Web COBIOPHAD – January 19

1. GENERAL INFORMATION ABOUT DRUG ALLERGY

[1] - Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. Antibiotic allergy. Lancet. 2019 Jan; 393(10167):183–98.

Abstract:

Antibiotics are the commonest cause of life-threatening immune-mediated drug reactions that are considered off-target, including anaphylaxis, and organ-specific and severe cutaneous adverse reactions. However, many antibiotic reactions documented as allergies were unknown or not remembered by the patient, cutaneous reactions unrelated to drug hypersensitivity, drug-infection interactions, or drug intolerances. Although such reactions pose negligible risk to patients, they currently represent a global threat to public health. Antibiotic allergy labels result in displacement of first-line therapies for antibiotic prophylaxis and treatment. A penicillin allergy label, in particular, is associated with increased use of broad-spectrum and non-β-lactam antibiotics, which results in increased adverse events and antibiotic resistance. Most patients labelled as allergic to penicillins are not allergic when appropriately stratified for risk, tested, and re-challenged. Given the public health importance of penicillin allergy, this Review provides a global update on antibiotic allergy epidemiology, classification, mechanisms, and management.

DOI: 10.1016/S0140-6736(18)32218-9

[2] - Warrington R, Silviu-Dan F, Wong T. Drug allergy. Allergy, Asthma Clin Immunol. 2018 Sep 12;14(S2):60.

Abstract:

Drug allergy encompasses a spectrum of immunologically-mediated hypersensitivity reactions with varying mechanisms and clinical presentations. This type of adverse drug reaction not only affects patient quality of life, but may also lead to delayed treatment, unnecessary investigations, and even mortality. Given the myriad of symptoms associated with the condition, diagnosis is often challenging. Therefore, referral to an allergist experienced in the identification, diagnosis and management of drug allergy is recommended if a drug-induced allergic reaction is suspected. Diagnosis relies on a careful history and physical examination and, in some instances, skin testing and graded challenges. Induction of drug tolerance procedures may also be required. The most effective strategy for the management of drug allergy is avoidance or discontinuation of the offending drug. When available, alternative medications with unrelated chemical structures should be substituted. Cross-reactivity among drugs should be taken into consideration when choosing alternative agents. Additional therapy for drug hypersensitivity reactions is largely supportive and may include topical corticosteroids, oral antihistamines and, in severe cases, systemic corticosteroids. In the event of anaphylaxis, the treatment of choice is injectable epinephrine. If a particular drug to which the patient is allergic is indicated and there is no suitable alternative, induction of drug tolerance procedures may be considered to induce temporary tolerance to the drug. This article provides a background on drug allergy and strategies for the diagnosis and management of some of the most common drug-induced allergic reactions, such as penicillin, sulfonamides, cephalosporins, radiocontrast media, local anesthetics, general anesthetics, acetylsalicylic acid and non-steroidal anti-inflammatory drugs, and therapeutic monoclonal antibodies.

DOI: 10.1186/s13223-018-0289-y

[3] - Mawhirt SL, Fonacier LS, Calixte R, Davis-Lorton M, Aquino MR. Skin testing and drug challenge outcomes in antibiotic-allergic patients with immediate-type hypersensitivity. Ann Allergy, Asthma Immunol. 2017 Jan;118(1):73–9.

Abstract:

Background: The evaluation of antibiotic immediate-type hypersensitivity is intricate because of nonstandardized skin testing and challenge method variability. To determine the safety outcomes and risk factors for antibiotic challenge reactions in patients reporting a history of antibiotic immediate-type hypersensitivity.

Methods: A 5-year retrospective review of patients evaluated for immediate-type antibiotic allergy was conducted. Data analyzed included patient demographics, index reaction details, and outcomes of skin testing and challenges, classified as single-step or multistep.

Conclusion: In the present population, younger women with multiple reported antibiotic allergies were at greatest risk for challenge reactions. Negative skin testing results did not exclude reactions, and index severity was not predictive of challenge outcome. **The multistep and full-dose methods demonstrated a comparable reaction risk for anaphylaxis.**

DOI: 10.1016/j.anai.2016.10.003

[4] - Torres MJ, Blanca M, Fernandez J, Romano A, Weck A, Aberer W, et al. Diagnosis of immediate allergic reactions to beta-lactam antibiotics. Allergy. 2003 Oct;58(10):961–72.

DOI: 10.1034/j.1398-9995.2003.00280.x

2. WEBSITES OF INTEREST

1 – European Academy of Allergy and Clinical Immunology: https://www.eaaci.org/

2 – Sociedad Española de alergología e inmunología clínica: https://www.seaic.org/

3 – The British Society for Allergy & Clinical Immunology: https://www.bsaci.org/

4 – Le Réseau National de Surveillance Aérobiologique: http://www.pollens.fr/accueil.php

5 – German Society for Allergology and Clinical Immunology: http://www.dgaki.de/

6 – Romanian Society of Allergology and Clinical Immunology: https://www.sraic.eu/

7 – The Norwegian Asthma and Allergy Association: https://www.naaf.no/

8 - The American Academy of Allergy, Asthma & Immunology: https://www.aaaai.org/

3. SCIENTIFIC PAPERS

[1] – Vultaggio A, Virgili G, Gaeta F, Romano A, Maggi E, Matucci A. High Serum β-Lactams Specific/Total IgE Ratio Is Associated with Immediate Reactions to β-Lactams Antibiotics. Muyldermans S, editor. PLoS One. 2015 Apr 16;10(4):e0121857.

Abstract:

Total serum IgE result from the combination of specific and non-specific pools. High specific/ total IgE ratio may reflect high level of allergen-specific IgE on mast cells. No data regarding its applications to drug allergies is available. One hundred seventy-one patients with a history of immediate reactions to β-lactams, confirmed by positive skin testing, and 122 control subjects tolerant to β-lactams, were studied. CAP System was used for the detection of serum total and specific IgE antibodies. The specific/total IgE ratio was tested for diagnostic accuracy compared with conventional criteria. We finally performed a simulation study to expand our investigation of the performance of the specific/total IgE ratio index in a scenario in which the new CAP detection threshold is lowered further. Specific/total IgE ratio values ≥0.002 were observed more frequently in reactive than in controls. Seventy-four of 80 subjects with values ≥0.002 were allergic to β-lactams, yielding a positive predictive value of 92.5%. The application of specific/total IgE ratio significantly improves the positive likelihood ratio and the overall diagnostic performance. In addition, we showed the capability of this new criterion to identify true reactive patients even among subjects with high levels of total IgE (>200 kU/L). Significant increase in both receiver operator characteristic (ROC) curve and sensitivity were observed in imputed case of the simulation study. The β-lactams-specific/total IgE ratio may be an additional index compared to the common criterion of positivity to a single hapten in the allergological work-up of patients with β-lactams immediate adverse reactions and in vitro tests reduce the need for challenge testing, limiting them to selected cases.

DOI: 10.1371/journal.pone.0121857

[2] – Buonomo A, Pascolini L, Rizzi A, Aruanno A, Pecora V, Ricci A, et al. Cross-reactivity and Tolerability of Ertapenem in Patients With IgE-Mediated Hypersensitivity to β-Lactams. J Investig Allergol Clin Immunol. 2016 Apr 1;26(2):100–5.

Abstract:

Background and Objective: Administration of carbapenems to β-lactam-allergic patients has always been considered potentially harmful because of a 47.4% rate of cross-reactivity to imipenem reported in a single study. Nevertheless, recent studies have shown that the rate of cross-reactivity of imipenem and meropenem with penicillins is lower than 1%. The aim of this study was to evaluate the possibility of using ertapenem in patients with an established IgE-mediated β-lactam allergy.

Patients and Methods: We studied all participants who came to our allergy unit and had a clinical history of immediate hypersensitivity reactions to β-lactams. The inclusion criteria were a positive skin test result to at least 1 β-lactam molecule and/or positive specific IgE (when available). All participants underwent immediate-type skin tests with several β-lactam molecules including ertapenem. Challenges with intravenous ertapenem were performed on 2 different days in patients with negative skin test results.

Results: We examined 49 patients with a clinical history of immediate reactions to β-lactams. All the patients had positive skin tests and/or positive specific IgE to at least 1 β-lactam reagent and negative carbapenem skin tests. Thirty-six patients agreed to undergo the challenges and 35 tolerated the full dose of ertapenem.

Conclusions: The practice of avoiding carbapenems in patients with β-lactam allergy should be abandoned considering the very low rate of cross-reactivity. β-Lactam-allergic patients who need ertapenem therapy should undergo skin tests and, if negative, a graded challenge to assess tolerability.

DOI: 10.18176/jiaci.0019

[3] – Mota I, Gaspar Â, Chambel M, Piedade S, Morais-Almeida M. Hypersensitivity to beta-lactam antibiotics: a three-year study. Eur Ann Allergy Clin Immunol. 2016 Nov;48(6):212–9.

Abstract:

Background. Beta-lactams antibiotics (BL) are the most frequent elicitors of allergic drug reactions. The aim of our study was to characterize the patients referred with suspected hypersensitivity (HS) to BL. Methods. Over a three-year period (2011-2013), a total of 234 adult and paediatric patients (pts) with suspected HS to BL were investigated according to the European Network for Drug Allergy guidelines. Results. HS to BL was confirmed in 43 pts (18%), without differences between adult and paediatric pts; anaphylaxis was reported by 20 pts. Diagnosis was ascertained by: serum-specific IgE antibodies in 5 pts (12%), skin prick tests in 5 (12%), intradermal tests in 25 (58%), 3 with delayed reading, and the remaining 8 (18%) by drug provocation tests. Penicillins / derivatives were the culprit drugs in 39 pts, mainly amoxicillin, and cephalosporins in 4. Conclusions. In most of these patients with suspected HS to BL, allergological work-up was negative and HS was excluded. One fourth of confirmed cases had a plausible non-IgE mediated mechanism.

ISSN: 1764-1489

[4] – Marraccini P, Pignatti P, D'Alcamo A, Salimbeni R, Consonni D. Basophil Activation Test Application in Drug Hypersensitivity Diagnosis: An Empirical Approach. Int Arch Allergy Immunol. 2018;177(2):160–6.

Abstract:

Background: The diagnosis of drug hypersensitivity reactions (DHRs) is based both on clinical history and in vivo tests, such as specific IgE and cutaneous tests, when available. The aim of this work was to evaluate the basophil activation test (BAT) as a supplementary tool for drug challenges and drug allergy diagnosis.

Method: We evaluated 204 outpatients reporting DHRs. Available serum-specific IgE drugs were determined and cutaneous tests were performed when appropriate. BAT was performed immediately after blood sampling. The expression of CD63 was evaluated with flow cytometry.

Results: The drugs that caused adverse reactions were mainly antibiotics (49%). Non-steroid anti-inflammatory drugs (NSAID) were cited as responsible for DHRs in 37%, with the remaining 14% being due to other drugs. BAT revealed a high specificity (92%) and low sensitivity for antibiotics (40%). For the suspected reactions to penicillin, both the in vitro tests supported 94% of the diagnoses. We also observed a high specificity in the case of challenge with NSAIDs (100% specificity).

Conclusions: BAT is effective in discriminating adverse drug reactions, whilst only more critical cases require integrated evaluations and more complex clinical examinations. It is relevant that the concordance of anamnesis and in vitro tests reduce the need for challenge testing, limiting them to selected cases.

DOI: 10.1159/000490116

[5] – Thinnes A, Merk HF, Wurpts G, Röseler S, Lehmann S, Tenbrock K, et al. Individual risk assessment in the diagnosis of immediate type drug hypersensitivity reactions to betalactam and non-betalactam antibiotics using basophil activation test: a single center experience. Cutan Ocul Toxicol. 2018 Oct 2;37(4):309–18.

Abstract:

Background: Drug hypersensitivity reactions of immediate type pose a challenging problem, especially, if standard diagnostic procedures do not lead to conclusive results. The aim of this investigation is to identify, whether basophil activation test (BAT) is able to provide additional benefit in the diagnostic evaluation of immediate type drug hypersensitivity reactions to antibiotics in comparison with the routine allergological diagnostic methods.

Conclusions: Although skin tests remain the most important part of the primary diagnostic investigation, BAT is an additional valuable and sensitive in vitro test in the diagnostic procedure of immediate type allergic reactions to antibiotics. However, **further standardized investigations are needed in order to calculate exact sensitivity and specificity of this diagnostic tool in both, adult and pediatric populations**.

DOI: 10.1080/15569527.2018.1448990

[6] – Torres MJ, Adkinson NF, Caubet J-C, Khan DA, Kidon MI, Mendelson L, et al. Controversies in Drug Allergy: Beta-Lactam Hypersensitivity Testing. J Allergy Clin Immunol Pract. 2019 Jan;7(1):40–5.

Abstract:

All beta-lactam use is associated with a certain rate of adverse reactions. Many of these adverse reactions result in an allergy to the beta-lactam being entered into the patient's medical record. Unfortunately, only a small minority of these recorded allergies are clinically significant immunologically mediated drug hypersensitivity. An unconfirmed allergy to beta-lactams is a significant public health risk, because patients so labeled typically do not receive narrow-spectrum penicillins and cephalosporins when clinically indicated. The alternative antibiotics they receive result in poorer clinical outcomes, increased incidence of serious antibiotic-resistant infections, prolonged hospitalizations, and greater health care utilization. There is a wide variation in beta-lactam allergy incidence and prevalence around the world, based in part on the specific beta-lactams used and overused. There is a wide variation in specific protocols used to confirm current tolerance of beta-lactams and remove these inaccurate allergy reports. Harmonizing testing protocols, when possible, may lead to more widespread use of narrow-spectrum beta-lactams, when clinically indicated, and improve patient safety worldwide. Further research is needed to better understand the regional differences in reporting beta-lactam allergy as this relates to regional differences in beta-lactam use and overuse, the frequency of clinically significant immunologically mediated beta-lactam hypersensitivity, and the optimal testing strategies to confirm current tolerance, based on presenting clinical symptoms.

DOI: 10.1016/j.jaip.2018.07.05

4. ALLERGY CONGRESS

January

1. Sociedad Española de Alergología e Inmunología Clínica (SEAIC)
   XV Reunión CYNA. Controversias y Novedades en Alergia.
   25th-26th January 2019
   Madrid, Spain
   https://www.seaic.org/inicio/reunion-cyna-madrid

February

2. American Academy of Allergy, Asthma & Immunology (AAAAI)
   2019 Annual Meeting
   22nd- 25th February 2019
   San Francisco, California.
   http://annualmeeting.aaaai.org

March

3. European Academy of Allergy and Clinical Immunology (EAACI)
   RHINA 2019
   21st – 23rd March 2019
   Eastbourne, United Kingdom.
   https://www.eaaci.org/focused-meetings/rhina-2019

April

4. Sociedad Castellano Leonesa de Alergia e Inmunología Clínica (SCLAIC)
   Congreso Regional SCLAIC 2019
   5th – 6th April 2019
   Burgos, Spain.
   http://www.sclaic.es/actividades.php

5. World Allergy Organization (WAO)
   WISC 2019
   4th – 6th April 2019
   Beirut, Lebanon
   https://www.worldallergy.org/beirut2019

May

6. American Association of Immunologists
   Annual Meeting
   9th – 13th May 2019
   San Diego, California.
   http://www.immunology2019.org

7. Sociedad Latinoamericana de Alergia, Asma e Inmunología (SLAAI)
   XX Congreso Latinoamericano de Alergia, Asma e Inmunología
   11th – 13th May 2019
   Asunción, Paraguay.
   http://slaai2019py.com

8. Sociedad Española de Inmunología Clínica y Alergología Pediátrica (SEICAP)
   XLII Congreso Nacional
   16th – 18th May 2019
   Valencia, Spain.
   http://www.seicapcongreso.com/modules.php?name=home

June

9. European Academy of Allergy and Clinical Immunology (EAACI)
   EAACI Congress 2019
   1st – 5th June 2019
   Lisbon, Portugal.
   https://www.eaaci.org/eaaci-congresses/eaaci-2019

10. World Immunopathology Organization (WIPO)
    XIII World Asthma, COPD & Allergy Forum
    29th June -2nd July 2019
    Saint Petersburg, Russia
    http://www.wipocis.org/Page605.html

October

11. Sociedad Española de Alergología e Inmunología Clínica (SEAIC)
    Simposio Internacional de la Sociedad Española de Alergología e Inmunología Clínica.
    23rd – 26th October 2019
    Gran Canaria, Spain
    http://www.congresoseaic.org/SEAIC2018

12. World Allergy Organization (WAO)
    World Allergy Congress 2019
    12th – 14th December 2019
    Lyon, France
    https://www.wac2019-allergy.com/

5. BIOSENSORS CONGRESS

1. Biosensors & Bioelectronics.
   October 25-26, 2019
   Vancouver – Canada
   https://biosensors.conferenceseries.com/

2. Biosensors and Bioelectronics
   June 17-18, 2019
   Washington, USA
   https://www.meetingsint.com/conferences/biosensor-bioelectronics

3. ICNBB 2019: International Conference on Nanomaterials for Biosensors and Bioelectronics
   April 16 - 17, 2019
   Lisbon, Portugal
   https://waset.org/conference/2019/04/lisbon/icnbb

4. 7th International Symposium on Sensor Science
   May 09-11, 2019
   Napoli, Italy
   https://i3s2019napoli.sciforum.net/

5. BioEngineering, BioDetection & BioSensors 2019
   April 1-2, 2019
   Coronado Island, California
   https://selectbiosciences.com/conferences/index.aspx?conf=BB2019

6. 11th Euro Biosensors & Bioelectronics Congress
   September 16-17, 2019
   Rome, Italy
   https://www.omicsonline.org/conferences-list/nanotechnology-in-biosensors

7. AchemAsia
   May 21–23, 2019
   Shanghai, People's Republic of China.
   https://www.achemasia.de/en/home.html

8. Achema 2021
   June 14-18, 2021
   Frankfurt, Germany
   https://www.achema.de/

9. Pittcon 2019
   March 17 - 21, 2019
   Pennsylvania, Philadelphia, Pennsylvania, USA
   https://pittcon.org/

6. MEDICAL FAIR

[1] – Duphat: Dubai – 26. - 28. February 2019.
https://duphat.ae/

[2] – Thüringer GesundheitsMesse: Erfurt – 16. - 17. March 2019:
https://www.thueringer-gesundheitsmesse.de/gesundheitsmesse/

[3] – iMF International Medical Forum: Kiev – 17. - 19. April 2019:
http://medforum.in.ua/

[4] – BIOMEDevice Boston: Boston – 15. - 16. May 2019.
https://biomedboston.com/

[5] - FEMI: Miami – 26. - 28. June 2019:
https://www.fimeshow.com/en/home.html

[6] - Analytica Anacon India: Hyderabad – 19. - 21. September 2019:
https://www.analyticaindia.com/

[7] – Compamed: Düsseldorf – 18 - 21. November 2019
https://www.compamed.de/

[8] – MEDICA: Düsseldorf – 18 - 21. November 2019
https://www.compamed.de/

[9] – Public Health: Kiev – October 2019:
http://www.publichealth.com.ua/

[10] – MEDiT: Rímini – 30. Novembre - 02. December 2019.
https://biomedboston.com/

7. EUROPEAN PROJECTS

1 – Automation of novel multi-parameter allergy test that is cost-efficient and delivers instantly correct results: AllergyExplorer

Grant agreement ID: 811470
Start date: 1 June 2018
End date: 31 May 2020

Objective:

Allergies and asthma affect at least a quarter of the population and the WHO has declared allergy a major health problem of the 21st century. Currently, medical practitioners must pre-select very few allergens for in-vitro testing, based on prior anamnesis, under time and cost pressure. Independent experts estimate that almost half of the patients are diagnosed insufficiently. The consequences for the patients are not optimal treatment and reduced quality of life. For the public health systems more than 140 Bn Euro are spent each year which could be saved if all allergic patients were treated adequately. We have developed a multi-parameter allergy test covering close to 100% of the globally relevant allergens in a single lab test. Instead of forcing medical practitioners to pre-select very few allergens for in-vitro, our solution substantiates any
therapeutic decision by offering a complete immunological profile for every tested individual. We expand testing to the molecular level which provides valuable decision points such as enhanced risk assessment, improving the success of allergen immunotherapy or clearer recommendations for avoidance. We eliminate the trade-off between cost and quality of allergy diagnosis. Our allergy test is technically validated and registered as an in-vitro diagnostics device in Europe. We are already selling and delivering the non-automated manual test systems to customers all over Europe. In this project, we will fully automate the test instrumentation so we can target the customer segments of highly automated clinical routine labs. This will multiply our selling potential and expand our customer reach.
The global market of in-vitro diagnosis of allergy is growing fast at almost double-digit rate globally, and amounted to approx. 700 million USD annual revenues in 2016. There is a de-facto monopoly of a single US supplier and this project will return jobs and revenues to the European Union.

https://cordis.europa.eu/project/rcn/216843/factsheet/en

2 – Point-of-care device based on KETs for diagnosis of food allergies: AllerScreening

Grant agreement ID: 768641
Start date: 1 October 2017
End date: 30 September 2021

Objective
Food allergy is an immune-based disease that has become an important public health problem that affects children and adults and may be increasing in prevalence. In the US, food allergy affects 5% of children under the age of 5 years and 4% of teens and adults, and its prevalence appears to be on the increase. Globally, it is estimated that over 6% of the population, around 200 to 250 million people, suffer from some food allergies, affecting more than 17 million people only in Europe.
The main objective of this proposal is translating an optical diagnostic technology already proven in which the novel AllerScreening platform is based on, to the clinical routine, addressing a priority healthcare unmet need from the laboratory to the clinic. The unique features of AllerScreening will allow clinicians to early detect main food allergies (at least the 90% of European food allergies) through a simple test using a drop of sera, reducing the cost and technical requirements of the current clinical practice. This new and innovative cost-effective sensing system for the in vitro component diagnosis of food allergies will be feasible thanks to the multiplexed disposable BioKits and the optical Pont-of-Care (PoC) reader in which the novel AllerScreening platform is based on, allowing the adoption of a novel PoC diagnostic device specific for food allergies.

https://cordis.europa.eu/project/rcn/211458/factsheet/en

8. RECENT NEWS

[1] - Allergic to Penicillin? You May Not Be:
https://www.nytimes.com/2019/01/22/well/live/allergic-to-penicillin-you-may-not-be.html

[2] - Patients believed allergic to penicillin have increased risks of MRSA and *C. difficile*:
https://www.sciencedaily.com/releases/2018/06/180627190252.htm

[3] - Reported penicillin allergy appears to increase the risk of surgical site infections:
https://www.sciencedaily.com/releases/2017/10/171009084353.htm