

*Allergy Unit
Hospital Universitario de Fuenlabrada
Madrid, Spain
†Instituto de Investigaciones Sanitarias
Fundación Jiménez Díaz
Madrid, Spain
‡Reserch & Development Department
Bial-Aristegui
Bilbao, Spain
mgandolfo.hflr@salud.madrid.org

- [2] Cuesta-Herranz J, Pastor C, Figueredo E, et al. Identification of Cucumisin (Cuc m 1), a subtilisin-like endopeptidase, as the major allergen of melon fruit. *Clin Exp Allergy*. 2003;33:827–833.
- [3] López Torrejón G, Crespo JF, Sánchez-Monge R, et al. Allergenic reactivity of the melon profilin Cuc m 2 and its identification as major allergen. *Clin Exp Allergy*. 2005;35:1065–1072.
- [4] Asensio T, Crespo JF, Sánchez-Monge R, et al. Novel plant pathogenesis-related protein family involve in fruit allergy. *J Allergy Clin Immunol*. 2004;114:896–899.
- [5] González-Mancebo E, López-Torrejón G, González-de-Olano D, et al. Identification of potential allergens involved in systemic reactions to melon and water-melon. *Ann Allergy Asthma Immunol*. 2010;104:271–272.
- [6] Pastor C, Cuesta-Herranz J, Cases B, et al. Identification of major allergens in watermelon. *Int Arch Allergy Immunol*. 2009;149:289–290.
- [7] Asero R, Mistrello G, Roncarolo D, et al. Immunological cross-reactivity between lipid transfer proteins from botanically unrelated plant-derived foods: a clinical study. *Allergy*. 2002;57:900–906.
- [8] Tordesillas L, Sirvent S, Díaz-Perales A, et al. Plant lipid transfer protein allergens: no cross-reactivity between those from foods and olive and Parietaria pollen. *Int Arch Allergy Immunol*. 2011;156:291–296.

References

- [1] Figueredo E, Cuesta-Herranz J, De-Miguel J, et al. Clinical characteristics of melon (*Cucumis melo*) allergy. *Ann Allergy Asthma Immunol*. 2003;91:303–308.

Hospital admissions for allergy and eczema varied across regions in England, 2008–2011

Allergic disorders are common throughout the United Kingdom, affecting males and females of all ages and peoples from all social classes and ethnic groups. In the 1990s, the largest increases in rates have been for anaphylaxis and food allergy. Anaphylaxis rates rose from 6 to 41 per million between 1990–1991 and 2000–2001, and food allergy rates rose from 5 to 28 per million over this period.¹ Moreover, direct National Health Service costs for managing allergic problems were estimated at over 1 billion UK pounds per annum, and treatments for asthma and other allergic disorders have accounted for 10% of primary care prescribing costs.¹ In terms of population prevention, avoiding preventable hospital admissions would be an effective strategy. Therefore, I investigated recent hospital admissions for all allergies in England.

Hospital Episode Statistics (HES) between July 1, 2008 and June 30, 2011 were obtained from Lightfoot Solutions, using the sfn system (<http://www.lightfootsolutions.com>), which enables access to real-time HES data.² The HES database contains information about all patients admitted to National Health Service hospitals in England.³ It was first established in 1989 and currently collects data on more than 12 million hospital admissions each year. No apparent barriers to access exist because all UK residents are entitled to primary care consultations, which are free at the point of use, and most residents are registered with a practice. The HES online system with complete information is available from 1997/1998, and the dataset contains many variables, including age, sex, primary and secondary diagnoses, and in-hospital death.³ The basic unit of the dataset is the consultant episode, covering the continuous period during which a patient was under the care of 1 consultant. Episodes of care were linked into admissions, and those ending in transfer to another hospital were linked together to avoid multiple counting.⁴ The main reason for admission (“primary diagnosis”) is coded using the *International Classification of Diseases*, version 10 (ICD-10) codes.⁵ In the current study, J30.1, J30.2, J30.3, J30.4, J45.0, K52.2, L50.0, L56.1, T78.0, T78.1, T78.2, T78.4, T80.5, and T88.6 were used for accounting allergies admissions.³ In addition, 2010 mid-year population estimates for year and age were obtained from the UK National Statistics (<http://www.statistics.gov.uk>).⁴ Moreover, because deprivation in particular has been shown to play a major role in risk of hospital admissions,⁵ it⁶ (including 7 domains such as

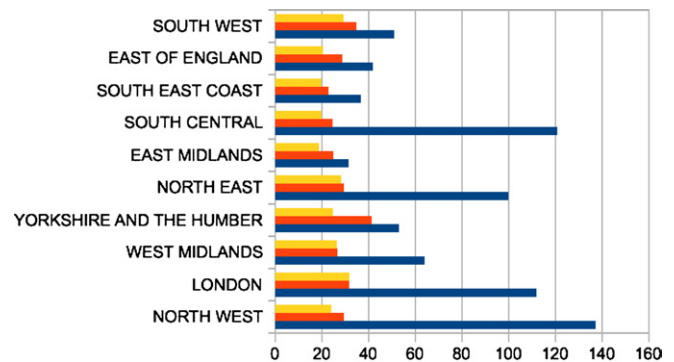


Fig. 1. Hospital admissions for all allergies by regions (top to down, showing regions with 20% most deprivation: the lowest to the highest).

income, employment, health and disability, education and skill, barriers to housing and services, crime, and living environment) was therefore included for comparisons. All graphs were produced using Excel (Microsoft Corp, Redmond, Washington).

In the northwest (137.20 per 100,000) and south central (120.73 per 100,000) regions (Fig 1), apparent peaks in allergy admissions were seen for those younger than 15 years, followed by London (111.85 per 100,000) and the northeast (99.81 per 100,000). Conversely, in London (31.67 per 100,000), the southwest (29.25 per 100,000) and northeast (28.17 per 100,000), higher allergies admissions were observed for those older than 76 years old. For adults aged between 16 and 75 years, generally similar allergies admissions patterns were found across regions, with a slightly higher rate in Yorkshire (41.27 per 100,000) and the southwest (34.72 per 100,000). Table 1 shows average annual hospital admissions rates for allergic diseases in the United Kingdom from July 1, 2008 to June 30, 2011 by age group and sex per 100,000 population (all admissions divided by 3). Interestingly, asthma admissions and other related admissions were all higher in males among those younger than age 15 but lower than female in those aged 16 and older.

Strengths of this study lie in its large nationally representative population-based sample and provision of recent clinical situations. Although the accuracy of HES depends on clinical diagnoses recorded in patients' medical records and may lead to misclassification bias, in recent years the quality of coding has improved, and HES data have been of good quality and used extensively for re-

Disclosures: Authors have nothing to disclose.

Funding Source: I.S. is supported by European Regional Development Fund and the European Social Fund. Convergence Programme for Cornwall and the Isles of Scilly.

Table 1

Average annual hospital admissions rates for allergic diseases in the United Kingdom from July 1, 2008 to June 30, 2011 by age group and gender per 100,000 population

	0–15 Years	16–75 Years	76+ Years
Allergic rhinitis and sinusitis (J30.1 to J30.4)			
Male	22.72	4.04	0.24
Female	9.63	5.92	0.30
Asthma (J45.0)			
Male	561.44	62.58	77.58
Female	55.15	147.09	151.20
IgE-mediated GI reactions (K52.2)			
Male	2.88	0.28	0.66
Female	1.34	0.43	1.18
Allergic urticaria (L50.0, L56.1)			
Male	7.85	0.82	0.66
Female	4.01	1.51	0.84
Anaphylaxis (T78.0 to T78.4, T80.5, T88.6)			
Male	33.92	8.86	9.91
Female	15.93	16.00	11.74
All causes			
Male	690.46	84.66	103.51
Female	96.79	181.21	184.43

Values are admissions per 100,000 person-years.

search.⁷ Still, the ethnicity data available were not sufficiently comprehensive to allow further exploration of ethnicity differences. Furthermore, the percentage of patients (J30.4) that underwent sinus surgery cannot be obtained. In conclusion, apparent geographic variations in hospital admissions for allergies were observed in recent years. More hospital admissions attributable to allergies were recorded in the more deprived areas. Because reducing hospital admissions continues to play an important role in

primary care, future prevention policy on reducing hospital admissions for allergy that is regionally specific for identifying and reducing over-utilization of health care costs should be considered.

Acknowledgment

The author would like to acknowledge the Convergence Programme for Cornwall and the Isles of Scilly.

Ivy Shiue, PhD*†

*European Centre for Environment and Human Health
University of Exeter
Exeter, United Kingdom

†The William A. & Barbara R. Owens Institute for Behavioral Research
University of Georgia
Atlanta, Georgia
ivy.shiue@pcmd.ac.uk

References

- [1] Gupta R, Sheikh A, Strachan DP, Anderson HR. Increasing hospital admissions for systemic allergic disorders in England: analysis of national admissions data. *BMJ*. 2003;327:1142.
- [2] Hospital Episode Statistics. Available at <http://www.hesonline.nhs.uk>. Accessed May 15, 2012.
- [3] Wu TY, Jen MH, Bottle A, Liaw CK, Aylin P, Majeed A. Admission rates and in-hospital mortality for hip fractures in England 1998 to 2009: time trends study. *J Public Health (Oxf)*. 2011;33:284–291.
- [4] Office of National Statistics. Available at <http://www.statistics.gov.uk>. Accessed May 15, 2012.
- [5] Majeed A, Bardsley M, Morgan D, O'Sullivan C, Bindman AB. Cross sectional study of primary care groups in London: association of measures of socioeconomic and health status with hospital admission rates. *BMJ*. 2000;321:1057–1060.
- [6] The English Indices of Deprivation 2010. Available at <http://www.communities.gov.uk/publications/corporate/statistics/indices2010>. Accessed on May 15, 2012.
- [7] Campbell S, Campbell M, Grimshaw J, Walker A. A systematic review of discharge coding accuracy. *J Public Health Med*. 2001;23:205–211.

Ultrarush venom immunotherapy and the lipoxin a₄ inflammation resolution pathway

Venom immunotherapy (VIT) stimulates T_H1 cytokines and allergen-specific, interleukin 10 (IL-10)–producing, T-regulatory cells, thereby inducing tolerance.¹ We previously reported that intercellular adhesion molecule 1 is overexpressed in allergic patients and decreases after ultrarush VIT.² Thus, VIT can correct the imbalance in T-lymphocyte subpopulations and in IL-4 and tumor necrosis factor α production. Despite these achievements, the mechanisms of ultrarush VIT-induced tolerance remain incompletely understood.

Proinflammatory mediators are released during allergic reactions to Hymenoptera venoms, whereas the pivotal role of mediators that actively terminate inflammation is emerging.³ Among these, the lipoxins exert potent bioactions to stop inflammation and promote resolution.³ Lipoxin A₄ (LXA₄) reduces asthmatic bronchoconstriction and airway inflammation⁴ and stimulates IL-10 release.⁵ LXA₄ generation and LXA₄ receptor expression are reduced in asthmatic patients,⁶ supporting a role of LXA₄ in immunoallergic disorders.

To determine whether VIT is associated with changes in LXA₄ generation, we measured urinary immunoreactive LXA₄ (iLXA₄) in 13 patients (4 women and 9 men; mean [SD] age, 45.5 [14.0] years and 37.1 [8.7] years, respectively) undergoing ultrarush VIT. Hymnox (Roxall Italia, Rome, Italy), an aqueous preparation of *Vespula* species

or *Apis mellifera*, was administered subcutaneously to 13 patients, according to an established protocol.² At the end of the incremental phase, the cumulative dose, administered in 13 fractions every 15 minutes (3 hours), was 111.101 μ g. All patients received a maintenance dose of 100 μ g on day 15 and thereafter once a month for 24 months. Urine samples were collected at baseline and at the end of the incremental phase. iLXA₄ was measured according to a method developed in our laboratory.⁷ Ultrarush VIT efficacy was monitored over time by evaluating the systemic allergic reaction to unintentional Hymenoptera stings after ultrarush VIT compared with the systemic allergic reaction before ultrarush VIT.

iLXA₄ increased after ultrarush VIT (mean [SD], 0.0088 [0.003] vs 0.013 [0.006] ng/mg of creatinine; $P = .046$, Wilcoxon signed rank test). By stratifying patients for the specific IgE (sIgE) to total IgE (tIgE) ratio, which correlates with the clinical response to allergic-specific immunotherapy, we separated patients into 2 groups: group A, 7 patients with an sIgE/tIgE ratio less than 0.05; and group B, 6 patients with an sIgE/tIgE ratio greater 0.05. Basal iLXA₄ levels were higher in group A patients (mean [SD], 0.0103 [0.0022] vs 0.0071 [0.0033] ng/mg of creatinine; $P = .03$, Mann-Whitney test). All group B patients displayed a significant increase in urinary iLXA₄ after ultrarush VIT (mean [SD], 0.0071 [0.0033] vs 0.016 [0.0056] ng/mg of creatinine; $P = .03$, Wilcoxon test) (Fig 1). No significant changes were denoted in group A, although 3 patients had an increase in urinary iLXA₄ after ultrarush VIT (Fig 1). We observed an

Disclosures: Authors have nothing to disclose.

Funding Support: This study was supported by the Italian Ministry of University and Research.