

- 7 Aho S, Mahoney MG, Uitto J. Plectin serves as an autoantigen in paraneoplastic pemphigus. *J Invest Dermatol* 1999; **113**:422–3.
- 8 Ohzono A, Sogame R, Li X et al. Clinical and immunological findings in 104 cases of paraneoplastic pemphigus. *Br J Dermatol* 2015; **173**:1447–52.
- 9 Poot AM, Diercks GF, Kramer D et al. Laboratory diagnosis of paraneoplastic pemphigus. *Br J Dermatol* 2013; **169**:1016–24.
- 10 Leger S, Picard D, Ingen-Housz-Oro S et al. Prognostic factors of paraneoplastic pemphigus. *Arch Dermatol* 2012; **148**:1165–72.
- 11 Geller S, Gat A, Zeeli T et al. The expanding spectrum of IgA pemphigus: a case report and review of the literature. *Br J Dermatol* 2014; **171**:650–6.
- 12 Ishii N, Teye K, Fukuda S et al. Anti-desmocollin autoantibodies in nonclassical pemphigus. *Br J Dermatol* 2015; **173**:59–68.

Occupational contact urticaria: a diagnosis not to be missed

DOI: 10.1111/bjd.14250

Linked Article: Bensefa-Colas, et al. *Br J Dermatol* 2015; **173**:1453–61.

Skin is the most commonly injured organ in industry. Occupational skin diseases (OSDs) account for 35% of all occupational-related diseases.¹ Dermatologists, workers and employers need to be vigilant with regard to the different manifestations of these important skin diseases as there can be a significant impact on the quality of life of workers, resulting in physical, psychological and financial hardships.

Contact dermatitis consisting of irritant and allergic contact dermatitis (with > 2000 known allergens) is the most common OSD, with atopy as an important cofactor. Although less common at 5% of all OSDs, occupational contact urticaria (OCU) is important not to miss clinically and should be confirmed with appropriate investigations such as skin prick testing, specific IgE tests and open testing.²

Occupational contact urticaria caused by natural rubber latex (NRL) has been well documented, especially with glove use by healthcare workers (HCW) and any other workers wearing gloves throughout the day.³ The reactions vary from mild erythema, with itching at the site of contact, to severe anaphylactic reactions occasionally leading to death.

In this issue of the *BJD*, Bensefa-Colas et al., working with the French National Network for Occupational Disease Vigilance and Prevention (RNV3P), have described their epidemiological findings for OCU over a 10-year period.⁴ They describe 251 cases of OCU, with 50% due to NRL. Over the study period there was a significant decline of NRL OCU (19% per year in HCW and 15% per year in all workers), especially after 2006, with no decline in other causes of OCU.

The article has an impressive study database, with experienced occupational physicians based in 32 centres with

> 69 000 work-related diseases recorded in the RNV3P between 2001 and 2010. As with any national or multicentre databases, some limitations may be present, including under-reporting, and the conclusions cannot necessarily be extrapolated to the whole population when based in specific specialized centres. The authors felt that there was a financial contractual obligation to accurately report that the reduction in NRL OCU was true. The reduction is likely owing to the ban on the use of powdered latex gloves in French hospitals and provides further evidence of the benefits of preventative measures for HCW.

This reduction in NRL OCU in HCW (and other workers) reflects clinical experience and epidemiological data across Europe and the U.K. for type 1 OCU due to NRL. This is owing to better awareness in workers, strict implementation of NRL-avoidance policies and vigilant occupational health departments with early referral to dermatology cutaneous allergy experts for advice and investigation.

Contact urticaria (CU) is a transient wheal and flare reaction appearing after contact with certain specific agents. These areas develop within 10–60 min of the skin contact and resolve within 2–24 h. CU has two main mechanisms: (i) immunological (IgE-mediated) and (ii) nonimmunological.²

In general, the most common type is nonimmunological CU. With sufficient provocation, nearly all exposed persons will develop a reaction. Previous sensitization is not required. It is due to the release of vasoactive substances (histamine, prostaglandin, leucotrienes, substance P) without the involvement of immunological processes. The reaction remains localized and does not cause systemic manifestations or generalized urticaria. The concentration, substance and skin site will determine the reaction strength. Substances known to trigger this type of CU include nettles, caterpillar hair, moths and other insects (gardeners); alcohols and Balsam of Peru (HCW); and cinnamic acid, cinnamic aldehyde, sodium benzoate, sorbic acid, fruits and vegetables (cooks). Other more exotic exposures triggering nonimmunological CU include jellyfish, sea anemones and corals.

Immunological (allergic) CU is caused by an antigen–antibody type 1 IgE-mediated hypersensitivity reaction. Raised serum-specific IgE antibody levels have been demonstrated with immunological CU. The stages of contact urticaria syndrome were well described in 1975 by Maibach and Johnson.⁵ The contact urticant (antigen) penetrates the epidermis and reacts with specific IgE antibodies on dermal mast cells and triggers the release of histamine and other inflammatory mediators, for example kinin and prostaglandins. This will determine the degree of skin symptoms, including erythema and oedema. Other symptoms may include conjunctivitis, rhinitis, asthma and anaphylactic shock. Protein contact dermatitis may be a manifestation of immunological CU presenting with hand and fingertip eczema.⁶

Causes of immunological CU include NRL exposure; medications, including antibiotics (e.g. cephalosporins, gentamicin, streptomycin); foods (e.g. potato, apple, flour, fish and meat); animal and plant products (e.g. animal dander, cow placenta,

cockroaches); cosmetics (e.g. hair bleaching products and, rarely, paraphenylenediamine); and chemicals (e.g. isocyanates, chlorhexidine, aluminium and platinum salts).

Royal College of Physician guidelines for the management of occupational NRL allergy have been published, with free resources available for departmental and patient use.⁷ Recent U.K. standards of care for occupational contact dermatitis and OCU have been published in the *BJD*.⁸ All these measures can support high levels of vigilance by workers and their employers not to miss less common forms of OSD such as OCU.

In conclusion, the identification of OSD such as contact allergy and OCU needs a high level of clinical acumen and detailed occupational history-taking, clinical examination and appropriate investigations such as patch testing and skin prick testing. This important paper reinforces the need to still be vigilant for OCU, including latex allergy, and to manage avoidance measures actively.⁴

Conflicts of interest

Invited external reviewer for National Health Service Plus, Royal College of Physicians, Faculty of Occupational Medicine. Latex Allergy: Occupational Aspects of Management: A National Guideline. London: Royal College of Physicians, 2008.

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References

- Salako K, Chowdhury MMU. Occupational skin disorders. In: *Current Diagnosis & Treatment: Occupational & Environmental Medicine* (LaDou J, Harrison RJ, eds), 5th edn. New York: Lange, 2014; 324–45.
- Wakelin SH. Contact urticaria. *Clin Exp Dermatol* 2001; **26**:132–6.
- Chowdhury MMU, Maibach HI (eds). *Latex Intolerance: Basic Science, Epidemiology and Clinical Management*. Boca Raton, FL: CRC Press, 2005.
- Bensefa-Colas L, Telle-Lamberton M, Faye S et al. Occupational contact urticaria: lessons from the French National Network for Occupational Disease Vigilance and Prevention (RNV3P). *Br J Dermatol* 2015; **173**:1453–61.
- Maibach HI, Johnson HL. Contact urticaria syndrome: contact urticaria to diethyl toluamide (immediate type hypersensitivity). *Arch Dermatol* 1975; **111**:726–30.
- Amaro C, Goossens A. Immunological occupational contact urticaria and contact dermatitis from proteins: a review. *Contact Dermatitis* 2008; **58**:67–75.
- NHS Plus, Royal College of Physicians, Faculty of Occupational Medicine. *Latex Allergy: Occupational Aspects of Management: A National Guideline*. London: Royal College of Physicians, 2008.
- Adishes A, Robinson E, Nicholson PJ et al. UK standards of care for occupational contact dermatitis and occupational contact urticaria. *Br J Dermatol* 2013; **168**:1167–75.

Navigating uncertainty: a valuable cost-effectiveness analysis in the rapidly changing field of metastatic melanoma treatment

DOI: 10.1111/bjd.14306

Linked Article: Matter-Walstra, et al. *Br J Dermatol* 2015; **173**:1462–70.

Treatment options for metastatic melanoma are rapidly increasing, with multiple new therapies released in the past several years and more actively under investigation.^{1–4} Because metastatic melanoma in particular has such a poor prognosis, there is understandable motivation at all levels – from researchers to policy-makers to providers – to make new treatment options accessible to patients. However, particularly when these new treatments have limited benefit (extending life by months without a significant chance of cure or durable response) and the cost of treatment is substantial, it is our responsibility as a medical community to consider whether relative cost to its effectiveness represents a reasonable use of medical resources.⁵

In this issue of the *BJD* Matter-Walstra et al.⁶ performed a thorough and rigorous cost–utility analysis of trametinib plus dabrafenib as first-line therapy for metastatic BRAF V600-positive melanoma in the Swiss setting and found this strategy to have an incremental cost-effectiveness ratio (ICER) of CHF385 603 per quality-adjusted life year. A common threshold used to decide if something is cost-effective is whether the ICER is less than the per capita gross domestic product of the setting (in this case about CHF85 000).⁵ Their choice to compare this combined treatment option with vemurafenib alone is appropriate – vemurafenib is the most popular current standard of care in this population. However, it's worth noting that there are alternative comparisons that would yield different results. If they had compared this therapy to chemotherapy alone, this would have shown a greater increase in effectiveness but a much greater increase in cost, and likely yielded an even higher ICER. A previous analysis showed vemurafenib itself to have poor cost-effectiveness relative to chemotherapy.⁷ Other possible comparisons – in particular, treatment strategies that involve ipilimumab or other immunotherapy – would be interesting given compelling evidence of benefit from these treatments, but would involve much more uncertainty due to the lack of data on direct comparisons.⁸

There are several factors making cost-effectiveness analysis for novel metastatic cancer treatments difficult leading to uncertainty in the results. Most notably, there are limits in the data available for inputs. In the case of trametinib and dabrafenib, the largest trial showing improved efficacy over