

Editorial

Drug hypersensitivity – allergy passion

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Twelve papers on drug hypersensitivity and allergy can be read in this issue of *Allergy* (1–12)! This reflects not only the dynamic input of the teams working in this field, but also the true problem of these diseases given their prevalence. Drug hypersensitivities represent >15% of all adverse drug reactions. They affect 10–20% of hospitalized patients and >7% of the general population (13). They may be potentially life-threatening, prolong hospitalization, affect the drug prescribing patterns of physicians and result in socioeconomic costs. The connection between adverse drug reactions and drug intake is rarely proven and both under diagnosis and over diagnosis can occur (13). The diagnostic procedure of drug allergies has greatly improved over the past 7 years, thanks to the consensus reports of the European Network for Drug Allergy/the core group of the EAACI drug allergy interest group (14–20). Drug allergy work up always begins with a suggestive clinical history and case reports such as those published in this Journal (10–12, 21) are very informative. However, larger series are required in order to achieve more satisfying answers to specific questions such as the following: (i) the decrease over time of beta-lactam specific IgE (5); (ii) the usefulness of flow cytometry in rocuronium anaphylaxis (4); (iii) drug provocation tests (8); (iv) validation of the newly available PPL and MDM reagents (9). When a sufficient number of papers on a specific subject are published, systematic reviews can be edited, such as the report contained in this issue on biological reagents (2). ENDA consensus reports should be challenged and we are glad to see that our report on drug provocation is valid (8). To date, we have mainly delivered position statements and general considerations. We should now evaluate and establish standard operation procedures. We should also implement a reactive approach, for example, this issue provides details on how to perform beta-lactam skin

testing since the worldwide withdrawal of Allergopen® and PrePen® PPL and MDM (1).

Drugs are capable of inducing all the types of immunological reactions (20, 22–31) described by Gell and Coombs (i.e. allergic drug hypersensitivities). They sometimes also mimic drug allergy but do not involve an immunological mechanism (i.e. non-allergic-drug hypersensitivities) (32–34). Only a few drug allergen determinants and a few mechanistic pathways have been pinpointed. A great deal remains to be learnt and in this issue you can read more about the specificity of the beta-lactam IgE-dependent immune-response (5) as well as how penicillin V desensitization works (7). New information on different individual risks with regard to pharmacological pathways (e.g. drug metabolizing enzymes such as CYP450s) or immunological factors should ultimately find persons at a higher or lower risk to drug allergy. This issue covers part of this subject with single nucleotide polymorphisms associated to beta-lactam IgE-dependent allergies (3), complementing other studies (35, 36). A better and clearer understanding of how patients are sensitized and how they react to chemical compounds will help the global field of the human–environmental xenobiotics interaction.

Although drug allergy is a daily problem for practitioners and some patients (13, 37), the level of awareness is dramatically low as compared to that of asthma and food allergies, which are actually less prevalent. Again, compared with respiratory allergies, there is almost no institutional (including regulatory agencies) or pharmaceutical support concerning drug allergies, at least at European and American levels. This in turn leads to a misunderstanding of the pathomechanisms, a weakness in the drug allergy work up, a lack of ready-to-use diagnostic tools and consequently a lack of preventive actions. We need help from other specialists (toxicolo-

gists, pharmacologists, chemists, geneticists and others) in order to exchange views and dramatically improve the level of knowledge regarding drug allergy. This is the objective of the project that ENDA would presently like to promote (38). The objective of the so-called World Network for Drug Allergy is to establish an international

network of centers of excellence devoted to the field of drug allergy and hypersensitivity in order to raise awareness and to optimize and to enhance research in this area. The support of EAACI and its official publication *Allergy* is important.

References

1. Torres MJ, Blanca M and the European Network for Drug Allergy (ENDA) and the EAACI interest group on drug hypersensitivity. Importance of skin testing with major and minor determinants of benzylpenicillin in the diagnosis of allergy to betalactams. Statement from the European Network for Drug Allergy concerning AllergoPen withdrawal. *Allergy* 2006;**61**:910–911.
2. Pichler WJ. Adverse side-effects to biological agents. *Allergy* 2006;**61**:912–920.
3. Guglielmi L, Fontaine C, Gougat C, Avinens O, Eliaou J-F, Guglielmi P et al. IL-10 promoter and IL4-R α gene SNPs are associated with immediate β -lactam allergy in atopic women. *Allergy* 2006;**61**:921–927.
4. Ebo DG, Bridts CH, Hagendorens MM, Mertens CH, De Clerck LS, Stevens WJ. Flow-assisted diagnostic management of anaphylaxis from rocuronium bromide. *Allergy* 2006;**61**:935–939.
5. Antúnez C, Fernández T, Blanca-Lopez N, Torres MJ, Mayorga C, Canto G et al. IgE antibodies to betalactams: relationship between the triggering hapten and the specificity of the immune response. *Allergy* 2006;**61**:940–946.
6. Tamayo E, Álvarez FJ, Rodríguez-Ceron G, Gómez-Herreras JI, Castrodeza J. Prevalence of positive prick test to anaesthetic drugs in the surgical population. *Allergy* 2006;**61**:952–953.
7. Woo H-Y, Kim Y-S, Kang N-I, Chung W-C, Song C-H, Choi I-W et al. Mechanism for acute oral desensitization to antibiotics. *Allergy* 2006;**61**:954–958.
8. Wöhrl S, Vigl K, Stingl G. Patients with drug reactions – is it worth testing?. *Allergy* 2006;**61**:928–934.
9. Rodríguez-Bada JL, Montañez MI, Torres MJ, Mayorga C, Canto G, Perez-Inestrosa E et al. Skin testing for immediate hypersensitivity to betalactams: comparison between two commercial kits. *Allergy* 2006;**61**:952–953.
10. Hyry H, Vuorio A, Varjonen E, Skyttä J, Mäkinen-Kijunen S. Two cases of anaphylaxis to macrogol 6000 after ingestion of drug tablets. *Allergy* 2006;**61**:1021.
11. Artesani MC. Anaphylactic shock to defibrotide. *Allergy* 2006;**61**:1022.
12. Madero F, Sastre J, Carmes J, Quirce S, Herrera-Pombo JL. IgG $_4$ -mediated allergic reaction to glargine insulin. *Allergy* 2006;**61**:1022–1023.
13. Gomes ER, Demoly P. Epidemiology of hypersensitivity drug reactions. *Curr Opin Allergy Clin Immunol* 2005;**5**:309–316.
14. Demoly P, Kropf R, Bircher A, Pichler WJ. Drug hypersensitivity questionnaire. *Allergy* 1999;**54**:999–1003.
15. Brockow K, Romano A, Blanca M, Ring J, Pichler W, Demoly P. General considerations for skin test procedures in the diagnosis of drug hypersensitivity. *Allergy* 2002;**57**:45–51.
16. Aberer W, Bircher A, Romano A, Blanca M, Campi P, Fernandez J et al. Drug provocation testing in the diagnosis of drug hypersensitivity reactions: general considerations. *Allergy* 2003;**58**:854–863.
17. Torres MJ, Blanca M, Fernandez J, Romano A, de Weck A, Aberer W et al. Diagnosis of immediate allergic reactions to beta-lactam antibiotics. *Allergy* 2003;**58**:961–972.
18. Romano A, Blanca M, Torres MJ, Bircher A, Aberer W, Brockow K et al. Diagnostic of non-immediate reactions to beta-lactam antibiotics. *Allergy* 2004;**59**:1153–1160.
19. Brockow K, Christiansen C, Kanny G, Clement O, Barbaud A, Bircher A et al. Management of hypersensitivity reactions to iodinated contrast media. *Allergy* 2005;**60**:150–158.
20. Torres MJ, Sanchez-Sabate E, Alvarez J, Mayorga C, Fernandez J, Padial A et al. Skin test evaluation in nonimmediate allergic reactions to penicillins. *Allergy* 2004;**59**:219–224.
21. Asero R. Teicoplanin-induced anaphylaxis. *Allergy*; DOI: 10.1111/j.1398-9995.2006.01021.x
22. Ebo DG, Wets RD, Spiessens TK, Bridts CH, Stevens WJ. Flow-assisted diagnosis of anaphylaxis to patent blue. *Allergy* 2005;**60**:703–704.
23. Pichler WJ. Delayed drug hypersensitivity reactions. *Ann Intern Med* 2003;**139**:683–693.
24. Pichler WJ, Tilch J. The lymphocyte transformation test in the diagnosis of drug hypersensitivity. *Allergy* 2004;**59**:809–820.
25. Boussetta K, Ponvert C, Karila C, Bourgeois ML, Blic J, Scheinmann P. Hypersensitivity reactions to paracetamol in children: a study of 25 cases. *Allergy* 2005;**60**:1174–1177.
26. Kuechler PC, Britschgi M, Schmid S, Hari Y, Grabscheid B, Pichler WJ. Cytotoxic mechanisms in different forms of T-cell-mediated drug allergies. *Allergy* 2004;**59**:613–622.
27. Kleinhans M, Boer A, Kaufmann R, Boehncke WH. Fixed drug eruption caused by articain. *Allergy* 2004;**59**:117.
28. Gonzalez-Mahave I, Del Pozo MD, Blasco A, Lobera T, Venturini M. Urticaria due to pentoxifylline. *Allergy* 2005;**60**:705.
29. Dewachter P, Mouton-Faivre C. Anaphylaxis to macrogol 4000 after a parenteral corticoid injection. *Allergy* 2005;**60**:705–706.
30. Padial A, Posadas S, Alvarez J, Torres MJ, Alvarez JA, Mayorga C et al. Nonimmediate reactions to systemic corticosteroids suggest an immunological mechanism. *Allergy* 2005;**60**:665–670.
31. Vermeulen C. Reactions to several antibiotics several years after cutaneous tests for penicillin derivatives. *Allergy* 2004;**59**:113.
32. Liccardi G, D'Amato G, Canonica GW, Lobefalo G, Noschese P, Piccolo A et al. Safety of celecoxib in patients with adverse reactions to nimesulide. *Allergy* 2005;**60**:708–709.

33. Kowalski ML, Ptasińska A, Jedrzejczak M, Bienkiewicz B, Cieślak M, Grzegorzczak J et al. Aspirin-triggered 15-HETE generation in peripheral blood leukocytes is a specific and sensitive Aspirin-Sensitive Patients Identification Test (ASPITest). *Allergy* 2005;**60**:1139–1145.
34. Kowalski ML, Lewandowska-Polak A, Wozniak J, Ptasińska A, Jankowski A, Wagrowska-Danilewicz M et al. Association of stem cell factor expression in nasal polyp epithelial cells with aspirin sensitivity and asthma. *Allergy* 2005;**60**:631–637.
35. Qiao HL, Yang J, Zhang YW. Specific serum IgE levels and FcεRIβ genetic polymorphism in patients with penicillins allergy. *Allergy* 2004;**59**:1326–1332.
36. Qiao HL, Yang J, Zhang YW. Relationships between specific serum IgE, cytokines and polymorphisms in the IL-4, IL-4Rα in patients with penicillins allergy. *Allergy* 2005;**60**:1053–1059.
37. Moneret-Vautrin DA, Morisset M, Flabbee J, Beaudouin E, Kanny G. Epidemiology of life-threatening and lethal anaphylaxis: a review. *Allergy* 2005;**60**:443–451.
38. WONDA (World Network for Drug Allergy). *EAACI Newsletter* 2006; **9**: 8–9.