

Self-reported Drug Allergy in Health Care Workers in Conservative and Surgical Medicine Departments

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■ Abstract

Background: Drug allergy comprises 10% to 30% of all adverse drug reactions, and according to data from the literature, sensitivity to drug allergens is 2 to 3 times more common in health care workers than in the general population.

Objective: The aims of this study were to estimate the prevalence of self-reported drug allergy in health care workers and compare the data obtained between doctors and nurses from conservative medicine (CM) and surgical medicine (SM) departments.

Methods: This was an analytic questionnaire-based survey conducted using the European Network of Drug Allergy questionnaire adapted to the Lithuanian population. The questionnaires were completed by 346 individuals.

Results: Nurses from SM departments reported allergy symptoms more frequently than doctors from the same departments (38.1% vs. 16.7%, $P=0.01$) and nurses from the CM departments (38.1% vs. 18%; $P=0.02$). The most common drugs reported to cause hypersensitivity symptoms were similar in the CM and SM departments: antibiotics (8.8% and 12.7%), local anesthetics (2.9% and 6.9%), and group B vitamins (1.2% and 2.1%). Skin damage was indicated as the most common clinical manifestation.

Conclusions: Based on the data reported by the questionnaire respondents, drug allergy was most prevalent among nurses from the SM departments, and antibiotics and local anesthetics were the most common substances that induced the symptoms.

Key words: Drug allergy. Hypersensitivity. Health care workers. Conservative medicine. Surgical medicine.

■ Resumen

Introducción: La alergia a medicamentos constituye un 10-30% de las reacciones adversas a medicamentos, siendo 2-3 veces más frecuente entre los trabajadores de la sanidad.

Objetivo: En este estudio se estimó la prevalencia de alergia a medicamentos referida por trabajadores de la sanidad y se comparó dependiendo del área de trabajo del personal sanitario, según fuera médico o quirúrgico.

Métodos: Para ello se aplicó un cuestionario adaptado del de ENDA 1999 para una población de 346 sujetos en Lituania.

Resultados: En los resultados se observó como las enfermeras de los departamentos quirúrgicos presentaban síntomas de alergia a medicamentos con más frecuencia que los médicos (38.1% vs. 16.7%, $p=0.01$), y que las enfermeras de departamentos médicos (38.1% vs. 18%; $p=0.02$).

Conclusiones: Los medicamentos que provocaban con más frecuencia síntomas de hipersensibilidad en ambas áreas fueron los antibióticos (8.8% y 12.7%), seguido de los anestésicos locales (2.9% y 6.9%), y el grupo B de Vitaminas (1.2% y 2.1%). Las manifestaciones clínicas más frecuentes fueron las cutáneas.

Palabras clave: Alergia a medicamentos. Hipersensibilidad. Trabajadores de la sanidad. Medicina conservadora. Medicina quirúrgica.

Introduction

Drug hypersensitivity is one of the most common adverse drug reactions related to increased sensitivity to drug allergens. It is a serious problem because of its potential for inducing morbidity and mortality [1]. Drug allergy comprises about 10% to 30% of all adverse drug reactions [1-4], and it is estimated that only 1 out of 6 such reactions is allergic [2,5]. According to the literature, sensitivity to drug allergens is 2 to 3 times more common in health care workers than in the general population [1,2,6,7]. Adverse drug reactions—including drug allergy—are related to drug exposure rather than genetic factors [4]. Health care workers are at risk of developing drug allergy because they are regularly exposed to the same medications in their daily work, and can become particularly sensitized to the drugs they handle [8].

Studies have shown that the prevalence of drug allergy among nursing staff is increasing worldwide, a change that may also be influenced by the continuous appearance of new medications [9].

Drug allergy develops through immunologic mechanisms and has different clinical manifestations, the most common of which is skin damage, which manifests through type 1 and type 4 hypersensitivity reactions [2,10]. The most common drug-related causes of allergy symptoms are antibiotics, drugs for epilepsy and heart disease, anesthetics, cancer drugs, vaccines, aspirin, morphine, and preservatives used in drug compounds [2,6]. Penicillin appears to be the most common cause of drug allergy [6,7].

The aim of the present study was to evaluate the prevalence of self-reported drug allergy in health care workers, and to compare the data obtained between doctors and nurses working in conservative medicine (CM) and surgical medicine (SM) departments.

Participants and Methods

The study was an analytic questionnaire survey based on the European Network of Drug Allergy questionnaire [11] adapted to the Lithuanian population. Permission for the study was obtained from the Bioethics Centre at the Lithuanian University of Health Sciences (Number: BC-MF-02). The questionnaire contained 56 questions divided into 7 parts: general information (age, sex, occupation, department, and length of employment); drugs reported to cause allergy; symptoms of drug allergy; other types of allergy; family history of drug allergy; family history of other allergies; and methods used to diagnose drug allergy. The questionnaire was distributed to doctors and nurses working at the Hospital of the Lithuanian University of Health Sciences Kauno Klinikos. The participants were employed in CM departments (Skin and Venereal Diseases, Endocrinology, Gastroenterology, Rheumatology, and Family Medicine) and SM departments (Otorhinolaryngology, Ophthalmology, Urology, Plastic and Reconstructive Surgery, Neurosurgery, General Surgery, and Maxillofacial Surgery). In total, 500 questionnaires were distributed and 346 were returned completed (by 196 doctors

Table 1. Characteristics of Questionnaire Respondents

| | Conservative Medicine Departments (n=154) | Surgical Medicine Departments (n=192) |
|--|--|--|
| Men/ women, No. | 20/134 | 78/114 |
| Doctors/ nurses, No. | 98/56 | 98/94 |
| Mean (SD) age, y | 39.0 (11.9) | 39.5 (12.3) |
| Mean (SD) years worked, No. | 17.8 (15.5) | 15.0 (12.5) |
| Self-reported drug allergy, % of participants | 17.5 | 15.1 |

and 150 nurses); 154 questionnaires were completed by CM department workers and 192 by SM department workers. The respondents were aged between 24 and 75 years (mean [SD] age, 39.26 [12.09] years). The characteristics of the participants are shown in Table 1.

All analyses were performed using the SPSS statistical software package (version 13). A *P* value of <.05 was considered statistically significant. The prevalence of responses was compared using the Pearson χ^2 criterion. A receiver operator curve (ROC) was used to evaluate the risk of drug allergy according to length of employment at the hospital. Multiple logistic regression analysis was also carried out, with the presence of drug allergy as the dependent variable.

Results

The prevalence of self-reported drug allergy did not differ significantly between the CM and SM departments (17.5% vs 15.1%) (Table 1). Drug hypersensitivity was confirmed

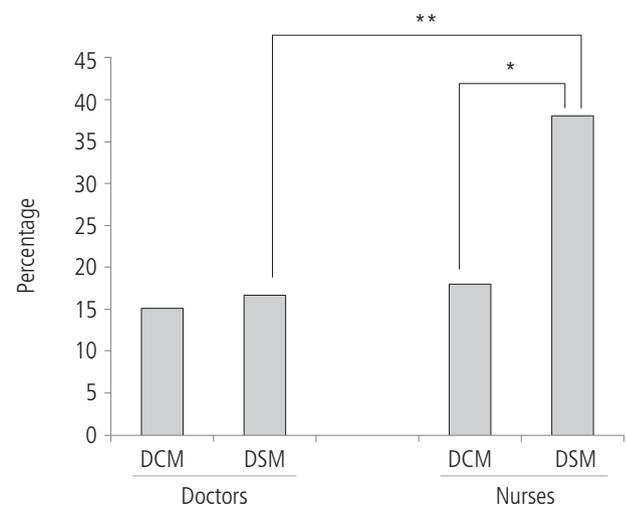


Figure 1. Self-reported prevalence of drug allergy. DCM indicates departments of conservative medicine; DSM, departments of surgical medicine.

**P*<.05

***P*≤.01

by an allergist and clinical immunologist in 37.04% of CM respondents and in 31.03% of SM respondents. A significantly higher proportion of nurses working in the SM departments reported allergy symptoms compared with doctors from the same departments and nurses from the CM departments (Figure 1).

Antibiotics and local anesthetics were the most common medications reported to cause drug allergy symptoms (Table 2). Penicillin was the most commonly attributed cause of symptoms, reported by 12.7% of SM workers and 8.8% of CM workers. The most common symptoms attributed to this allergy were rash (6.3%), itching (5.5%), redness (5.0%), sneezing (4.6%), ocular symptoms (3.8%), cough (3.4%), and edema (3.4%) (Figure 2).

Skin damage was the most common symptom of drug allergy in both groups (Figure 2). We noticed that workers from the SM departments reported hand rash more frequently than those from the CM departments (22.3% vs 12.5%, $P=.045$).

Table 2. Most Common Drugs Reported to Cause Allergy Symptoms

| | | Local Anesthetics | Antibiotics | Group B Vitamins |
|-----------------------------------|--------------------|--------------------|--------------------|-------------------|
| Surgical medicine departments | Doctors and nurses | 6.9% | 12.7% | 2.1% |
| | Doctors | 1.7% | 6.7% | 0% |
| | Nurses | 14.3% ^a | 21.4% ^b | 4.3% ^b |
| Conservative medicine departments | Doctors and nurses | 2.9% | 8.8% | 1.2% |
| | Doctors | 3.5% | 8.1% | 1.0% |
| | Nurses | 2.0% | 10.0% | 1.8% |

^a $P \leq .01$ (nurses vs doctors in surgical medicine departments).

^b $P < .05$ (nurses vs doctors in surgical medicine departments).

Compared with doctors, nurses from the SM departments reported more frequently that their drug allergy symptoms were due to local anesthetics, antibiotics, and group B vitamins (Table 2).

We found that a reported family history of allergy was more common in health care workers who noted drug allergy than in those who did not (Figure 3).

According to our data, sensitivity to drugs increased with length of employment at the hospital. The area under the ROC was 0.586 ($P=.04$), indicating that duration of employment was a prognostic factor in predicting the risk of the development of drug allergy (Figure 4). The incidence of cases increased after more than 3 years of employment at the hospital (refraction index, 3.8). Almost the same proportion of doctors from the SM and CM departments (10.5% and 5%, respectively) indicated a connection between the manifestation of drug-induced symptoms of allergy and duration of employment at the hospital. In the case of nurses, this relationship was noted

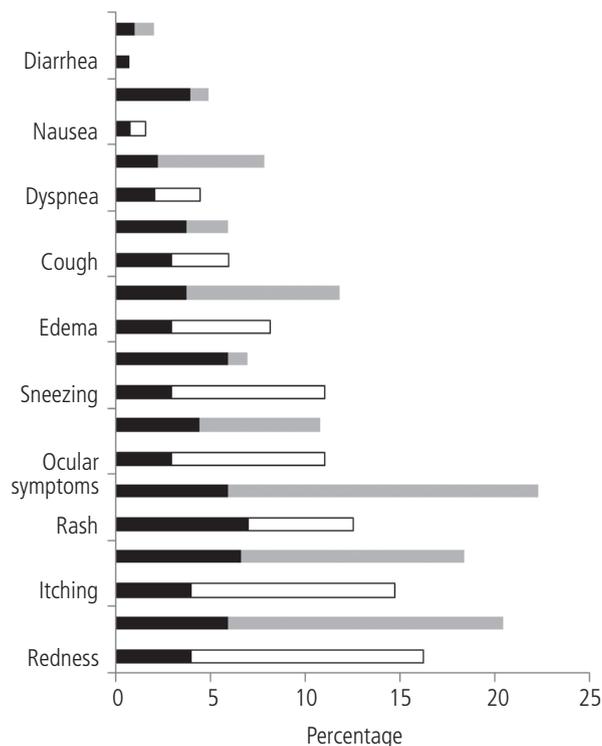


Figure 2. Most common symptoms of self-reported drug allergy.

Legend:
 Grey: Departments of surgical medicine.
 White: Departments of conservative medicine.
 Black: Penicillin-induced symptoms.

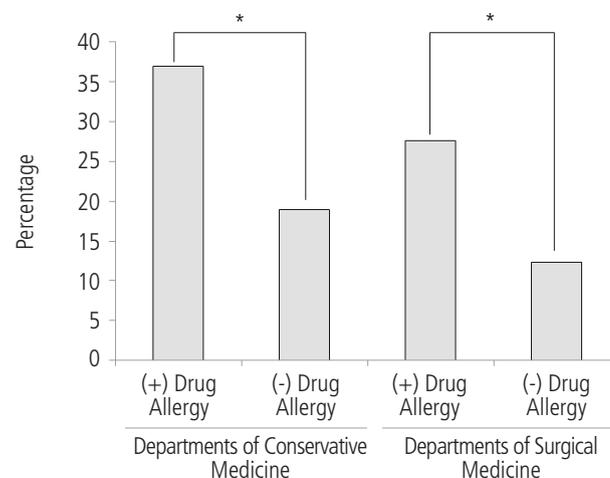


Figure 3. Proportion of respondents indicating a family history of allergy according to the self-reported presence (+) or absence (-) of drug allergy. * $P < .05$.

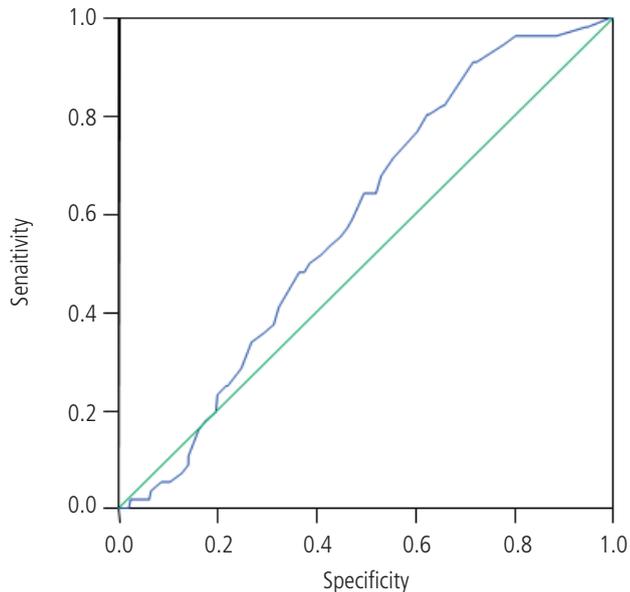


Figure 4. Relationship between the manifestation of drug allergy and length of employment (years) at the hospital. The area under the receiver operator curve is 0.586 ($P=0.04$); refraction index, 3.8.

more frequently by those working in the SM departments (28.6% vs 12%, $P=0.04$).

Multiple logistic regression analysis showed that increasing age had a significant impact on the development of drug allergy (odds ratio, 1.026; 95% CI, 1.003 to 1.051).

Discussion

Our study has shown that medical workers (and nurses in particular) from SM departments reported drug-induced allergy more frequently than their colleagues from the CM departments. To our knowledge, there have been no previous studies of the prevalence of self-reported allergy among health care workers in Lithuanian hospitals. In a search of the Pubmed database, we also failed to find any studies about differences in the prevalence of drug-induced allergy between doctors and nurses in CM and SM departments.

A comparison of our results with data from previously published studies shows that drug allergy symptoms are more common in health care workers than in the general population [1-3,6,7]. The prevalence of self-reported drug allergy among health care workers in our series was 16.18%. According to the literature, more than 7% of the general population experience adverse drug reactions and over 15% of these are hypersensitivity reactions [3]. In a study performed by Kvedariene et al [12] in Lithuania, 11.2% of adults reported drug allergy: 6.9% to antibiotics, 2.1% to nonsteroidal anti-inflammatory drugs, and 1.2% to local anesthetics [12]. The prevalence of drug allergy in hospitalized patients reported in the literature is variable, with rates ranging from 3% to 20% [13]. Drug allergy symptoms can

be influenced by high doses, long-term or frequent exposure, route of administration (application of ointment on skin with dermatitis, parenteral administration), previous use of drugs, cross-sensitization, age, sex (drug allergy is more common in women), genetic predisposition, and the presence of other diseases [2,14,15].

Similarly to other studies performed in health care workers and the general population, our study showed that cutaneous reactions (redness, rash, and/or itching) were the most frequent clinical manifestation of drug allergy, and that antibiotics—in particular penicillin—were the most commonly reported cause of symptoms [2,4,8,11,13,16-20]. In our series, allergy to penicillin accounted for 33.93% of all the drug allergies reported. All the respondents who indicated symptoms of allergy to antibiotics were allergic to penicillin. Skin prick tests have shown that approximately 7% of people without clinical manifestations of allergy react to the penicillin allergen [17]. Although the number of deaths due to adverse drug reactions is not known, anaphylactic reactions occur in 32 out of 100 000 persons treated with penicillin [13,17,28]. A study conducted by Khanferyan et al [6] in hospitals in South Russia showed that penicillin was responsible for drug allergy symptoms in 29.5% of health care workers, and accounted for 68.7% of all antibiotics that caused allergy. In a French study, Bousquet et al [21] analyzed 210 individuals with penicillin allergy and showed that 36.7% of patients with proven hypersensitivity to β -lactam antibiotics experienced urticaria as a single symptom, 19.1% experienced anaphylaxis without shock, 17.6%, anaphylactic shock, and 19.1%, maculopapular exanthema [21]. In our study, the most common symptoms of penicillin allergy, apart from skin damage, were sneezing, ocular symptoms, and cough. There were no reports of anaphylactic shock. Our study and the aforementioned study by Bousquet et al. showed a similar tendency in that skin damage was the most common symptom of penicillin allergy.

Our study showed that local anesthetics were indicated as the second most common cause of allergy among health care workers. However, according to the literature, local anesthetics rarely cause allergy symptoms, even during interventional procedures [22-25]. In a study by Rood [25], it was found that the most likely causes of adverse reactions to lidocaine were psychogenic, and there were no cases of allergic reactions. However, in a study by Beliauskiene et al [26], benzocaine, a local anesthetic, was found to be the main contact allergen in patients with chronic leg ulcers and surrounding dermatitis; 34.4% of these patients had a positive patch test reaction to benzocaine. In our search of the literature, we found no data on allergy symptoms among people exposed to local anesthetics on multiple occasions. Our respondents were exposed on a daily basis, and this could have led to the development of hypersensitivity. Allergy to local anesthetics was more common among nurses working in SM departments (14.3%) than in CM departments, where these drugs are used less often. This could explain our findings. On the other hand, we did not use any specific tests to confirm self-reported allergy to local anesthetics, and thus the symptoms could have been caused by adverse drug reactions rather than by immunological mechanisms.

In our series, symptoms of drug allergy were more common

in nurses from SM departments than in doctors from the same departments or in nurses from CM departments. This might be related to the fact that drugs—especially antibiotics and local anesthetics—are more widely used in surgical medicine. A study by Cetinkaya et al [7] in 2004 in a hospital in Istanbul, Turkey, showed that nurses can develop occult sensitization to β -lactam antibiotics. The nurses used these antibiotics in their daily practice and had no history of drug allergy. The frequency of positive skin reactions to penicillin allergen in that study was 12%.

Many factors may influence increased sensitivity to medications, and genetic predisposition is thought to be one of the risk factors for drug allergy [14]. Our study showed that a reported family history of allergy was more common in SM and CM department workers who indicated drug allergy. On investigating a possible genetic predisposition for drug allergy, Huang et al [27] concluded that the IL-4R α Q576 allele was related to penicillin allergy, the IL-4R α I75 allele was associated with urticaria, and the Q576/I75 haplotype might be related to penicillin allergy [27]. A study performed by Apter et al [28] at the University of Pennsylvania in the United States also showed that self-reported allergy to penicillin may be influenced by *interleukin-4* single nucleotide polymorphisms, and postulated that the development of allergy to penicillin may be associated with a history of penicillin allergy among first-degree relatives, a history of other adverse drug reactions, and atopy. The role of genetic predisposition based on family history in Lithuanian children with allergy to penicillin was described in 2008 in a study by Malyte et al [29], who observed adverse drug reactions in 8.9% of children with a family history of drug hypersensitivity reactions and in only 2.4% of children without such a history. In our study, we detected a similar tendency: reports of allergy among relatives were more common in respondents who reported drug allergy than in those who did not. Other authors, however, have claimed that adverse drug reactions—including allergic reactions—are not strictly related to genetic predisposition but rather acquired due to exposure to medications [4].

Allergy to antibiotics has been reported to be more prevalent among females [30]. A study performed by the Mayo Clinic College of Medicine in the US state of Minnesota reported a greater risk of allergy to penicillin in females with a history of this allergy [30]. In our study, 78.95% of the participants who reported penicillin allergy were women. However, the fact that the majority of respondents in our study were women might explain why we detected a higher prevalence of penicillin allergy—and drug allergy in general—in this population.

Previous use and long-term exposure to drugs are well-known risk factors for developing drug allergy symptoms [14,15]. Khanferyan et al [6] found that 20% of health care workers showed the first symptoms of allergic disease after they had started working at a hospital, with prevalence increasing with length of employment (6.7% after 1 year and 47% after 7 or more years). Our study yielded similar results as drug allergy symptoms were more common in health care workers who had been in long-term employment at the hospital. This might be explained by the fact that immunoglobulin (Ig) E-mediated reactions to drugs frequently used in daily practice are generally believed to depend on the prior development of an immune response to

the hapten/carrier complex. This sensitization phase is usually asymptomatic. On renewed contact with the drug, the hapten-carrier complex is formed again, and drug-specific IgE binds to mast cells, and causes mast cell degranulation—and thus symptoms of allergic reactions [2].

To sum up, our study shows that symptoms of drug-induced allergy were reported more frequently by nurses working in SM departments than by doctors from the same departments or nurses from CM departments. The respondents who noted drug allergy attributed their condition to family factors and length of employment. The drugs most frequently indicated as the cause of symptoms were antibiotics and local anesthetics, and the most common manifestations were redness, rash, and itching.

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References

1. Nagao-Dias AT, Barros-Nunes P, Coelho HL, Solé D. Allergic drug reactions. *Jornal De Pediatria*. 2004;80:259-66.
2. Pichler WJ, Adam J, Daubner B, Gentinetta T, Keller M, Yerly D. Drug hypersensitivity reactions: pathomechanism and clinical symptoms. *Med Clin North Am*. 2010;94:645-64.
3. Brockow K. Diagnosis of drug allergy. In Final programme and abstracts SAM 2010. EAACI; 2010. p. 20.
4. Nagao-Dias AT, Teixeira FM, Coelho HL. Diagnosing immune-mediated reactions to drugs. *Allergol et Immunopathol*. 2009;37:98-104.
5. Lochmatter P, Zawodniak A, Pichler WJ. In vitro tests in drug hypersensitivity diagnosis. *Immunol Allergy Clin North Am*. 2009;29:537-54.
6. Khanferyan RA, Grigorieva VV, Sundatova TV, Reuk SV, DuBuske LM. The prevalence of allergic diseases among health care workers in the South of Russia. *J Allergy Clin Immunol*. 2004;113:321.
7. Cetinkaya F, Ozturk AO, Kutluk G, Erdem E. Penicillin Sensitivity among hospital nurses without a history of penicillin allergy. *J Adv Nurs*. 2006;58:126-9.
8. Barbaud A. Occupational dermatitis in health care personnel. *Rev Prat*. 2002;52:1425-32.
9. Chaari N, Sakly A, Amri C, Mahfoudh A, Henchi MA, Khalfallh T, Bchir N. Occupational allergy in healthcare workers. *Recent Pat Inflamm Allergy Drug Discov*. 2010;4:65-74.
10. Choi IS, Han ER, Lim SW, Lim SR, Kim JN, Park SY, Chae SK, Lim HH, Seol YA, Bae YI, Won YH. Beta-lactam antibiotic sensitization and its relationship to allergic diseases in tertiary hospital nurses. *Allergy Asthma Immunol Res*. 2010;2:114-22.
11. Demoly P, Kropf R, Birhcer A, Pichler WJ. Drug hypersensitivity: questionnaire. *Allergy*. 1999;4:999-1003.
12. Kvedariene V, Rudzeviciene O, Silkina O, Kavaliauskaite L, Drusyte S, Volugyte I, Nargela R, Demoly P. Hypersensibilite

- medicamenteuse dans la region de Vilnius, Lituanie. *Revue francaise d'allergologie et immunologie clinique*. 2007;47:279.
13. American Academy of Allergy, Asthma and Immunology. The Allergy Report: Science Based Findings on the Diagnosis & Treatment of Allergic Disorders. American Academy of Allergy, Asthma and Immunology (AAAAI) 1996-2001. 2001. [cited 2012 Jan 5]. Available from: <http://www.aaaai.org>.
 14. Thong B, Motala C, Vervloet D. Drug Allergies. Resource Center: information for health professionals. January 2007. [cited 2012 Jan 5]. Available from: <http://www.worldallergy.org>.
 15. Birnbaum J, Vervloet D. Allergy to Anaesthetic Agents. Resource Center: information for health professionals. October 2007. [cited 2012 Jan 5]. Available from: <http://www.worldallergy.org>.
 16. Branellec A, Thomas M, Fain O, Kettaneh A, Stirnemann J, Letellier E. Frequency of self-reported penicillin allergy in the area of Seine-Saint-Denis (France). *Rev Med Interne*. 2008;29:271-6.
 17. Nugent JS, Quinn JM, McGrath CM, Hrcir DE, Boleman WT, Freeman TM. Determination of the incidence of sensitization after penicillin skin testing. *Ann Allergy Asthma Immunol*. 2003;90:398-403.
 18. The International Collaborative Study of Severe Anaphylaxis. Risk of anaphylaxis in a hospital population in relation to the use of various drugs: an international study. *Pharmacoepidemiol Drug Saf*. 2003;12:195-202.
 19. Borch JE, Andersen KE, Bindslev-Jensen C. The prevalence of suspected and challenge-verified penicillin allergy in a university hospital population. *Basic Clin Pharmacol Toxicol*. 2006;98:357-62.
 20. Gomes E, Cardoso MF, Praca F, Comes L, Marino E, Demoly P. Self-reported drug allergy in general adult Portuguese population. *Clin Exp Allergy*. 2004;34:1597-601.
 21. Bousquet PJ, Kvedariene V, Co-Minh HB, Martins P, Rongier M, Arnoux B, Demoly P. Clinical presentation and time course in hypersensitivity reactions to beta-lactams. *Allergy*. 2007;62:872-6.
 22. Mertes PM, Laxenaire MC. Anaphylactic and anaphylactoid reactions occurring during anaesthesia in France. Seventh epidemiologic survey (January 2001-December 2002). *Ann Fr Anesth Reanim*. 2004;23:1133-43.
 23. Grzanka A, Misiołek H, Filipowska A, Miśkiewicz-Orczyk K, Jarzab J. Adverse effects of local anaesthetics – allergy, toxic reactions or hypersensitivity. *Anestezjol Intens Ter*. 2010;42:175-8.
 24. Wildsmith JA, Mason A, McKinnon RP, Rae SM. Alleged allergy to local anaesthetic drugs. *Br Dent J* 1998;184:507-10.
 25. Rood JP. Adverse reaction to dental local anaesthetic injection – 'allergy' is not the cause. *Br Dent J*. 2000;189:380-4.
 26. Beliauskiene A, Valiukeviciene S, Sitkauskiene B, Schnuch A, Uter W. Contact sensitization to the allergens of European baseline series in patients with chronic leg ulcers. *Medicina*. 2011;47:480-5.
 27. Huang CZ, Yang J, Qiao HL, Jia LJ. Polymorphisms and haplotype analysis of IL-4Ralpha Q576R and I75V in patients with penicillin allergy. *Eur J Clin Pharmacol*. 2009;65:895-902.
 28. Apter AJ, Schelleman H, Walker A, Addya K, Rebeck T. Clinical and genetic risk factors of self-reported penicillin allergy. *J Allergy Clin Immunol*. 2008;122:152-8.
 29. Malyte J, Kvedariene V, Rudzeviciene O, Butiene I, Norkuniene J, Vogulyte I, Drusyte S, Demoly P. Hypersensitivity and family history of β -lactams induced reaction in Lithuanian children. *Eur J Dermatol. Drug hypersensitivity meeting*. 2008;18. p.269.
 30. Park MA, Matesic D, Markus PJ, Li JT. Female sex as a risk factor for penicillin allergy. *Ann Allergy Asthma Immunol*. 2007;99:54-8.

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