

CURRENT APPROACH TO MEDICO-LEGAL ASPECTS OF ALLERGIC REACTIONS

Ovidiu Nicolae Berghi¹, Mihai Dumitru², Daniela Vrinceanu², Romica Cergan^{3,*}, Ionut Isaia Jeican⁴,
Calin Giurcaneanu⁵, Adrian Miron⁶

¹*Allergology and Clinical Immunology, Saint Mary Laboratories*, ²*“Carol Davila” University of Medicine and Pharmacy, ENT Department*, ³*“Carol Davila” University of Medicine and Pharmacy, Anatomy Department*, ⁴*“Iuliu Hatieganu” University of Medicine and Pharmacy, Anatomy Department*, ⁵*“Carol Davila” University of Medicine and Pharmacy, Dermatology Department*, ⁶*“Carol Davila” University of Medicine and Pharmacy, General Surgery Department, Bucharest, Romania*

Abstract: Allergies affect one of four people on Earth in their lifetime. Drugs are substances intended to heal or to alleviate diseases but administering them should be under strict control. Immune system may recognize in some people drugs as potential threats and produce IgE antibodies against them. In some cases, this sensitisation can lead to unwanted and dangerous reactions called drug allergies. Errors may appear even in cases of experienced allergology specialists, but these are covered by malpractice licences worldwide. One possible source of legal consequences is the lack of proper allergy training of the staff performing the drug allergy skin tests in current practice. In this situation the limitation derives from interpreting the skin reactions to an undiluted drug as an allergy and unnecessary restraining the patient from receiving that medication. Another aspect revealed is that deadly drug allergic reactions are reported mostly in unauthorized healthcare settings. This article presents a review of medical literature regarding medico-legal aspects of these potential harmful situations.

Keywords: malpractice, drug, allergy.

INTRODUCTION

Medical malpractice occurs when a doctor, other health care professional or a medical unit, through a negligent act or omission, causes a medical problem to a patient. The mistake might be the result of errors in diagnosis, treatment, aftercare, or health management [1,2]. According to Bono *et al.* a simple mistake or error in diagnosis or error during a medical procedure does not define medical malpractice [2]. The authors affirm that a patient or an attorney must demonstrate four elements for a case to go to trial: 1) causation asks the question: did the act or omission cause the poor outcome? 2) duty to the patient asks the question: did the doctor have a responsibility for the care of this patient? 3) negligence or breach of duty: was the clinician negligent in taking care of this patient? 4) damages refer to compensation for loss or injury and/or medical bills [2].

Allergy occurs when a sensitised person

reacts to substances from the surrounding environment that are benign to most people. These substances are called allergens and can be found in dust mites, pets, pollens, foods, insects, ticks, moulds, and medications. Atopy represents the genetic tendency to develop allergic diseases. When atopic people encounter the allergens, they develop an immune reaction that provokes allergic inflammation. This can cause symptoms in the: nose and/or eyes, resulting in allergic rhinitis (hay fever) and/or conjunctivitis, skin resulting in eczema or hives (urticaria) and lungs resulting in asthma. Most allergic reactions are mild to moderate, and do not cause important problems. However, a minority of people may experience a severe allergic reaction called anaphylaxis, which requires immediate lifesaving medication. Allergens most implicated in causing anaphylaxis include foods, medications and insects [3-5].

*Correspondence to: Romica Cergan, Associate Professor, “Carol Davila” University of Medicine and Pharmacy, Anatomy Department, 050474, 8th Eroii Sanitari Blvd., Bucharest, Romania, E-mail: r.cergan@gmail.com

ERRORS IN ALLERGOLOGY

Errors regarding allergic reactions may be divided into two categories: allergic reactions provoked by allergists during testing procedures and allergic reactions provoked by other health professionals.

Allergology tests can be realised in two ways: *in vitro* and *in vivo*. *In vitro* tests pose no risk to the patient because they involve the contact between the patient's blood and a reactant in laboratory without any contact between the patient and the allergen. *In vivo* tests implicate the contact between the patient and the allergen. To demonstrate the allergic supposed nature of a reaction from the past the allergist shall put in direct contact the patient with the presumed allergen using various procedures. One of them is skin prick test where the allergist places a drop of solution on the forearm of the patient and pierce it with a special disposable lancet. This test is used for diagnosing respiratory and food allergies and is part of the more complex drug allergy testing. Generally, it is a safe procedure, and it can be done in hospital and outpatient facilities by allergists. Some negative reactions may appear when this test is realised in patients with unstable asthma, in this situation the physician being responsible for starting an asthma attack. A special precaution it is also advisable when testing pollen extracts in pollen season [6]. Skin prick test present greater flexibility and is usually less costly. Intradermal skin tests are more sensitive but less specific than SPT. They require more precise techniques and are more labour-intensive and time consuming. These tests have occasionally been associated with serious systemic allergic reactions and even death from anaphylaxis [7-9].

According to experts, physicians must take some precautions when they perform skin testing: evaluate patient before the procedure, including the presence of current allergic symptoms, condition of the skin (normal skin vs dermatographism), the history of medication taken by the patient and time of last dose. The specialist must also verify the potency and stability of the allergen extract used, to assure that are used appropriate concentrations of extracts and positive and negative control solutions and to record the reactions at the proper time. It is also mandatory to have ready for use emergency equipment, including epinephrine [4].

Common errors may appear both in prick testing and intradermal testing. Most frequent errors for prick test are the obtaining of false results because placing test too close together (< 2 cm) which can lead to overlapping reactions and induction of bleeding or

negative results when a puncture instrument provoke insufficient penetration of skin [4].

Intradermal testing is also subject to common errors: false results provoked by test sites too close together, volume injected too large, high concentration of allergen and bleeding and negative false results when the injection is performed subcutaneous. In some situations, too many tests performed at the same moment may induce a systemic reaction [4].

DRUG ALLERGIES

Drug allergy represents a major health problem. In order to discern if a negative reaction to a medicine from the patient's medical history was truly allergic it is necessary to perform drug allergy tests. Medical malpractice regarding drug allergy can appear in two situations: when the drug is administrated by a health professional or during a drug allergy test provocation.

Drug-induced allergy is a paradoxical disorder involving a hyperresponsivity to medicines prescribed for therapeutic purposes. Several studies have evaluated along last decades the incidence and gravity of malpractice regarding drug allergies. An analysis from South Korea revealed that antibiotics, radiocontrast media and non-steroidal anti-inflammatory drugs were the most common drugs that had caused drug – induced anaphylaxis [10]. Still, if not properly diagnosed, self – declared allergies to contrast media may deprive patients of important imaging investigations (CT, MRI, intraoperative cholangiograms) with potential detrimental consequences. Jeffres *et al.* reviewed medical negligence and malpractice cases in which a patient with a known penicillin allergy received a β -lactam and experienced an adverse reaction related to the β -lactam. The authors included 27 cases where the patients were known with penicillin allergy, received a β -lactam, and experienced an adverse event. Were included all sources from United States federal and state cases. Limited professional liability was found for clinicians who prescribed cephalosporins or carbapenems to a patient with a known penicillin allergy when the cases received legal outcomes [11].

Poetker and Smith reviewed the existing data of the year 2015 of the medicolegal implications of commonly used oral medications in the speciality of Otolaryngology. Antibiotics, corticosteroids, and narcotics were the classes of medications frequently associated with litigation in the USA [12]. Same two authors realised an OVID research implicating in the first step 272 articles and included in the final review

13 articles regarding medico-legal implications of antibiotic use. Antibiotics were the most common medication associated with litigation in the USA and allergic reactions were the first reason for litigation [13]. An analysis of claims against the NHS in England 1995-2007 about litigation related to drug errors in anaesthesia has found that from ninety-three claims a number of thirty-one involved allergic reactions and in 20 of them, the patients allegedly received a drug to which they were known to be allergic [14].

102 deaths were due to adverse drug reactions and allergies in a retrospective multicentre study on medical malpractice cases with lethal outcome. Leading drug groups were contrast media, anti-coagulants, marcumar, heparine, lyse therapy followed by antibiotics and non-steroidal anti-rheumatics (NSAR), diclophenac and metamizole. Fewer situations were seen with local anaesthetics, chemotherapeutics (methotrexate), opioids. Cases with death due to side-effects and allergies were mostly seen in hospitals, mainly seen in elderly patients with several pre-existing diseases [15].

A comparative review study evaluated anaphylactic deaths in Maryland (United States) and Shanghai (China) of forensic autopsy cases from 2004 to 2006. A total of 28 cases of anaphylactic death were identified, 17 from Maryland and 11 from Shanghai. Of the 17 Maryland cases 5 involved allergic reaction to drugs with some of cases having history of asthma and previous allergic reactions to certain foods and/or drugs. In Shanghai, all 11 deaths resulted from anaphylactic reaction to antibiotics, 10 of which occurred in clinics illegally operated by unlicensed physicians [16].

The diagnostic of drug allergy must be done by allergists. The specialist may use different techniques to do it, with drug challenges being the gold-standard diagnostic procedure to determine patient's tolerance to a drug. It can be also used skin tests (especially for penicillin allergy), patch testing and delayed intradermal testing. The test must be preceded by a written informed consent and carried out in a facility fully prepared to treat an allergic reaction and with an easy access to intensive therapeutic unit in case of a severe reaction [17]. A major source of medical malpractice is the performing of allergy tests by unqualified personnel. In many situations the test is realized by nurses unqualified for this procedure, that have no allergology training in this activity. The most common mistake is to perform an intradermic test with an undiluted drug. In many cases it will appear a wheal after just few minutes. This reaction shall be considered an allergy and the patient shall be labeled wrong as allergic. In fact, the reaction

is an irritation, because most substances if they are injected intradermic/subcutaneously will provoke an irritation at the site of injection. Because of lack of allergology base knowledge this reaction shall be interpreted as a drug allergy [18-21].

Nevertheless, given the increasing incidence and prevalence of allergies, asthma and allergic rhinitis in general population there is a supplementary risk of encountering a severe reaction during routine allergy tests [22]. Supplementary efforts should be put into preventing severe airway obstruction during drug hypersensitivity testing to prevent iatrogenic cases developing reactions to novel allergens [23]. Special care should be taken also in cases with topic medication applied on mucosa or skin [24]. Another future aspect to discuss could be the allergic reaction to implantable substances used in ambulatory cosmetic procedures [25].

In conclusion, drug allergy is an undesired medical event. In some situations, this is a result of an unknown drug sensitisation. In other situations, the reaction is the result of an error in taking the complete medical history of a patient regarding adverse events to drugs in the past. Measures to reduce the incidence and severity of this type of reactions are taking an exhaustive allergic medical history before recommending a medicine for any physician and obtaining an informed consent before any drug provocation and performing the procedure only by allergy specialists in well-equipped facilities.

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Rodziewicz TL, Houseman B, Hipskind JE. Medical Error Prevention. 2020. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020.
2. Bono MJ, Wermuth HR, Hipskind JE. Medical Malpractice. [Updated 2020]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020.
3. Costache A, Berghi ON, Cergan R, Dumitru M, Neagos A, Popa LG, Giurcaneanu C, Vrinceanu D. Respiratory allergies: Salicaceae sensitization (Review). *Exp Ther Med*. 2021;21(6):609.
4. Anca Mirela Chiriac, Jean Bousquet, Pascal Demoly. *In Vivo* Methods for the Study and Diagnosis of Allergy. *Middleton's Allergy Principles and Practice*. 2020; 9(2): 1097- 1110.
5. Anne M. Ditto. Drug Allergy. Chapter 17. Part A. Introduction, Epidemiology, Classification of Adverse Reactions, Immunochemical Basis, Risk Factors, Evaluation of Suspected Drug Allergy, and Patient Management Considerations. P308 - 354. *Patterson's Allergic Diseases*. Eight Edition. 2019.

6. Heinzerling L, Mari A, Bergmann KC, Bresciani M, Burbach G, Darsow U, Durham S, Fokkens W, Gjomarkaj M, Haahtela T, Bom AT, Wöhrl S, Maibach H, Lockey R. The skin prick test - European standards. *Clin Transl Allergy*. 2013;3(1):3.
7. Bagg A, Chacko T, Lockey R. Reactions to prick and intradermal skin tests. *Ann Allergy Asthma Immunol*. 2009 May;102(5):400-2.
8. Birch K, Pearson-Shaver AL. Allergy Testing. [Updated 2020]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020.
9. Tourlas K, Burman D. Allergy Testing. *Prim Care*. 2016;43(3):363-374.
10. Hyeon CW, Lee JY, Jang S, Cho SI, Kim S, Lee W, Shin S. Medical malpractice related to drug-induced anaphylaxis: An analysis of lawsuit judgments in South Korea. *Medicine (Baltimore)*. 2019; 98(23):e15996.
11. Jeffres MN, Hall-Lipsy EA, King ST, Cleary JD. Systematic review of professional liability when prescribing β -lactams for patients with a known penicillin allergy. *Ann Allergy Asthma Immunol*. 2018;121(5):530-536.
12. Poetker DM, Smith TL. Medicolegal Implications of Common Rhinologic Medications. *Otolaryngol Clin North Am*. 2015;48(5):817-826.
13. Poetker DM, Smith TL. What rhinologists and allergists should know about the medico-legal implications of antibiotic use: a review of the literature. *Int Forum Allergy Rhinol*. 2015;5(2):104-110.
14. Cranshaw J, Gupta KJ, Cook TM. Litigation related to drug errors in anaesthesia: an analysis of claims against the NHS in England 1995-2007. *Anaesthesia*. 2009; 64(12):1317-1323.
15. Madea B, Musshoff F, Preuss J. Medical negligence in drug associated deaths. *Forensic Sci Int*. 2009;190(1-3):67-73.
16. Shen Y, Li L, Grant J, Rubio A, Zhao Z, Zhang X, Zhou L, Fowler D. Anaphylactic deaths in Maryland (United States) and Shanghai (China): a review of forensic autopsy cases from 2004 to 2006. *Forensic Sci Int*. 2009;186(1-3):1-5.
17. Roland Solensky, Elizabeth J. Phillips. *Drug Allergy*. Middleton; Allergy Principles and Practice. 2020; 9 (2): 1261-1282.
18. Krau SD, McInnis LA, Parsons L. Allergy skin testing: what nurses need to know. *Crit Care Nurs Clin North Am*. 2010;22(1):75-82.
19. Powrie K. Identification and management of drug allergy. *Nurs Stand*. 2018;33(1):45-50.
20. Miron A, Giulea C, Tudose I, Petrache D, Giurcaneanu C. Pyoderma gangrenosum, rare parietal complication after colorectal surgery. *Chirurgia (Bucur)*. 2014; 109(2):248-253.
21. Calu V, Toma EA, Enciu O, Miron A. Clostridium difficile Infection and Colorectal Surgery: Is There Any Risk? *Medicina (Kaunas)*. 2019; 55(10):683.
22. Vrinceanu D, Berghi ON, Cergan R, Dumitru M, Ciuluvica RC, Giurcaneanu C, Neagos A. Urban allergy review: Allergic rhinitis and asthma with plane tree sensitization (Review). *Exp Ther Med*. 2021;21(3):275.
23. Berghi ON, Vrinceanu D, Cergan R, Dumitru M and Costache A: Solanum melongena allergy (A comprehensive review). *Exp Ther Med* 22: 1061, 2021.
24. Mehedintu C, Bratila E, Cirstoiu M, Petca A, Brinduse LA, Berceanu C, Barac RI, Andreescu CV, Petca RC, Sandru F, Ionescu OM. Evaluation of Effectiveness and Tolerability of Boric Acid in the Treatment of Vaginal Infection with Candida Species. *Revista de Chimie*. 2019; 70(7):2375-2378.
25. Vasile D, Iancu R, Bogdanici C, Ungureanu E, Ciobotea D, Ciuluvica R, Iancu G. Chemo-physical properties and biomedical applications of hyaluronic acid in medicine, *Rev. Chim*. 2017; 68(2):384-386.