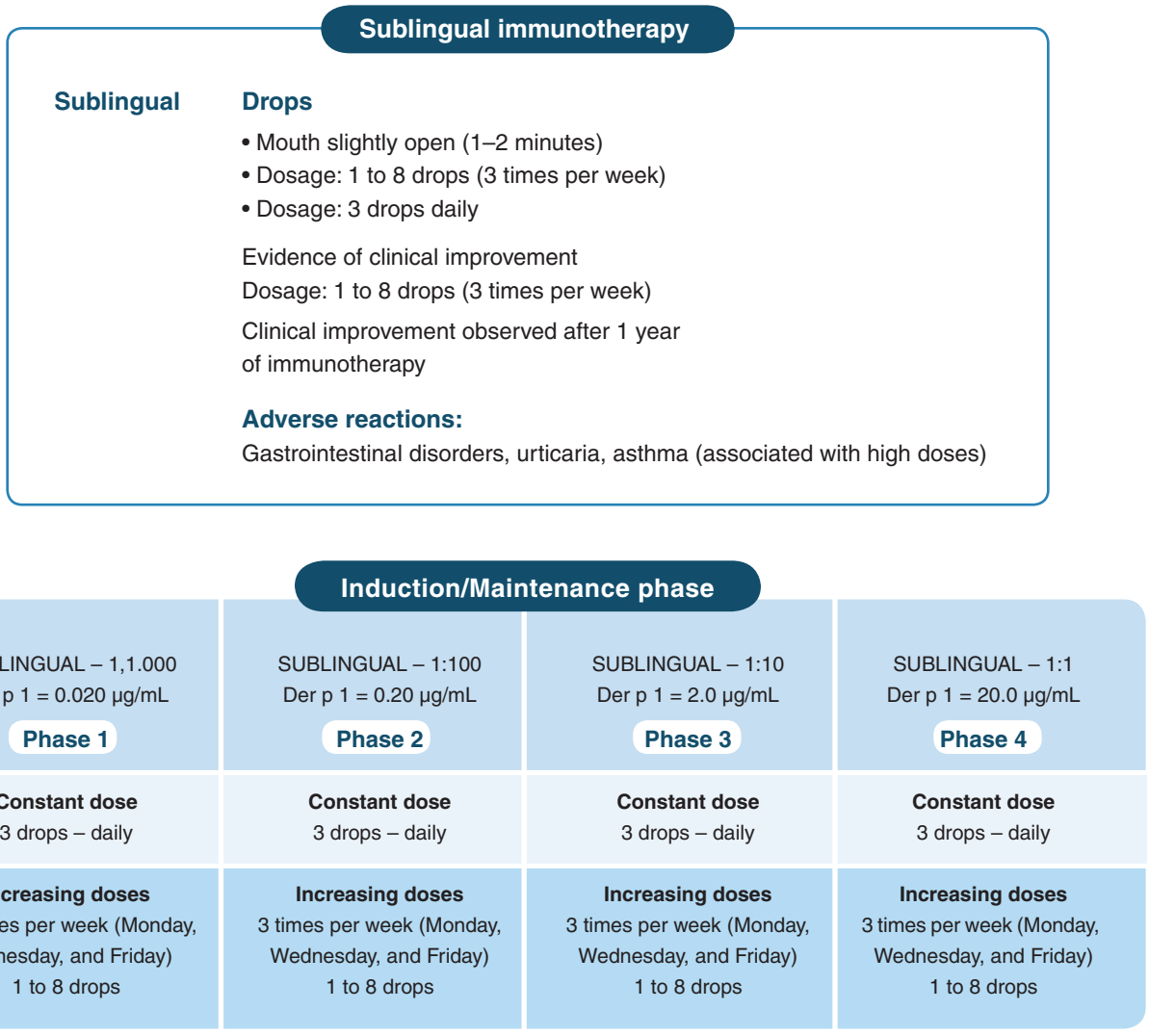

Figure 4
Administration of allergen-specific sublingual immunotherapy

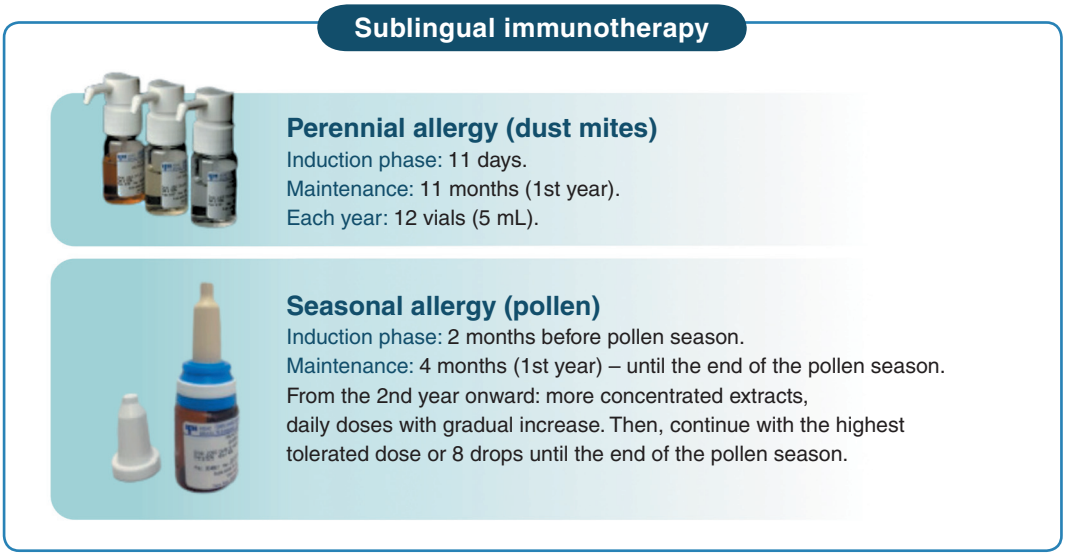

Figure 4 *(continued)*
Administration of allergen-specific sublingual immunotherapy

Documentation

- Document the procedure in the patient's medical record.
- The Informed Consent Form and immunotherapy administration sheet are attached to this document.

Adverse reactions

- In case of adverse reactions, immediately contact the physician in charge.

Special measures

- Instruct the patient to store the allergen vial in the refrigerator after dilution.
- Instruct the patient to correctly fill out the immunotherapy administration sheet and bring it to each follow-up appointment.

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Prepared by: Registered Nurse (COREN-certified).

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Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 29 – Date: __/__/__ – Revision: __/__/__

Procedure

Administration of allergen-specific subcutaneous immunotherapy.

Person(s) responsible

Physician and nurse.

Objectives

– Establish standardized procedures for the injection of allergen-specific subcutaneous immunotherapy. Standardizing the administration method and prescription improves the safety of allergen immunotherapy practices.

Necessary materials

– Informed Consent Form for immunotherapy administration.
– Necessary resources and prior preparation.
– Immunotherapy administration record sheet.
– Pre- and post-application evaluation of immunotherapy.

Activities

– The protocol for the administration of allergen-specific subcutaneous immunotherapy is described in Figure 5.

Documentation

– Document the procedure in the patient's medical record.
– The Informed Consent Form and the immunotherapy administration record sheet are attached to this document.

Administration

– Wash hands.
– Don gloves.
– Correctly identify the patient and medication.
– Disinfect the vial cap with 70% ethyl alcohol and aspirate the medication.
– Explain the procedure to the patient.
– Disinfect the application site with 70% alcohol.
– Administer immunotherapy subcutaneously, rotating application sites.

Induction phase: Standardized extract

Phase 1	Phase 2	Phase 3	Phase 4
1:10,000 0.0005 µg	**1:1,000 0.005 µg**	**1:100 0.05 µg**	**1:10 0.5 µg**
0.10 mL	0.10 mL	0.10 mL	0.10 mL
0.20 mL	0.20 mL	0.20 mL	0.20 mL
0.30 mL	0.30 mL	0.30 mL	0.30 mL
0.40 mL	0.40 mL	0.40 mL	0.40 mL
0.50 mL	0.50 mL	0.50 mL	0.50 mL

Figure 5
Administration of allergen-specific subcutaneous immunotherapy

- Instruct the patient to report any abnormalities.
- Properly dispose of gloves and syringe without recapping the needle.
- Wash hands.
- Complete forms and release the patient.

References

- Conselho Federal de Medicina, CFM. Resolução nº 1.794/2006, publicada no Diário Oficial da União (D.O.U.) 11 de agosto de 2006, Seção I, pg. 127. Available from: www.sistemas.cfm.org.br. Accessed on Apr 28 2021.
- Anvisa – Resolução da Diretoria Colegiada – RDC Nº 233, de 17 de agosto de 2005, publicada no Diário Oficial da União (DOU) em 22 de agosto de 2005. Available from: www.bvsms.saude.org.br. Accessed on Apr 28 2021.
- Anvisa – Resolução da Diretoria Colegiada – RDC Nº 67, de 08 de outubro de 2007, publicado no Diário Oficial da União (DOU). Available from: www.bvsms.saude.org.br. Accessed on Apr 28 2021.
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Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 30 – Date: __/__/__ – Revision: __/__/__

Procedure

Subcutaneous administration of medication.

Person(s) responsible

Physician and nurse.

Objectives

- Administer medications via the subcutaneous route.

Necessary materials

- Tray.
- Allergen extract.
- Sharps disposal container.
- Syringe (1 mL).
- Needle (13 × 4.5).
- Cotton balls.
- 70% ethyl alcohol (INPM).

Main activities

- Perform hand hygiene.
- Don gloves.
- Check prescription.
- Ensure the patient's privacy by closing curtains, placing screens, or closing doors.
- Choose the application site on the body, rotating sites appropriately.
- Clean the site with a cotton ball soaked in 70% alcohol: position the cotton ball in the center of the area and clean outward in a circular motion covering approximately 5 cm.
- Open the syringe packaging and attach the needle, maintaining asepsis.
- Draw the medication from the ampoule or vial.
- Remove the needle cap with the nondominant hand using a direct motion.
- Pinch the subcutaneous fold of the area with the thumb and index finger.
- Hold the syringe between the thumb and index finger of the dominant hand.
- Hold the syringe like a dart, palm facing down.
- Insert the needle at a 45° to 90° angle (90° for obese patients).
- Inject the medication slowly (1 mL/10 seconds).
- Withdraw the needle at the same angle of insertion, applying a cotton ball or dry gauze.
- Do not recap the needle.
- Discard the syringe in a sharps disposal container.
- Perform hand hygiene.
- Document the procedure in the patient's medical record.

Special measures

- The subcutaneous route can accommodate 0.5 to 1.0 mL.
- Avoid the periumbilical region.
- Palpate the selected site for nodules, redness, or pain and inspect the skin surface for bruises, inflammation, or edema. Avoid sites showing these conditions.
- Since puncturing a blood vessel through this route is very rare, aspiration before medication administration is not necessary.

Actions in case of noncompliance

- In case of noncompliance, immediately notify the clinic's Technical Supervisor.

References

- Potter PA, Perry AG. Fundamentos de enfermagem. Rio de Janeiro: Elsevier; 2009. p.686-754.
- Luvas cirúrgicas e luvas de procedimentos: Considerações sobre seu uso. Boletim Informativo de Tecnovigilância. Brasília, n.2, abr-jun, 2011.
- Conselho Regional de Enfermagem de Minas Gerais. Uso de luvas de procedimento para a administração de medicamentos. Fev, 2010.
- Potter PA, Perry AG. Guia Completo de Procedimentos e Competências de Enfermagem. Rio de Janeiro: Elsevier; 2012. p. 308-14.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 31 – Date: __/__/__ – Revision: __/__/__

Procedure

Pharmacovigilance – Adverse reactions.

Person(s) responsible

Physician and nurse.

Objectives

- Standardize the management of adverse reactions and support analyses and statistical studies for the recognition of new adverse reactions, identification of predisposing factors for side effects, and the ongoing prevention of adverse reactions to immunotherapy.

Necessary materials

- Notification form.
- Standardized questionnaire (pharmacovigilance form).

Activities

- Complete the designated form (Figure 6).

Local reaction

- Local reactions are classified by measuring the largest diameter of the reaction.
- Immediate reactions with a diameter smaller than 5 cm and delayed reactions smaller than 10 cm are considered clinically irrelevant.
    1. Induration, itching, or edema at the injection site: apply ice or topical corticosteroid if the reaction exceeds 10 cm in diameter, and administer oral antihistamines. Assess the need to adjust the dosage regimen in case of more intense reactions.
    2. Itching and/or swelling of the lips, tongue, or oropharynx during sublingual administrations: administer oral antihistamines and/or systemic corticosteroids, depending on the severity of the reaction. Assess the need to adjust the dosage regimen in case of more intense reactions.

Systemic reaction

- Signs and/or symptoms away from the injection site.
- Systemic reactions usually begin a few minutes after vaccine administration and rarely occur after 30 minutes. They can be classified as:
    1. Mild systemic reactions: localized urticaria, rhinitis or mild asthma, nausea, or slight abdominal pain.

CLINIC LOGO	**QUESTIONNAIRE – IMMUNOTHERAPY PHARMACOVIGILANCE**

Spontaneous report of suspected adverse reactions

Dilution batch	

Patient information

Patient (initials)	Date of birth	Age	Sex ( ) Male ( ) Female

Diagnosis of allergic disease

( ) Asthma ( ) Rhinitis ( ) Atopic dermatitis ( ) Hymenoptera venom allergy ( ) Allergy to hematophagous arthropod bites ( ) Others

Information about the allergen extract (suspected)

Allergen(s) used: ( ) Mite ( ) Epithelium ( ) Pollens ( ) Fungi ( ) Hematophagous insects ( ) Hymenoptera venom

Extract source laboratory name:

Batch: Beyond-use date:

Treatment number:	Beyond-use date:	Date of reaction:

Concentration/dilution:

( ) 1:1,000.000 ( ) 1:100,000 ( ) 1:10,000 ( ) 1:1,000 ( ) 1:100 ( ) 1:10 ( ) 1:1

Route of administration:

( ) Subcutaneous, aqueous solution, dose _____ mL ( ) Subcutaneous, depot system, dose _____ mL

( ) Sublingual, dose _____ gotas ( ) Sublingual, dose _____ sprays

Time elapsed between administration and reaction

( ) Within the first 30 minutes

( ) After 30 minutes but before 1 hour

( ) ___ hours after administration

Local reaction

( ) Edema ( ) Erythema ( ) Papule larger than 10 mm

( ) Itching ( ) Papule smaller than 10 mm

( ) Possible reaction to aluminum hydroxide (depot)

Systemic reaction

( ) Grade I – Nonspecific (malaise, headache, lethargy, likely not IgE-mediated)

( ) Grade II – Mild (mild rhinitis and/or asthma)

( ) Grade III – Moderate (urticaria, angioedema, severe asthma) – immediate treatment required

( ) Grade IV – Severe (anaphylactic shock or anaphylaxis) – Immediate treatment required

Figure 6
Questionnaire – "Spontaneous report of suspected adverse reactions"

Other adverse reactions and symptoms:

Possible causes of the adverse reaction:

( ) Incorrect dosage ( ) New vial
( ) Asthma symptoms ( ) Medication use (eg, beta-blockers, etc.)
( ) Period of exacerbation ( ) Other causes – Specify: _____

Did the reaction disappear after immunotherapy suspension?	Did the reaction reappear after immunotherapy reintroduction?
( ) Yes ( ) No ( ) Not applicable	( ) Yes ( ) No ( ) Not applicable

Outcome attributed to the event

( ) Death ( ) Life-threatening ( ) Hospitalization ( ) Significant medical event ( ) None of the above

Concomitant medications

Medication name	Dose and route of administration	Date of administration
1		
2		
3		

Physician information

Prior to administration, the patient:

( ) Was evaluated by the physician, was well, and not experiencing an allergy attack.
( ) Applied immunotherapy elsewhere without possibility of physician evaluation.
( ) _____

Was the report sent to health authorities?

( ) Yes ( ) No

Relationship to immunotherapy:

( ) Unrelated ( ) Remote relation ( ) Possible relation ( ) Probable relation

Name: _____
Address: _____
City: _____
State: _____
ZIP code: _____
Medical license #: _____

Date and physician's signature:

Reserved for entity/company use

Date received:	Received by:
Manufacturer:	Importation/compounding:

Important: Filling out this report does not necessarily imply that the product caused the adverse reaction.

Figure 6 *(continued)*
Questionnaire – "Spontaneous report of suspected adverse reactions"

2. Moderate systemic reactions: slow onset (>15 minutes) of generalized urticaria and/or moderate asthma, vomiting, diarrhea, or severe abdominal pain.
3. Severe systemic reactions: rapid onset (<15 minutes) of generalized urticaria, angioedema, or severe asthma.
4. Anaphylactic shock: rapidly progressing reaction characterized by skin itching, erythema, generalized urticaria, laryngeal stridor (angioedema), asthma, and hypotension, possibly leading to loss of consciousness. Following a systemic reaction, the physician should carefully weigh the benefit-risk ratio of continuing or discontinuing immunotherapy treatment.

Management of severe systemic allergic reactions (anaphylaxis)

1. Immediate treatment is required to halt the progression of anaphylaxis.
2. Administer intramuscular adrenaline (epinephrine) at a 1/1,000 dilution:
   – Adults: 0.3 to 0.5 cc.
   – Children: 0.01 mg/kg/dose, up to a maximum of 0.3 cc (for children under 40 kg).
   – This dose can be repeated every 5 to 15 minutes, if necessary, up to a total of 3 applications.
3. Administer intramuscular antihistamine (promethazine). For example: 2 mg for adults or 0.025 mg/kg/dose for children (may also be administered intravenously); alternatively, hydroxyzine 25 mg for adults or 1 mg/kg/dose for children.
4. Deliver oxygen at a flow rate of 6 to 8 L/min via nasal cannula or face mask.
5. Establish venous access.
6. Administer intravenous corticosteroids (eg, methylprednisolone 125 mg for adults or 1–2 mg/kg for children; or hydrocortisone 200 mg for adults or 4 mg/kg/dose for children) to prevent delayed symptoms. If venous access cannot be established, corticosteroids may be administered orally or intramuscularly.
7. Administer intravenous fluids or plasma expanders, if necessary.
8. In case of bronchospasm, also administer inhaled salbutamol (via nebulizer or pressurized aerosol).

Documentation

– Document the incident in the patient's medical record.
– Notify relevant authorities.

References

– Conselho Federal de Medicina, CFM. Resolução nº 1.794/2006, publicada no Diário Oficial da União (D.O.U.) 11 de agosto de 2006, Seção I, pg. 127. Available from: www.sistemas.cfm.org.br. Accessed on Apr 28 2021.
– Brasil - Agência Nacional de Vigilância Sanitária - Anvisa. Resolução da Diretoria Colegiada – RDC Nº 233, de 17 de agosto de 2005, publicada no Diário Oficial da União (DOU) em 22 de agosto de 2005. Available from: www.bvsms.saude.org.br. Accessed on Apr 28 2021.
– Brasil - Agência Nacional de Vigilância Sanitária - Anvisa. Resolução da Diretoria Colegiada – RDC Nº 67, de 08 de outubro de 2007, publicado no Diário Oficial da União (DOU). Available from: www.bvsms.saude.org.br. Accessed on Apr 28 2021.
– Agência Nacional de Vigilância Sanitária - Anvisa. Resolução da Diretoria Colegiada - RDC N° 54, de 10 de dezembro de 2013, publicada no Diário Oficial da União (DOU) nº 240, de 11 de dezembro de 2013. Available from: www.gov.org.br. Accessed on Apr 28 2021.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 32 – Date: __/__/__ – Revision: __/__/__

Procedure

Dispensation of allergen-specific immunotherapy vial for sublingual administration.

Person(s) responsible

Physician.

Objectives

– Establish procedures for the dispensation of immunotherapy vials for sublingual administration following the application of the first dose of allergen-specific immunotherapy. Standardizing the method of administration and prescription improves the efficacy and safety of allergen immunotherapy practices.

Necessary materials

– Informed Consent Form for immunotherapy administration.
– Necessary resources and prior preparation.
– Immunotherapy administration record sheet.
– Provide instructions and dispense the sublingual vial for home treatment. Reinforce guidance about possible adverse reactions.

Activities

– Request the patient to sign the Informed Consent Form for immunotherapy administration.
– Deliver the vial and the dose administration record sheet to the patient, along with information about the vaccine and potential reactions.
– Provide guidance on the adequate storage of the vial.

Documentation

INFORMED CONSENT FORM (ICF) AFTER IMMUNOTHERAPY INFORMATION SESSION

Patient _____

General information

Allergen immunotherapy is a treatment used worldwide for respiratory allergies (such as allergic rhinitis and asthma) and insect bite allergies. It consists of the administration of increasing doses of an allergen (the agent causing the allergy) via the sublingual or subcutaneous route to increase the individual's "resistance" or develop tolerance to that specific allergen.

How is treatment performed?

The indication for allergen immunotherapy is based on the patient's medical history and results from skin tests or blood tests. Increasing doses of the allergen extract are administered either sublingually or subcutaneously. The complete treatment duration is up to 3 years.

Possible side effects during immunotherapy

General symptoms occur in approximately 0.1% of all cases and may include: red patches (urticaria) over the body, eye and throat itching, nasal congestion, throat or chest tightness, cough, wheezing, shortness of breath, dizziness, nausea, and vomiting. Severe reactions (anaphylaxis) are very rare. In the vast majority of cases, reactions resolve with appropriate medications.

I am aware that I may suspend the treatment at any time without it causing any embarrassment or affecting my medical care in any way. My physician remains available to continue my treatment under any circumstances.

I declare that I have read all the information above and clarified all my doubts with the physician responsible for the treatment. I understand all the risks and benefits of allergen-specific immunotherapy and agree to the treatment and all terms outlined in this informed consent form. I am signing this document freely and voluntarily, in joint decision with my physician.

_____ _____

Signature of patient or guardian | Responsible physicians

City _____ , Date: ___/___/ ____

– Attached: dose administration record sheet.

References

– Conselho Federal de Medicina, CFM. Resolução nº 1.794/2006, publicada no Diário Oficial da União (D.O.U.) 11 de agosto de 2006, Seção I, pg. 127. Available from: www.sistemas.cfm.org.br. Accessed on Apr 28 2021.
– Anvisa – Resolução da Diretoria Colegiada – RDC Nº 233, de 17 de agosto de 2005, publicada no Diário Oficial da União (DOU) em 22 de agosto de 2005. Available from: www.bvsms.saude.org.br. Accessed on Apr 28 2021.
– Anvisa – Resolução da Diretoria Colegiada – RDC Nº 67, de 08 de outubro de 2007, publicado no Diário Oficial da União (DOU). Available from: www.bvsms.saude.org.br. Accessed on Apr 28 2021.
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Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 33 – Date: __/__/__ – Revision: __/__/__

Procedure

Dispensation of allergen-specific immunotherapy vial for injectable administration.

Person(s) responsible

Physician.

Objectives

– In special cases, such as patients who live too far away to attend weekly appointments or patients who are unable to attend due to professional activities, vials of injectable immunotherapy will be dispensed and delivered to the patient for administration at another location.

Necessary materials

– Informed Consent Form for immunotherapy administration.
– Necessary resources and dose administration record sheet for the person responsible for the injection (for administration in a facility equipped for emergency treatment). Patient must sign to acknowledge receipt of the vial.
– Provide instructions and dispense the vial for treatment outside the facility. Reinforce guidance about possible adverse reactions.

Activities

– Request the patient to sign the Informed Consent Form for immunotherapy administration.
– Deliver the package containing the vial and the dose administration record sheet and provide information about the vaccine and possible adverse reactions.
– Provide instructions on the correct storage of the vaccine (keep it in the refrigerator door).

Documentation

INFORMED CONSENT FORM (ICF)
AFTER IMMUNOTHERAPY
INFORMATION SESSION

Patient: _____

General information

Allergen immunotherapy is a treatment used worldwide for respiratory allergies (such as allergic rhinitis and asthma) and insect bite allergies. It consists of the administration of increasing doses of an allergen (the agent causing the allergy) via the sublingual or subcutaneous route to increase the individual's "resistance" or develop tolerance to that specific allergen.

How is treatment performed?

The indication for allerge immunotherapy is based on the patient's medical history and on skin or

blood tests (such as the RAST test). Increasing doses of the allergen extract are administered either sublingually or subcutaneously. The complete treatment duration is up to 3 years.

Possible side effects during immunotherapy

General symptoms occur in approximately 0.1% of all cases and may include: red patches (urticaria) over the body, eye and throat itching, nasal congestion, throat or chest tightness, cough, wheezing, shortness of breath, dizziness, nausea, and vomiting. Severe reactions (anaphylaxis) are very rare. In the vast majority of cases, reactions resolve with appropriate medications.

I am aware that I may suspend the treatment at any time without it causing any embarrassment or affecting my medical care in any way. My physician remains available to continue my treatment under any circumstances.

I declare that I have read all the information above and clarified all my doubts with the physician responsible for the treatment. I understand all the risks and benefits of allergen-specific immunotherapy and agree to the treatment and all terms outlined in this informed consent form. I am signing this document freely and voluntarily, in joint decision with my physician.

_____ _____

Signature of patient or guardian | Responsible physicians

City _____ , Date: ___/ ___ / ____

– Attached: dose administration record sheet.

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 34 – Date: __/__/__ – Revision: __/__/__

Procedure

Confidentiality and privacy of patient medical records.

Person(s) responsible

Receptionist, assistant, administrative assistant, and administrative staff.

Objectives

– Ensure the confidentiality and integrity of patient information documented in medical records.

Important

– Article 69 of the Medical Code of Ethics: "It is prohibited for the physician to fail to create a medical record for each patient."

– A medical record (patient record) is a set of standardized, organized, and concise documents intended to record all information related to medical and paramedical care provided to the patient.

– The medical record is a permanent document maintained by physicians and health care facilities (CFM Resolution No. 1331/89). It may later be used by interested parties as legal evidence until the expiration of the statute of limitations for lawsuits, which is twenty (20) years.

Necessary materials

– Patient's medical record

– Digital storage for medical records in a recognized cloud-based system using a secure database solution (ProDoctor Cloud). The software is hosted in internationally recognized data centers that ensure, beyond information security, compliance with the Brazilian GDPR and Federal Board of Medicine (Resolution 2.299/2021) requirements.

– A Confidentiality and Privacy Agreement for patient record information.

Activities

1. Explain the concept and importance of patient records.
2. Emphasize the need to store records in a restricted area protected against moisture.
3. Explain the legal requirement for storing patient records for the mandatory period.
4. Explain that all notes in the medical record are confidential.
5. Require employees to sign the Confidentiality and Privacy Agreement, committing not to disclose any patient information contained in the medical record.

References

1. Conselho Federal de Medicina, CFM. Código de Ética Médica. Resolução CFM nº 1.931, de 17 de setembro de 2009. Brasília: CFM; 2010. p. 70.

Annex

CONFIDENTIALITY AND PRIVACY AGREEMENT

By this instrument, and in accordance with applicable law, the Employee: _____

_____,

and the Clinic: _____

_____.

agree as follows:

Given that proper and diligent performance of activities in the medical office requires discretion regarding the technical and confidential information contained in patient records:

The employee hereby agrees to:

I) Maintain confidentiality, refraining from using such confidential information for personal or third-party gain.

II) Use such information solely for the purpose of properly performing their professional duties at the clinic.

III) Protect confidential information disclosed to them with the same degree of care used to protect the clinic's own records.

The employee may only disclose patient information to a third party with prior written consent from the clinic or under judicial order, in which case the employee must immediately inform the physician in writing.

The employee is expressly prohibited from producing copies or backups of patient records without prior authorization from the physician.

By signing this agreement, the employee acknowledges and accepts the obligation to maintain the confidentiality of patient information. Failure to comply with any of the confidentiality provisions set forth herein will subject the employee to disciplinary and administrative actions by the employer.

Executed in two (2) counterparts of equal form and content, signed before two witnesses.

City: _____ , on _____

of _____ , 20____ .

_____

Employee/Secretary

_____

Physician

Witnesses:

Name: _____

CPF (Taxpayer Identification Number): _____

Name: _____

CPF (Taxpayer Identification Number): _____

Prepared by: Registered Nurse (COREN-certified).

Reviewed by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 35 – Date: __/__/__ – Revision: __/__/__

Procedure

Cleaning the vaccination room.

Person(s) responsible

Receptionist, assistant, and general services assistant.

Objective

– Prevent cross-infection, provide comfort and safety to patients and staff, and maintain a clean and comfortable environment.

Necessary materials

– Bucket.
– Closed-toe shoes.
– Disinfectant (quaternary ammonium solution or bleach).
– Hand brush, sponge.
– Cleaning gloves.
– Floor cloth (clean), cleaning cloth, dustpan, squeegee.
– Appropriate clothing for cleaning (apron).
– Soap.
– Waste disposal bags.
– Natural bristle broom.
– PPE (safety goggles, long-cuff gloves, mask, and cap).

Main activities

– For concurrent cleaning of the vaccination room, employees must:
  • Wear appropriate clothing and closed-toe shoes.
  • Gather all necessary cleaning materials (bucket, disinfectant solution, squeegee, floor cloth or mop, cleaning gloves, dustpan).
  • Wash hands with soap and water and/or use alcohol gel.
  • Don gloves before starting cleaning.
  • Prepare the disinfectant solution for cleaning, adding 1/50 parts of water.
– Note: the agent used to disinfect the vaccination room is preferably quaternary ammonium solution.
– Wash floors with water and neutral soap, using a broom to scrub the entire floor.
– Remove excess water and soap using a squeegee and damp cloth.
– Dry the floor using a clean cloth.
– Afterwards, use a cloth dampened with quaternary ammonium solution to clean the entire floor again to remove remaining dirt.
– Dry the floor using a dry cloth.
– Rinse the cloth in a clean water bucket and reapply quaternary ammonium solution until the floor is fully clean.
– Gather any debris from the floor into a dustpan using a mop or a damp cloth wrapped around the mop head.
– Empty the waste basket, closing the bag correctly.

Terminal cleaning procedures

– For terminal cleaning of the vaccination room, employees must:
  • Wash hands before and after cleaning the room and/or sanitize them with 70% alcohol gel.
  • Don gloves before starting cleaning.
  • Gather all necessary cleaning materials.
  • Prepare the disinfectant solution for cleaning, adding 1/50 parts of water.

Note 1

– For powder laundry detergent, use one tablespoon of detergent per 5 liters of water.
– Gather any debris from the floor into a dustpan using a natural bristle broom with a damp cloth wrapped around the broom head.
– Empty the waste basket, closing the bag correctly.

Note 2

– Waste bags are disposable and should never be reused.
– Wipe down the waste baskets with a damp cloth that has been soaked in the disinfectant solution.
– Start cleaning from the ceiling, using a natural bristle broom with a dry cloth wrapped around the broom head.

- Clean the light fixtures by removing any detachable parts, washing them with soap, and then drying them.
- Wipe down windows, stained glass, and frames with a cloth soaked in the disinfectant solution, followed by a damp cloth, and finally a dry cloth.
- For the exterior of windows, stained glass, and frames, use a natural bristle broom (or brush) and the disinfectant solution to wash, and then rinse them.
- Clean tiled walls with a cloth soaked in the disinfectant solution, then wipe with a damp cloth and finish with a dry cloth.
- Clean the light switches with a damp cloth and then dry them.
- Wash the sink and faucet as follows:
  - For stainless steel sinks, use a sponge and the disinfectant solution.
  - For porcelain sinks, use a sponge, water, and a cream cleaner.
  - Rinse all sinks and wipe them down with a cloth dampened with the disinfectant solution.
- Clean the floor using a natural bristle broom with a cloth dampened with the disinfectant solution wrapped around the broom head, and then wipe it with a dry cloth.

Note 3

- Avoid sweeping the floor to prevent dust from spreading around the room.
- Clean from the farthest point of the room toward the exit, repeating as needed until the area is clean (at least three times).

Special measures

- The vaccination room is cleaned daily at the end of each work shift, and whenever necessary.
- Once a week the floor is washed with soap and water and then disinfected with a disinfectant solution. A more thorough cleaning takes place every two weeks, when the ceiling, walls, windows, light fixtures, lamps, and doors are cleaned.

Observations

- Concurrent cleaning of the vaccination room should be conducted at least twice daily at scheduled times or as needed. Terminal cleaning involves thorough cleaning and disinfection of all surfaces (horizontal, vertical, internal, and external) and equipment within the room. Terminal cleaning of the vaccination room should be conducted every 15 days, including a comprehensive cleaning of the floor, ceiling, walls, doors, windows, furniture, light fixtures, lamps, and air-conditioning filters.

Prepared by: Registered Nurse (COREN-certified).

Revised by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 36 – Date: __/__/__ – Revision: __/__/__

Procedure

Cleaning in case of spillage of bodily fluids (urine, feces, vomit, and secretions).

Person(s) responsible

Receptionist, assistant, and general services assistant.

Objective

- Standardize the cleaning routine within the clinic in case of spillage of bodily fluids (urine, feces, vomit, and other secretions) in order to prevent the spread of microorganisms and maintain a clean and comfortable environment.

Necessary materials

- Water.
- Neutral soap.
- Quaternary ammonium solution.
- 70% ethyl alcohol.
- Squeegee.
- Bucket.
- PPE (gloves, safety goggles, mask, gown, and closed-toe shoes).
- Cleaning cloth.
- Paper towel.

Main activities

– Wash hands before and after the activity.
– Don PPE.
– Gather all required materials.

Disinfection technique for organic matter

1. Remove any organic matter, such as bodily fluids (urine, feces, vomit, secretions) or blood spills (even small ones or splashes), from all affected surfaces using a paper towel or cloth, discarding it in the infectious waste bin immediately.
2. Proceed with disinfection as described below.

For floors and walls

Use quaternary ammonium solution: first, clean the surface to be disinfected with soap or detergent using a squeegee. Rinse and dry. After cleaning, moisten a clean cloth with the pure solution and apply it to the area where the organic matter has been removed, leaving it to act for 10 minutes. If necessary, rinse and dry.

For furniture

Use 70% alcohol: first, clean the surface to be disinfected with soap or detergent using furniture cloths. After cleaning the furniture, rub it with 70% alcohol until it evaporates completely, repeating this step three consecutive times.

Special measures

– Cleaning should be conducted whenever necessary.
– Cleaning should be conducted as soon as possible.
– If an outsourced company handles cleaning, provide their name.

References

– Brazil. Ministério da Saúde. Segurança do paciente em serviços de saúde: Limpeza e Desinfecção de Superfícies. Anvisa; 2012.
– Ferreira AM, de Andrade D, Rigotti MA, de Almeida MTG, Guerra OG, Santos Junior AG. Avaliação da desinfecção de superfícies hospitalares por diferentes métodos de monitoramento. Rev Latino-Am Enfermagem. 2015;23(3):466-74.

Prepared by: Registered Nurse (COREN-certified).

Revised by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 37 – Date: __/__/__ – Revision: __/__/__

Procedure

Mandatory reporting.

Person(s) responsible

Physician and nurse.

Objective

– Standardize the routine practice for mandatory reporting of diseases, conditions, and health events.

Necessary materials

– Computer with Internet access.
– Patient's complete sociodemographic and clinical data.
– Belo Horizonte City Hall access link for mandatory reporting (http://notificacao.pbh.gov. br/individual.php).

Main activities

– Conduct a thorough clinical evaluation if any notifiable disease is suspected.
– Request tests or referral to a specialist if necessary.
– Gather all the required data to complete the mandatory reporting form accurately:
  • Date of first symptoms.

- Patient's name.
- Sex.
- Date of birth.
- Age.
- Mother's name.
- Contact telephone number.
- City of residence.
- Full address.
- District.
- Reference point.
- E-mail.

– Report any strong suspicion and/or confirmed cases (through a report or corroborating examination) to your city's municipal system.

– Provide appropriate guidance to the patient.

The flowchart of the mandatory reporting process and the content of the reporting form used by the Belo Horizonte City Hall are illustrated in Figures 7 and 8.

Special measures

– The communication of the occurrence of specific diseases or health conditions to public health authorities, whether by health professionals or any citizen, is termed "reporting" and must be kept confidential.

– Suspected cases must be reported without waiting for confirmation to ensure timely implementation of necessary prevention and control measures.

– According to Anvisa's guidelines, both monitoring and mandatory reporting of diseases can be facilitated through the City Hall's Portal (http://notificacao.pbh.gov.br/individual.php).

Annex

– Contact telephone numbers and addresses:

– Municipal Regional Health Authority:
Address:
Phone:

– Municipal Health Department:
Address:
Phone:

– Epidemiological Surveillance Management Unit (GVIGE - central level)

References

– Belo Horizonte City Hall [website]. Available from: https://prefeitura.pbh.gov.br/saude/informacoes/vigilancia/vigilancia-epidemiologica.

– Belo Horizonte City Hall [website]. Available from: https://prefeitura.pbh.gov.br/saude/informacoes/vigilancia/vigilancia-epidemiologica/fichas-de-notificacao-compulsoria.

– Brazil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Coordenação-Geral de Desenvolvimento da Epidemiologia em Serviços. Guia de Vigilância em Saúde: volume único [recurso eletrônico] / Ministério da Saúde, Secretaria de Vigilância em Saúde, Coordenação-Geral de Desenvolvimento da Epidemiologia em Serviços. 3rd ed. Brasília: Ministério da Saúde, 2019. Available from: https://prefeitura.pbh.gov. br/sites/default/files/estrutura-de-governo/saude/ Guia%20de%20Vigil%C3%A2ncia%20em%20 Sa%C3%BAde%202019.pdf. Accessed on May 2024.

Notifiable diseases/events

– Serious workplace accidents
– AIDS (patients aged 13 years or older)
– AIDS (patients under 13 years of age)
– Venomous animals
– Human anti-rabies
– Botulism
– Cholera
– Pertussis
– HIV-exposed children
– Dengue-Chikungunya
– Diphtheria
– Acute Chagas disease
– Work-related illness/Work-related cancer
– Work-related illness/Occupational dermatoses
– Work-related illness/RSI/MSD
– Work-related illness/NIHL
– Work-related illness/Pneumoconioses
– Work-related illness/Work-related mental disorders
– Febrile exanthematous diseases/Measles/Rubella
– Epizootic

- Sporotrichosis
- Schistosomiasis
- Exposure to biological material
- Yellow fever
- Spotted fever
- West Nile fever
- Typhoid fever
- HIV-positive pregnant women
- Hansen's disease
- Hantavirus disease
- Viral hepatitis
- Exogenous intoxication
- American tegumentary leishmaniasis
- Visceral leishmaniasis
- Leptospirosis
- Malaria
- Meningitis
- Acute flaccid paralysis/Poliomyelitis
- Plague
- Human rabies
- Rotavirus
- Acquired syphilis
- Congenital syphilis
- Syphilis in pregnant women
- Congenital rubella syndrome
- Severe acute respiratory syndrome
- Outbreaks
- Outbreak - FBD
- Accidental tetanus
- Neonatal tetanus
- Tuberculosis
- Complicated varicella
- Interpersonal/self-directed violence

For questions:

- Epidemiological Surveillance Management Unit (GVIGE - central level)

  +55 (31) 3277.7767/7768
- Out of Hours CIEVS service - 98835.3120
- Municipal Health Department

  Address: 2336 Afonso Pena Ave - Funcionários, Belo Horizonte, MG, Brazil

  Opening hours: 8am to 6pm

  Phone: +55 (31) 3277.7722

Prepared by: Registered Nurse (COREN-certified).

Revised by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

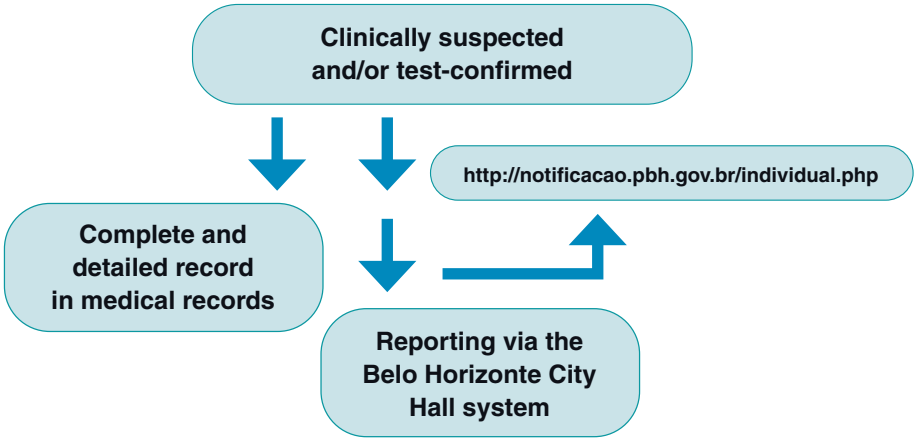

Figure 7
Flowchart of the mandatory reporting process

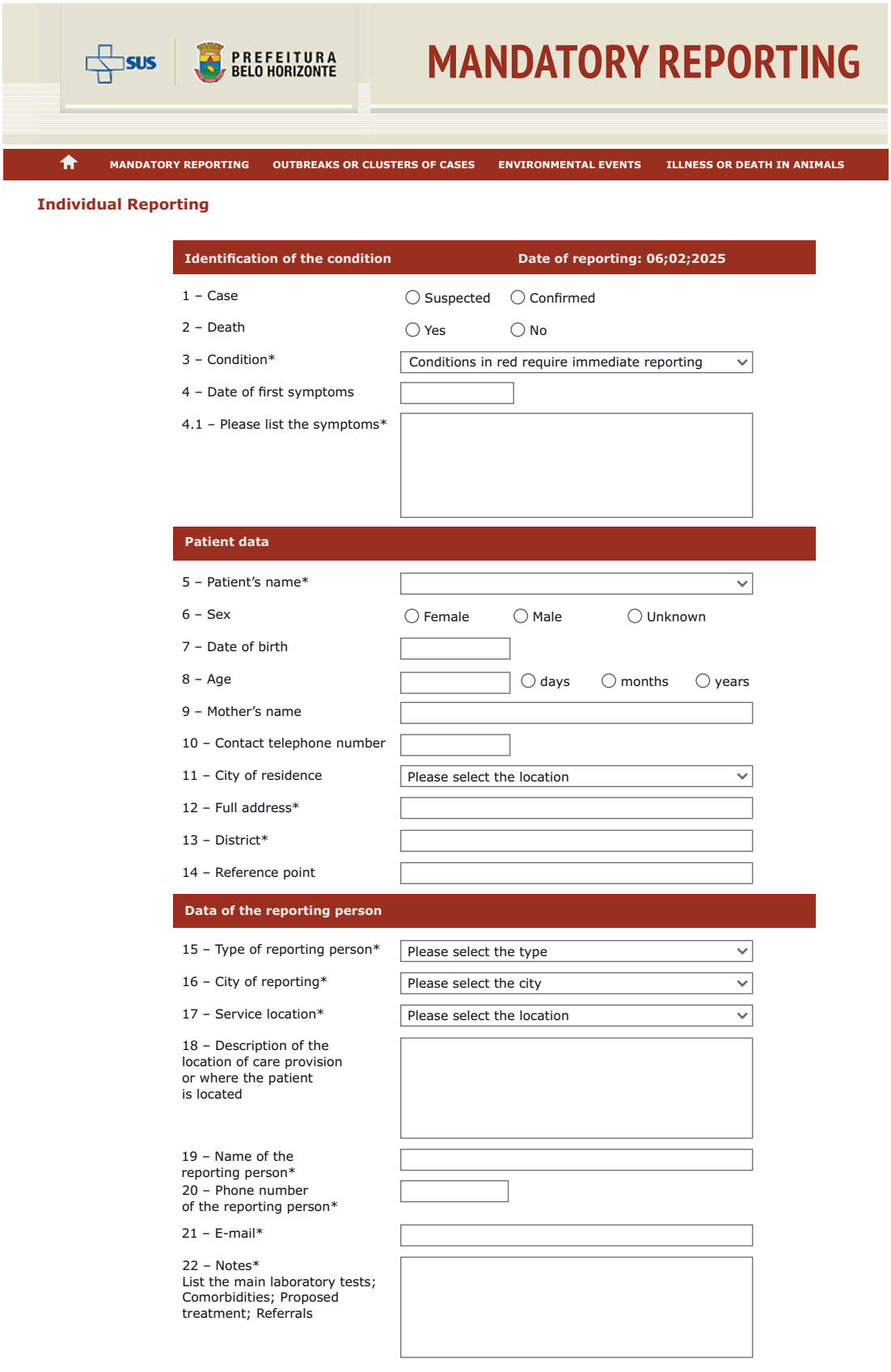

Figure 8
Belo Horizonte City Hall electronic form for mandatory reporting

SOP No. 38 – Date: __/__/__ – Revision: __/__/__

Procedure

Calibration of sphygmomanometers.

Person(s) responsible

Secretary, physician, and nurse.

Objective

– Standardize the calibration routine for sphygmomanometers within the clinic to ensure they function correctly and maintain the quality of the care provided.

Necessary materials

– Sphygmomanometers.

Main activities

– Send devices for calibration according to the attached schedule (secretaries).
– Report any changes in a device's functioning (physicians and nurses) so that it can be sent for corrective maintenance when needed.
– Store devices in a suitable place to maximize their lifespan.

Special measures

– Upon delivery after calibration and/or maintenance, devices should be evaluated to check for any damage or malfunction.
– The sphygmomanometer cuff should be cleaned with cotton soaked in 70% ethyl alcohol after each use. If it becomes excessively dirty, it should be washed with soap and water as necessary.

References

– Portaria Inmetro nº 24, de 22 de fevereiro de 1996, Regulamento Técnico Metrológico que estabelece as condições a que devem satisfazer os esfigmomanômetros mecânicos do tipo aneroide, destinados a aferir a pressão arterial.

Calibration schedule

– Annual calibration in the month of _____. Mention where the calibration is conducted and have the validity seal.

Prepared by: Registered Nurse (COREN-certified).

Revised by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 39 – Date: __/__/__ – Revision: __/__/__

Procedure

Infection control.

Person(s) responsible

Physician, nurse, administrative staff, and secretary.

Objective

– The office or clinic does not have inpatients. It provides diagnostic and treatment services for patients with allergic diseases, as well as vaccination and immunobiological agent administration.
– A license from the competent health authority is a mandatory requirement for operation. Failure to possess this license would constitute a breach of current legal and regulatory standards.
– It is the responsibility of everyone at the clinic to monitor and adhere to the cleaning and disinfection protocols outlined in the SOPs to prevent the spread of diseases and contamination.
– The use of PPE is critical to safeguarding the health of all clinic personnel.
– The 5 moments for hand hygiene is a measure adopted and recommended by the Ministry of Health.
– Soap and 70% alcohol dispensers should be available throughout the facilities for common use by employees and patients.
– Environmental disinfection should be performed using a quaternary ammonium solution.
– To ensure proper and compliant disposal, waste should be kept under supervision following the guidelines established in the Health Care Waste Management Plan.
– All diagnostic, therapeutic, and auxiliary utensils and instruments used in the clinic that may come into contact with biological agents must be disposable.

– The clinic is responsible for the periodic checking and calibration of all equipment and devices, in accordance with current legislation.
– All patients must have a computerized record containing their data, as well as their illness, ensuring easy access to information on an individual basis.

Actions in case of noncompliance

– For other instances of noncompliance, notify the clinic's Technical Supervisor so appropriate action can be taken.

Reference

– Brazil. Agência Nacional de Vigilância Sanitária. Segurança do paciente em serviços de saúde: limpeza e desinfecção. Brasília: Anvisa, 2012. Available from: https://www.gov.br/anvisa/pt-br/centraisdeconteudo/publicacoes/servicosdesaude/publicacoes/manual-de-limpeza-e-desinfeccao-desuperficies.pdf/view. Accessed on May 5 2021.

Prepared by: Registered Nurse (COREN-certified).

Revised by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 40 – Date: __/__/__ – Revision: __/__/__

Procedure

Power outage contingency plan – Refrigerators.

Person(s) responsible

Physician, nurse, administrative staff, and secretary.

Objective

– Safeguard immunobiological agents and their quality should the refrigerator fail for any reason.

Necessary materials

– Contingency Plan Flowchart.
– Contact telephone numbers.

Main activities

– In the event of a power interruption or equipment malfunction, it is crucial to keep the refrigerator closed and monitor the internal temperature closely.
– For example, the Indrel RW22D® refrigerator has an autonomy of 48 hours, provided the doors remain closed, according to the manual.
– The internal temperature must be strictly checked every 10 minutes using an external digital thermometer.
– The refrigerator system is programmed to contact up to three designated telephone numbers in case of a breakdown, temperature fluctuation, or power outage. It will automatically dial these numbers and play a pre-recorded message to alert users of any issues.
– If there is an unscheduled power outage, contact the energy provider to ascertain the estimated restoration time.
– If the equipment malfunctions, notify the equipment maintenance department immediately to explore potential solutions.
– If power restoration is not expected, the equipment issue cannot be resolved promptly, or the internal temperature approaches 7 °C, immediately transfer the immunobiological agents to a cooler, ensuring the temperature remains between +2 and +8 °C (SOP 41 – Cooler assembly).
– The clinic must have reusable ice packs readily available for use when storing immunobiological agents in coolers.
– When transferring vaccines to a cooler, ensure they are packaged to prevent mechanical shocks (do not leave them loose inside the cooler).

Actions in case of noncompliance

– In all cases, the nurse should develop educational activities to address the issue, ensuring the correction and application of this SOP.

Prepared by: Registered Nurse (COREN-certified).

Revised by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 41 – Date: __/__/__ – Revision: __/__/__

Procedure

Cooler assembly.

Person(s) responsible

Physician, nurse, administrative staff, and secretary.

Objective

– Ensure immunobiological agents are kept at a standardized temperature between 2 and 8 °C to maintain their immunizing potential.

Necessary materials

– Reusable ice packs.
– Polyurethane cooler.
– Maximum and minimum thermometer.

Coolers

– Coolers are typically made from thermal materials such as polyurethane or expanded polystyrene (e.g. Styrofoam, Insonor), with the latter being the most common for transporting immunobiological agents between laboratories and vaccination rooms.
– Each cooler must be capable of maintaining a storage temperature between +2 and +8 °C for a specific duration.
– Before use, inspect the cooler for any cracks or holes, and ensure the lid is in good condition.
– After each use, thoroughly wash and dry the coolers. Store them without the lid until they are completely dry. Once dry, replace the lid and store them in a suitable location (Figure 9).

Cooler assembly

Special measures

– Maintain the internal temperature between +2 and +8 °C. Monitor this using an extension cable thermometer, preferably, or a linear thermometer. Replace the recyclable ice packs as needed to stay within the temperature range.
– Use recyclable ice packs that have been stored in the refrigerator freezer. Allow them to acclimatize before use, as their temperature in the freezer can reach approximately -7 °C.
– When arranging the immunobiological agents inside the cooler, ensure they are surrounded (islanded) by recyclable ice. For the cooler mentioned above, this typically involves using three to five 500 mL recyclable ice packs.
– Always keep the cooler out of direct sunlight and away from any heat sources, such as stoves or heaters.

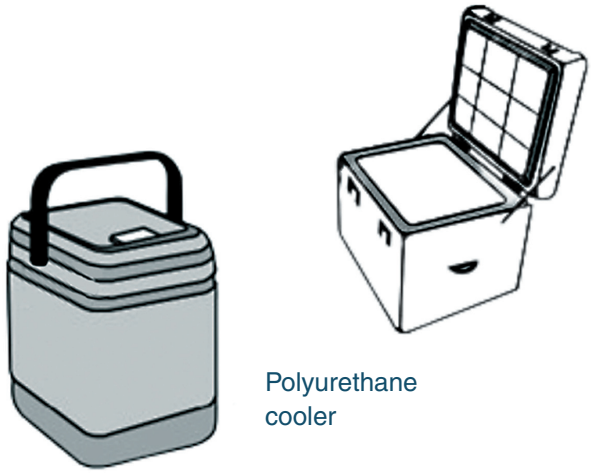

Figure 9
Polyurethane cooler

Cooler assembly

– Ice pack acclimatization: remove the reusable ice packs from the refrigerator and place them on sinks or countertops that have been previously cleaned with 70% alcohol. Leave the ice packs in place until the “fog” that typically covers their frozen surface has dissipated.
– Simultaneously, take one ice pack and place it on an insulating material, such as the lid of a Styrofoam box. Position the bulb of a thermometer with an extension cable underneath this ice pack, to monitor when the packs reach the minimum required temperature of 0 °C.

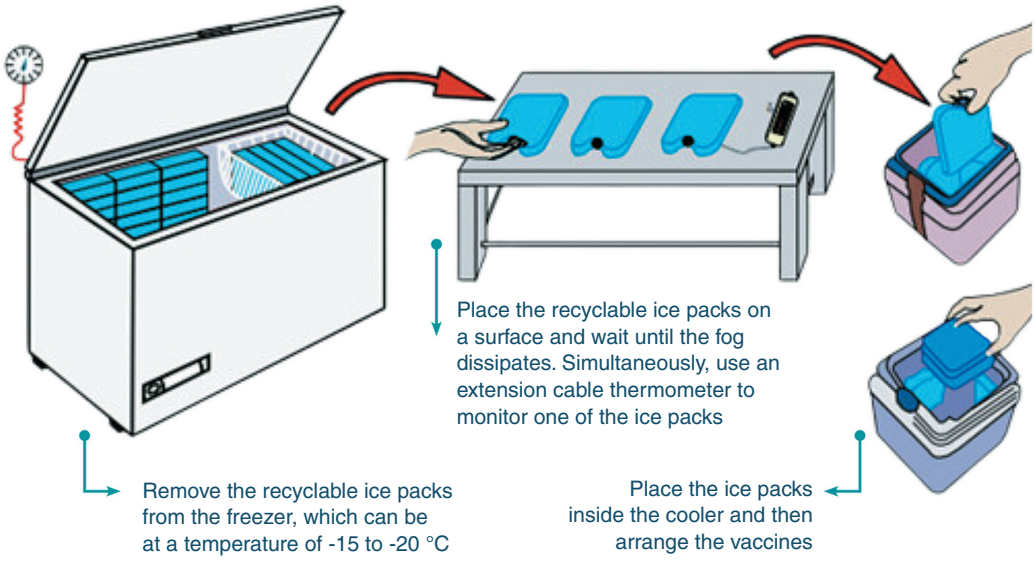

Figure 10
Cooler assembly

– Once the "fog" has dissipated and a positive temperature is confirmed by the extension cable thermometer located underneath one of the packs, arrange the items in the coolers as shown in Figure 10.
– Meanwhile, prior to placing the vaccines inside, it is recommended to use the extension cable thermometer to measure and confirm the internal temperature of the cooler.

Actions in case of noncompliance

– In all cases, the nurse should develop educational activities to address the issue, ensuring the correction and application of this SOP.

Prepared by: Registered Nurse (COREN-certified).

Revised by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 42 – Date: __/__/__ – Revision: __/__/__

Procedure

Patient identification.

Person(s) responsible

All staff members.

Objective

– Ensure that every patient receives the intended care (procedure or treatment) by verifying their identity before any action is taken.

Necessary materials

– Patient's medical record.

Required actions

– Call the patient by their full name.

– Verify the patient's identity by cross-referencing their name and date of birth with the information in their medical record.

Observation

– Even if the health care professional is familiar with the patient, it is crucial to follow these identification protocols to ensure the correct patient receives the correct care.

Reference

– Ministério da Saúde. Portaria N° 529: Portaria Nº 529, de 1º de Abril de 2013. Available from: https://bvsms.saude.gov.br/bvs/saudelegis/gm/2013/prt0529_01_04_2013.html. Accessed on Sep 13 2022.

Prepared by: Registered Nurse (COREN-certified).

Revised by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 43 – Date: __/__/__ – Revision: __/__/__

Procedure

Fall prevention.

Person(s) responsible

All staff members.

Objective

– Enhance patient safety by preventing, minimizing, or eliminating any fall risks during their treatment period.

Necessary materials

– Patient's medical record.

Required actions

– Identify and document each patient's fall risk on their care form and/or medical records.
– Clearly mark any steps or uneven surfaces with visible signage.
– Pay close attention to patients' footwear, advising them to avoid shoes that may increase the risk of slipping and falling.
– Provide clear instructions to both the patient and their family members on effective fall prevention strategies.

Observations

1. The following situations are considered falls:

– Finding a patient on the floor.
– A patient being supported during a fall, even if they do not reach the floor.
– A patient slipping from a chair, armchair, or toilet onto the floor.

2. Factors that can increase the risk of falling

– Altered mental state (confusion or agitation).
– Neurological disorders.
– Impaired gait and balance.
– Underlying health conditions and chronic diseases.
– Sensory impairments affecting hearing, vision, and touch.
– A history of previous falls.
– Pregnancy.
– Obesity.
– Use of medications that affect the central nervous system.
– Age (those aged > 60 years and children).
– Urinary or bowel urgency.

A fall risk is considered to be present if one or more of these risk factors are identified.

3. Reporting and actions in the event of a fall

– Transport the patient on a stretcher and notify the attending physician for evaluation and a physical examination.
– If the attending is not immediately available, the staff member should request an evaluation from another physician or arrange for a referral to the emergency department.
– Document the circumstances of the fall and the medical actions taken in the patient's medical record.

Reference

– Ministério da Saúde. Portaria Nº 529, de 1º de Abril de 2013. Available from: https://bvsms.saude.gov.br/bvs/saudelegis/gm/2013/prt0529_01_04_2013.html. Accessed on Sep 13 2022.

Prepared by: Registered Nurse (COREN-certified).

Revised by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

SOP No. 44 – Date: __/__/__ – Revision: __/__/__

NURSING REGULATIONS AT THE CLINIC:

Introduction

The Clinic _____
is located at _____ ,
_____
registered under CNPJ number _____ , and is private in nature. Its main activity is to provide care for patients within the specialty of Allergy and Immunology. You can contact the clinic by phone:
_____
or _____ ,
via e-mail: _____
or through our Instagram page: _____

The health insurance plans accepted at the clinic include:
_____
_____ .

Objective

Define and outline the objectives of nursing professionals within the clinic.

Duties and responsibilities

The Nursing Technical Supervisor holds responsibility for the following tasks:

- Planning, supervising, and monitoring all health care activities.
- Actively participating in the clinic management process through effective collaboration with support sectors, including administration, reception, and offices.
- Implementing and overseeing the systematization of patient care protocols.
- Updating and disseminating the internal nursing regulations on an annual basis, while also providing support to medical directors.
- Developing and revising SOPs annually and whenever new activities are introduced.
- Ensuring adequate health care coverage in the vaccination room, spirometry services, and skin testing procedures.
- Monitoring audits conducted by health surveillance and other regulatory agencies, and implementing necessary adjustments to maintain compliance.
- Participating in the recruitment, interviewing, and onboarding processes for new nursing staff members.
- Overseeing the maintenance, preservation, and inventory control of all nursing-related assets and equipment.
- Identifying and addressing any maintenance requirements, coordinating with the relevant support services to resolve these needs.
- Conducting regular assessments of material and equipment needs and collaborating with the administrative department to develop a purchasing schedule.
- Providing training to nursing staff under their supervision during onboarding, transitions to new roles or departments, and whenever there are updates to processes and procedures, as well as encouraging and facilitating their team's participation in institutional events.
- Developing and managing the nursing quality process (manuals, regulations, SOPs, and protocols).
- Monitoring and supervising the temperature of vaccine and medication refrigerators, ensuring accurate recording on designated forms.
- Maintaining oversight of the emergency cart.
- Conducting daily functionality checks of the AED and documenting these checks on the appropriate form.
- Performing activities related to the clinic's Infection Control service.
- Executing tasks that are specifically designated as exclusive to nurses.

Staff and requirements

– Requirements for the positions listed below:

II - Nursing Technical Supervisor

– COREN-certified, with jurisdiction in the area where the practice will take place;
– At least 2 years of proven professional experience.

Working hours and shifts

The Clinic _____

operates from Monday to Friday, between ____ : ____

AM and _____ : _____ PM.

All clinic employees are required to be in uniform and report to work at their scheduled time as specified in their employment contract.

The medical director has the authority to modify work hours as necessary, and any such changes will be communicated to the affected employee in advance.

The standard work schedule is as follows:

– Physicians: Monday to Friday, from xx:xx to xx:xx, with a break from xx:xx to xx:xx.
– Nurses: Tuesday and Thursday, from xx:xx to xx:xx.
– Administrative assistant: Monday to Friday, from xx:xx to xx:xx.
– Secretary I: Monday to Friday, from xx:xx to xx:xx.
– Secretary II: Monday to Friday, from xx:xx to xx:xx.

General Provisions

These regulations are to be followed by all employees of the Clinic _____ .

The nursing SOPs will be accessible as PDF files in a shared folder on the server and also available in print within the room (where they must be stored). Employees should refer to these documents if they have any questions. The SOPs will be updated annually or whenever their content requires changes.

These regulations may be subject to amendments due to the adoption of new relevant legislation, the implementation or discontinuation of units or services within the clinic, or at the discretion of the board of directors.

Any proposed changes to these regulations must be submitted to the medical board for their approval.

Situations not explicitly addressed in these regulations will be resolved through collaboration between the medical team, nursing staff, and administration.

These internal regulations will be made available to all clinic employees following approval by the board of directors. They will be reviewed/updated biannually or when their content is modified.

Prepared by: Registered Nurse (COREN-certified).

Revised by: Registered Nurse (COREN-certified).

Approved by: Clinic's Technical Supervisor (Physician).

Conclusions

The implementation of SOPs in allergists' offices will help organize and standardize daily tasks and procedures. This will ensure that every team member follows the same protocols, which is crucial for maintaining patient safety and the efficient operation of the clinic. Furthermore, these SOPs will assist us in complying with the health regulations and standards set forth by regulatory bodies such as the Brazilian Federal Board of Medicine and National Health Surveillance Agency.

Recommended reading

– Agência Nacional de Vigilância Sanitária - Anvisa. Segurança do Paciente em Serviços de Saúde – Higienização das mãos [Internet]. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/seguranca_paciente_servicos_saude_higienizacao_ maos.pdf.
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4. Brazil. Ministério da Saúde - Agência Nacional de Vigilância Sanitária - Resolução - RDC Nº 222, de 28 de março de 2018. Available from: https://bvsms.saude.gov.br/bvs/saudelegis/anvisa/2018/rdc0222_28_03_2018.pdf . Accessed on Aug 10 2023.
5. Prefeitura Municipal de Belo Horizonte. Vigilância sanitária [Internet]. Available from: https://prefeitura.pbh.gov.br/saude/informacoes/vigilancia/vigilancia-sanitaria. Accessed on Aug 15 2023.
6. Prefeitura Municipal de Belo Horizonte: Vigilância Sanitária – Legislações - Roteiro de Inspeção para consultório de Alergologia e/ou Pneumologia [Internet]. Available from: https://prefeitura.pbh.gov.br/saude/informacoes/vigilancia/vigilancia-sanitaria/legislacoes. Accessed on Aug 5 2024.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Special Article

Starting an Allergy and Immunology practice. Part 3 – GDPR for doctors: Basic concepts and responsibilities

Construindo o consultório do Alergista e Imunologista. Parte 3 – LGPD para médicos: conceitos básicos e responsabilidades

Eduardo Magalhães de Souza Lima[1], Adriana Aragão Craveiro Leite[2], Celso Taques Saldanha[2], Fátima Rodrigues Fernandes[2], Gustavo Falbo Wandalsen[2], Luís Felipe Chiaverini Ensina[2], Fábio Chigres Kuschnir[3], Dirceu Solé[4], Henrique Cunha Lima[5], Fernanda Amaral Duarte[6], Lorenzzo Anonini Itabaiana[7]

ABSTRACT

The Brazilian General Data Protection Regulation (GDPR) regulates the processing of personal data, establishing specific rules for its protection. Medical practices must comply with the GDPR as well as with the Medical Ethics Code, as they handle sensitive health-related data. Noncompliance can result in severe administrative and legal penalties. To ensure compliance, it is crucial to implement a Data Protection and Governance Program, which includes security measures and the documentation of data processing activities. In addition, obtaining liability insurance, particularly cyber insurance, is recommended as a way of mitigating the risks that doctors naturally face when conducting their activities.

Keywords: Computer security, data protection, information protection, liability, insurance.

RESUMO

A Lei Geral de Proteção de Dados (LGPD) regulamenta o tratamento de dados pessoais, impondo regras específicas sobre sua proteção. Clínicas médicas devem cumprir a LGPD além do Código de Ética Médica, pois lidam com dados sensíveis, como informações de saúde. O não cumprimento dessa Lei pode resultar em penalidades administrativas e judiciais severas. Para conformidade, é crucial implementar um Programa de Governança em Proteção de Dados, que inclui medidas de segurança e registro de operações de tratamento. Recomenda-se, ainda, a contratação de seguros de responsabilidade, em especial seguros cibernéticos, como forma de mitigar os riscos que os médicos naturalmente incorrem no desenvolvimento de suas atividades.

Descritores: Segurança computacional, proteção de dados, proteção da informação, responsabilidade, seguro.

Introduction

You run a private medical practice and handle personal data from several patients every day. These data are essential for providing care and often contain sensitive information about patients' health conditions.

In 2018, a law was passed in Brazil to regulate the processing of personal data across all sectors of the economy: the Brazilian General Data Protection Regulation (GDPR).[1] Although enacted in 2018, the

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2. Member of the Statute, Regulations, and Standards Committee of ASBAI – 2023/2024 Term.
3. President of ASBAI – 2023-2024 Term.
4. Research Director at ASBAI – 2023-2024 Term.
5. Attorney, Master of Digital Law from the Universidade Federal de Minas Gerais (UFMG). Professor of Data Protection and Digital Law at the Pontifícia Universidade Católica de Minas Gerais (PUC Minas) and CEDIN.
6. Attorney, Master of Laws from the UFMG. IT Technician specialized in computer programming – CEFET-MG.
7. Attorney, Master's Student of Law and Technology at UFMG, Postgraduate in Digital Law from PUC Minas.

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Arq Asma Alerg Imunol. 2024;8(4):362-70.

http://dx.doi.org/10.5935/2526-5393.20240049-en

GDPR only came into full effect in August 2021. During the nearly 4-year transition period, the imposition of administrative sanctions was suspended, giving data controllers time to comply with the new requirements and allowing the establishment of the Brazilian Data Protection Authority (Autoridade Nacional de Proteção de Dados, ANPD) – the agency responsible for enforcing the law. Since then, the ANPD has received numerous complaints, launched administrative and sanctioning proceedings, and even issued its first fine for noncompliance with the GDPR in 2023.

The Brazilian GDPR outlines how personal data must be handled and intersects with other regulations, such as the Medical Code of Ethics. For this reason, it should be studied by everyone who handles personal data, regardless of the volume of data or the size of the medical practice.

This article will address the main precautions that must be taken when handling patient data, including an overview of key GDPR concepts and the context of digitalization in health care services. It will also describe the legal responsibilities – both administrative and civil –physicians may assume in the course of data processing.

Basic concepts

What is personal data?

Personal data are any information relating to an identified or identifiable natural person. In other words, personal data must relate to a physical individual and either directly identify them or have the potential to do so. An example of the first case is the CPF (Taxpayer Identification Number), which directly identifies its holder. In the second case, it is necessary to consider whether a combination of information can identify someone. For example, in a game of Secret Santa, as more characteristics of a person are revealed, they become increasingly identifiable. This means that even seemingly trivial information, such as hair color, height, or clothing, can identify someone depending on the context.

Therefore, a person's health information may also lead to their identification, whether because they have a rare disease or because they are a public figure whose health condition is widely known.

The Brazilian GDPR also defines a specific category of personal data that requires a higher level of protection: sensitive personal data. These are data that could lead to discrimination against the individual, such as those related to racial or ethnic origin, religious beliefs, political opinions, or health data. Such data may only be processed under restricted circumstances, requiring additional precautions. For example, these data cannot be shared for commercial advantage, unless the sharing is strictly necessary for the provision of services. A hospital, for instance, may share health data with health insurance providers, but may not sell them to a pharmaceutical company.

Important note: Many people mistakenly believe that data such as CPF numbers, balance sheets, and bank statements are classified as sensitive personal data. This is not the case. While such information is indeed important and must be protected, it is not defined as sensitive under the Brazilian GDPR. Understanding this distinction is crucial for identifying the appropriate legal basis for processing different types of data – which will vary depending on whether the data are regular or sensitive. Do not worry if you are not familiar with the term "legal basis." We will cover what it is and why it matters in the following sections.

Processing of personal data

The Brazilian GDPR applies to all activities that fall under what it defines as "processing of personal data." Therefore, in addition to understanding what qualifies as personal data, it is also essential to understand the concept of data processing. The GDPR outlines a broad range of actions that constitute data processing. The terms used in the law include: collection, production, reception, classification, use, access, reproduction, transmission, distribution, processing, filing, storage, elimination, evaluation or control of information, modification, communication, transfer, dissemination, or extraction.

In practice, any action taken with personal data falls under this definition. Whether you are receiving, storing, sending, or analyzing data, you are engaging in data processing as part of your daily workflow. These examples are simply different forms of the broader concept of processing, which includes every possible interaction with personal data.

Even if you receive a physical medical record and store it in a drawer, that still counts as an activity involving personal data processing. The GDPR applies not only to digital data, but also to physical records. Therefore, for each data processing activity, it is essential to determine the most suitable legal basis for that specific action.

What are legal bases?

Legal bases are the legal justifications for processing of personal data in compliance with the GDPR. Data may only be used if its processing is justified by one of these legal bases, which is why they are so important.

The Brazilian GDPR allows for data processing under several different circumstances. There are 10 legal bases for the processing of general (nonsensitive) personal data and 8 legal bases specifically for the processing of sensitive personal data, as shown in Table 1.

The most well-known legal basis is consent, which refers to the unequivocal indication of the data subject's will to authorize the use of their data. Despite its popularity, consent is not necessarily the most suitable legal basis in all situations – in fact, in many practical scenarios, avoiding it is preferable. For instance, you are likely aware that medical records must be stored for a minimum of 20 years if they are in physical (paper) format.[2,3] Law No. 13.787/2018 allows for the destruction of physical or digitized records after 20 years; however, CFM Resolution No. 1.821/2007 establishes a different rule, requiring permanent storage of digitized or microfilmed records. As a result,

Table 1
Legal bases for general and sensitive personal data

General personal data	Sensitive personal data
Consent	Consent
Compliance with legal or regulatory obligations	Compliance with legal or regulatory obligations
Execution of public policies provided for in laws and regulations or supported by contracts, agreements, or similar instruments	Execution of public policies provided for in laws or regulations
Research conducted by a research body	Research conducted by a research body
Execution of a contract or preliminary procedures related to a contract to which the holder is a party, at the request of the data subject.	–
Regular exercise of rights in judicial, administrative, or arbitration proceedings	Regular exercise of rights, including in contracts and in judicial, administrative, or arbitration proceedings
Protection of the vital interests of the data subject or another natural person	Protection of the vital interests of the data subject or another natural person
Health protection	Health protection
Legitimate interests pursued by the controller or by a third party	–
Credit protection	Prevention of fraud and security of the data subject, in the processes of identification and authentication of registration in electronic systems

it is the Data Protection Officer (DPO)'s responsibility to analyze the applicable regulation in each case to determine the appropriate retention period.

Therefore, consent is not a suitable legal basis for the storage of medical records, as the data must be retained regardless of whether the patient consents, making consent irrelevant in such contexts. In these cases, the suitable legal basis would be "compliance with a legal or regulatory obligation." Another commonly used legal basis in health care is "execution of a contract." Often, it is necessary to use patient data to fulfill a contract – either directly with the patient or through a health insurance provider involved in the service.

Additionally, patient records may be used for legal defense in judicial proceedings, such as in cases involving allegations of medical error. The Medical Code of Ethics[4] permits the breach of medical confidentiality for justified reasons or with the patient's prior consent (Articles 73 and 89). The Brazilian GDPR also recognizes that sensitive data may be used in legal actions to exercise rights when the data subject is a party to the case. In such instances, there is legal support for using medical records in court, but several rules must be followed to ensure proper handling.

Another frequently used legal basis in medical settings is "health protection." This is often the most suitable basis for activities performed by health care professionals, health care services, or public health authorities. However, to rely on this basis, the processing of data must be conducted by licensed health professionals who are subject to confidentiality obligations imposed by their respective regulatory boards – such as the Federal Boards of Medicine, Pharmacy, or Nursing.

Another relevant legal basis is "legitimate interests." This can be applied in cases involving support or promotion of your clinic's activities. For example, with appropriate safeguards, you may use patients' email addresses to send relevant updates or informational content. It is important to note, however, that this basis cannot be used for processing sensitive personal data, such as health information from medical records, for marketing purposes or the interests of third parties.

Finally, when dealing with the data of children and adolescents, the Brazilian GDPR establishes a special legal framework that offers a higher level of protection. Legal bases in these cases are more restrictive, and all processing must prioritize the best interests of the child or adolescent.

Evaluating and applying legal bases is a complex task that should be undertaken by a qualified specialist. Beyond determining which legal basis is suitable for each activity, the professional must also be capable of structuring the entire data processing infrastructure to ensure full compliance with the GDPR.

Physician responsibilities

Noncompliance with the GDPR can lead to significant financial penalties for physicians, as well as serious reputational damage and loss of patient trust. For this reason, compliance with the law is essential to prevent such consequences. Below is a breakdown of the main areas of legal responsibility.

Administrative responsibility

The first type of liability under the Brazilian GDPR is administrative, meaning it arises from noncompliance with the law and falls under the oversight of the ANPD. Violating the GDPR can subject private medical practices to sanctions ranging from warnings to fines of up to 2% of the organization's gross revenue from the previous fiscal year (excluding taxes), capped at R$ 50,000,000.00 per infraction.[5]

While the risk of a fine may seem alarming, it is also important to consider that other penalties may apply – such as the partial or total suspension of activities involving personal data processing. In these cases, you will be prohibited from processing data, which could mean the inability to perform your professional activities. Furthermore, even if a sanction is later overturned, the reputation of your clinic may be harmed.

Another form of administrative responsibility, although not directly linked to data protection, may arise through professional oversight bodies, such as the Federal and Regional Medical Boards. There have already been cases of disciplinary actions, such as by the Regional Medical Board of Ceará (CREMEC),[6] where a physician displayed identifiable clinical cases and patient images in professional advertisements. In this case, inadequate handling of personal data led to an administrative penalty and revocation of the physician's license.

Judicial responsibility

Physicians may also face judicial (civil) liability. This applies in situations where, through action or omission, negligence, or recklessness, one person causes harm to another. In such cases, civil damages – whether compensatory or general – are awarded to the harmed party.

The extent of this liability will be determined by the judge if the patient feels harmed. In data protection scenarios, legal action may be taken if a data breach exposes a patient's sensitive data. If such a breach results in harm to the patient's reputation or leads to discrimination, the physician may be held legally responsible.

Although difficult to quantify, civil damages awarded in similar scenarios can serve as reference for estimates. For instance, in cases involving financial institutions, the Court of Justice of Minas Gerais has typically awarded general damages averaging BR 8,000.00.[7] While the circumstances differ from those involving medical professionals, judges may reference such amounts in cases of GDPR violation.

In addition to general damages, if the patient demonstrates that financial losses have also occurred, compensatory damages may also be awarded as a result of inadequate data processing.

Contractual responsibility

A third type of liability arises from contractual obligations. If you work with health insurance providers, you have likely signed an affiliated provider agreement that outlines specific data protection responsibilities. Even in private agreements, similar clauses may exist, including penalties for noncompliance.

Regardless of the contract, safeguarding patient data is a legal obligation, and failing to do so may be deemed a breach of contract. This means that any damages or losses caused by such failure may result in the application of penalties.

In the face of risk and uncertainty, what should be done? How to comply with the GDPR?

Complying with the Brazilian GDPR in medical practice is a multidisciplinary effort that requires collaboration among professionals from different fields. The objective is to ensure adequate protection of patient data.

It should be noted that compliance with data protection regulations cannot be achieved through a one-time effort, such as merely publishing a privacy policy on the clinic's website. Because data processing is a continuous, day-to-day activity, the compliance process must also be ongoing. For this reason, the most effective way to meet the requirements of the Brazilian GDPR is to establish a permanent Data Governance Program. This program should be managed by a DPO, who can be either a natural person (individual) or a legal entity (company or law firm). The key role of the DPO is to continuously monitor the practice's data processing activities.

In addition to preparing and providing standard documents, the DPO should also be able to identify the applicable legislation, monitor ongoing legal updates, and ensure the practice remains compliant – while also identifying opportunities for improvement. The work performed may vary depending on the size and needs of the practice, but generally follows a structured set of phases, as outlined below.

Documentation of data processing activities

Documenting a data processing operation is similar to creating a Standard Operating Procedure (SOP). An SOP is a document that describes, in detail, the steps required to perform a specific task in the medical office. It serves as a standardized protocol designed to ensure consistency, allowing any team member to follow the procedure correctly. SOPs may cover a wide range of procedures, from patient care workflows to hand-washing techniques.

As part of the Data Governance Program, the DPO is responsible for documenting all internal processes of the clinic: from patient care workflows to administrative operations. For each process, the DPO will specify which data are being processed, who has access to the data, where the data are stored, what security measures are in place, and any other relevant details necessary to understand the complete lifecycle of personal data.

Conduction of diagnostic assessment

After mapping all data flows – a process that serves as a "snapshot" of how personal data are handled in the clinic – a diagnostic assessment should be conducted in accordance with the Brazilian GDPR. One of the main actions during this phase is the selection of a legal basis for each data processing

activity. This step is especially important because, as previously mentioned, no data processing may occur without a valid legal basis, under penalty of violating the GDPR.

This phase should also include a risk classification of each process. According to ANPD Resolution 02/2022, processes may be considered high-risk if they: (a) Involve the processing of a large volume of personal data, (b) pose a risk to fundamental rights and freedoms, (c) involve the use of innovative technologies, surveillance technologies, or automated processes, or (d) involve data of children or older adults.

It is important to note that this analysis is not straightforward, as many uncertainties remain. For example, the definition of what constitutes a "large volume" of data is still being developed by the ANPD, and there is no objective benchmark yet for how many patients would qualify a practice as "handling a high volume." Therefore, it is strongly recommended that this diagnostic evaluation be performed by the DPO.

Gap identification and risk mitigation

Both the documentation of data processing activities and the performance of a diagnostic assessment are not only mandatory under the Brazilian GDPR but also play a critical role in identifying procedural gaps and mitigating risks. For instance, when mapping the patient care workflow, the DPO may discover that patient records are being stored in an unlocked drawer. This storage method leaves sensitive data vulnerable to unauthorized access. The DPO might recommend installing locks or safes to create a physical layer of data security.

Another common gap in medical practices is data duplication. For example, patient documents might be saved simultaneously on a local computer, email inbox, cloud drive, and also printed on paper. While this may seem to provide additional security, it can actually increase the risk of data breaches – such as unauthorized data access by a third party –, especially when there is no centralized control over where and how the data are stored.

Challenges and precautions in implementing a Data Governance Program for physicians

Implementing a Data Governance Program presents challenges across all sectors. Mapping every process, identifying risks, and implementing corrective measures are tasks that demand precision and care.

In the medical field, the implementation of such a program requires special attention in specific areas. For the purposes of this article, two key focus points will be discussed: storage of electronic medical records and the physician's relationship with health insurance providers.

Electronic Patient Records (PEP) and Electronic Health Records (EHR)

The digital transformation of health care has become increasingly prominent. As digital technologies evolve, traditional paper documents that once structured patient information, such as medical records, have become digitalized.

On the one hand, this transformation has brought numerous benefits in terms of data accessibility for both physicians and patients. On the other hand, it has introduced redundancy between physical and digital files, along with security risks.[8] In many cases, physical copies of digitized documents continue to be stored in boxes or filing cabinets without adequate control, increasing the risk of unauthorized access. Additionally, the law mandates retention periods for these documents, after which they must be destroyed. Without active oversight, there is a risk that these documents will be improperly stored indefinitely.

If it comes as a surprise that personal data are subject to a retention period, it is important to understand that all data processing must be tied to a specific purpose. Data may only be used as long as necessary to fulfill the stated purpose. Once that purpose is achieved, the data must be deleted, or the organization may be found in violation of the GDPR.

For example, consider a situation in which you have concluded care for a patient, with no ongoing treatment plans, and the patient's file has not been accessed for some time. One could say that the purpose for processing the data has ended, and this could justify shredding the physical medical record. However, Law No. 13,787/2018 requires that paper medical records be retained for a minimum of 20 years from the date of the last entry. After this period, the data must be destroyed, as the legal purpose for its retention would also have ended.

Just like medical records, all documents in a medical practice are subject to specific retention periods. Analyzing these timelines and developing a

records retention schedule is one of the responsibilities of the DPO.

Another important DPO task related to electronic records is the evaluation of software vendors. It is common in the medical field to use software platforms for the management of medical records. However, selecting a platform that does not comply with the Brazilian GDPR requirements can result in legal liability for the physician, as discussed in the "Physician responsibilities" section. Therefore, before signing any contract with a vendor, it is essential to conduct a thorough assessment of the company – known as vendor due diligence – based on a checklist of GDPR requirements. This evaluation determines the vendor's maturity in data protection practices and helps to identify potential risks associated with the partnership.

Relationship with health insurance providers

Another important challenge for physicians involves their interactions with health insurance providers. Typically, the affiliation agreements signed with these providers include specific data protection clauses that establish mutual responsibilities. As a result, a physician working with multiple providers will be subject to different contractual obligations related to data protection.

For example, a contract with Provider X may stipulate that, in the event of a data security incident, the physician must notify the provider and take appropriate action within 72 hours. Meanwhile, a contract with Provider Z may impose a stricter deadline of 24 hours for the same actions. Therefore, it is important that the physician maintain strict control and awareness of these obligations to avoid violating contractual terms.

Some health insurance providers may also require that patient documents be stored in accordance with specific standards, such as using segregated databases. When reviewing the agreement, the DPO can identify such obligations and, if necessary, perform a risk analysis of the clauses.

For this reason, it is strongly recommended that physicians carefully review all data protection clauses during the affiliation process with any health insurance provider.

Liability insurance

Liability insurance is a form of financial protection that professionals, including physicians, can acquire to protect themselves against civil liability claims and the costs associated with legal proceedings. This insurance typically covers legal defense costs, compensations, and settlements arising from allegations of medical negligence.

Insurance options for physicians

As is well known, physicians face a variety of risks in their daily practice that can affect both their professional careers and their patients' well-being. These risks may range from medical errors (which can lead to lawsuits) to failures in the IT security infrastructure of clinics and offices. In this context, insurance coverage for physicians is highly recommended, as it provides both financial and professional protection, in addition to offering greater peace of mind and security in the practice of medicine.

There are several types of insurance that can help health care professionals feel more secure in their work. Among the most relevant are the following:

– *Professional liability insurance:* designed to protect physicians against claims of damage caused by errors, omissions, or negligence in the practice of medicine. It typically covers legal expenses, compensation payouts, and other costs related to legal proceedings.
– *Equipment insurance:* covers damage or loss of medical equipment due to theft, fire, or other unexpected events.
– *Health and life insurance:* provides financial protection for physicians and their families in the event of serious illness, accidents, or death.
– *Cyber insurance:* covers risks related to information technology and data privacy. This type of insurance helps physicians manage the consequences of cyber incidents, such as data breaches, ransomware attacks, or security violations.

Given the increasing relevance of cyber threats, it is worth taking a closer look at cyber insurance.

Cyber insurance

With the increasing digitalization of health care, cybersecurity has become a central concern. As discussed earlier, patient data is both sensitive and valuable, making it a frequent target of cyberattacks. In addition, data breaches can result in serious legal and financial consequences for physicians and their practices, as well as cause significant reputational harm.

To prevent these risks, it may be worthwhile to invest in a good cyber insurance policy, which typically covers the following:

– Incident response costs: covers the expenses involved in responding to a cyberattack, including hiring IT specialists to contain and resolve the issue.
– Notification and credit monitoring: includes the costs of notifying patients about a data breach and offering credit monitoring services to prevent fraud.
– Data privacy and security liability: protects against legal actions and fines resulting from failure to properly secure personal data.
– Revenue loss and data recovery: compensates for lost income due to operational disruptions and covers the cost of restoring lost or compromised data.

Physicians should view cyber insurance as an essential component of their risk management strategy. With the widespread use of EHRs and digital patient management systems, the likelihood of suffering a cyberattack is significantly increased.

By investing in comprehensive coverage, physicians can focus on what they do best – caring for their patients – while remaining protected from the multiple risks associated with their profession.

Conclusion

The GDPR has introduced a new paradigm for the processing of personal data in Brazil, significantly impacting a range of sectors – including health care. Medical practices, which handle a wide array of patient information on a daily basis, must adapt to this legislation to ensure adequate data protection and to avoid serious consequences.

As outlined, personal data refers to any information related to an identified or identifiable natural person, while sensitive data includes information that may lead to discrimination, such as racial or ethnic origin, religious beliefs, political opinions, and health information. The Brazilian GDPR places an additional layer of protection on sensitive data, strictly limiting the circumstances under which they can be processed.

Personal data processing is a relevant concept that encompasses a wide range of activities, from data collection and storage to data processing and sharing. Each of these actions must be supported by a valid legal basis. In the medical field, the most relevant legal bases include patient consent, compliance with a legal or regulatory obligation, execution of a contract, and health protection. Choosing the correct legal basis is crucial, as an incorrect choice may lead to GDPR violations.

Physicians must be aware of the administrative, judicial, and contractual responsibilities that may arise from noncompliance. Administratively, the ANPD may impose sanctions ranging from warnings to significant fines, or even suspend data processing activities. Judicially, civil liability may lead to claims for general or compensatory damages, depending on the consequences of a data breach or misuse. Contractually, penalties may be enforced if data protection clauses are breached.

To mitigate these risks and ensure compliance, it is essential to implement a Data Governance Program. Such program must be ongoing and include continuous monitoring of data processing activities, the establishment of appropriate security measures, and the detailed documentation of processing operations. The DPO plays a key role in this process, ensuring that all activities are in line with the applicable legislation.

Moreover, the digitalization of medical records, such as PEPs and EHRs, demands special attention. Choosing vendors that comply with the Brazilian GDPR and managing the data lifecycle effectively are key steps in preventing breaches and ensuring patient privacy.

In conclusion, GDPR compliance presents a complex and ongoing challenge for medical practices. However, by implementing a robust governance program and adopting proper security practices, clinics can effectively protect patient data, avoid penalties, and build trust in their services. Investing in compliance not only prevents legal sanctions but also fosters ethical and responsible medical practice, ultimately benefiting both healthcare professionals and their patients.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Review Article

Contact dermatitis to alkyl glycosides: are we aware of its importance?

Dermatite de contato aos alquil glicosídeos: estamos cientes da importância?

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ABSTRACT

Alkyl glycosides are nonionic surfactants derived from fatty alcohols and glucose. They are widely used in personal care products such as shampoos, sunscreens, and moisturizers due to their mild and biodegradable properties. Important cases of allergic contact dermatitis to substances from this family have been reported. The PubMed, SciELO, and LILACS databases were searched for articles on contact dermatitis to alkyl glycosides published in the last 10 years, in English or Portuguese, involving human participants. Contact dermatitis to alkyl glycosides is a significant and emerging condition due to the widespread use of these surfactants. Its prevalence is relatively high but often underestimated due to the lack of inclusion of elements of this family in many baseline series. However, decyl glucoside has already been included in the American series and was recently included in the European baseline series. In view of this, we highlight the need to include alkyl glycosides in the Brazilian baseline and cosmetic series to prevent this contact allergy from remaining underdiagnosed. This would allow for the adequate diagnosis of suspected cases and development of more effective prevention strategies, such as innovations in the formulation of alternative products.

Keywords: Allergic contact dermatitis, glycosides, surface-active agents, cosmetics.

RESUMO

Os alquil glicosídeos são surfactantes não iônicos derivados de álcoois graxos e glicose. São amplamente utilizados em produtos de higiene pessoal, como xampus, filtros solares e hidratantes, devido às suas propriedades suaves e biodegradáveis. Importantes casos de dermatite de contato alérgica a substâncias desta família têm sido relatados. As fontes da pesquisa incluíram artigos científicos publicados nas bases de dados PubMed, SciELO e LILACS. Os critérios de seleção dos artigos incluídos abordam a dermatite de contato relacionada aos alquil glicosídeos, publicados nos últimos 10 anos, em inglês e português, e com seres humanos como sujeitos de estudo. A dermatite de contato aos alquil glicosídeos é uma condição significativa e emergente, devido ao uso disseminado desses surfactantes. Sua prevalência é relativamente alta, mas muitas vezes subestimada devido à ausência de inclusão de elementos desta família em muitas baterias padrões. No entanto, decil glicosídeo já havia sido incluído em série americana e foi recentemente incluído na série base europeia. Diante disso, destacamos a necessidade de incluir os alquil glicosídeos em série base nacional e em série de cosméticos, para não deixarmos oculta esta alergia de contato. Desta forma, poderíamos diagnosticar adequadamente os casos suspeitos, e com isso desenvolver estratégias de prevenção mais eficazes, como a inovação na formulação de produtos alternativos.

Descritores: Dermatite alérgica de contato, glicosídeos, tensoativos, cosméticos.

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Introduction

Surfactants are substances that reduce the surface tension between two liquids or between a liquid and a solid. They can act as detergents, emulsifiers, or foaming agents.[1] Alkyl glucosides are a type of nonionic biodegradable surfactant commonly used in cleaning products. They are made by reacting glucose with a long-chain fatty alcohol, usually derived from coconut or palm oil.[2] Recently, some cases of contact dermatitis caused by glucosides have been reported. The most common ones associated with allergic reactions are decyl glucoside and lauryl glucoside.[3] These are found in rinse-off products such as shampoos, soaps, and hair dyes. However, they are also used in leave-on products such as sunscreens, moisturizers, and deodorants. They can even be found in baby wipes and therefore are widely used by the population.

Although considered less irritating than other surfactants such as sodium lauryl sulfate, glucosides are believed to cause a relatively high incidence of allergic contact dermatitis.[1] On the other hand, this rate may actually be underestimated because there are few large studies on the topic and many baseline series do not include these substances.[2]

Reports of contact eczema caused by this group of allergens have become more common, leading the American Contact Dermatitis Society (ACDS) to name them allergen of the year in 2017.[3] Indeed, decyl glucoside had already been added to the North American Contact Dermatitis Group (NACDG) baseline series back in 2009. In 2022, the European Society of Contact Dermatitis (ESCD) also recommended adding decyl glucoside to its baseline series.[4] In Brazil, however, this group of allergens is rarely discussed, and no alkyl glucosides are currently included in baseline series. This review aims to highlight the importance of these substances in allergic contact dermatitis and to show why they should be routinely included in baseline series.

Methods

This is a narrative literature review conducted between April and May 2024. Three electronic databases were used to select the articles: PubMed, Scientific Electronic Library Online (SciELO), and Latin American and Caribbean Health Sciences Literature (LILACS). For the article selection process, Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) were used, with the keywords *alkyl glucosides* and *contact dermatitis* combined using the Boolean operator *and*.

To ensure the literature selected was appropriate for this review, the following inclusion criteria were applied: studies involving humans, articles published within the last 10 years, and articles written in English or Portuguese. Scientific publications that were not closely related to the topic — based on title and abstract screening — were excluded.

Results

A total of 43 articles related to the topic were identified, of which 19 were duplicates. After reviewing the abstracts of the remaining 24 studies, 4 were excluded. As a result, 20 articles were included in this review. No publications in Portuguese were found, highlighting the importance of this review. The article selection process is shown in Figure 1.

Discussion

Alkyl glucosides are a group of 19 surfactants derived from renewable sources. They are used in both rinse-off products (eg, cleaning agents) and leave-on products (eg, cosmetics). Currently, decyl glucoside is the most widely used. However, cetearyl, lauryl, and coco glucosides are also commonly used.[5]

They are considered safe for use[5] and are commonly found in products labeled as "hypoallergenic" or safe for sensitive skin.[4] However, alkyl glucosides in sunscreens, cosmetics, and cleaning products can cause sensitization through a mechanism that is still unclear. When tested, most patients react to multiple alkyl glucosides.[5] Women are more commonly affected, which may be due to their higher use of cosmetics.[4] Most cases are not work-related. However, allergic reactions can occur in occupational settings, especially among health professionals, cleaners, and salon professionals.[5] Conditions such as atopic dermatitis can increase glucoside penetration due to a impaired skin barrier.[2] Individuals with atopic dermatitis may be at greater risk of developing allergic contact dermatitis to weaker allergens, such as those in this group.[6]

The clinical presentation varies depending on the areas of product application.[2] The hands, face, and neck are commonly affected by exposure to shampoos, sunscreens, and liquid soaps. Nonexposed

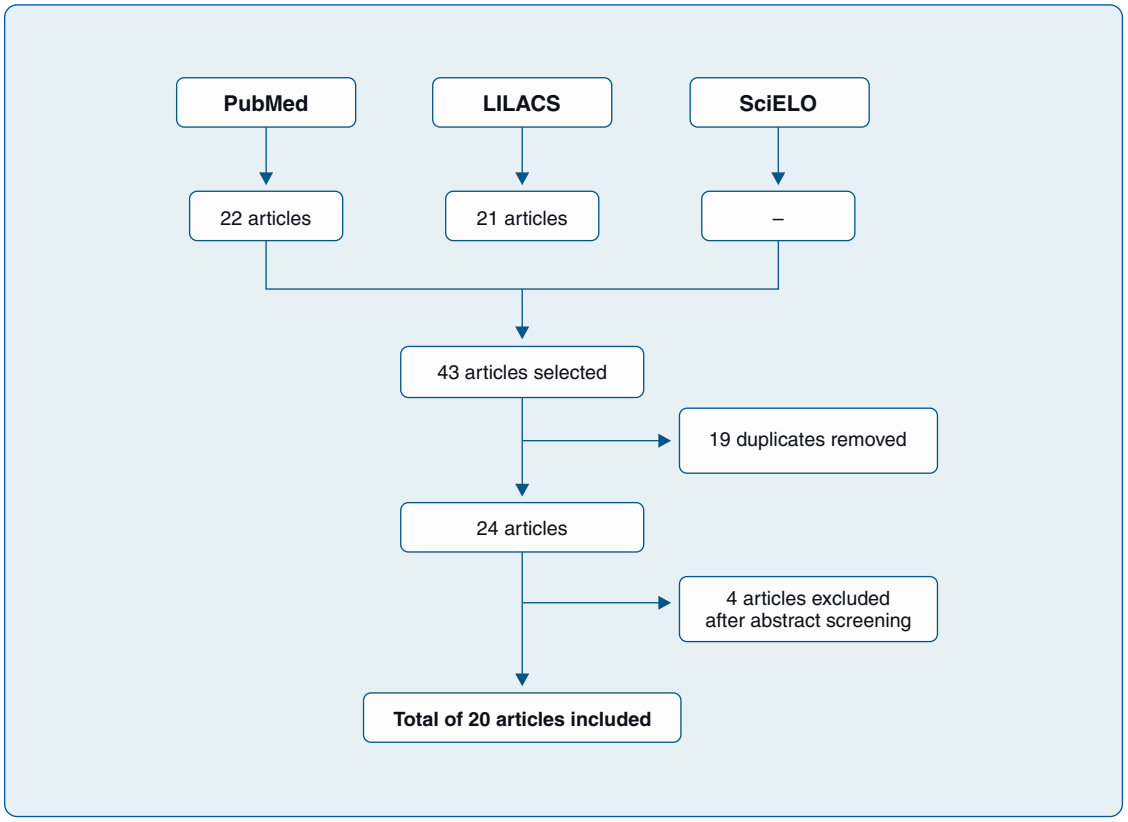

Figure 1
Flowchart of the article selection process

areas such as the breasts, abdomen, and genitals can be affected by antiseptics, skin cleansers, and baby wipes.[5] In occupational exposure, eczema most often affects the hands — such as in hairdressers handling hair products or nurses applying creams and antiseptics.[2]

In most cases, strict avoidance of the products involved and treatment with topical corticosteroids lead to the resolution of dermatitis.[5] Because of likely significant cross-reactivity, the safest approach is to avoid all alkyl glucosides.[7]

Rinse-off products

Shampoos are the most common cause of contact dermatitis from alkyl glucosides.[5] Hair care products are the most frequent source of such allergens.[7] They usually contain a mix of different glucosides, and their exact composition is not always clear. Since shampoos and cosmetics also contain preservatives, fragrances, and other allergens, testing both the patients' products and the individual ingredients is important.[5] An interesting study analyzing the ingredients of shampoos marketed as "hypoallergenic" or "for sensitive skin" found that 56.7% of these shampoos contained alkyl glucosides, of which coco glucoside was the most common.[8]

Sunscreens

Until recently, decyl glucoside was considered a "hidden" allergen in sunscreens containing Tinosorb® M because, while used during manufacturing, it was not listed as an ingredient.[7] It is now known that this widely used sunscreen contains the active ingredient bisoctrizole, along with propylene glycol, xanthan gum,

and decyl glucoside.[9] One case involved a woman who developed itchy eczema on her face, especially around the eyelids, after using different cosmetics. Patch testing was positive for decyl glucoside, Tinosorb® M (which contains decyl glucoside), and her facial cream (which also contained Tinosorb® M). This case highlights the importance of checking for hidden allergens in facial creams, since most of them contain UV filters. On the other hand, previous sensitization to alkyl glucosides through cosmetics may increase the likelihood of an allergic reaction to the decyl glucoside present in Tinosorb® M.[9]

Other personal care products

The general population is increasingly seeking products labeled as "natural," "hypoallergenic," or "clean," under the assumption that these items are typically free from harmful ingredients. A study assessing the prevalence of allergenic ingredients in such personal care products (Table 1) reported that alkyl glucosides were the sixth most commonly found allergen, present in 20.7% of the total consumer items.[10] In another study that evaluated the prevalence of surfactants in products listed in the American Contact Dermatitis Society Contact Allergen Management Program (CAMP), glucosides were found in 10% of the products analyzed.[11] Thus, they represented the third most common surfactant group and were the most frequently found in household-use substances.[11]

An interesting study analyzed the composition of facial moisturizers marketed for men. It found that 26.2% of these products contained alkyl glucosides, with cetearyl glucoside being the most frequently identified.[12]

There are case reports highlighting specific glucosides, such as one involving a woman who applied an anti-wrinkle facial cream only once. She developed acute dermatitis affecting her face and neck. Patch testing confirmed an allergy to arachidyl glucoside, an ingredient in the product that has rarely been reported as a cause of allergy. In that case, the patient also had positive reactions to other glucosides that were not present in the cream she used.[13]

Medications and hospital-use products

A survey was conducted to identify common allergens in surgical disinfectants (products used by health professionals for scrubbing and surgical asepsis). Among the 267 products analyzed, alkyl glucosides were found in 6% of them. However, just as the use of glucosides in personal care products has increased, their presence in soaps and cleaning products used in surgical settings may also become more common.[14]

In two case reports, contact dermatitis was linked to the same topical medication (Ialuset cream®). The only confirmed sensitivities were to the undiluted product and to 5% cetearyl glucoside, a component of the cream. In these cases, no sensitivity to other tested glucosides was observed.[15]

Another case involved a 70-year-old patient with a chronic ulcer on her ankle that had persisted for 6 months. She was initially treated with foam dressing without success. Due to marked erythema and exudation, a local infection was suspected. The dressing was then replaced with another foam dressing containing an antiseptic (polyhexanide). However, her condition did not improve. Allergic eczema was then considered, and patch testing was performed. The test was positive for the dressing material and borderline positive for lauryl glucoside, but negative for the antiseptic. The exact composition of the dressing was not disclosed by the manufacturers. However, chemical analysis of the product confirmed the presence of the glucoside in

Table 1
Prevalence of alkyl glucosides in so-called "natural" products

Product category	Alkyl glycosides[a]
All "natural" products	20.7%
Soap	43.0%
Shampoo	40.3%
Conditioner	4.2%
Deodorant	0.0%
Sunscreen	24.8%
Moisturizer	13.4%
Hair treatment	3.1%
Toothpaste	0.0%

[a] Includes lauryl, coco, decyl, and other related glucosides.
Adapted from Tran et al.[10]

the foam, supporting the relevance of the borderline test result.[16]

In the United States

A large study by the NACDG, involving 24,000 patients evaluated over a 10-year period, compared glucoside-positive vs glucoside-negative patients and showed that sensitized individuals had significantly higher rates of occupational skin disease, atopic dermatitis, and/or asthma. More than 80% of the reactions to glucosides were considered to have current clinical relevance.[7] In the most recent NACDG survey, decyl glucoside showed a positivity rate of 2.1%, confirming the need for its inclusion in baseline series. Lauryl and coco glucosides both had a positivity rate of 1.4%, while cetearyl glucoside had a lower rate of only 0.4%.[17]

In Europe

An evaluation of the inclusion of glucosides in the European baseline series found a positivity rate of 1.73% for decyl glucoside, supporting its inclusion in that series. On the other hand, the positivity rate for lauryl glucoside was only 0.3%, suggesting that it may be more appropriately placed in the cosmetics series.[18]

A recent study by a Spanish group tested alkyl glucosides (decyl and lauryl glucosides) in 3,629 patients. They found a positivity rate of 0.8%. The mean age of positive patients was 55.5 years and most of them were women (56.7%). Presumably, 26.7% of the positive cases had atopic dermatitis. Among sensitized individuals, the most affected body areas were the hands and the face. The products most commonly involved were leave-on products.[4]

In Brazil

There are no alkyl glucosides included in the Brazilian baseline series or in the Latin American baseline series. Similarly, glucosides are not present in the cosmetics series. Only decyl and lauryl glucosides are found in the hair product series, which is still rarely used in Brazil. This may explain the absence of reported cases of sensitivity to this group of surfactants in the country.

Patch testing and possible screening for glucosides

The NACDG and the ESCD test decyl glucoside at 5% in petrolatum as the vehicle, while lauryl glucoside is tested by both organizations at 3% in petrolatum.[17,18] Columbia University published a study showing that 13% of individuals who reacted to lauryl glucoside did not react to decyl glucoside. Likewise, 23% of those who reacted to decyl glucoside did not react to lauryl glucoside. Based on these findings, the study concluded that no single glucoside could serve as a screening agent for allergy to another glucoside. Since these reactions are usually clinically relevant, specialists are advised to test for all possible alkyl glucosides when there is suspicion of cosmetic allergy.[19]

Cross-reactivity

Most patients tested for different glucosides show multiple positive reactions, likely due to their structural similarity.[2] This suggests that sensitization may represent a group allergy with possible cross-reactivity. However, industrial production processes are known to produce impurities resulting in mixtures of different glucosides.[2,5] As a result, positive patch test reactions to different glucosides may actually reflect simultaneous exposure rather than true cross-reactivity.[5] A British study evaluating five specific glucosides found that 79.3% of patients reacted to more than one alkyl glucoside. However, the authors noted that these simultaneous reactions did not occur consistently, and therefore recommended testing multiple members of this chemical family.[20]

In a series of 30 cases that reacted to glucosides, 25 patients also showed reactions to unrelated chemical substances, with many of them presenting multiple sensitivities. An increased risk of polysensitization may be explained by genetic predisposition, frequent and/or prolonged exposure, or acquired susceptibility resulting from skin barrier disruption.[21]

Conclusions

Glucosides are important and emerging allergens. They are widely present in popular household products. Many clinical cases of allergic contact dermatitis still show no positive results in patch testing. Therefore, the possibility of a glucoside allergy should be considered. To improve diagnosis, these substances need to be included in the national baseline series and in the cosmetics series. Only then will it be possible to take a step forward in accurately diagnosing these patients.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Review Article

Type 2 inflammatory diseases: safety profile of biologics and small molecules during pregnancy

Doenças inflamatórias do tipo 2: perfil de segurança de imunobiológicos e pequenas moléculas na gestação

Catarina Monteiro Palumbo[1], Marcelo Vivolo Aun[1,2]

ABSTRACT

Type 2 chronic inflammatory diseases are highly prevalent among women of childbearing age. When poorly controlled, they are associated with pregnancy complications, which justifies the study of different options for their management. This study aimed to review the literature on the use of advanced therapies, such as biologics and small molecules, for type 2 diseases, focusing on their safety profile during pregnancy. Observational studies available in the literature from 2010 to 2024 were analyzed to determine the risk of maternal and fetal complications arising from exposure to these medications during pregnancy. No randomized clinical trials involving human participants were found on the topic. No study showed a direct association between exposure to omalizumab or dupilumab and negative outcomes. There is insufficient evidence in humans to predict increased risk of complications with the use of mepolizumab, benralizumab, tezepelumab, reslizumab, or tralokinumab. Janus kinase inhibitors are absolutely contraindicated after conception due to risks observed in animal studies. Further research is needed to better understand the safety of advanced therapies during pregnancy, with the goal of making more informed clinical decisions in the future.

Keywords: Molecular targeted therapy, pregnancy, asthma, atopic dermatitis, hypersensitivity.

RESUMO

As doenças inflamatórias crônicas do tipo 2 são altamente prevalentes em mulheres em idade fértil. Quando mal controladas, se associam a complicações gestacionais, o que justifica o estudo de diferentes alternativas para o seu manejo. Esse artigo objetiva revisar a literatura sobre o uso de terapias avançadas, como imunobiológicos e pequenas moléculas, em doenças do tipo 2, com enfoque em seu perfil de segurança durante a gestação. Foram analisados os estudos observacionais disponíveis na literatura de 2010 a 2024, visando avaliar o risco de complicações maternas e fetais advindas da exposição a estas medicações na gestação. Não foram encontrados ensaios clínicos randomizados em humanos sobre o tema. Em nenhum estudo sobre omalizumabe e dupilumabe a exposição foi diretamente associada a desfechos negativos. Não há dados suficientes em humanos para predizer aumento de risco de complicações no uso de mepolizumabe, benralizumabe, tezepelumabe, reslizumabe ou tralokinumabe. Os inibidores das Janus quinase são absolutamente contraindicados após a concepção, pelo risco observado na exposição de animais. São necessários mais estudos sobre o tema, para melhor compreensão da segurança de terapias avançadas na gestação, visando decisões clínicas mais embasadas no futuro.

Descritores: Terapia de alvo molecular, gravidez, asma, dermatite atópica, hipersensibilidade.

Introduction

Chronic type 2 inflammatory diseases, such as atopic dermatitis (AD), asthma, chronic rhinosinusitis with nasal polyps (CRSwNP), and eosinophilic esophagitis (EoE), are a group of conditions with varied phenotypes but shared pathophysiological characteristics, which taken together affect 20–30% of

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the world population.[1,2] Chronic spontaneous urticaria (CSU), despite having a distinct pathophysiology, is associated with atopy and also involves the main cells and molecules of type 2 inflammation, sharing some of its therapeutic targets.[3,4]

Poor control of these conditions is associated with morbidity and reduced quality of life, with high direct and indirect societal costs.[5] Although there are well-established and individualized management strategies, many patients do not tolerate conventional therapies or do not achieve complete remission of symptoms with these therapies alone. The advent of advanced therapies, such as biologics and advanced small-molecule drugs, has revolutionized the treatment and prognosis of these conditions, allowing more effective control of disease activity.[6]

The prevalence of allergic diseases in women of childbearing age is estimated at 18–30%.[7] During pregnancy, a series of immune-system changes result in dominance of the T helper 2 (Th2) cell response throughout the fetal growth period, which may predispose women with these diseases to flares, worsening of symptoms, or even onset of new atopic conditions.[8] Some of the first-line drugs of choice for management are also contraindicated in pregnancy, and must be discontinued after conception. However, inadequate disease control is consistently associated with adverse maternal and fetal outcomes.[9-12]

Currently, of the 11 medicinal products approved by the U.S. Food and Drug Administration (FDA) for the management of type 2 inflammatory diseases,[6] none are formally indicated for use during pregnancy. There are no randomized clinical trials demonstrating safety in this population[13]; however, there are multiple records of pregnant patients who received biologicals and small molecules for these indications between 2010 and 2024. The aim of this study is to conduct a comprehensive review of the literature on the use of advanced therapies for asthma, chronic rhinosinusitis with nasal polyps, atopic dermatitis, eosinophilic esophagitis, and chronic spontaneous urticaria, with a focus on their safety profile during pregnancy.

Background

Pathophysiology of type 2 inflammation

The type 2 immune response is classically defined as an adaptive response which involves the activation of Th2 lymphocytes and the release of group 2 effector cytokines, culminating in the recruitment of eosinophils and the production of IgE.[14,15] This pattern of immune response can be triggered by helminths, but also by other pathogens and irritating substances.[16,17] Allergens can trigger a non-targeted, dysregulated Th2 inflammatory response, resulting in allergies, anaphylaxis, and atopic diseases.[14,17] The host skin and epithelial barrier play an important protective role against noxious environmental stimuli and invasion by parasites.[17] In patients with persistent inflammation, the epithelial barrier is damaged, exacerbating and perpetuating atopic diseases.[18]

Exposure to exogenous insults triggers the release by epithelial cells of alarmins, such as thymic stromal lymphopoietin (TSLP), interleukin (IL) 25, and IL33. These substances play a role in the activation of antigen presenting cells (APCs)[19] and ILC2 cells—major sources of IL5 and IL13[15]—even before the onset of the adaptive immune response.[14] APCs present antigens in lymph nodes,[19] leading to activation of naive CD4 T lymphocytes into Th2 lymphocytes and the production of effector cytokines such as IL4, IL5, and IL13.[14] The process of polarization toward the Th2 response has not been completely elucidated, but appears to be mediated by the presence of alarmins.[14,20]

Th2 lymphocytes interact with B lymphocytes (BLs),[21] resulting in the production of IgE by an IL4- and IL13-dependent mechanism.[6] IL4, in addition to encouraging the differentiation of more immature T lymphocytes into Th2, induces isotype switching in BLs. IL13, in turn, mediates the proliferation of IgE-producing BLs.[19] IL5 stimulates the development of eosinophils, promoting activation of their precursors in the bone marrow, maturation, and differentiation.[6,22] In the bloodstream, eosinophils release cytotoxic protein granules that induce tissue damage and dysfunction.[22] They also play roles in the regulation of mast cell proliferation and degranulation.[6,22]

IgE antibodies activate mast cells and basophils, releasing histamine, leukotrienes, tryptase, and prostaglandins, which perpetuate the inflammatory response through the recruitment of immune cells[6] and act on the epithelial barrier, resulting in hypersecretion of mucus and contraction of smooth muscle cells.[16]

Several signaling pathways are involved in type 2 inflammation. Highlights among these include the Janus kinase (JAK) and Bruton's tyrosine kinase (BTK) pathways, which have been studied as targets for the development of advanced therapies.[6] Suppression of the type 2 immune response is carried out by regulatory T (Treg) and B (Breg) lymphocytes,

which secrete IL10 and transforming growth factor beta (TGF-β). The activity and concentration of these regulatory factors appears to be altered in type 2 inflammatory diseases.[6,23]

Type 2 inflammatory diseases in pregnancy

The prevalence of allergic diseases in woman of childbearing age ranges from 18 to 30%, with asthma, AD, allergic rhinitis, and food allergies being most common.[7] During pregnancy, several immune adaptations occur, aiming to strike a balance between effective immunity against pathogens and appropriate immunomodulation for each stage of fetal development. While more pro-inflammatory states are required for implantation, placentation, and during the third trimester, an anti-inflammatory immune milieu predominates throughout the fetal growth stage.[8]

Between 13 and 27 weeks of gestation, the period of fetal and placental growth, the immune response shifts to a dominance of the Th2 pattern and a key role for regulatory lymphocytes. Treg and Th9 lymphocytes control effector lymphocyte responses against paternal antigens, protecting fetal cells from rejection and apoptosis, which helps promote an anti-inflammatory environment.[8,24] Type 2 cytokines are also believed to be involved in maternal-fetal tolerance.[24] However, exacerbation of Th2 immunity during this period may be associated with onset or clinical deterioration of autoimmune and/or atopic diseases.[13,24]

Asthma is the most prevalent respiratory disease in this group, affecting up to 13% of pregnant women worldwide. Although the course is variable, approximately 30% of women experience a worsening of symptoms during pregnancy. Asthma exacerbations have a negative impact on maternal and fetal outcomes and may be related to reduced prescription and adherence to medications during the gestational period. Guidelines generally recommend continuing any drugs used before conception, but this is hindered by a lack of evidence on their safety profile.[25]

Multiple studies have demonstrated a significant association between poorly controlled asthma and negative maternal and fetal outcomes. In a systematic review and meta-analysis by Wang et al.[9] based on 40 prospective and retrospective cohorts, maternal asthma was significantly correlated with increased risk of gestational diabetes, cesarean section, antepartum hemorrhage, postpartum hemorrhage, placental abruption, and premature rupture of membranes. An update of the systematic review and meta-analysis by Robijn et al.[10] on neonatal adverse events in pregnant women with asthma demonstrated a high risk of congenital malformations, perinatal mortality, and neonatal hospitalization. However, compared to the original study,[26] the risk of neonatal death lost statistical significance.

AD is the most common dermatosis during pregnancy, accounting for 30–50% of cutaneous conditions in this population.[27] In 80% of cases there is no previous history of AD, while the remaining 20% are recurrences or relapses occurring after conception.[28] Among women with eczema, the course of the disease varies during pregnancy; approximately half experience worsening of symptoms, especially in the second trimester.[27] This can be explained by the immune-system changes discussed above, but also by the consequences of hormonal changes in the skin. Recent studies indicate that estrogen has a positive impact on the epithelial barrier, while progesterone appears to have a negative effect. These hormones also stimulate Th2 lymphocytes and alter the cytokine balance, contributing to gestational atopic eruptions.[29]

Preconception planning should include measures to reduce disease activity to a minimum,[27] as few systemic therapies for AD have been proven safe during pregnancy. Emollients and low-to-medium-potency topical corticosteroids are considered first-line treatments. UVA1 and UVB therapies are restricted to more serious cases, as is ciclosporin, which is a pregnancy category C drug. Other topical and systemic medications may be considered; however, the evidence base is limited.[29]

Maternal and fetal outcomes of pregnancies in patients with eczema are poorly studied. In a Danish retrospective cohort, Hamann et al.[11] found statistical significance of AD as a protective factor against gestational diabetes mellitus and as a risk factor for premature rupture of membranes and staphylococcal neonatal sepsis. These associations, however, were not sustained in an analysis adjusted for BMI. Another possible complication, although few cases have been reported, is eczema herpeticum during pregnancy. Eczema herpeticum develops secondary to compromised epithelial integrity[30] and may be associated with miscarriage, premature birth, and intrauterine growth restriction.[27]

There are few data in the literature on CRSwNP during pregnancy. It is estimated that around 18–30% of pregnant women experience symptoms of

rhinitis, which significantly worsen their quality of life, especially in the third trimester.[31] There are no studies on the prevalence of CRSwNP in this population. Maternal and fetal outcomes have also been scarcely studied.

Management of CRSwNP during the gestational period is based on corticosteroids, with topical agents being preferable to systemic ones.[32] Alhussien et al.[33] concluded that fluticasone propionate, mometasone, and budesonide are the safest options during pregnancy. There are no data in the literature regarding the maintenance or introduction of biologics in pregnant women with this condition.

CSU affects 3–5% of the population at some point in their lives, occurring most frequently in women.[34] Despite the severity of this condition in female patients, there is little data regarding their follow-up during pregnancy. The PREG-CU study by Kocatürk et al.[35] evaluated 288 women with this disease in 13 countries. Of these, 63% discontinued or changed treatment after conception. Antihistamines were the most commonly used medications, and were not associated with worse maternal or fetal outcomes. There were no differences in complications between women with CSU and the general population. Urticaria flares requiring emergency treatment were significantly associated with preterm birth, suggesting that robust disease control is essential during pregnancy.[35]

Although more frequent in males, EoE still has a substantial prevalence in women (32.83 cases per 100,000), with incidence peaking between the second and third decades of life.[36,37] Huang et al.[37] did not report adverse gestational events related to the use of systemic corticosteroids during pregnancy. A cohort study by Röjler et al.[36] did not demonstrate any positive association between presence of EoE and low birth weight, instrumental delivery, induction of labor, gestational diabetes, or preeclampsia. However, there is still little information on its proper management and possible complications during pregnancy.

Advanced therapies

Advanced therapies have revolutionized the treatment and prognosis of atopic diseases, allowing more effective control of disease activity and, in many patients, remission of symptoms. Currently, there are 7 biologics approved by the U.S. FDA for use in these conditions: omalizumab, dupilumab, mepolizumab, benralizumab, tezepelumab, reslizumab, and tralokinumab. In addition, there are four small-molecule targeted therapies: abrocitinib, upadacitinib, baricitinib, and ruxolitinib. Table 1 summarizes key information on these advanced therapies.[6,38-56]

In Brazil, the following have been approved by Anvisa (the National Health Regulatory Authority) for the treatment of asthma: omalizumab, dupilumab, mepolizumab, tezepelumab, and benralizumab.[49-53,57] An international consensus published in 2024[58] including 141 experts involved in asthma treatment in 32 countries concluded that biologics can be used during preconception, pregnancy, and breastfeeding in women with severe asthma. Among them, omalizumab, mepolizumab, benralizumab, reslizumab, and dupilumab achieved consensus (≥ 75% of respondents). There was also agreement that these therapies can be started during pregnancy, with the same indication criteria applied to non-pregnant women and an emphasis on shared decision-making with the patient.

Advanced therapies approved for AD management in Brazil are dupilumab, abrocitinib, upadacitinib, and baricitinib.[50,54-56] For CRSwNP, the therapeutic armamentarium includes omalizumab, dupilumab, and mepolizumab.[49-51,59] Both the FDA and Anvisa have approved dupilumab for EoE[39,50] and omalizumab for CSU.[38,49]

Other medications are in clinical development and/or at different phases of clinical research. Potential therapeutic targets of interest include cytokines (TLSP, IL33, and ST2), IL4/ IL4 Rα and IL13/ IL13 Rα1, IL5 and IL-5Rα, JAK, IgE, BTK, mast cells, and various others (IL31, IL-31Rα, NK1R, CCR4, GATA3, OX40, OX40L).[6]

Safety profile of advanced therapies during pregnancy

The use of advanced therapies during pregnancy is poorly supported by evidence, and there is no formal indication for their prescription during this period.[38-48] Table 2 summarizes the pregnancy risk categories assigned to each of these medications. Pregnancy category B refers to medications in which animal studies have not been associated with increased fetal risk, but controlled studies have not been conducted in pregnant women. This category also includes drugs in which animal studies have demonstrated risks which were not confirmed by subsequent controlled studies in humans. Category C includes medications in which animal studies have demonstrated risk to the fetus,

Table 1
Advanced therapies currently approved by the FDA and Anvisa

Drug (trade name)	Mechanism/ target	Indications (FDA and Anvisa approved) FDA	Anvisa	Route of administration
Omalizumab (Xolair®)	IgE	Asthma, CRSwNP, CSU	Asthma, CRSwNP, CSU	Subcutaneous
Dupilumab (Dupixent®)	IL4/13-Rα	Asthma, AD, CRSwNP, PN, EoE	Asthma, AD, CRSwNP, PN, EoE	Subcutaneous
Mepolizumab (Nucala®)	IL 5	Asthma, CRSwNP, EGPA, HES	Asthma, CRSwNP, EGPA, HES	Subcutaneous
Benralizumab (Fasenra®)	IL 5-Rα	Asthma	Asthma	Subcutaneous
Tezepelumab (Tezspire®)	TSLP	Asthma	Asthma	Subcutaneous
Reslizumab (Cinqair®)	IL 5	Asthma	N/A	Intravenous
Tralokinumab (Adbry®)	IL 13	AD	N/A	Subcutaneous
Abrocitinib (Cibinqo®)	JAK1	AD	AD	Oral
Upadacitinib (Rinvoq®)	JAK1	AD, RA, PA, UC	AD, RA, PA, UC, AS	Oral
Baricitinib (Olumiant®)	JAK1/2	AD, RA	AD, RA, AA	Oral
Ruxolitinib (Opzelura®)	JAK1/2	AD	N/A	Topical

FDA = Food and Drug Administration, ANVISA = Brazilian National Health Regulatory Agency, AD = atopic dermatitis, PN = prurigo nodularis, CRSwNP = chronic rhinosinusitis with nasal polyps, EoE = eosinophilic esophagitis, CSU = chronic spontaneous urticaria, RA = rheumatoid arthritis, UC = ulcerative colitis, PA = psoriatic arthritis, EGPA = eosinophilic granulomatosis with polyangiitis, HES = idiopathic hypereosinophilic syndrome, N/A = not approved, AS = ankylosing spondylitis, AA = alopecia areata.
Adapted from[6,38-56].

but controlled studies have not been conducted in humans.[60]

Because advanced therapies have specific biological targets, they are believed to carry a lower risk of adverse maternal and fetal outcomes when compared to conventional systemic drugs. However, there is evidence of transplacental passage of monoclonal antibodies, especially at the later stages of pregnancy, which could pose risks to the fetus.[13] The following section will review the available literature on use of these therapies during pregnancy.

Omalizumab

The use of omalizumab during pregnancy has been studied in patients with asthma and CSU. There are no randomized clinical trials. The EXPECT observational study, by Namazy et al.,[61] is a prospective cohort published in 2015 which analyzed 191 patients exposed to one or more doses of omalizumab at any time during pregnancy or up to 8 weeks before conception. Among the 169 pregnancies with reported outcomes, there were 160 live births (including 4 twin pregnancies), 1 stillbirth, and 11 miscarriages.

Table 2
Pregnancy risk categories of advanced therapies with marketing authorization in Brazil

Drug	Pregnancy risk category
Omalizumab	B
Dupilumab	B
Mepolizumab	B
Benralizumab	B
Tezepelumab	B
Abrocitinib	C
Upadacitinib	C
Baricitinib	C

Adapted from [49-56].

A total of 21 congenital anomalies were described, with a 4.4% rate of major defects and an 8.8% rate of conditional defects. Premature birth weight, low birth weight, and small for gestational age status were seen, respectively, in 14.5%, 3.2%, and 10.9% of cases. These findings did not differ from studies of fetal complications in patients with asthma not on biologics.

The QECC (Quebec External Comparator Cohort) study, published in 2020 by Namazy et al.,[62] compared the EXPECT cohort (n = 230) to a population of pregnant patients with asthma not on biologics (n = 1143). The prevalence of major birth defects was similar between groups (8.9% in QECC vs. 8.1% in EXPECT), which corroborates the conclusion that exposure to omalizumab does not appear to increase the risk of this outcome. Furthermore, the proportion of live births was similar in both studies (99.3% in QECC vs. 99.1% in EXPECT), with a higher number of small-for-gestational-age children in the former (15.8% in QECC vs. 9.7% in EXPECT).[61-62]

Another retrospective observational study, by Gemicioglu et al.,[63] analyzed 20 patients with asthma who had received at least one dose of omalizumab during pregnancy. There were 8 episodes of asthma exacerbation (36.4%), 5 cases of premature birth (21.5%), and 3 cases of low birth weight (13%). No congenital anomalies or other maternal-fetal outcomes were reported.

A retrospective analysis of the safety profile of omalizumab in women with CSU by Patruno et al.[64] found 1 miscarriage among 29 patients who received one or more doses during pregnancy or up to 8 weeks preconception. No other adverse events were observed, leading to the conclusion that the use of omalizumab for CSU does not appear to be associated with negative outcomes. A subgroup of EXPECT containing 30 patients with CSU was also analyzed by Namazi et al.[65] The results were similar to those found in asthma, and the study concluded that no increased risk was observed in the omalizumab group.

Finally, we reviewed 9 case reports, the main data and outcomes of which are compiled in Tables 3 and 4. Five patients with severe, difficult-to-control asthma and multiple exacerbations became pregnant while taking omalizumab and chose to continue it throughout pregnancy.[66-69] Three continued taking the drug until full term, while one discontinued use after the first trimester. Four episodes of exacerbation were reported. One patient[68] delivered a low-birth-weight female infant (544 g) prematurely in the 26th week of gestation. This may have been related to the severity

Table 3
Case reports on the use of omalizumab during pregnancy in patients with asthma[49-56]

Author	Timing of exposure	Patients	Exacerbations	Fetal complications	Maternal/ gestational complications	Live births
Majou et al.[66]	Throughout pregnancy	1	2	0	0	1
Kuprys-Lipinska et al.[67]	Throughout pregnancy	2	0	0	0	2
Hirashima et al.[68]	First trimester	1	1	Prematurity, low birth weight	0	1
Kuschnir et al.[69]	Throughout pregnancy	1	1	0	0	1

Table 4
Case reports on the use of omalizumab during pregnancy in patients with chronic spontaneous urticaria

Author	Timing of exposure	Patients	Exacerbations	Fetal complications	Maternal/ gestational complications	Live births
Liao et al.[70]	Variable	2	1	0	0	2
Losappio et al.[71]	Throughout pregnancy	1	0	0	0	1
González-Medina et al.[72]	Variable	2	0	0	0	2
Ghazanfar et al.[73]	Throughout pregnancy	1 (2 pregnancies)	0	0	1 post-term pregnancy (42 weeks)	2
Cuervo-Pardo et al.[74]	Throughout pregnancy	4	0	0	0	4

of her asthma prior to pregnancy. No congenital anomalies or other adverse maternal or fetal outcomes were observed.

The 10 patients with CSU who were monitored received omalizumab in the first trimester or throughout their pregnancies.[70-74] In one case, the drug was started after conception,[72] while in another, the dosage was increased at 12 weeks due to a severe exacerbation.[70] No stillbirths, miscarriages, premature birth weight, low birth weight, congenital birth defects, or other negative outcomes were reported.

There are no studies on the safety profile of this medication during pregnancy in women with CRSwNP. Omalizumab is currently classified as pregnancy category B by the FDA, but it is not approved for use during pregnancy.[38]

Dupilumab

The use of dupilumab during pregnancy was studied in women with AD and pemphigoid gestationis. An observational study on the use of systemic and topical therapies in the United States[75] estimated that, of 3,563 patients with the disease, 2% were taking this drug before conception. The data show that the drug was discontinued in most cases, with only 0.7% taking it in the first and 0.3% taking it in the second and third trimesters. This may be related to the lack of robust evidence proving the safety of this biologic during pregnancy.

An Italian retrospective cohort study by Avallone et al.[76] evaluated 29 patients with severe AD who received dupilumab during pregnancy. The drug was discontinued in all cases once pregnancy was discovered, with a median exposure time of 6 [2-24] weeks. There was no statistically significant difference in any gestational, fetal, or neonatal outcomes, even after multivariate analysis adjusted for confounders. Another observational study analyzed a worldwide pharmacovigilance database (VigiBase).[77] No perinatal adverse events were consistently associated with the use of dupilumab during pregnancy.

We have also reviewed 8 case reports[78-85] and 3 case series,[86-88] which are compiled in Table 5. The patients analyzed in these reports all started dupilumab for moderate to severe AD, with high Eczema Area Severity Index (EASI) scores, a large body surface area affected, significant impact on quality of life, and/or lack of disease control despite multiple previous trials of therapy. The most frequent comorbidities included asthma, rhinitis, and conjunctivitis. Improvement of symptoms and regression of AD were observed in all women.

In most cases, the drug was used throughout the gestational period. Only one case series[87] was restricted to preconception. All three patients in whom the drug was discontinued subsequently experienced disease flares,[78,80,84] with two requiring reintroduction of therapy. In one case[85] dupilumab was initiated during pregnancy (24 weeks).

Regarding maternal complications, there were two cases of gestational diabetes and one emergency cesarean section due to suspected intrauterine growth restriction.[80,84,85] Low birth weight was reported in a singleton pregnancy (2480 g) and in two premature twins born at 35 weeks (1500 g and 2000 g, respectively).[80,88] No congenital anomalies, miscarriages, stillbirths, or any other gestational or fetal adverse events were observed. Follow-up of offspring[78,86] showed no changes in growth or development. Dupilumab use by men during conception was not associated with any adverse outcomes.[87]

There are no randomized clinical trials on this topic. There are also no published articles on the use of dupilumab during pregnancy in patients with asthma who have comorbid CRSwNP or EoE.

Mepolizumab

There are no randomized clinical trials of mepolizumab during pregnancy. It has also not been studied in CRSwNP. We found only one case report, by Vittorakis et al.,[89] regarding treatment with biologics in a patient with severe eosinophilic asthma. During pregnancy planning, an attempt was made to discontinue mepolizumab, which resulted in a severe disease flare requiring reintroduction. The patient became pregnant and remained on medication throughout her gestation, experiencing only two disease flares which were treated with brief cycles of systemic corticosteroids. The child was born at 40 weeks of gestation, weighing 2750 g, with no birth defects. Maternal and fetal eosinophil counts after delivery were less than 1.5%. No gestational or neonatal adverse events were reported. Another report, by Ozden,[90] focused on two previously infertile patients who conceived after starting mepolizumab. One chose to terminate the pregnancy, while the other discontinued the medication and delivered a healthy infant with no congenital anomalies.

Table 5
Case reports and case series on the use of dupilumab for management of atopic dermatitis during pregnancy

Author	Timing of exposure	Patients	Exacerbations	Fetal complications	Maternal/ gestational complications	Live births
Di Lernia et al.[78]	Throughout pregnancy	1	1, after attempted withdrawal of medication	0	0	1
Alvarenga et al.[79]	Throughout pregnancy	1	0	0	0	1
Akhtar et al.[80]	Throughout pregnancy	1	1, after attempted discontinuation of dupilumab at 27 weeks (2480 g)	Low birth weight (2480 g)	Emergency cesarean section due to suspected intrauterine growth restriction	1
Costley et al.[81]	Throughout pregnancy	1	NRA	0	0	1
Gracia-Darder et al.[82]	Throughout pregnancy	1	0	0	0	1
Kage et al.[83]	Throughout pregnancy	1	0	0	0	1
Lobo et al.[84]	Up to 24 weeks of gestation	1	1, after discontinuation of dupilumab at 24 weeks	0	Gestational diabetes	1
Mian et al.[85]	Started after 24 weeks of gestation	1	NRA	0	Gestational diabetes	1
Hong et al.[86]	Variable 1-3 = 1st and 3rd trimesters 4 = 3rd trimester	4	1 mild 1 moderate 0 severe	0	0	4
Bosma et al.[87]	2 fathers at conception 2 mothers pre-conception	4	NRA	0	0	4
Escolà et al.[88]	Variable (average exposure 6.8 ± 2.9 months)	11	NRA	2 premature twins (35 weeks) with low birth weight (1500 g and 2000 g)	0	12 (1 twin pregnancy)

NRA = not reported in article.
Adapted from [78-88].

Benralizumab

We found a single case series by Naftel et al.[91] on the use of benralizumab for asthma during pregnancy. No adverse neonatal events, low birth weight, or congenital anomalies were observed in the four patients reported. All deliveries occurred at full term, except for one scheduled cesarean section at 36 weeks. One patient had a history of multiple asthma-related complications during previous pregnancies, including two premature births (at 32 and 36 weeks). After starting benralizumab, she achieved and maintained satisfactory control of her symptoms, with no complications during pregnancy. Flares were reported in two women, one of which was related to an attempt at drug discontinuation. The patient with the worst disease control was a smoker who did not cease her habit during pregnancy, and experienced four disease flares.

One case report by Saco and Tabatabaian[92] described significant worsening of asthma and eosinophilia after discontinuation of benralizumab in a pregnant patient. At 20 weeks of gestation, the decision was made to reintroduce the biologic, with significant improvement in the patient's condition. The report does not discuss any possible maternal or fetal complications. There have been no randomized clinical trials of benralizumab in pregnancy.

Tezepelumab

There are no published articles in the literature on the use of tezepelumab during human pregnancy. The FDA warns that any potential adverse events would be worse during the third trimester, as more substances cross the placental barrier during this period. A study of primates exposed throughout gestation to tezepelumab at doses more than 168 times that administered to humans demonstrated placental passage of the biologic, but no evidence of fetal adverse events.[42]

Reslizumab

There are no published studies on the use of reslizumab during human pregnancy. Studies in rodents exposed to 6 to 17 times the maximum recommended human dose did not find any fetal adverse events. However, this biologic is known to have a prolonged half-life and to cross the placental barrier, which may be associated with negative outcomes, particularly in the second and third trimesters.[43]

Tralokinumab

There are no published studies on the use of tralokinumab during human pregnancy. There is an ongoing study which is currently collecting data through an online platform.[93] In primates administered doses up to ten times higher than the maximum recommended human dose, no gestational or fetal developmental complications were reported.[44]

Small-molecule JAK inhibitors (abrocitinib, baricitinib, upadacitinib, ruxolitinib)

Expert consensus on systemic treatment of AD in special populations[94] contraindicates the use of all JAK inhibitors during pregnancy and lactation. This is based on the teratogenic effects reported for these drugs in animal studies. Accordingly, all patients of childbearing age on anti-JAK therapy are advised to use contraceptive methods.

There are no published articles in the literature on the use of abrocitinib during human pregnancy. A pregnancy outcomes registry is available but is still at the data collection stage. A safety analysis in rats exposed to 11 times the maximum recommended human dose demonstrated an increased incidence of skeletal variants and dystocia. An increase in fetal lethality and a reduction in postnatal survival were also observed at doses up to 17 times higher than recommended.[45]

Kammerer[95] reviewed cases of accidental exposure to baricitinib during pregnancy. Data extracted from a pharmacovigilance system found 77 maternal and 14 paternal exposures. Incidences of complications were similar to those recorded in the general population. The outcomes of interest included the number of live births, miscarriages, and elective terminations of pregnancy. Two fetal malformations were identified: anencephaly and hip dysplasia. In animal studies,[47] rodents exposed to 11 to 46 times the maximum recommended dose of baricitinib had a higher incidence of low weight and skeletal malformations. Increased fetal lethality has also been reported in rabbits. At 2- to 7-fold doses, no developmental changes were observed.

Rats exposed to 1.6 to 15 times the maximum recommended dose of upadacitinib had an increased incidence of skeletal malformations and low weight. In rabbits, an increased incidence of cardiac malformations, fetal losses after implantation, and low birth weight was observed.[46]

Finally, we found no studies on the use of topical ruxolitinib for AD during pregnancy. During drug development, oral administration of doses 22 times higher than recommended did not result in any congenital malformations in rodents.[48]

Final comments

Type 2 inflammatory diseases are highly prevalent in women of reproductive age, and their management during pregnancy is still controversial. Although not formally recommended after conception, some biologics are an acceptable second-line treatment option, especially for patients who cannot tolerate or are unable to achieve disease control with conventional therapies. Conversely, all small-molecule targeted therapies for these conditions are currently contraindicated during pregnancy and lactation.

The present article reviewed observational studies on the use of immunobiologics in humans during pregnancy. Among this class, omalizumab and dupilumab had the largest number of available studies, the findings of which do not demonstrate any increased risk of adverse outcomes directly related to treatment. Disease severity before conception is a major confounding factor in such studies, as poor control of type 2 inflammatory conditions is known to be associated with gestational complications. Furthermore, the sample sizes of exposed women are small, and all available studies are observational, which limits the validity of their conclusions.

There is a dearth of literature on mepolizumab and benralizumab, precluding any conclusions about their safety during pregnancy. There are also no published studies on the use of tezepelumab, reslizumab, or tralokinumab during human pregnancy. Animal studies have not found evidence of congenital malformations or any other complications. Again, the limited data precludes any conclusions regarding the potential gestational risk associated with these medications.

Conversely, animal studies with Janus kinase inhibitors have conclusively demonstrated fetal complications and malformations, which is consistent with the current absolute contraindication to their use during pregnancy.

Given the maternal and fetal risks, there have been no randomized clinical trials on this topic with any of the drugs of interest, which is a major limitation to generalization of our findings. The decision to continue therapy with biologics during pregnancy must be made on a case-by-case basis, considering the risk-benefit ratio for each patient. Further studies on this subject are needed to allow more evidence-informed clinical decisions in future.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Review Article

Mixed rhinitis: a new phenotype?

Rinite mista: um novo fenótipo?

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ABSTRACT

Rhinitis is not a homogeneous condition and can manifest in different subtypes, depending on the underlying pathophysiological mechanisms (endotypes) and clinical manifestations (phenotypes). Idiopatic rhinitis (IR) is the most prevalent subtype within the group of nonallergic rhinitis and requires the exclusion of allergic rhinitis (AR) as a diagnosis. Mixed rhinitis (MR) can be considered in patients who present symptoms after exposure to allergens and nonspecific stimuli, representing a combination of Nonallergic rhinitis (NAR) and AR. The PubMed, Google Scholar, EMBASE, and SciELO databases were searched for articles published in English, Portuguese, French, or Spanish in the last decade. The following search strategy was used: mixed rhinitis OR allergic rhinitis OR nonallergic rhinitis OR chronic rhinitis OR nasal irritants AND children OR adults. The prevalence of chronic rhinitis in the general population is estimated to be between 10% and 40%. Among adults, the prevalence of MR corresponds to 30% to 50% of these patients. In children with AR, 42.9% were classified as having MR. Clinically, MR manifests itself in more severe conditions, with worse control and a greater need for medication combinations. The use of a standardized and culturally validated instrument for the study population is essential for the identification of patients with MR, as well as for improving the understanding of this rhinitis endotype in terms of disease progression and pharmacological management.

Keywords: Rhinitis, allergic rhinitis, vasomotor rhinitis, irritants.

RESUMO

A rinite não é uma condição homogênea e pode se manifestar por diferentes subtipos, segundo os mecanismos fisiopatológicos subjacentes (endotipos) e manifestações clínicas (fenótipos). A rinite idiopática (RI) é o subtipo mais prevalente dentro do grupo das rinites não alérgicas e requer a exclusão da rinite alérgica (RA) como diagnóstico. A rinite mista (RM) pode ser considerada em pacientes que apresentam sintomas após exposição a alérgenos e estímulos inespecíficos, uma combinação de RI e RA. Os autores realizaram revisão narrativa de artigos publicados em inglês, português, francês e espanhol, na última década nas bases de dados PubMed, Google Scholar, EMBASE e SciELO. As palavras-chaves usadas nessa busca foram: *mixed rhinitis OR allergic rhinitis OR non allergic rhinitis OR chronic rhinitis OR nasal irritants AND children OR adults*. A prevalência de rinite crônica na população geral está estimada entre 10% e 40%; entre adultos, a prevalência de RM corresponde entre 30% e 50% desses pacientes. Em crianças com RA, 42,9% delas foram classificadas como tendo RM. Clinicamente, a RM manifesta-se por quadros mais graves de rinite, com pior controle e maior necessidade de associação de medicamentos. O emprego de instrumento padronizado e validado para a cultura da população em estudo é primordial para a identificação de pacientes com RM, além de permitir o melhor entendimento desse fenótipo de rinite com relação à evolução e controle medicamentoso.

Descritores: Rinite, rinite alérgica, rinite vasomotora, irritantes.

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Introduction

Rhinitis is an inflammatory condition of the mucous membrane of the nose, characterized by symptoms such as nasal congestion, runny nose, sneezing, and nasal itching.[1,2] It is one of the most common conditions in children and adolescents, significantly affecting their quality of life and general well-being.[3,4] In Brazil, it is estimated that more than one third of the population of children, adolescents, and adults have rhinitis, and its prevalence is increasing.[5,6]

Worldwide, rhinitis causes increased use of health services, poor quality of life, and low performance at work/school. Rhinitis is an independent risk factor for asthma, and several comorbidities may be involved in uncontrolled nasal symptoms: sinusitis, otitis media, eustachian tube dysfunction, chronic cough, obstructive sleep apnea, chronic headache, and fatigue.[7-9] The disease is also a risk factor for behavioral changes and learning difficulties in children.[4,10] Despite their impact, chronic forms of rhinitis have been trivialized and seen as nothing more than a nuisance, both by the general population and by health professionals.

Rhinitis is not a homogeneous condition and can manifest in different subtypes, depending on the underlying pathophysiological mechanisms (endotypes) and clinical manifestations (phenotypes), making it difficult to develop assertive guidelines for its diagnosis and treatment.[10]

Rhinitis classification

The most widely used and accepted classification system for rhinitis divides the disease into 3 main groups according to etiology[11]:

– *infectious rhinitis:* acute, self-limiting, and usually caused by viruses;
– *allergic rhinitis:* induced by a specific allergen in a patient with proven allergic sensitization; and
– *noninfectious and nonallergic rhinitis:* a heterogeneous group without allergic sensitization or signs of infection.

This classification system provides a useful framework for understanding the cause of rhinitis and guides appropriate treatment for each patient.

Infectious rhinitis is usually caused by viruses, its course is self-limiting, and treatment is based on symptom control.[12-15] Also called acute rhinosinusitis, it is characterized by inflammation of the nasal cavity and paranasal sinuses, causing runny nose, nasal obstruction/congestion, and facial pain. Coughing is a very common symptom, especially in children.[16]

Symptoms of uncomplicated viral rhinitis resolve in 7 to 10 days, with significant improvement after day 5. If symptoms persist after 10 days or worsen after a period of improvement, complications with secondary bacterial infection (acute bacterial rhinosinusitis) may be considered, and antibiotics may be indicated. *Streptococcus pneumoniae*, *Hemophilus influenzae*, and *Moraxella catarrhalis* are the most frequently involved bacteria in these cases. Coexisting allergic rhinitis (AR) may contribute to persistent nasal symptoms, hindering differential diagnosis with bacterial infection, which occurs in 5% to 13% of pediatric cases.[17,18]

In influenza virus infections, oseltamivir is indicated for at-risk patients (older adults, children < 2 years of age, and individuals with cardiac or respiratory comorbidities).[12,19] Topical corticosteroids may also be considered for their local anti-inflammatory action, especially in more severe cases. They act by neurogenic modulation, reducing edema and mucus production, thus contributing to symptom improvement.[18]

AR is a common, well-defined condition. It is triggered by an immunoglobulin E (IgE)-mediated response after inhalation of environmental allergens, such as pollen, dust mites, cockroach feces, animal dander, rodent dander, and fungi. AR is diagnosed when skin or serological tests demonstrate specific IgE in response to exposure to one or more allergens.[11]

Allergens inhaled through the nose are processed by antigen-presenting cells in the nasal mucosa and are then presented to TCD4+ lymphocytes. During the sensitization phase, T lymphocytes produce cytokines that stimulate the production of a specific IgE against the antigen. This IgE binds to high-affinity receptors on the surface of mast cells and basophils. Upon re-exposure to the allergen, the specific allergen peptides are recognized by IgE bound to mast cells and basophils, resulting in activation of a signaling cascade that leads to the release of preformed and newly synthesized mediators, such as histamine, leukotrienes, prostaglandins, and platelet activating factor. The late-phase reaction occurs approximately 4 to 12 hours after exposure to the allergen, with the release of chemokines that attract type 2 T helper cells, activated eosinophils, and mast cells to the nasal epithelium. These cells

release cytokines, such as interleukin (IL)-4, IL-5, and IL-13, as well as enzymes and other mediators, which perpetuate allergic inflammation, resulting in chronic symptoms such as nasal congestion and runny nose.[10] The response of type 2 T helper cells mainly involves eosinophils and IgE. However, type-2 innate lymphoid cells, which are also present in the nasal mucosa, can produce the same cytokine profile, contributing to local inflammation.[18]

According to the Allergic Rhinitis and its Impact on Asthma guidelines,[1] AR is classified based on symptom duration and severity, namely: mild intermittent, moderate-severe intermittent, mild persistent, or moderate-severe persistent.[1]

Furthermore, the sensitization pattern can be used to differentiate monosensitized vs polysensitized patients. This information can facilitate AR treatment, since polysensitized patients may require more aggressive and individualized treatment.[10]

Noninfectious, nonallergic rhinitis (NAR) is a chronic condition of the nasal mucosa that manifests predominantly with symptoms of nasal congestion and rhinorrhea, without evidence of allergic sensitization (ie, negative skin prick test and/or serum specific IgE). Although the most common symptoms are congestion and anterior and posterior rhinorrhea, other associated symptoms include throat clearing, cough, eustachian tube dysfunction, sneezing, decreased sense of smell, and facial pain/pressure. It is important to note that itchy eyes, throat, and ears are not common symptoms.[1]

NAR is not a single disease with a single underlying cellular mechanism, but rather a group of several different conditions that cause similar nasal symptoms. Some examples of these conditions include: drug-induced rhinitis, rhinitis in older adults, hormonal rhinitis, rhinitis during pregnancy, nonallergic occupational rhinitis, gustatory rhinitis, and idiopathic or vasomotor rhinitis (IR). Several tests may be involved when assessing patients suspected of NAR, such as skin tests, serum IgE levels, nasal provocation tests, pulmonary function tests, X-rays, or computed tomography.[20]

IR is the most prevalent subtype of the NAR group, requiring the exclusion of AR for diagnosis. Different studies have used varying terminologies to refer to this condition, including intrinsic rhinitis, IR, vasomotor rhinitis, and nonallergic rhinopathy. The pathophysiological mechanism of IR is unrelated to allergy, structural defects, or underlying systemic diseases, and it is usually not associated with nasal eosinophilia.[10]

IR symptoms include nasal congestion, runny nose, sneezing, and itchy nose. Treating IR can be challenging because the symptoms can be triggered by a variety of factors, including emotional stress, temperature changes, and alcohol consumption. Treatment options include medications such as decongestants, anticholinergics, and nasal steroids, as well as preventive measures such as avoiding known triggers.[21]

However, in addition to these 3 groups, there is another type: mixed rhinitis (MR), a specific subtype that combines characteristics of AR and NAR and has aroused increasing interest.[10,11]

MR may be considered for patients who present symptoms after exposure to allergens and nonspecific stimuli, a combination of NAR and AR. The degree to which chronic allergic inflammation contributes to hyperreactivity to other stimuli remains unknown, but, in any case, it is believed that other mechanisms trigger symptoms in this type of rhinitis.[7]

The specific endotypes of NAR are not yet fully understood, but the underlying mechanism is believed to be neurogenic.[10] A study assessing the nasal secretions of patients with AR, MR, and NAR in search of biomarkers that could distinguish the disease groups, found no differences in the investigated proteins and peptides. Patients with MR and AR had lower levels of IL-12 than those with NAR, but the groups could not be individually differentiated.[21] The lack of a distinct and consistent cellular inflammatory pattern in the nasal mucosa indirectly supports a neurogenic mechanism. Common symptom triggers include chemical irritants, such as strong odors, tobacco smoke, perfumes/fragrances, and cleaning agents, as well as changes in temperature, humidity, and atmospheric pressure. Other triggers may include changes in position, alcohol consumption, or eating habits.[10]

These irritants are thought to trigger the release of tachykinins, which, by inhibiting sympathetic mediators, result in increased parasympathetic response and nasal congestion and/or rhinorrhea. This neural/vascular pathophysiological mechanism has not yet been clearly documented, and it is now believed that some forms of NRA may be disorders of the non-adrenergic, non-cholinergic (NANC) nervous system.[10,22]

Innervation of the nasal cavity

The neural supply to the nasal mucosa consists primarily of autonomic fibers, including the sympathetic and parasympathetic systems, and NANC neurotransmission mediated by neuropeptides (Figure 1). The sympathetic and parasympathetic components of the autonomic nervous system contribute equally to the delicate homeostasis between vasoconstriction and vasodilation and nasal gland secretion. Imbalance among these components is likely to contribute to the glandular hypersecretion and increased nasal congestion observed in patients with NRA.[20]

Nasal sensory innervation comes from the ophthalmic and maxillary divisions of the trigeminal nerve and supplies the septum, lateral walls, the anterior nasal floor, and the inferior meatus. The parasympathetic fibers travel from their origin in the superior salivary nucleus of the midbrain to the geniculate ganglion, where they join the greater superficial petrosal nerve, which joins the deep petrosal nerve to form the vidian nerve. This nerve then passes to the sphenopalatine ganglion, where preganglionic parasympathetic fibers synapse and postganglionic fibers supply the nasal mucosa. The nasal glands receive direct parasympathetic nerve supply, and their electrical stimulation in animals induces glandular secretions that are blocked by atropine. Furthermore, stimulation of the human nasal mucosa with methacholine, a cholinomimetic drug, produces a marked increase in atropine production in nasal secretion. Stimulation of parasympathetic fibers also causes vasodilation.[20,22]

Sympathetic innervation originates as preganglionic fibers in the thoracolumbar region of the spinal cord, which pass through the vagosympathetic trunk and are relayed to the superior cervical ganglion. Postganglionic fibers also join the petrosal nerves to form the vidian nerve, which passes through the

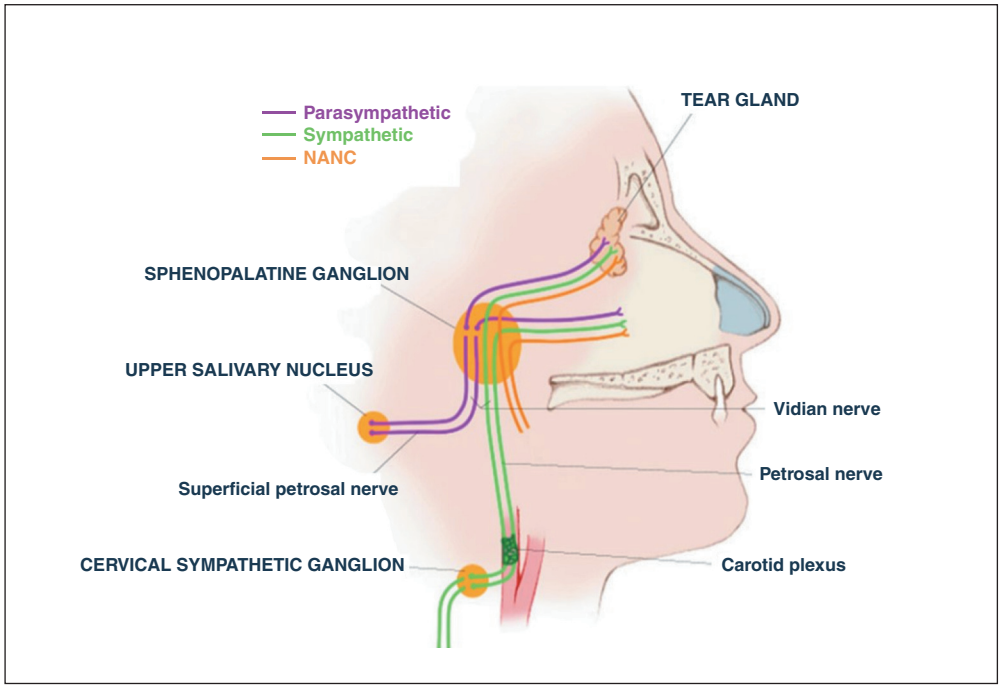

Figure 1
Sympathetic, parasympathetic and non-adrenergic non-cholinergic innervation of the nasal mucosa[22]
NANC = non-adrenergic, non-cholinergic.

sphenopalatine ganglion without synapses and is distributed in the nasal mucosa. Sympathetic fibers supply the nasal vasculature, but do not establish a direct relationship with the nasal glands; their exact role in secretion control is unclear. In animals, stimulation of these fibers causes vasoconstriction and decreases nasal airway resistance. Adrenergic agonists are also commonly used in humans, both topically and orally, to reduce nasal congestion.[20,22]

The presence of sympathetic and parasympathetic nerves and their transmitters in the nasal mucosa has been known for decades, but recent immunohistochemical studies have established the presence of additional neuropeptides. These neuropeptides are secreted by nociceptive unmyelinated C fibers (tachykinins, calcitonin gene-related peptide, neurokinin A, and gastrin-releasing peptide), parasympathetic nerve endings (vasoactive intestinal peptide [VIP] and histidine methionine peptide), and sympathetic nerve endings (neuropeptide Y). Substance P, a member of the tachykinin family, is frequently found as a cotransmitter with neurokinin A and calcitonin gene-related peptide, and high concentrations are present in blood vessels, glandular acini, and the nasal mucosal epithelium, where its receptors are located. High concentrations of calcitonin gene-related peptide receptors are found in small muscular arteries and arterioles of the nasal mucosa. The distribution of VIP fibers in human airways closely corresponds to that of cholinergic nerves. VIP is abundant in the human nasal mucosa, and its receptors are located in arterial vessels, submucosal glands, and epithelial cells, as is the case with substance P. In addition to identifying neuropeptides in the nasal mucosa, several studies have supported its potential contribution to nasal symptoms. VIP stimulates the secretion of serous cells, dilates nasal vessels, and can regulate mucociliary clearance in dogs. Nasal challenge with substance P induces few changes in normal individuals, but it causes a significant increase in vascular permeability, nasal airway resistance, and eosinophil and neutrophil chemotaxis in individuals with rhinitis.[10,20,22]

Nonspecific stimuli can cause the release of substance P, neurokinin A, VIP, and calcitonin gene-related peptide in the nasal mucosa, mainly through sensory C fibers, which are primarily activated by transient response potential (TRP) calcium ion channels, whose ligands are affected by temperature, mechanical or osmotic stimuli, and a wide variety of chemical irritants. For example, TRPV1, for which capsaicin has been shown to be a specific ligand, is activated by high temperatures. Acute exposure to capsaicin can activate TRPV1, whereas continued exposure to it can desensitize this receptor.[10] TRPA1 mediates the effects of noxious stimuli, such as low temperatures and environmental irritants. These channels have been increasingly recognized as an important mediator of nasal response to noxious chemical, mechanical, and osmotic stimuli.[20] These neuropeptides may also stimulate the release of histamine and other inflammatory mediators by local immune cells, resulting in additional IR symptoms, such as itching and sneezing.[22]

Mixed rhinitis

MR, characterized by the coexistence of AR and NAR, can occur in up to 85% of patients with AR and is more common than isolated types of the disease.[23] AR is triggered by exposure to aeroallergens, while NAR can be caused by factors such as weather changes and chemical irritants. MR presents with a combination of allergic and nonallergic symptoms, making its diagnosis and treatment challenging. Understanding the prevalence of MR and its associated factors in children and adolescents is essential for better treatment planning and improved quality of life.

Several studies have investigated the prevalence of MR in different populations, finding variable results. It is important to note that although this condition is relevant in all age groups, it is especially important to study its prevalence and impact on children and adolescents, since it can affect their development. Like all types of chronic rhinitis, MR can negatively affect school performance, sleep, and mental health in affected children and adolescents. Early identification of MR and adequate symptom control are essential to avoid short- and long-term complications. The presence of other respiratory disorders, such as asthma, has been associated with a higher risk of MR in children and adolescents.[24]

Another important aspect to consider is the influence of environment and lifestyle on MR. Factors such as exposure to environmental pollutants, passive smoking, inadequate diet and physical inactivity can contribute to the condition's development and worsening. Understanding these environmental determinants is crucial for effective prevention and treatment initiatives.

Triggering factors

In general, inadequate diet and physical inactivity can play an important role in the development and worsening of any chronic inflammatory disease. Excessive consumption of processed foods and foods rich in saturated fats, refined sugar, and additives, can lead to a chronic systemic inflammatory state, which can affect the upper airways and worsen rhinitis symptoms. Physical inactivity combined with an inadequate diet can lead to weight gain, overweight, and obesity. Excessive adiposity can also lead to changes in the immune system and chronic inflammation, which can exarcebate nasal symptoms.[25,26]

Conversely, diets rich in essential nutrients, such as vitamins, minerals, and antioxidants ensure proper immune function, reduce oxidative stress, and facilitate self-regulation of the inflammatory response.[26,27] Although a direct relationship between inadequate diet, physical inactivity, and rhinitis has not yet been established, a balanced nutrient-rich diet, and an active and healthy lifestyle can help reduce systemic inflammation, strengthen the immune system, and improve respiratory health, reducing rhinitis symptoms.[26]

Several agents and substances can act as direct irritants to the nasal mucosa, promoting local inflammation and worsening rhinitis symptoms. Goblet cells are a type of glandular cell in the nasal epithelium. They are responsible for the production and secretion of mucus, which helps moisten and protect the nasal passages. When the nasal mucosa is irritated, these cells can be stimulated to increase mucus production as part of the protective response, causing nasal congestion and rhinorrhea. The nasal epithelium is also lined with ciliated epithelial cells whose surface contains microscopic cilia. These cilia move in coordinated waves to help move mucus and foreign particles out of the nasal passages. In response to direct irritation of the nasal mucosa, the movement of cilia is increased in epithelial cells to remove irritants and protect the mucosa. However, this movement may decrease upon exposure to tobacco smoke. In both cases, harmony is lost and either the runny nose intensifies or allergens and other irritants can penetrate more easily.[28]

When a local inflammatory response occurs, several types of inflammatory cells are recruited to that area, including neutrophils, eosinophils, and mast cells. These cells release inflammatory mediators, such as histamine, leukotrienes, and cytokines, which act on vasodilation, increase vascular permeability, and activate other components of the immune system, amplifying inflammation.[28] Local chronic inflammatory response can also lead to remodeling of the nasal mucosa.[16]

Mold is a main trigger of rhinitis symptoms and can produce symptoms through allergic and non-allergic responses. Mold spores contain proteins that function as allergens. In sensitized individuals, specific IgEs on the surface of mast cells and basophils bind to these proteins, causing mast cell degranulation and histamine release, which determine the appearance of allergic nasal symptoms. In addition to allergic reactions, contact with mold spores can directly irritate the epithelial cells of the nasal mucosa, leading to local inflammation. Some types of fungi also release mycotoxins, which also cause direct toxic effects on epithelial cells. These response types and sensitization to mold spores can vary between individuals, and symptom severity may depend on factors such as the concentration of mold spores present in the environment and the duration of exposure.[28,29]

Weather changes, which can play a significant role in triggering nasal symptoms, involve variations in temperature, humidity, and air pollutant concentrations. High temperatures and humidity can trigger the direct release of inflammatory mediators by mast cells, such as histamine, causing local vasodilation, increased mucus production, and nasal congestion.[30,31] However, low humidity or exposure to air pollutants can affect the function of the epithelial cells lining the nasal mucosa. Exposure to pollutants can also result in the excessive migration and activation of inflammatory cells, such as eosinophils and type 2 T helper cells. Sensory receptors can also detect changes in temperature, humidity, and other environmental characteristics, influencing airflow regulation, mucus production control, and sneeze reflex response.[32] Some individuals may be more sensitive to certain weather factors than others. It is also important to consider the complex interplay between weather factors and other triggers, such as allergens and irritants.[28]

Many cleaning products contain irritating chemicals, such as bleach, ammonia, acids, and solvents, which act as direct irritants to the nasal mucosa. When these products are used, their volatile chemicals are released into the air and are inhaled, causing irritation and inflammation of the nasal epithelium.

Chronic exposure to these harsh chemicals can lead to chronic rhinitis.[28]

Active or passive exposure to tobacco smoke has detrimental effects on the nasal epithelium. Tobacco smoke contains many irritants and toxic substances, such as nicotine, tar, and carbon monoxide. When inhaled, these agents can directly irritate the nasal epithelium, affecting its integrity and function. As mentioned previously, exposure to tobacco smoke also causes reduced ciliary movement. This can result in less effective removal of mucus and harmful particles from the respiratory system, an increased risk of infection, and easier penetration of allergens and irritants, exacerbating nasal symptoms. Exposure to tobacco smoke can also stimulate increased mucus production. Smoking compromises nasal epithelial function and the overall health of the respiratory system, including the lungs.[28]

Diagnosis

Chronic rhinitis is a very common disease with increasing incidence, especially in Western countries, where the actual prevalence is estimated to be 10%-40% in the general population. Despite this epidemiological burden, the disease is usually considered mild and underestimated.[33] Despite the classic distinction between AR and NAR, thousands of patients meet the diagnostic criteria for AR but have symptoms triggered by primary irritants in addition to allergens, which suggests neural and vascular involvement. For these patients, a diagnosis of MR has been considered, which could apply to 30% to 50% of patients with chronic rhinitis.[24] In these cases, inflammation of the nasal mucosa is exacerbated by IgE-mediated response to allergens, in addition to the entire cascade of neural stimuli described above. Exposure to NAR triggers is difficult to control without depending heavily on the patient's attitude. It is also difficult to control exposure to inhalant allergens, such as dust mites and other aeroallergens. Therefore, controlling NAR symptoms becomes even more challenging. Understanding the cellular mechanisms involved in nasal reactions to irritants is essential for developing appropriate prevention and management strategies to minimize their negative impact on respiratory health.

In an attempt to identify patients with a high response to primary irritants, in 2012, Bernstein et al. developed the Irritant Index Questionnaire.[7] In a population of > 300 adults, the results of this instrument led to reclassifying 25% of those previously diagnosed with AR as having MR. Patients with MR had a higher frequency of symptoms, greater severity, and a higher occurrence of sinusitis and asthma than those who remained diagnosed with AR.[7]

Although the prevalence of NAR in children is unknown, it is estimated that the ratio of NAR to AR is at least 1:3.[34,35] It is known that some of these patients must represent the MR subgroup, but no study has evaluated pediatric populations regarding this diagnosis.[33]

In the Brazilian population, especially children and adolescents, no study has investigated the role of primary irritants as triggers of nasal symptoms. Chronic rhinitis, which is associated with more persistent symptoms, is an important cause of morbidity and affects several aspects of daily life in all age groups, including children and adolescents. An instrument measuring the magnitude of the action of primary irritants as triggers of nasal symptoms has proven effective for assessing chronic rhinitis in adults.[7] It is necessary to understand and quantify the role of primary irritants as a cause of nasal symptoms among children and adolescents.

Nasal irritant questionnaire to identify mixed rhinitis

Based on Bernstein et al.'s Irritant Index Questionnaire,[7,35] our group developed a questionnaire including all of the above mentioned irritants, in addition to several common to our population (makeup, hair dye, nail polish, artificial nail glue, deodorant, fabric softener, and e-cigarette smoke), totaling 27 items, including the following irritants: perfume, hair spray, cosmetics, bleach, washing powder, ammonia, disinfectant, solvent, paint, sawdust, gas stations, cold air, weather changes, cigarette smoke, mold or mildew, periods of severe air pollution, recently printed newspaper, kitchen odors, varnish, and household cleaning products, in addition to the list in parentheses above.[36]

In a pilot study, we asked 40 patients with AR whether they reported discomfort or not when exposed to these irritants. Items receiving < 20% affirmative responses were excluded. This resulted in our Nasal Irritant Questionnaire (Figure 2).[36] To better assess the role of these agents in the final questionnaire, it was decided to increase

NASAL IRRITANT QUESTIONNAIRE

Do you sneeze or have an itchy, runny, or stuffy nose when you come into contact with the following substances? Mark an "X" on the score you give for your symptoms:
0 is no symptoms at all and **10** is unbearable (the worst possible)

	0	1	2	3	4	5	6	7	8	9	10
1) Changes in the weather?	0	1	2	3	4	5	6	7	8	9	10
2) Wall paint or varnish?	0	1	2	3	4	5	6	7	8	9	10
3) Mold or damp indoor spaces?	0	1	2	3	4	5	6	7	8	9	10
4) Cigarette smoke?	0	1	2	3	4	5	6	7	8	9	10
5) E-cigarette or hookah (bong) smoke?	0	1	2	3	4	5	6	7	8	9	10
6) Sawdust?	0	1	2	3	4	5	6	7	8	9	10
7) Severe air pollution (fire, smoke)?	0	1	2	3	4	5	6	7	8	9	10
8) Cold air, cold wind, or air conditioning?	0	1	2	3	4	5	6	7	8	9	10
9) Perfumes?	0	1	2	3	4	5	6	7	8	9	10
10) Paint thinners or acetone?	0	1	2	3	4	5	6	7	8	9	10
11) Bleach or chlorine?	0	1	2	3	4	5	6	7	8	9	10
12) Cleaning products (air fresheners, floor wax)?	0	1	2	3	4	5	6	7	8	9	10
13) Disinfectants?	0	1	2	3	4	5	6	7	8	9	10
14) Ammonia (including hair bleach and dye)?	0	1	2	3	4	5	6	7	8	9	10
15) Cosmetics (lotions) or makeup?	0	1	2	3	4	5	6	7	8	9	10
16) Fabric softener?	0	1	2	3	4	5	6	7	8	9	10
17) Washing powder?	0	1	2	3	4	5	6	7	8	9	10
18) Deodorants?	0	1	2	3	4	5	6	7	8	9	10

Eight or more questions with scores ≥ 5 = **HIGH RESPONSE TO NASAL IRRITANTS**
Fewer than 8 questions with scores ≥ 5 = **LOW RESPONSE TO NASAL IRRITANTS**

Figure 2
Nasal Irritant Questionnaire[36]

the granularity of the responses, changing the options to a numerical scale from 0 to 10, with 10 corresponding to the worst possible reaction. Using the same evaluation criteria as for visual analogue scales, scores ≥ 5 for each question were considered significant. For patients with a high response to irritants (≥ 8 items that scored ≥ 5), an MR diagnosis was considered.[36]

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Original Article

Prevalence of anaphylaxis among individuals with allergic diseases in the state of São Paulo, southeastern Brazil, through an online questionnaire

Prevalência de anafilaxia entre indivíduos portadores de doenças alérgicas no estado de São Paulo através de questionário online

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ABSTRACT

Introduction: Anaphylaxis is a severe, potentially fatal systemic reaction, making rapid and accurate diagnosis essential for adequate treatment. Despite the seriousness of the condition, studies focusing on its prevalence in Brazil are scarce, limiting the understanding of its real impact and hindering the planning of preventive measures for anaphylaxis in the country. This study aimed to contribute to the understanding of the prevalence of anaphylaxis in individuals with allergic diseases in the state of São Paulo, southeastern Brazil. **Methods:** The study was conducted using the digital platform Google Forms, with anonymous participation from residents of the state of São Paulo, and was previously approved by the Research Ethics Committees of the involved institutions. Two validated questionnaires were disseminated through social media, targeting individuals up to 7 years old and those older than that age. **Results:** A total of 309 questionnaires were collected from individuals aged 7 years or older who reported having an allergy. Based on suggestive anaphylaxis scores, 46 individuals (14.9%) were potentially anaphylactic. The reported causes were medications (56.5%), foods (47.8%), insect stings (26.0%), latex (4.3%), and undetermined (4.3%). Other diagnoses included rhinitis (60.8%), dermatitis or eczema (41.3%), asthma (30.4%), and isolated anaphylaxis (30.4%). Among children up to 6 years, 11 months, and 29 days, 84 questionnaires indicated allergies, with 21.4% showing suggestive scores of anaphylaxis. The causes in this group were foods (72.2%), insect stings (22.2%), and medications (22.2%). Dermatitis was reported in 38.8% of the questionnaires, asthma in 55.5%, rhinitis in 44.4%, and isolated anaphylaxis in

RESUMO

Introdução: Anafilaxia é uma reação sistêmica grave potencialmente fatal, sendo fundamental um diagnóstico rápido e preciso para que o tratamento seja realizado de forma adequada. Apesar da gravidade da doença, os estudos voltados para sua prevalência no Brasil são escassos, limitando o conhecimento do real impacto e dificultando o planejamento de medidas preventivas para a anafilaxia no país. Este estudo objetiva, assim, contribuir para o conhecimento da prevalência da anafilaxia em indivíduos portadores de algum tipo de doença alérgica no estado de São Paulo. **Métodos:** O estudo foi realizado através da plataforma digital Google Forms com envolvimento anônimo dos participantes residentes do estado de São Paulo, previamente aprovado pelos Comitês de Ética em Pesquisa das instituições envolvidas. Foram divulgados, através de mídias sociais, dois questionários validados direcionados a indivíduos com até 7 anos e acima dessa idade. **Resultados:** Foram obtidos 309 questionários de indivíduos com sete anos ou mais que referiam ter algum tipo de alergia. Através dos escores sugestivos de anafilaxia, obteve-se 46 pessoas (14,9%) possivelmente anafiláticas. Entre estas, as causas foram medicamentos em 56,5%, alimentos em 47,8%, ferroadas de insetos em 26,0%, látex em 4,3%, e indeterminado em 4,3%. Outros diagnósticos: rinite, 60,8%; dermatite ou eczema, 41,3%; asma, 30,4%; diagnóstico isolado de anafilaxia, 30,4%. Entre crianças de até 6 anos 11 meses e 29 dias, 84 questionários referiram alergia, sendo que 21,4% apresentaram escores sugestivos de anafilaxia, cujas causas foram: alimentos em 72,2%, insetos em 22,2%, e medicamentos em 22,2%. Dermatite apareceu em 38,8% dos questionários, asma em 55,5%, rinite em 44,4%, e anafilaxia

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5.55%. **Conclusion:** Anaphylaxis is not a rare condition among individuals with atopy, especially in young children. The causes of anaphylaxis reported were similar to those found in the medical literature, with medications predominating in the older population and foods being more common in children.

Keywords: Prevalence, epidemiology, anaphylaxis, precipitating factors, allergens.

isoladamente em 5,55%. **Conclusão:** A anafilaxia não é doença rara entre portadores de atopia, especialmente nas crianças pequenas, e as causas foram similares às referidas pela literatura médica, predominando medicamentos na população mais velha, e alimentos nas crianças.

Descritores: Anafilaxia, epidemiologia, fatores desencadeantes, prevalência, alérgenos.

Introduction

Anaphylaxis is a severe, acute, potentially life-threatening systemic reaction triggered by a hypersensitivity mechanism. Anaphylaxis is characterized by the sudden onset of systemic clinical symptoms, which may progressively or simultaneously affect multiple systems, including the skin, mucous membranes, respiratory and cardiovascular systems, central nervous system, and gastrointestinal tract.[1] A later study showed high sensitivity for these diagnostic criteria, with moderate specificity. This indicates that while the criteria are extremely useful, the diagnosis may be overestimated in nearly 20% of cases.[2] The World Allergy Organization (WAO) has recently defined new clinical criteria to help diagnose anaphylaxis in both adults and children.[3] The goal of simplifying these criteria is to allow faster recognition of anaphylactic reactions, as experts agree that the condition is becoming more common, especially in the pediatric population.[4]

The triggers of anaphylaxis vary depending on age group and population habits. Food is the most common cause in children, adolescents, and young adults, and it has been identified as the main factor responsible for the increase in incidence in recent years. In contrast, medications, insect venom, and idiopathic anaphylaxis are more frequently seen in older patients.[5]

In Brazil, research on the epidemiology of anaphylactic reactions is still limited. The causative agents appear to be similar to those reported in international medical literature, with medications, food, and insects being the most common triggers.6 Given the challenges of conducting epidemiological studies in the country, Gagete et al.[7] proposed a new tool for population-based studies on anaphylaxis and its potential causes.

Online surveys and social media are part of today's reality, especially in the post-COVID-19 world. The Internet is a powerful tool that brings people and ideas together and can be useful for gathering relevant data. Thus, the present study aimed to assess the prevalence of anaphylaxis and its main triggers among individuals in the state of São Paulo, southeastern Brazil, who have any diagnosis of "allergy." Data were collected using a standardized questionnaire distributed electronically through various social media platforms.

Methods

The validated and standardized questionnaire developed by Gagete et al.[7] was sent electronically to Internet users, without requiring participant identification. This tool separates individuals aged 7 years and older (Q.1 questionnaire) from children aged 0 to 6 years, 11 months, and 29 days (Q.2 questionnaire), with each version tailored specifically to the age group. The forms were created using the Google Forms platform. This platform allows respondents to view each question one at a time, with new questions appearing as previous ones are answered, while earlier ones are hidden. It also automatically organizes responses into an Excel spreadsheet, facilitating later data analysis. Each questionnaire contains multiple questions and subquestions based on anaphylaxis diagnostic criteria, which are described in greater detail in the original publication.[7] In summary, the questions address symptoms, symptom progression, whether the diagnosis was made by a specialist, and the triggering factors. Responses are assigned positive and negative scores, and the total score indicates the likelihood of an individual having experienced anaphylaxis. To avoid bias associated with the word "anaphylaxis," considering that many different terms are used to describe the condition (such as "glottic edema," "giant urticaria," "cow's milk protein allergy," etc.), the questionnaire does not mention anaphylaxis as the focus; instead, it uses the broader term

"allergy." This approach encourages a wider range of allergic individuals to respond. As a result, the questionnaire includes negatively weighted questions for the differential diagnosis between anaphylaxis and other conditions such as severe asthma and acute urticaria.

The link to the questionnaires, along with an explanatory letter, was distributed through the following channels:

– all email contacts registered by the project authors;
– social media platforms such as WhatsApp, Facebook, and Instagram belonging to the project authors;
– respondents were also asked to share the questionnaire with their own contacts.

The Prática Clínica platform was used for sample size calculation,[8] considering a 5% margin of error, a 95% confidence level, and a maximum estimated prevalence of 6%. The sample size was calculated based on the population of the state of São Paulo, which is approximately 44 million according to the 2022 census,[9] resulting in a required sample size of 87 individuals. However, for this study, we considered 87 to be the minimum sample size and included in the analysis all questionnaires collected over the 6-month study period (from June to December 2022). The study was approved by the Research Ethics Committee (CEP USP) of the Hospital das Clínicas, School of Medicine, University of São Paulo – HCFMUSP (CAAE 45043621.2.0000.0068).

Results

A total of 309 Q.1 questionnaires were collected from individuals who reported being "allergic," with ages ranging from 7 to 81 years. Additionally, 84 Q.2 questionnaires were completed for children whose respondents reported some type of allergy.

Regarding Q.1 questionnaires, 46 individuals (14.9%) scored within the range indicating a possible diagnosis of anaphylaxis. Of these, 36 (78.3%) were female. The reported triggers for these 46 individuals included: medications, 26 (56.5%); food, 22 (47.8%); insect stings (bee, wasp, or ant), 12 (26.0%); latex, 2 (4.3%); and unknown causes, 2 (4.3%) (Figure 1). The total number exceeds 46 because some respondents reported multiple reactions triggered by different agents. Other diagnoses reported among these individuals with possible anaphylaxis included: rhinitis, 28 (60.8%); dermatitis or eczema, 19 (41.3%); asthma, 14 (30.4%); and isolated diagnosis of

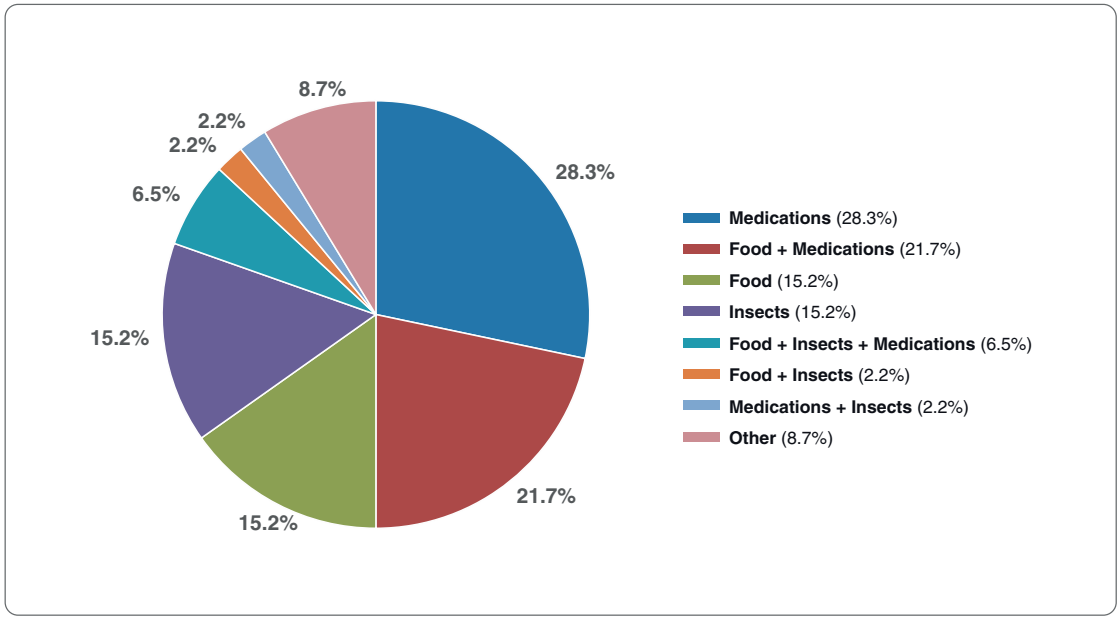

Figure 1
Reported causes of anaphylaxis in Questionnaire 1

anaphylaxis, 14 (30.4%). Among the 26 respondents who identified medications as the cause, nonsteroidal anti-inflammatory drugs (NSAIDs) were reported as the trigger in 18 cases (69.2%), antibiotics in 3 cases (11.5%), and muscle relaxant, vitamin, and vaccine in 1 case each (3.8% each). One respondent did not identify the medication involved (3.8%). Among the 22 respondents who identified food as a trigger, the breakdown was as follows: milk, 10 (45.4%); seafood, 6 (27.2%); egg, 4 (18.1%); fish, 2 (9.0%); and tree nuts, peanut, sesame, fruit, sunflower seed, and wheat, 1 each (4.5% each).

Among the 46 individuals with possible anaphylaxis, 33 (71.7%) reported that a physician confirmed the diagnosis through tests and/or examinations. Of these 46 patients, 5 reported that they had never received a medical diagnosis of the condition (or a related term such as "glottic edema" or "giant urticaria"). Regarding the number of episodes, 6 respondents reported only 1 episode; 8 had 2 episodes; 3 had 3 episodes; and 29 had 4 or more episodes.

Regarding Q.2 questionnaires, of 84 respondents indicating allergy, 18 had scores suggestive of anaphylaxis (21.4%). The reported triggers included: food, 13 (72.2%); insect stings, 4 (22.2%); and medications, 4 (22.2%). Asthma was reported in 10 questionnaires (55.5%), dermatitis in 7 (38.8%), rhinitis in 8 (44.4%), and an isolated diagnosis of anaphylaxis in 1 (5.55%). Of the 18 individuals with probable anaphylaxis, 9 were female (50.0%) and 9 were male (50.0%). For food-related causes of probable anaphylaxis, the following were reported: milk in 8 individuals (61.3%), egg in 3 (23.0%), tree nuts in 2 (15.3%), wheat in 1 (7.6%), food dye in 2 (15.3%), peanut in 4 (30.7%), fish in 2 (15.3%), and soy in 2 (15.3%). The number of reported causes is greater than the number of individuals because 5 of them indicated more than one trigger (Figure 2).

Among insect-related cases, 1 respondent reported a bee sting, 2 reported mosquito bites, and 2 reported ant stings. Regarding the 4 respondents who identified medications as the cause, 3 reported antibiotics. The respondents for all 15 children with probable anaphylaxis stated that a physician had confirmed the etiology. As for the number of episodes, the responses were as follows: 2 individuals (11.1%) reported only 1 episode; 4 (22.2%) reported 2 episodes; 2 (11.1%) reported 3 episodes; and 10 (55.5%) reported 4 or more episodes of possible anaphylaxis.

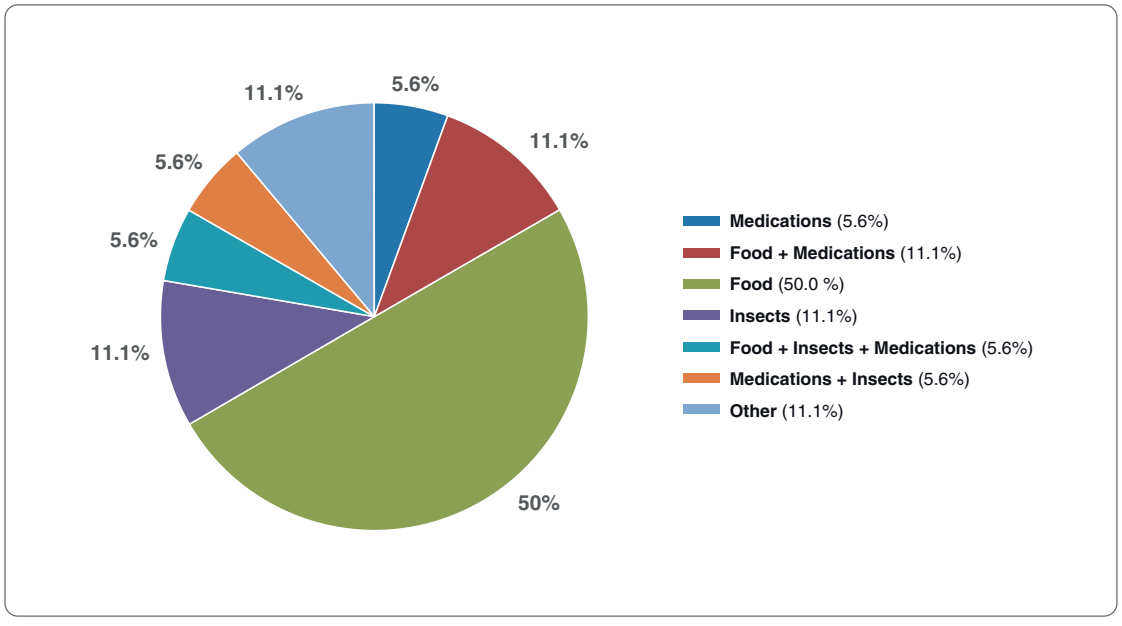

Figure 2
Reported causes of anaphylaxis in Questionnaire 2

Discussion

Anaphylaxis is a medical emergency where etiological diagnosis and patient guidance are the responsibility of allergist specialists. Anaphylactic reactions have been on the rise for reasons that are not yet fully understood,[10] making the study of this condition increasingly important. In Brazil, self-injectable epinephrine is still not available, despite being considered the cornerstone of self-management during an anaphylactic reaction while waiting for medical care. The reasons for the lack of approval of this device in the country remain unclear. However, one possible explanation may be the limited number of epidemiological studies demonstrating the need for such a resource in the Brazilian population.

Conducting epidemiological studies poses many challenges, especially concerning anaphylaxis, since the term "anaphylaxis" was not included in the International Classification of Diseases (ICD) until its 11th edition. Previous studies have shown that several ICD-9 codes suggestive of allergic reactions in the medical records of children treated in emergency settings — when later reviewed based on presented symptoms — were actually cases of anaphylaxis. However, these cases were recorded with diagnoses such as "unspecified allergic reaction" (999.3), "adverse food reactions" (995.7), and "allergic urticaria" (708.0), among others. This issue persists in ICD-10, which includes only codes such as "unspecified allergy" (T78.4), "personal history of allergy" (Z88.0 to Z91.0), and "anaphylactic shock" (T78.0, T78.2, T80.5, and T88.6).[11] However, ICD-11 explicitly includes the term "anaphylaxis," and once this new classification system is fully implemented, it will certainly facilitate epidemiological research.[12]

Questionnaires are widely used in epidemiological studies, despite challenges related to respondents' understanding of the content. These tools have proven useful in many areas of medicine, particularly in allergy and immunology. Well-known examples include the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire[13] and the online Latin American survey on anaphylaxis (OLASA).[14] The latter study, which involved several Latin American countries including Brazil, identified medications as the predominant triggers of anaphylactic reactions, especially NSAIDs and antibiotics. Food was the second most frequent cause, with common triggers including fish, milk, fruits, wheat, peanuts, egg, tree nuts, and cassava. Other causes reported were insect venom, immunotherapy, latex, exercise, and iodinated contrast agents. Other studies in Latin America have also used questionnaires to identify food-related anaphylaxis.[15-17] In Brazil, a recently published research protocol outlines a study that will use a questionnaire to investigate the prevalence of self-reported food allergies in older adults.[18] Additionally, Gagete et al., using a validated questionnaire, reported a 6.2% prevalence of anaphylaxis in the city of Botucatu, state of São Paulo, southeastern Brazil, where medications were the main cause, especially metamizole.[7] Sousa et al., using the same instrument in children and adolescents in the city of Imperatriz, state of Maranhão, northeastern Brazil, found a 5.78% prevalence of anaphylaxis.[19]

In this study, we used previously standardized questionnaires to investigate the prevalence of anaphylaxis among Internet users in the city of São Paulo who reported having some type of allergy. The prevalence rate was 14.9% with the Q.1 questionnaire and 21.4% with the Q.2 questionnaire. These rates are significantly higher than those previously reported in the general population using the same instruments. This may reflect a higher prevalence of anaphylaxis among individuals with preexisting allergic conditions, as these conditions may increase the likelihood of developing anaphylaxis.[20] There is also evidence supporting a positive correlation between anaphylaxis and a prior allergic condition.[21]

Our data also show that, among older children and adults (Q.1 questionnaire), medications were the most common triggers of anaphylactic reactions, followed closely by food. In contrast, among younger children (Q.2 questionnaire), food was clearly the leading cause of anaphylaxis, which is consistent with findings from previous studies conducted in Brazil and worldwide.[14,22] Another noteworthy finding is that 5 Q.1 respondents scored very high for symptoms, suggesting possible anaphylaxis even though no formal diagnosis of anaphylaxis had been made. While this could be a false positive, the lack of follow-up with respondents suggests that the study population may not have received proper guidance on when to seek specialist care for accurate diagnosis and treatment. This becomes even more evident considering that most respondents reported experiencing more than 1 episode, with 29 individuals indicating they had experienced 4 or more possibly anaphylactic reactions. It is likely that these individuals have not received proper guidance on how to prevent future episodes of anaphylaxis.

Questionnaire-based population studies face several challenges. A significant challenge is motivating individuals to respond to electronically distributed surveys, especially given the routine nature of such communications today. We should consider the potential for bias, as individuals with more severe allergies or those who have experienced more severe episodes may be more inclined to participate. However, the use of symptom scores and cutoff points for the diagnosis of possible anaphylaxis can help identify individuals who might otherwise remain undiagnosed, since many are mislabeled or do not consult specialists. Another challenge is ensuring respondents fully understand the questions. In a country where public education is increasingly inadequate, questionnaires are likely to be answered primarily by the more educated segment of the population, which can lead to results that do not represent all social classes. Moreover, conducting surveys online assumes that respondents have access to a mobile device and an Internet connection, which is still not a reality for the entire population.

Despite the challenges, epidemiological studies are essential to understand the true impact of anaphylaxis on the Brazilian population. Further research is needed to increase awareness of this important condition among the public, health professionals, and health authorities.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Original Article

Prevalence of sensitization to contact allergens in Brazil

Prevalência de sensibilização a alérgenos de contato no Brasil

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ABSTRACT

Introduction: Allergic contact dermatitis is a subtype of contact dermatitis triggered by immunological mechanisms. Patch testing is the gold-standard diagnostic method, and the screening series used should include the most prevalent and relevant haptens for each population. This study aimed to determine the prevalence of sensitization to the contact allergens of the Brazilian baseline series used in clinical practice among patients with suspected contact dermatitis. **Methods:** This was a cross-sectional observational study of patch tests using the Brazilian baseline series of 30 substances in patients with suspected contact dermatitis. **Results:** Of 2996 patch tests performed, 2054 (68.6%) were positive for at least 1 allergen, and 31.4% were negative for all allergens. The most frequently positive allergens were nickel sulfate (29.9%), thimerosal (16%), cobalt (15.3%), fragrance mix (15.1%), and balsam of Peru (8.6%). **Conclusion:** Nickel was the most common cause of contact sensitization in our Brazilian population. However, in approximately 30% of patch tests, the causative substance was

RESUMO

Introdução: A dermatite de contato alérgica é um subtipo de dermatite de contato, desencadeada por mecanismos imunológicos. O teste de contato é o procedimento diagnóstico padrão ouro, e a bateria empregada deve basear-se em uma série de haptenos mais prevalentes e relevantes para cada população. O objetivo do estudo foi conhecer a prevalência de sensibilização aos alérgenos da bateria padrão brasileira, utilizados na prática clínica, em pacientes com suspeita de dermatite de contato. **Métodos:** Estudo transversal observacional de testes de contato com a bateria padrão brasileira composta por 30 substâncias em pacientes com suspeita de dermatite de contato. **Resultados:** Entre os 2.996 testes de contato realizados, 2.054 (68,6%) foram positivos a pelo menos um alérgeno, e 31,4% foram negativos a todos os alérgenos. Os mais frequentemente positivos foram: sulfato de níquel (29,9%), timerosal (16%), cobalto (15,3%), perfume mix (15,1%), e bálsamo-do-peru (8,6%). **Conclusão:** O níquel permanece como causa mais frequente de sensibilização de contato na

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not identified. Studies on the prevalence of sensitization to contact allergens should be conducted in different populations to assess changes over time.

Keywords: Contact dermatitis, allergic contact dermatitis, nickel, haptens, epidemiologic studies.

nossa população. Entretanto, em cerca de 30% dos testes não foi identificada a substância causadora da doença. Estudos para conhecer a prevalência de sensibilização aos alérgenos de contato devem ser realizados de forma seriada em diferentes populações para avaliar as mudanças ao longo do tempo.

Descritores: Dermatite de contato, dermatite alérgica de contato, níquel, haptenos, estudos epidemiológicos.

Introduction

Contact dermatitis (CD) is a common inflammatory skin disease that affects approximately 20% of the general population.[1,2] It occurs after skin exposure to an exogenous substance, which can be either an allergen or a nonspecific irritant.[3] CD is subdivided into allergic CD (ACD) and irritant CD (ICD), with the latter being more common (up to 80% of CD cases).[1,2] ACD is triggered by a type IV delayed hypersensitivity reaction to a contact allergen in previously sensitized individuals, while ICD is triggered by non-immunological mechanisms.[1] These two types of dermatitis are clinically indistinguishable.

A patch test (also known as an epicutaneous test) is the gold-standard diagnostic method for identifying allergens that cause ACD. Patch testing should be performed according to international guidelines and best practice recommendations.[4] In 2023, the Brazilian Association of Allergy and Immunology (ASBAI) conducted an online survey of 223 associates, and the results showed that 98.7% of them treat patients with CD and 81.2% perform patch tests on their patients.[5]

According to De Groot,[6] approximately 5200 substances have been catalogued as potential causative agents of CD (known as haptens or contact allergens), but it is impractical to test for all of them. The prevalence of sensitization to contact allergens is continuously changing, reflecting both lifestyle changes and new industrial products.[7] In addition to time trends, geographical differences in exposure and sensitization prevalences have been observed.[7]

Given the changing trends of contact allergens, the American Contact Dermatitis Society created the "Allergen of the Year" award in 2000 to draw attention to emerging and under-recognized allergens that require surveillance as well as those that have become obsolete and clinically irrelevant.[8]

Within this context, in the 1980s it was determined that each country should have its own standard battery of regional allergens for systematic screening in patch tests.[9] However, the term "baseline series" (BS) is currently preferred over "standard battery," as the latter is insufficient to diagnose all contact allergies. Patch testing can be complemented to include allergens of local importance, which are determined based on exposure type and personal history.[9]

In 2000, the Brazilian Contact Dermatitis Study Group developed the Brazilian BS (BBS), which includes 30 substances.[10] This series has been a reference for dermatologists and allergists across Brazil since its creation, but it has never been updated.[10] In 2013, the Ibero-Latin American College of Dermatology developed the Latin American BS, consisting of 40 substances and incorporating several emerging allergens and more appropriate concentrations and vehicles. It became commercially available in Brazil as a supplemental series of allergens in November 2020.[11]

The composition of any BS of contact allergens should be reviewed and updated periodically in each country to more accurately reflect changes in exposure and sensitization over time, removing obsolete allergens and including emerging ones.[12]

Decisions about which haptens to retain or remove from the BS should be based on objective data concerning sensitization frequency, hence the importance of identifying the prevalence of positive reactions to contact allergens in the BS, as well as their clinical relevance.[11] Weak allergens with low rates of sensitization but high rates of exposure should be retained or included. Conversely, haptens with high sensitization rates but low clinical relevance should be removed. As a general rule, a contact allergen should demonstrate a sensitization prevalence of at

least 0.5% to 1% in the local population to be included in a BS.[11]

The aim of this study was to determine the prevalence of sensitization to the contact allergens of the BBS used in clinical practice among Brazilian patients with suspected ACD.

Methods

This retrospective cross-sectional observational study was conducted by members of the ASBAI Scientific Department of Contact Dermatitis and 4 training centers for allergy and immunology specialists registered with ASBAI between 2006 and 2021. The 30-substance BBS (FDA Allergenic Ltda.; IPI-ASAC do Brasil) was used for patch testing (Table 1).

A total of 2996 patch tests were performed, distributed as follows: 57 in the Immunology Department of the School of Medicine – Universidade de Passo Fundo, state of Rio Grande do Sul; 829 at Hospital Universitário Pedro Ernesto, affiliated with Universidade do Estado do Rio de Janeiro, state of Rio de Janeiro; 845 in the Unit of Skin Allergy and

Table 1
List of contact allergens from the Brazilian baseline series and positivity in the patch test (N = 2996)

Allergen	N (%)
Nickel sulfate 5%	898 (29.9)
Thimerosal 0.1%	480 (16.0)
Cobalt chloride 1%	457 (15.3)
Fragrance mix 7%	452 (15.1)
Balsam of Peru 25%	258 (8.6)
Potassium dichromate 0.5%	257 (8.5)
Neomycin sulfate 20%	222 (7.4)
Methylchloroisothiazolinone/methylisothiazolinone 0.5%	222 (7.4)
p-phenylenediamine (PPD) mix 0.4%	206 (6.9)
p-phenylenediamine 1%	204 (6.8)
Formaldehyde 1%	184 (6.1)
Carba mix 3%	146 (4.9)
Colophony 20%	93 (3.1)
Paraben mix 15%	90 (3.0)
Epoxy resin 1%	83 (2.8)
Turpentine 10%	83 (2.8)
Ethylenediamine 1%	80 (2.7)
Hydroquinone 1%	79 (2.6)
Promethazine 1%	79 (2.6)
Thiuram mix 1%	77 (2.6)
Benzocaine 5%	74 (2.5)
Quaternium-15 1%	55 (1.8)
Quinoline mix 6%	46 (1.5)
Nitrofurazone 1%	41 (1.4)
Propylene glycol 10%	39 (1.3)
Lanolin 30%	37 (1.2)
p-tert-butylphenol 1%	33 (1.1)
Anthraquinone 2%	30 (1.0)
Triclosan 1%	30 (1.0)
Mercapto mix 2%	29 (0.9)

Immunology at the Dermatology Institute Professor Rubem David Azulay – Santa Casa da Misericórdia do Rio de Janeiro, state of Rio de Janeiro; and 1265 in the Unit of Allergy and Immunology of the Department of Pediatrics and Pediatric Surgery of the São José do Rio Preto School of Medicine, state of São Paulo.

Readings of patch test results were performed at 48 h and at 96 h, according to the International Contact Dermatitis Research Group (ICDRG) guidelines, and scored as follows: (-) negative; (+) faint erythema, few papules; (++) erythema, papules, and vesicles; (+++) intense erythema, papules, and coalescing vesicles.

Results

Of 2996 patch tests performed, 2054 (68.6%) were positive for at least 1 BBS allergen, and 942 (31.4%) were negative for all allergens. The most frequent allergens were nickel sulfate (29.9%), thimerosal (16%), cobalt (15.3%), fragrance mix (15.1%), and balsam of Peru (8.6%) (Table 1). Mercapto mix (0.9%), anthraquinone (1.0%), triclosan (1.0%), p-tert-butylphenol (1.1%), and lanolin (1.2%) showed the lowest rates of positive patch-test reactions.

Discussion

In the present study, 68.6% of the patch tests had a positive reaction. Nickel sulfate was the most prevalent allergen in this sample, followed by thimerosal and cobalt chloride.

Along the same lines, the North American Contact Dermatitis Group (NACDG) patch testing results from 2019 to 2020 showed that, of 4121 patients tested, 69.7% had a positive reaction to at least 1 allergen.[13] They also showed a higher prevalence of sensitization to nickel (18.2%), followed by fragrance mix (12.8%).[13] In a previous study encompassing NACDG patch testing results from 2017 to 2018, nickel was the most prevalent allergen (16.2%), followed by methylisothiazolinone 0.2% aqueous (15.3%) and methylchloroisothiazolinone/methylisothiazolinone 0.02% aqueous (11.0%),[14] an emerging allergen not included in the BBS. The Spanish Research Group on Contact Dermatitis and Skin Allergy (GEIDAC), analyzing sensitization to contact allergens in 11,327 patients, found a higher prevalence of sensitization to nickel, methylisothiazolinone, cobalt, methylchloroisothiazolinone/methylisothiazolinone, and fragrance mix.[15]

Sandrin et al., analyzing a sample of 394 patients for sensitization to BBS contact allergens involved in ACD between 2018 and 2020 in a hospital in Santa Catarina, Brazil, reported a higher prevalence of the following haptens: nickel (33.5%), p-phenylenediamine (PPD) mix (23.2%), perfume mix (22.4%), fragrance mix (22.0%), and cobalt (18.9%).[16] As observed in our study, nickel was the most prevalent allergen, probably due to the population's high exposure to products containing this metal.

Our study has limitations. It was conducted at only 4 research centers, which limits the generalizability of the results to the Brazilian population. However, we included a significant number of tests performed by qualified professionals, thus ensuring their standardized execution and providing an initial overview of the prevalence of contact sensitization to the allergens tested in our study population.

Although our findings align with results for the most common allergens in other international BS, data on emerging allergens are lacking in our population. Since 2020, many Brazilian professionals have adopted the Latin American BS as a more comprehensive and current diagnostic tool than the BBS. The Latin American BS is innovative because it incorporates emerging allergens, similar to other international series, but the BBS remains the initial screening tool for ACD in Brazil and needs to be updated.[17]

It should be noted that some substances, such as anthraquinone, hydroquinone, triclosan, nitrofurazone, promethazine, and turpentine, have been included in the BBS but not in the Latin American, North American, European, or international BS, indicating their limited relevance.[18,19] For instance, promethazine is now rarely used in Brazil; its parenteral form was discontinued in February 2024, although its topical form is still marketed for insect bites and local itching. Photosensitivity cases related to promethazine are well documented, and in these cases, photopatch testing is recommended over conventional patch testing.[19] At present, major international BS do not include promethazine,[13,20] and the European Society of Contact Dermatitis recommends its inclusion in the BS only for photopatch testing.[21]

The antimicrobial nitrofurazone, while widely used in the past, has been replaced by more effective agents for the treatment of ulcers and burns.[22] Triclosan (commercially available as Irgasan) is an effective antibacterial agent against gram-positive bacteria and fungi. However, after risk assessment, experts have recommended discontinuing its use in

products such as hand soaps and cleaning supplies due to its high allergenic potential.[23]

Ethylenediamine is currently included in both the BBS and the North American BS, but not in the Latin American, European, or international BS.[17,18,20] Due to its low prevalence of sensitization (0.8%) and even lower relevance, it may soon be removed from the NACDG BS. As a component of aminophylline, reactions to ethylenediamine were more common in the past. However, aminophylline is no longer recommended in the most recent asthma management guidelines.[24] Regarding thimerosal, patch testing is no longer recommended in BS from several countries, and thus thimerosal was the first to be recognized as a "Nonallergen of the Year" by the American Contact Dermatitis Society in 2002 due to its frequently positive, but often irrelevant, reactions on patch testing (past relevance).[8]

Positive patch test results can be difficult to explain to patients when they lack current relevance, and thus patients often ask: if it has no clinical value, why test for it? Such discussion highlights the need to update the BBS by removing obsolete substances of limited relevance and adding new allergens that are clinically relevant to the Brazilian population.

To address this, the ASBAI Scientific Department of Contact Dermatitis formed a study group in 2022 to revise the BBS. Based on scientific evidence, 18 emerging allergens have been added, 13 allergens with no clinical relevance and a low prevalence of sensitization have been removed, and 10 allergens with a high frequency of positive reactions have been retained; some of them with modified concentrations and vehicles. This new BS of contact allergens will soon be tested in the Brazilian population, and the results will be published in this journal.

Conclusions

Nickel was the most common cause of ACD in our Brazilian population, although other emerging allergens, such as methylisothiazolinone and fragrances, are becoming more frequent. Studies on the prevalence of sensitization to the various ACD allergens are of utmost importance and should be periodically conducted to assess changes over time. This will allow us to update the BS of patch test allergens to better suit the Brazilian population, taking into account new allergens and decreased sensitization to existing ones.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Allergic contact dermatitis in children with polysensitization – Attention to new allergens and risks associated with childhood adultification

Dermatite de contato alérgica na infância com sensibilização a múltiplos componentes – Atenção aos novos alérgenos e aos riscos associados à adultização infantil

Bruno Emanuel Carvalho Oliveira[1], Sergio Duarte Dortas-Junior[2], Priscilla Filippo A. M. Santos[3]

ABSTRACT

We report the case of a 6-year-old girl with allergic contact dermatitis and polysensitization. Patch testing performed with the baseline series, cosmetic series, and nail products showed positive results for balsam of Peru, propylene glycol, cobalt chloride, Amerchol L-101, ethylene glycol dimethacrylate, and triethylene glycol dimethacrylate. She had a history of using her mother's perfumes, jewelry, and skincare products, having colored hair highlights, and using nail polish. The incorporation of adult typologies into the child's world and the aesthetic pressure on pediatric patients to consume products such as hair dyes, accessories, perfumes, creams, moisturizers, and nail polish contribute to the increased prevalence of contact dermatitis in this age group.

Keywords: Allergic contact dermatitis, children, allergens.

RESUMO

Relatamos o caso de uma paciente de 6 anos com dermatite de contato alérgica com sensibilização a múltiplos componentes. Foi realizado o teste de contato com bateria padrão, cosméticos e unhas com positividade para bálsamo-do-peru, propilenoglicol, cloreto de cobalto, amerchol L-101, dimetacrilato de etilenoglicol e dimetacrilato de trietilenoglicol. Havia relato do uso de perfumes, bijuterias, produtos para *skin care* da mãe, apresentava mechas do cabelo coloridas e unhas pintadas com esmalte. A incorporação de tipologias adultizadas ao universo infantil e a pressão estética para o consumo, pelos pacientes pediátricos, de produtos como tinturas e adornos para cabelos, perfumes, cremes, hidratantes e esmaltes de unha contribuem para o aumento da prevalência das dermatites de contato nesta faixa etária.

Descritores: Dermatite de contato alérgica, crianças, alérgenos.

Introduction

The term contact dermatitis (CD) refers to a polymorphic pattern of skin inflammation caused by exposure to exogenous substances. It is one of the most common dermatoses and mainly includes allergic CD (ACD) and irritant CD (ICD). In addition to these two subtypes, other forms have also been recognized based on different causes and clinical features, including: immediate skin reactions, which can be classified as immunologic contact urticaria, nonimmunologic contact urticaria, and protein CD;

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photoinduced CD; systemic CD; and noneczematous CD, which includes a wide range of manifestations, such as erythema multiforme-like lesions, pigmented purpuric dermatosis, lichen planus-like lesions, bullous, papular, and nodular eruption, granulomatous lesions, pustular rash, scleroderma-like lesions, and pigmented, lymphomatoid, and vascular-occlusive CD.[1]

In a recent meta-analysis of 28 studies, comprising 20,107 individuals who underwent patch testing, the pooled prevalence of CD was 20.1%. In children and adolescents under 18 years of age, the prevalence was 16.5%. The prevalence was significantly higher in females (27.9%) than in males (13.2%). The most common allergen was nickel (11.4%), followed by fragrance mix I (3.5%), cobalt (2.7%), *Myroxylon pereirae* (1.8%), chromium (1.8%), p-phenylenediamine (1.5%), methylchloroisothiazolinone/methylisothiazolinone (1.5%), and colophony (1.3%).[2]

Most contact allergens are low molecular weight chemicals, and many substances have sensitizing properties — over 4,000 have already been identified.[3]

Traditionally, ACD is defined as a type IV hypersensitivity skin reaction, according to the Gell and Coombs classification, mediated by T cells and divided into a sensitization phase and an elicitation phase. However, recent studies have provided new insights,[3] showing that cells of the innate immune system — including innate lymphoid cells, mast cells, neutrophils, and dendritic cells — play critical roles in both sensitization and elicitation.[4]

We report the case of a pediatric patient with ACD and polysensitization to raise awareness in the medical community of the frequency of ACD in children, the importance of clinical history, the use of standardized patch testing, sensitization to emerging allergens, and the risks associated with early exposure to adult products.

Case report

A 6-year-old girl from the city of Natal, Rio Grande do Norte, northeastern Brazil, was referred for evaluation of chronic skin lesions. Her mother, a manicurist who works with gel and artificial nails, reported that she had been painting the child's nails about once a month since the girl turned[5]. The patient also used perfumes, wore costume jewelry, applied her mother's skincare products, and had colored streaks in her hair.

Physical examination showed chronic eczematous lesions with lichenification and hyperpigmentation on the anterior neck and upper chest. She also had acute eczema with erythema, edema, vesicles, and oozing on the eyelids and at the earring perforation sites on both ears, as well as subacute eczema with scaling on the back of the neck.

Differential diagnoses such as atopic dermatitis, bacterial and fungal infections, scabies, psoriasis, dyshidrotic eczema, seborrheic dermatitis, juvenile plantar dermatoses, and dermatomyositis were considered and ruled out.

The patient has controlled allergic rhinitis, with a positive skin prick test for house dust mites. The mother denied any diagnosis of atopic dermatitis.

Patch testing was performed on the dorsal trunk in two stages, with a 4-week interval between them, due to the limited area available on the patient's back for applying chamber patches. In the first stage, testing was conducted using the baseline series (30 substances, FDA Allergenic®) and a cosmetic series (10 substances, FDA Allergenic®). The substances were applied using 8 mm Finn Chamber Aqua® devices. Readings were taken at 48 and 96 hours, following the guidelines of the International Contact Dermatitis Research Group. Positive reactions were observed for balsam of Peru (++), propylene glycol (+), cobalt chloride (++), and nickel sulfate (++) in the baseline series, and Amerchol L-101 (+) in the cosmetic series. In the second stage, due to the patient's use of nail polish, the mother's occupation as a manicurist, and the potential environmental exposure to (meth)acrylates, a nail-specific series (20 substances, IPI ASAC®) was tested using the same methodology. Positive reactions were found for ethylene glycol dimethacrylate 2% (++) and triethylene glycol dimethacrylate 2% (++).

The patient's mother was informed of the diagnosis of ACD caused by inappropriate substances used by the child for her age and was advised of the need to eliminate these exposures. Treatment included the use of an emollient cream and a short course of a medium-potency topical corticosteroid to manage skin lesions. She was also instructed to keep the child away from the manicure station. After 6 months of follow-up, the patient demonstrated complete remission of clinical symptoms and was discharged.

Discussion

The landscape of childhood is changing, and we are witnessing these transformations in the daily behaviors of children, who are increasingly being drawn toward adult-like roles and habits at an earlier age.

An American social critic and writer, Neil Postman (1931 to 2003), published a book in 1982 titled "The Disappearance of Childhood". The book was a publishing success as it encouraged readers to reflect on the shifting concept of childhood — an evolution that continues today. Postman drew parallels between communication technologies, consciousness, cultural values, and emotional development. In one particularly relevant passage, he wrote: *"Everywhere one looks, it may be seen that the behavior, language, attitudes, and desires—even the physical appearance—of adults and children are becoming increasingly indistinguishable."*[5,6]

This trend is concerning and closely tied to the current social model, as childhood is a brief developmental period that can be overlooked when adult behaviors and attitudes are adopted prematurely. A child is a person in formation, and childhood is a time of preparation for adult life. Therefore, children deserve to experience childhood fully, with their unique characteristics respected. They are agents of change and should be encouraged daily to imagine, create, and shape their own personalities.[7]

Children are increasingly exposed at an early age to concerns and demands that are not appropriate for the childhood stage. They are subjected daily to technological and media influences that promote consumerism and distance them from their own childlike world. The incorporation of adult-like behaviors and aesthetics into childhood has become more common, along with growing pressure to use skincare products, hair dyes and accessories, perfumes, creams, moisturizers, nail polish, among many others.

Once it was believed that young children rarely developed ACD due to the immaturity of their immune systems and limited exposure to allergens that trigger CD. However, data from recent decades have shown a prevalence comparable to that observed in adults.[8] Cases of ACD have been reported in infants as young as 1-week old,[9] and more than 20% of healthy, asymptomatic children are sensitized to common allergens such as nickel.[10,11] Despite growing awareness of pediatric ACD, fewer than 10% of patch tests in the United States are performed in children.[8]

The prevalence of ACD is increasing among children, and sensitization to contact allergens can begin as early as early childhood. Factors that may influence the development of sensitization in children include the presence of atopic dermatitis, other skin barrier defects, and frequent or repeated exposure to allergens.[12]

There is growing evidence of toxicity associated with ingredients found in cosmetics and personal care products. However, little is known about how and why children use these products. Medley et al.[13] conducted a survey with parents and caregivers of children aged ≤ 12 years regarding the use of children's makeup and body products (CMBPs), a category widely marketed to children across the United States. Examples of these products are presented in Table 1.

The study found that 70% of children had used CMBPs at some point in their lives. Of these, 60% had used body products, 44% hair products, 41% facial products, and 33% used nail, fragrance, and lip products. Eye products were used by 18% of the children. Acknowledging that children might also use makeup and products intended for adults, the authors investigated the proportion of products specifically designed and marketed for children. They found that only 36% of children used such products, meaning most of them were exposed to products made for adults.

The study served as an introduction to understanding early exposure to this unique, understudied class of products.

Diagnosing ACD in children can be challenging due to its clinical polymorphism and the wide range of differential diagnoses, but it should always be considered in cases of recalcitrant eczema. Recognizing key features of ACD — such as the distribution of dermatitis and its clinical course — can support the diagnosis. Family members may not always associate allergen exposure with the onset of symptoms. In the case presented, for example, the mother did not link her daughter's eczema to the materials she used at work. Parents should be asked about the use of products such as shampoos, soaps, lotions, detergents, topical medications, fabrics, footwear, materials used in sports and hobbies, and items such as jewelry, nail polish, and hair dyes. In cases of systemic CD, ingestion of contact allergens should be considered, including carmine

Table 1
Children's makeup and body products children's makeup and body products (CMBPs)

Body	Face paint, body paint, temporary tattoos, glitter, jewelry, stickers, tanning lotion
Eyes	Eyeshadow, eyeliner, mascara, eyebrow pencil, false eyelashes
Lips	Lip gloss, lipstick, lip tint, lip liner
Face	Foundation, concealer, powder, blush, bronzer, primer, highlighter, face masks
Nails	Nail polish, nail stickers, press-on nails
Hair	Hair sprays, dyes, gel, styling mousse/creams, hair glitter
Fragrances	Perfume, cologne, body spray

Adapted from Medley EA, et al.[13]

red,[14] nickel in oats and cocoa,[15,16] and balsam of Peru in ketchup.[17,18] Understanding environmental sources of allergens helps guide age-appropriate questions during medical history-taking. For infants and toddlers, questions should include diaper use, powders, and creams. In school-aged children, toys are known sources of exposure that can cause hand eczema. In adolescents, exposure may come from hair dyes,[19,20] perfumes,[21] nail polish,[22] and henna tattoos.[23,24] As observed in our case, the patient was sensitized to allergens typically seen in older age groups, which aligns with the phenomenon of early adult-like behavior.

Patch testing is the gold standard diagnostic procedure for ACD. In Brazil, there are some patch test series specifically designed for children; however, in their absence, adult test series should be used. In a study involving 1,142 children, Jacob et al.[25] identified the main allergens responsible for triggering ACD in those who underwent patch testing, including nickel, fragrance mix I, balsam of Peru (*Myroxylon pereirae*), bacitracin, formaldehyde, and propylene glycol, among 15 other allergens. In our case, the patient was sensitized to nickel, balsam of Peru, and propylene glycol.

A noteworthy aspect of our case was the child's sensitization to methacrylates. The decision to perform the nail-specific patch test series was guided by the mother's occupation and the child's use of nail polish.

Acrylates and methacrylates are derivatives of salts or esters of acrylic acid. They comprise a wide range of compounds in the class of plastics and synthetic resins, all sharing a common chemical structure based on acrylic acid. These substances are widely used in cosmetic products, dental restorations and prosthetics, surgical equipment, medical devices, household items, construction materials, printing inks, and other products such as artificial nails. Acrylic monomers undergo a polymerization reaction that requires a catalyst — either a chemical agent or a physical one such as UV light. In this reaction, the vinyl radical acts as the reactive group. Sensitization and subsequent lesion development are mainly caused by acrylic monomers, since the by-products and polymerized forms are considered to be weak sensitizers.[26-28]

Acrylic and gel nails do not fully polymerize after mixing, even when cured with UV light. As a result, monomers remain present when the nails are applied.

Artificial press-on nails do not contain acrylate monomers, so sensitization to these allergens does not occur through their use alone. However, the chemical compound found in nearly all adhesives used to apply these nails has been identified as a potential sensitizing allergen. Given the relevance of this issue, it is essential to provide proper safety recommendations for workers and implement techniques to reduce direct exposure to these sensitizers. These include the use of vinyl gloves, protective masks, safety goggles, and appropriate work attire.[29]

Contact sensitization to nail (meth)acrylates is an emerging health concern. In a study of 230 cases of ACD caused by nail (meth)acrylates, Raposo et al.[30] reported that 93% of patients had hand eczema. The most common sensitizers were 2-hydroxyethyl methacrylate (90% of tested patients), 2-hydroxypropyl methacrylate (64.1%), and ethylene glycol dimethacrylate (54.5%). Among these main components, our patient was sensitized to ethylene glycol dimethacrylate, although she did not present with hand eczema. Since ACD caused by nail (meth)acrylates is rare in childhood,[31] and, to date only a few cases have been described in literature, clinicians should be alert to the possibility of eczema developing from (meth)acrylate exposure in other areas of the body.

Finally, the key to treating ACD is avoiding further contact with the sensitizing agents. In our case, once the causative allergens were identified, removing the child from exposure and treating the lesions led to complete remission of eczema after 6 months of follow-up.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Alpha-gal syndrome: the first case report from the state of Rio Grande do Norte, northeastern Brazil

Síndrome alfa-gal: primeiro relato de caso do estado do Rio Grande do Norte

Bruno Emanuel Carvalho Oliveira[1]

ABSTRACT

We report the first clinical case of alpha-gal syndrome in an older man from the city of Brejinho, in the state of Rio Grande do Norte, northeastern Brazil, along with a brief literature review on the subject. The patient developed delayed anaphylaxis after consuming *buchada de bode* (a traditional Brazilian dish made from goat offal). Living in a rural area, he has frequent contact with tick-infested animals. Alpha-gal syndrome challenges traditional paradigms of food allergy and requires appropriate diagnosis and treatment due to its potentially fatal outcomes. Patients should be advised to avoid mammalian meat and further tick bites, as well as to carry an epinephrine auto-injector for emergencies.

Keywords: Anaphylaxis, viscera, red meat.

RESUMO

Apresentamos a descrição do primeiro caso clínico de síndrome alfa-gal em um idoso da cidade de Brejinho, no estado do Rio Grande do Norte, Brasil, e fizemos uma breve revisão da literatura sobre o tema. O paciente desenvolveu anafilaxia tardia após ingerir uma buchada de bode. Residente em uma zona rural, ele tem contato frequente com animais infestados por carrapatos. A síndrome alfa-gal desafia paradigmas tradicionais de alergia alimentar e requer diagnóstico e tratamento adequados devido aos seus resultados potencialmente fatais. Os pacientes devem ser orientados a evitar carne de mamíferos e novas picadas de carrapatos, além de possuir epinefrina autoinjetável para emergências.

Descritores: Anafilaxia, vísceras, carne vermelha.

Introduction

IgE antibodies specific to oligosaccharide galactose-alpha-1,3-galactose (alpha-gal) have been shown to cause two distinct forms of anaphylaxis in patients previously sensitized by a tick bite — *immediate-onset anaphylaxis*, which occurs after cetuximab use; and *delayed-onset anaphylaxis*, which occurs 3 to 6 hours after ingestion of non-primate mammalian meat (beef, pork, and lamb, hereafter referred to as red meat) —, leading to the diagnosis of an emerging disease called alpha-gal syndrome (AGS). Since then, it has become clear that, as allergists and immunologists, we need to think "outside the box."[1]

AGS appears to challenge several immunological paradigms. For example, anaphylaxis triggered by sensitization to carbohydrates is uncommon compared to reactions caused by protein triggers, and these systemic reactions develop hours after exposure, rather than minutes. Furthermore, reactions seem to

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lack specificity, since they are not to alpha-gal in the tick saliva but rather to the alpha-gal on mammalian meat, and occasionally alpha-gal in non-meat foods and pharmaceuticals. Reactions also tend to subside with strict dietary avoidance, which is unusual for other types of food allergy, especially those acquired in adulthood.[2,3]

For many years, recognition and diagnosis of AGS have been delayed, primarily because neither patients nor physicians have correlated delayed symptoms with the ingestion of red meat. The reasons for delayed onset of symptoms in AGS are not yet fully understood.[4]

This new form of delayed anaphylaxis has been diagnosed more frequently, as evidenced by the series of 2500 clinical cases published by Commins.[2] In Brazil, the most recent case was reported in 2021 by Lima et al.,[5] involving an adolescent from the city of Belém, in the state of Paraíba, northeastern Brazil. A recent review published in January 2024 by Wilson et al. reports fewer than 5 documented cases in Brazil.[6]

This report describes the first clinical case of AGS in an older man from the city of Brejinho, in the state of Rio Grande do Norte, northeastern Brazil.

Case report

A 78-year-old man born and living in Brejinho, Rio Grande do Norte, northeastern Brazil, was admitted to a private clinic for investigation of a clinical suspicion of idiopathic anaphylaxis. The patient reported that, approximately 3 hours after consuming *buchada de bode*, a traditional Brazilian dish made from goat offal, he developed urticarial lesions, bilateral palpebral angioedema, hypotension, dyspnea, and syncope. His family promptly took him to the city hospital, where he had a cardiac arrest and successfully received cardiopulmonary resuscitation. After stabilization, he was transferred to Natal, the capital of the state of Rio Grande do Norte, and admitted to the intensive care unit for 3 days.

The patient denied previous episodes of anaphylaxis, atopy, use of non-steroidal anti-inflammatory drugs, alcohol consumption, intense physical activity, emotional stress, or acute infection that could have acted as cofactors of anaphylaxis. His medical history included hypertension, for which he was taking losartan 50 mg twice daily. Both the patient and his family reported frequent exposure to ticks and tick bites in their residential area. Considering the possibility of AGS, a serum alpha-gal specific IgE test was performed by ELISA, yielding a result of 68.40 kU/L. There is a lack of commercially available specific IgE tests to goat meat or offal components, which highlights the importance and need of regionalizing commercial extracts for allergy testing.

Medical management included advising the patient to avoid red meat and offal products, providing a descriptive medical report on AGS with an emergency action plan, prescribing self-injectable epinephrine, and offering guidance on environmental control to prevent future tick bites.

Discussion

An estimated 7.6% of children and 10.8% of adults have IgE-mediated food-protein allergies in the United States, a condition that may cause anaphylaxis and death. The mortality rate due to food-related anaphylaxis in the United States is estimated at 0.04 deaths per million annually. AGS affects approximately 96,000 to 450,000 individuals in the United States and is currently a leading cause of anaphylaxis in adults. The seroprevalence of sensitization to alpha-gal ranges from 20% to 31% in the southeastern United States.[7]

Genetic susceptibility, changes in the microbiome, skin exposure to detergents, and pollutant exposure are factors that may contribute to the risk of food sensitization and IgE-mediated allergy.[8] For AGS, the most widely studied risk factor is ABO blood group status. The patient in our case report had O+ blood type. Evidence indicates that individuals with B antigen blood group may have some protection against alpha-gal sensitization and/or development of the clinical syndrome, although they can still be affected. Previous studies have shown that alpha-gal differs from the B-group blood antigen by a single fucose at the penultimate galactose residue, a similarity that might be related to the lower risk of alpha-gal sensitization. Male sex, rural residence, and an outdoor lifestyle have been associated with AGS, although these are presumably risk modifiers for tick exposure.[6]

A study in the United States assessed 122,068 serum specimens from 105,674 patients with suspected allergy to mammalian meat and reported an alpha-gal sensitization rate of 32.4%. Individuals aged 70

years and older were most likely to test positive, whereas those aged 0-9 years were the least likely to receive positive test results. Men showed a higher positive test rate than women (43.3% vs. 26.0%). From 2011 to 2018, the number of positive alpha-gal IgE antibody test results increased 6-fold, suggesting a potential rise in alpha-gal sensitization rates in the United States and/or an increase in testing frequency.[9]

A report from the Centers for Disease Control and Prevention (CDC) estimates that between 96,000 and 450,000 persons in the United States might have been affected by AGS since 2010.[10] Reactions to alpha-gal were initially observed in the United States in 2008 in patients treated with cetuximab,[11] a chimeric mouse-human IgG1 antibody containing an alpha-gal glycosylation site on the murine portion.[12] In 2009, a potential association between red meat allergy and tick bite reactions was first suggested in Australia,[13] and in the same year, the first clinical case was described in the United States.[14] In 2011, it was noted that reactions to cetuximab and red meat allergies were occurring in southeastern United States, coinciding with the distribution of the lone star tick (*Amblyomma americanum*).[15] Other tick species have also been associated with AGS, including *Ixodes holocyclus*, *Amblyomma sculptum*, *Ixodes Ricinus*, and *Haemaphysalis longicornis*.[16] Since then, accumulated circumstantial evidence has suggested that tick bites induce alpha-gal-specific IgE, leading to the development of AGS.[17]

Over the past decade, a growing number of studies have expanded the list of possible sensitizing agents leading to AGS. As an emerging disease, there is a crucial need for new information. Areas of uncertainty include understanding whether bites from *A. americanum* and other tick species are indeed the driving sensitizer for AGS. Additional sensitizers have been proposed, such as chigger bites[18] and flea bites.[19] Recently, compelling evidence has also suggested that *Ascaris* infection plays a causative role.[20] Studies exploring the higher rates of *Hymenoptera* venom allergy among patients with AGS have shown that the venom allergens cross-react with tick salivary components, although alpha-gal itself is not one of these cross-reactive antigens. It is not currently clear whether venom allergy is associated with AGS through shared environmental exposures or a direct immunological link, but avoiding stings appears to be important for the resolution of AGS.[21] These new sensitizers support the idea that AGS could be considered an immunoparasitologic syndrome.[3]

AGS is widely recognized as an allergy mediated by alpha-gal-specific IgE antibodies.[14] Humans, great apes, and Old World monkeys do not express alpha-gal; however, it is found in all other mammals, including cows, pigs, and goats.[22] Therefore, humans can be exposed to alpha-gal through the consumption of mammalian meat or products derived from mammals, including pharmaceuticals that contain mammalian components, such as heparin, immunobiological products (such as cetuximab and influenza, measles-mumps-rubella, rabies, varicella, and zoster vaccines),[23] and drugs containing gelatin.[24]

In predisposed individuals, after previous sensitization and subsequent consumption of red meat, delayed allergic reactions can occur, including urticaria, angioedema, gastrointestinal symptoms, or even anaphylaxis. Several theories aim to explain these delayed responses, with the theory involving lipid particles being the most compelling. However, this particular theory is difficult to investigate in humans and has not yet been proven.

The “glycolipid hypothesis” suggests that glycolipid forms of alpha-gal can explain the 3-6 hour delay in symptom onset after ingesting mammalian meat, a delay atypical for IgE-mediated food allergies but characteristic of AGS. This hypothesis is based on the known kinetics of lipid digestion, absorption, packaging, and circulation. Specifically, lipids are packaged into chylomicrons within the intestine and transit via the thoracic duct, entering the systemic circulation approximately 2-3 hours after a fatty meal. Over the subsequent few hours, these lipids progressively transition to smaller lipoprotein particles, such as low-density lipoproteins (LDLs), which are sufficiently small to pass through endothelial walls and enter interstitial tissues where mast cells reside. It is important to note that experimental evidence supporting this hypothesis is currently incomplete, and alternative explanations involving glycoprotein forms of alpha-gal cannot be ruled out. For instance, it is plausible that alpha-gal expression on highly stable proteins, such as collagen and laminin, contributes to delayed digestion and absorption kinetics in vivo.[6]

As observed in the case reported here, the patient developed severe anaphylaxis after consuming *buchada de bode*, a traditional dish from Northeastern

Brazil, culturally representative of the diet of people living in the Brazilian semiarid region (*sertão*), which typically includes goat meat and offal. It is prepared by washing, boiling, cutting, and seasoning goat meat and offal, which are then cooked in bags often made from the goat's stomach. While the name implies goat (*bode*) products, some variations may use offal from lamb, beef, or a combination of different meats.

A serum concentration of alpha-gal-specific IgE of 0.1 kU/L or more supports a diagnosis of AGS in patients who experience delayed allergic symptoms after consuming mammalian meat. In populations with high rates of alpha-gal sensitization, an alpha-gal IgE level of at least 2 kU/L or more than 2% of the total IgE concentration increases the likelihood of a positive mammalian meat oral food challenge (OFC) to greater than 50%.[7]

Diagnosing food allergy requires a detailed clinical history and diagnostic allergy tests, but caution is needed when ordering and interpreting test results to prevent misdiagnosis, which could lead to unnecessary dietary restrictions, expose patients to nutritional risks, and significantly decrease their quality of life. For AGS, skin prick tests using commercial extracts often yield negative or weakly positive results. In these cases, intradermal tests or prick-to-prick testing may be considered, since they demonstrate higher positivity rates.[6] While OFC can be used, its efficacy is limited due to the delayed onset of reactions. When food exclusion is indicated, its subsequent reintroduction should be monitored through an OFC, conducted by a trained specialist in a well-equipped or hospital setting. Food reintroduction at home, without medical supervision, poses risks and should be discouraged.[25]

Management of AGS cases involves advising patients to avoid red meat consumption and tick bites, providing them with an emergency care plan that details medication to use for mild and severe allergic reactions, and prescribing self-injectable epinephrine. Regular clinical follow-up visits are also recommended.[7]

Avoidance of red meat and offal can lead to complete symptom remission in more than 80% of cases, and approximately 5% to 20% of patients may also need to avoid dairy and gelatin. However, some adult patients have regained tolerance to mammalian meat after 1 to 2 years of avoiding additional tick bites.[26,27] It is important to note that the natural course of AGS often involves a reduction in IgE antibody response over time, which can lead to a lower frequency or inconsistency of reactions. Furthermore, patients should be informed that the allergenicity of red meat proteins is preserved even after different thermal cooking methods.[28]

For effective vector control, it is recommended to apply acaricides both to the house and to pets. When exposure to ticks is unavoidable, it is recommended to wear long sleeves, boots, and light-colored long pants to facilitate the visualization of ticks. After use, all clothes should be washed in boiling water for complete tick removal.[27]

Injectable epinephrine is the first-line treatment for severe allergic reactions and/or anaphylaxis. Epinephrine auto-injectors can be used to administer doses in rapid succession (e.g., at 5-minute intervals), which may be necessary to delay the progression of a reaction and reduce the severity of symptoms. A 2021 meta-analysis of 86 studies, including data from 36,557 anaphylactic reactions, showed that 1 in 10 reactions were treated with more than 1 dose of epinephrine, but only 2.2% (95% CI, 1.1%-4.1%) resulted in response failure after 2 doses of epinephrine.[29]

In patients with AGS, serum alpha-gal-specific IgE levels should be regularly monitored, typically every 6 to 18 months.[30] A mammalian meat OFC should be considered when serum alpha-gal-specific IgE levels are below 2 kU/L or less than 2% of the total IgE concentration,[2] although these thresholds may vary according to the population.[31] Strategies to reintroduce mammalian meat into the diet after AGS resolution depend on the patient's and physician's comfort level and should include supervised follow-up.

Oral immunotherapy using cow's milk or beef to treat AGS is still under investigation.[32,33] The development of a Food and Drug Administration (FDA)-approved pig, genetically engineered to not produce alpha-galactosyltransferase enzymes, may provide future avenues for hypoallergenic mammalian meat preparations and enable the use of mammalian products for the treatment of patients with AGS.[34]

Finally, in 2015, Ferreira et al. conducted a systematic review on AGS[27] and reported that, in Brazil, there was only clinical suspicion of this diagnosis. However, as confirmed by this case report, AGS is already present in Brazil and should not be overlooked.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Corn-induced anaphylaxis: rare but possible

Anafilaxia induzida por milho: rara, mas possível

Ana Paula Brito Dias[1], Daniela de Abreu e Silva Martinez[1], Sergio Duarte Dortas-Junior[1,2], José Elabras-Filho[1]

ABSTRACT

Anaphylaxis is defined as a life-threatening systemic allergic reaction that can present with a wide range of clinical signs and symptoms. The most common foods responsible for food hypersensitivity reactions are milk, eggs, peanuts, tree nuts, fish, and shellfish. There are few documented reports of corn allergy, particularly corn-induced anaphylaxis. In addition, corn starch is a common excipient in medications, increasing the risk of reactions in individuals allergic to corn. Here, we report a case of anaphylaxis in a woman following the ingestion of corn and a medication containing corn starch as an excipient.

Keywords: Anaphylaxis, food hypersensitivity, drug-related side effects and adverse reactions, starch.

RESUMO

A anafilaxia é caracterizada como uma reação alérgica sistêmica com risco de vida e importante impacto na qualidade de vida, que pode incluir uma variedade de sinais e sintomas clínicos. Os alimentos mais comuns que causam reações de hipersensibilidade alimentar são leite, ovo, amendoim, nozes, peixe e marisco. Existem poucos relatos de alergia ao milho documentados, particularmente anafilaxia induzida por milho. Além disso, o amido de milho é um excipiente comum em medicamentos, e indivíduos alérgicos ao milho têm um risco aumentado de apresentar reações. Relatamos o caso de uma paciente que apresentou anafilaxia devido à ingestão de milho e a um medicamento contendo amido de milho como excipiente.

Descritores: Anafilaxia, hipersensibilidade alimentar, efeitos colaterais e reações adversas relacionados a medicamentos, amido.

Introduction

Anaphylaxis is a severe systemic hypersensitivity reaction[1], with an acute presentation, that can significantly impair a patient's quality of life and may lead to shock, respiratory failure, or even death.[1-3] Food allergens are a major contributor to the rising prevalence of anaphylaxis, being the most common triggers in children.[1,2] Most food-related allergic reactions are caused by an IgE-mediated mechanism. Therefore, sensitization can be assessed through specific IgE testing or immediate-reading skin tests.[3] While numerous foods can trigger anaphylactic reactions, approximately 80% to 90% are attributed to allergens from eggs, milk, soy, wheat, fish, seafood, peanuts, and tree nuts.[4] Although cereals account for approximately 70% of global protein intake, their prevalence as causative

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agents in hypersensitivity events remains poorly documented.[5] Corn, a staple cereal for many populations, is an infrequent cause of food allergies, but when reactions occur, they can be potentially severe[6]. Beyond its dietary presence, starch—extracted from rice, potatoes, tapioca, and corn—is a common excipient in medications, with cornstarch found in nearly 37% of marketed medications. Corn-allergic individuals are more prone to reactions from cornstarch excipients in medications.[7,8] We report the case of a patient with a history of corn-induced anaphylaxis, diagnosed at a university hospital, who experienced a subsequent reaction after ingesting medication containing cornstarch as an excipient.

Case report

A 63-year-old female patient who worked as a cook, with a history of high blood pressure, type II diabetes mellitus, and allergic rhinitis, presented with angioedema of the eyelids and lips, progressing to dyspnea, after contact with ants near corn flour. Diagnosed with anaphylaxis at the emergency department, she responded well to epinephrine, antihistamine, and corticosteroid treatment. She also reported previous oropharyngeal itching when handling corn, a frequent occurrence due to her occupation. In a separate incident, she developed laryngeal angioedema and dyspnea approximately 10 minutes after ingesting food containing corn flour, requiring similar treatment as in the previous episode. Chemiluminescence was used to measure total IgE (206 IU/mL) and corn-specific IgE (9.95 KU/L) levels, as well as wheat-, mite-, ant-, and fungus-specific IgE levels (<0.10 KUA/L). Given the clear cause-effect relationship in the patient's history, the positive corn-specific IgE test, and the absence of new episodes post-dietary exclusion, we opted against a challenge test and made the diagnosis of corn-induced anaphylaxis. The patient was counseled to avoid corn and prevent accidental exposure. Following the elimination of corn and its derivatives from her diet and environment, she did not experience any new episodes. A few months after the last event, the patient experienced a runny nose and limiting sneezing, for which she took a second-generation antihistamine (loratadine). A few minutes later, she developed abdominal discomfort and oropharyngeal itching, symptoms similar to those of her previous reaction to corn. Upon reviewing the package insert, she identified cornstarch as an excipient in loratadine. Symptoms improved after switching to dexchlorpheniramine.

Discussion

Corn-induced anaphylaxis is rare and poorly documented in the literature.[5] Suspicion of this condition is typically based on the patient's clinical history and characteristic symptoms, after ruling out other potential causes and observing no new episodes following dietary exclusion. Oral food challenge testing is the gold standard for diagnosis, but it should be reserved for cases where the patient's history is unclear or the diagnosis remains uncertain. Given the prevalence of corn in global cuisine and the widespread use of starch as an excipient in medications, the risk of accidental ingestion and subsequent anaphylaxis is a major concern. In view of the foregoing, our team investigated the presence of starch in the 10 most prescribed medications of 2023, based on a survey by the Brazilian Association of Generic and Biosimilar Medicines Industries (PróGenéricos).[9] We reviewed package inserts from major suppliers and identified starch as an excipient in at least one formulation of the following common medications: losartan, dipyrone, hydrochlorothiazide, enalapril, atenolol, and simethicone (tablet) (Table 1). Additionally, we examined second-generation antihistamines, an important class of drugs commonly used in Allergy and Immunology, as illustrated in the case reported here, focusing on medications from major generic suppliers. Starch was consistently absent as an excipient only in desloratadine formulations (Table 2).

Conclusion

Managing corn-induced anaphylaxis requires careful attention beyond just dietary guidelines. When prescribing and dispensing medications, it is crucial to review the patient's prescriptions and provide clear guidance, as even different brands of medications with the same active pharmaceutical ingredient may contain different excipients.

Table 1
Ten most prescribed generic medications in Brazil in 2023 and respective evaluation of tablet formulations that contain or do not contain starch as an excipient, with cornstarch being one of the main excipients used

Active ingredient	Generics containing starch	Generics not containing starch
Losartan	CIMED, EMS, Prati, Teuto	Aché, Eurofarma, Medley, Neoquímica
Dipyrone	Medley [a]	CIMED, EMS, Eurofarma, Neoquímica
Hydrochlorothiazide	CIMED, EMS, Medley, Neoquímica	Not found
Nimesulide	Aché, Eurofarma, Medley, Neoquímica	CIMED, EMS
Sildenafil	Not found	Aché, CIMED, EMS, Eurofarma, Medley, Neoquímica
Atenolol	Aché, CIMED, Medley, Neoquímica	EMS
Simethicone	Aché, Neoquímica	CIMED, EMS, Medley
Tadalafil	Not found	Aché, CIMED, EMS, Eurofarma, Medley, Neoquímica
Simvastatin	Aché, EMS, Medley, Neoquímica	CIMED

[a] 500 mg formulation with starch as an excipient. 1 g formulation without starch described in the package insert.

Table 2
Main generic second-generation antihistamines used in Brazil with starch as an excipient as described in the package insert

Active ingredient	Generics containing starch	Generics not containing starch
Bilastine	Eurofarma, Neoquímica	EMS
Desloratadine	Not found	Aché, Eurofarma, Medley
Fexofenadine	EMS, Medley, Nova Química, Germed Pharma	Eurofarma
Levocetirizine	Eurofarma	Germed Pharma, Glenmark, EMS, Neoquímica
Loratadine	CIMED, Aché, Neoquímica	Not found

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Hierarchy in the diagnosis of inborn errors of immunity and the decline of functional diagnosis

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Dear Editor,

The immune system is a complex network of cells, tissues, and molecules that protects the body against infections and diseases. Its effective action is due to the diversity of its components, the interconnectivity between them, and the precise regulation of inflammatory and immunological response. In addition, immunity interacts with the microbiome and is influenced by external factors, such as exposure to pathogens and the environment. However, mutations in genes involved in immune response can compromise of this system's functioning, resulting in vulnerability to infections, immune dysregulation, and predisposition to neoplasia, a set of conditions known as inborn errors of immunity (IEI).[1]

These errors encompass several diseases and immune deficiencies and require a complex diagnostic approach. IEI are diagnosed at 3 levels: clinical, functional, and genetic. Despite technological advances, clinical diagnosis remains essential. It is the first step in identifying immunological conditions, allowing syndromes to be suspected based on symptoms, clinical signs, and susceptibility to infection. It is essential to direct subsequent laboratory investigations by grouping conditions into categories such as phagocyte disorders, defects in humoral immunity, cellular immunity, complement system, immune regulation, autoinflammatory disorders, predisposition to specific infections, etc. Although clinical diagnosis does not accurately identify the specific disease, it is crucial to the investigation process and to determine more specialized tests. Only after clinical diagnosis is it possible to define the functional tests necessary to clarify the pathological process and to direct genetic research.[2]

Functional diagnostics complement clinical assessment by providing objective data on immune system performance, demonstrating its response to pathogens or stimuli. Tests such as antibody dosage, lymphocyte phenotyping, and lymphoproliferation tests assess the immune response by verifying the production of antibodies and the activation of T, B and NK cells. In addition, phagocytosis disorders, such as chronic granulomatous disease and leukocyte adhesion deficiency, are investigated through tests such as nitroblue tetrazolium and dihydrorhodamine, which assess phagocyte capacity to produce reactive oxygen species to eliminate microorganisms and the expression of adhesion molecules. The CH50 and AH50 tests measure the functionality of the classical and alternative complement pathways, helping identify immunological defects. These tests are essential for identifying immune system dysfunction and guiding treatment.

Much of the syndromic diagnosis of IEI is performed through a combination of clinical and functional diagnoses.[3] Despite the importance of these tests in IEI diagnosis, their availability is limited. The evaluation of humoral immunodeficiencies is more common, with many laboratories offering assays to assess antibody levels and function, although analyzing cellular immunity, the complement system, innate immunity, and phagocytosis is challenging due to the scarcity of specialized laboratories, the high cost, and the low demand. Thus, combining clinical and functional diagnosis, although essential, often becomes unfeasible in certain conditions.

Genetic assessment of IEI is essential to identify immune system mutations, using techniques such as whole-exome sequencing, whole-genome sequencing, and gene panel sequencing. Its main advantages include accurate molecular diagnoses, which are essential in rare diseases, enabling genetic counseling and personalized treatment, such as molecularly targeted therapies, bone marrow transplantation, and gene therapy. However, challenges include the high cost of testing and limited access to specialized centers, in addition to the difficulty of interpreting the results, which requires extremely complex computational analyses. The analysis of genome and whole-exome tests is based on bioinformatics and mathematical tools to interpret huge volumes of genetic

data. The process includes aligning the DNA sequence with a reference genome, identifying variants, and filtering and classifying relevant variants. Predictive tools assist in the interpretation of variants of uncertain significance, and machine learning models identify genetic patterns. These data are integrated with clinical information to obtain more accurate diagnoses and guide treatment.[4]

Frequent identification of genetic variants of uncertain significance complicates clinical decisions, since these variants do not have a clearly defined impact on health. The time needed to obtain results can be long, delaying diagnosis and treatment. Furthermore, environmental and epigenetic factors, which influence disease progression, are not considered in genetic testing. The psychological impact on patients and families, especially in relation to hereditary risk, can be significant, reinforcing the importance of appropriate genetic counseling.[5]

Interpreting genetic results in IEI is complex, since not all identified mutations are clinically relevant. Many genetic variations do not cause pathology, resulting in the classification of several genetic alterations as variants of uncertain significance. The designation 'variant of uncertain significance' generates uncertainty about whether the variant is benign or pathogenic, making therapeutic decisions difficult. Reclassifying variants of uncertain significance depends on new scientific evidence, especially in rare diseases such as IEI, for which data are limited. Collaborative databases are essential to improve diagnosis and facilitate more effective decisions. Although genetic diagnosis has become more accessible, functional assays are in decline, becoming less available and less requested by clinicians. Genetic evaluation is often preferred over functional evaluation, especially to investigate processes such as phagocytosis and cellular immunity. However, a lack of functional assay data can result in bias and misdiagnosis, especially when relying solely on genetic diagnosis. This is compounded by the inaccuracy associated with variants of uncertain significance, which can lead to incorrect diagnosis.[6]

Without functional evidence demonstrating immune dysfunction, IEI diagnosis may be vulnerable to bias. Integrating functional and genetic testing is essential for a complete and accurate assessment of immune conditions. Although genetic diagnosis is a powerful tool, it is important not to overestimate it, since it does not solve all diagnostic challenges. Genetic analysis, while vital, is not a substitute for functional assays, which are crucial to identify true immune system dysfunction.

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The visual evolution of atopic dermatitis: from 18th- and 19th-century historical illustrations to photography and AI-generated images

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Dear editor,

The Roman historian Suetonius (born about 69 AD) provided an important historical account of the Roman emperor Augustus (63 BC - 14 AD), in which he described not only signs of atopic dermatitis but also conditions such as asthma and rhinitis. His description includes the following observations: *"His body is said to have been marred by … a number of hard, dry patches suggesting ringworm, caused by an itching of his skin and a too vigorous use of the scraper at the baths."* He further noted that Augustus was subject to *"certain seasonal disorders: in early spring a tightness of the diaphragm; and when the sirocco blew, catarrh."* There seems to be no doubt that the combination of lichenified skin lesions, asthmatic symptoms, and rhinitis indicates an atopic predisposition.

The earliest depictions of atopic dermatitis date back to the 18th century, with numerous historical images available. Examples include those found in Robert Willan's book "On cutaneous diseases," published in 1798, the photographic illustrations in George Henry Fox's book "Photographic Illustrations of Skin Diseases," and images from the first dermatology encyclopedia, "Pratique Dermatologique," published in 1900. Coauthored by the renowned French physicians Ernest Henri Besnier, Louis-Anne-Jean Brocq, and Lucien Jacquet, this work is a landmark in the history of dermatology because of its scientific rigor and visual richness. With an extensive collection of detailed clinical descriptions and meticulous illustrations of skin diseases, this treaty was consolidated due to its interdisciplinary approach, addressing dermatology with clinical and aesthetic accuracy. The high-quality illustrations faithfully captured the characteristics of skin lesions, making them an indispensable resource for physicians, researchers, and students. This work significantly influenced diagnostic standards and the understanding of skin diseases throughout the 20th century.

Many clinical descriptions of diseases similar to what we now call atopic dermatitis have been meticulously documented in earlier treaties, including Thomas Carrere's publication from 1740. Since then, prominent figures such as Alibert and Rayer in France, Hebra and Neumann in Vienna, and Duhring and Fox in the United States have greatly contributed to dermatology by creating illustrated atlases with striking images of adults and children suffering from atopic dermatitis and other conditions then considered manifestations of "infantile eczema." These visual atlases have deeply influenced medical practice, providing health care professionals with an essential visual reference for diagnosing and understanding dermatological conditions.

Robert Willan (1754-1812) was a British physician pioneer in the dermatology field and renowned for his innovative and systematic approach to the study of skin diseases. He was the first to systematically classify dermatological conditions based on the visual characteristics of skin lesions. His work contained detailed color illustrations, being one of the first works to include visual representations of skin diseases. While atopic dermatitis is not explicitly mentioned, we propose examining an image Willan labeled "Strophulus confertus" (Figure 1), which depicts lesions suggesting infantile atopic dermatitis. Images of pediatric dermatological conditions from the 18th century are rare, making this particular illustration highly valuable due to its striking similarity to atopic dermatitis.

Figure 1
"Strophulus confertus", Robert Willan (1754-1812)

Louis Duhring (1845-1913) was a renowned American dermatologist and considered one of the founders of dermatology in the United States. A former professor at the University of Pennsylvania, Duhring is celebrated for his contributions to the study of skin diseases. His book "Atlas of Skin Diseases," published in 1876, features magnificent plates that are remarkable for their artistic quality and precise depiction of signs and symptoms. One particularly striking image portrays an infant with eczema, standing out as one of the most beautiful and medically accurate artistic representations of infantile eczema from the 19th century. The artist masterfully captured the elementary lesions typical of the disease, creating a portrait of impressive aesthetic beauty (Figure 2). Duhring referred to the condition as "Eczema rubrum," describing it as *"… male infant, one year of age. … the child was perfectly healthy at birth. The disease of the skin manifested itself during the second month, appearing as … reddish spots on either cheek. These became redder…. The disease now attacked the forehead…, likewise in the form of reddish patches…. The patches… were from the beginning accompanied by swelling, thickening of the skin, slight scaling, and considerable heat and itching. In the course of four of five weeks…, the patches becoming moist and discharging from day to day a sticky, honey-like, clear, pale-yellowish exudation which immediately dried, forming yellowish crusts. (…) The case before us may be viewed as representative of a large number of infantile eczemas. (…) The disease tends to become chronic, the process, as a rule, repeating itself from time to time in a more or less aggravated form. It may continue for months or for years. (…) The face may be the only region attacked, or, as often happens, other parts of the body may be involved at the same time. The causes of infantile eczema,…, are often obscure. (…), resulting very commonly from improper diet, …. In many instances, indeed, no cause can be assigned for the eruption beyond the existence of a predisposition to eczema, which may be either hereditary or acquired."* Another plate in the book illustrates eczema in an adult, capturing the subject's facial expression and gaze, which carry deep symbolism and convey the profound impact of the disease (Figure 3). The accompanying description reads: *"… an Irish laboring man, forty-five years of age. (…) The skin of the face is everywhere dry and has a harsh feel."*

Figure 2
"Eczema rubrum", Louis Duhring (1845-1913)

Figure 3
45-year-old man presenting with dry, harsh skin in all facial areas, Louis Duhring (1845-1913)

George Henry Fox (1846-1937) was a prominent American dermatologist who published "Photographic Illustrations of Skin Diseases" in 1880. This work was among the first to use actual photographs to document

and illustrate skin diseases, a significant innovation at the time. The book features detailed images of several dermatological conditions, capturing the visual characteristics of lesions more accurately than the drawings and illustrations previously used. This marked an advance in the study and diagnosis of skin diseases, making their representations more accessible and faithful to clinical reality. One particularly striking image in the book is a photograph of a sleeping baby. Although originally black and white, Fox painted the child's face red to highlight crusts and wounds, making the intense inflammatory process more evident. This image captures a rare moment of lightness and rest for the baby, who was likely suffering intensely from the disease (Figure 4).

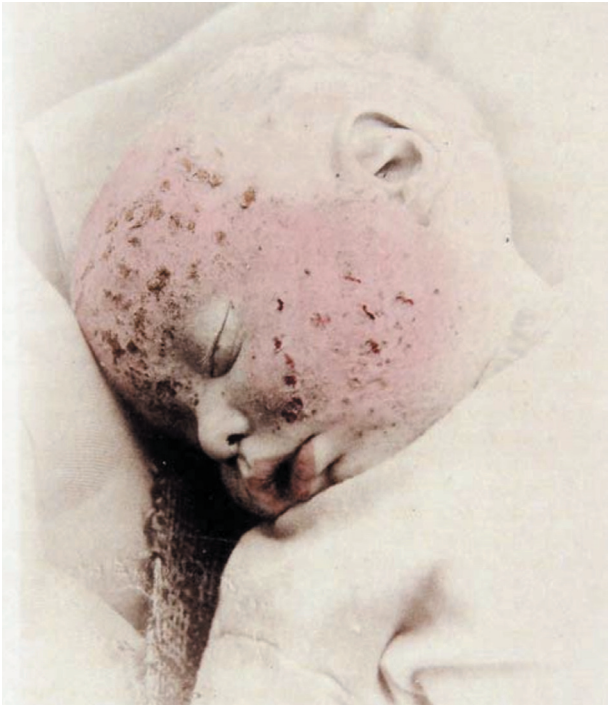

Figure 4
"Photographic Illustrations of Skin Diseases", George Henry Fox (1846-1937)

Historically, a series of color illustrations, lithographs, and black and white photographs have depicted the signs and symptoms of atopic dermatitis with increasing accuracy, often within high-quality artistic representations. By the early 20th century, the clinical presentation, progression, and heredity of the disease were well established, paving the way for a new era of research into its pathophysiology and treatment in the following decades.

Currently, artificial intelligence (AI) is playing an increasingly crucial role in medicine. Especially in dermatology, it provides innovative tools for the diagnosis, treatment, and investigation of skin diseases. AI can analyze vast amounts of clinical data and images, identifying patterns that might go unnoticed by the human eye. This technology not only improves the accuracy of dermatological diagnoses but also enables the generation of illustrations and photographs that simulate various skin diseases, such as atopic dermatitis. The ability of AI to reproduce realistic images has significant implications for several areas, including clinical research, medical education, and the training of health care professionals. For example, creating detailed visual representations of diseases allows students and professionals to learn how to identify clinical characteristics more effectively, thereby improving their diagnostic skills. Furthermore, AI can be used to develop predictive models, which are helpful in assessing prognosis and personalizing treatment.

Figure 5 displays an AI-generated image created in ChatGPT, based on a prompt to reproduce severe atopic dermatitis in a child. This representation is a valuable educational resource, allowing physicians and researchers to visualize and discuss the clinical and aesthetic aspects of the disease, which promotes a better understanding of patients' experience. With the continuous advancement of AI, this technology is

Figure 5
Artificial intelligence-generated image: severe atopic dermatitis in a child

expected to transform medicine by facilitating access to faster and more accurate diagnoses, enhancing medical education, and ultimately improving patient outcomes. Despite these benefits, close attention must be given to the correctness and reliability of the skin lesions represented. It is crucial to remember that a careful clinical examination and a detailed medical history remain our essential working tools and should never be undervalued, even with the introduction of these powerful technologies in medical practice.

The visual evolution of atopic dermatitis, from early medical illustrations to current AI-generated images, demonstrates a significant shift in both available techniques/technologies and our understanding of the disease over time. Historically, illustrations and photographs have effectively captured patients' experience and contributed to our knowledge, while current innovative visual tools offer new perspectives for diagnosis and treatment. This journey in visual representation not only chronicles the historical advancements in medicine but also reflects our ongoing commitment to empathy and to better understanding the conditions that impact patients' quality of life.

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