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## **Cutaneous Adverse Drug Reactions Referrals to a Liaison Dermatology Service**

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Dear Editor,

Adverse drug reactions (ADRs) are a common consequence of medications, with an estimated 10-20% of all hospitalised patients experiencing a drug side effect<sup>1-2</sup>; those affecting the skin being the most frequently recorded. The need to optimise management of cutaneous ADRs has been underlined by the recent publication of NICE Guidelines on Drug Allergy<sup>3</sup>, setting out a range of standards to enhance the diagnosis and management of patients developing allergic reactions to drugs. This study was undertaken to assess the number of drug allergy referrals, and the types of cutaneous drug reaction encountered in the in-patient population. We assessed the diagnostic accuracy of referring clinicians and the subsequent documentation of cutaneous ADR. Data was collected prospectively between December 2014 and March 2015.

Over the 4-month period, 373 hospital in-patient referrals were made to the liaison dermatology service, out of 8,413 patients admitted to the hospital during this period. 42/373 (11.2%) were referred as possible drug-related events, with 35/42 (83%) having developed a rash prior to admission to hospital. 27/42 patients were male (64.2%); average age was 50 years (mean=50.1 year). There were 2 paediatric patients, aged 1 and 7 years. 30/42 patients were referred by physicians and 12/42 by surgeons. In all cases the referring diagnosis was 'drug rash'.

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Accepted Article

Following review by the liaison dermatology service, 31/42 of referred patients (73.8%) were confirmed as cutaneous ADRs (see Table 1). The remaining 11/42 were found to be a variety of non-drug related inflammatory dermatoses. Thus, over the 4-month study period, 8% of the patients referred to the hospital liaison dermatology service (31/373) had a cutaneous ADR. Within the drug rash group, 13/31 patients (41.9%) had a pre-existing history of drug allergy/intolerance, 5 of whom were penicillin-allergic.

18/31 (58%) patients had an uncomplicated drug exanthem. 7/31 (22.6%) were diagnosed with drug reaction with eosinophilia and systemic symptoms (DRESS) based on RegiSCAR criterion<sup>10</sup>. The remaining 6 cutaneous ADRs are as listed in Table 2. Attribution of drug culpability was made in each case. Standard drug rash methodologies were used, including timelines and known notoriety as assessed using the WHO-UMC standardised causality assessment tool<sup>4</sup>. In 23/31 (74%) a single causative medication was identified (see Table 2), and these were all deemed either definite or probable. The cutaneous ADR and culprit drug was recorded in the electronic patient records and on the hospital drug chart.

In all patients, discontinuation of the culprit medication was carried out as soon as the diagnosis was made. Treatment of the drug rash varied according to the diagnosis and the symptoms. 29/31 (93.5%) patients received an emollient, 27/31 (87%) received a potent topical corticosteroid. 9 patients (7 with DRESS, 1 with erythema multiforme major, 1 with lichenoid drug reaction) received systemic corticosteroids (intravenous or oral). Four patients received intravenous corticosteroids; all were nursed on Intensive Care.

The electronic patient records were up-dated to indicate allergy to the medication. However, mention of a cutaneous ADR was made in only 6/31 (19%) of discharge summaries.

The data presented in this study confirms that allergic drug rashes are a significant cause of referral to the dermatology service. In the current study, 31 cases of a cutaneous ADR were diagnosed in a hospital in-patient population over a four month period. There was a slight male preponderance in our study, however this could be due in part to the small sample size. The commonest cutaneous ADR was drug-induced exanthem, occurring in 58% of patients (18/31). In all cases, the exanthem was uncomplicated and resolved swiftly once the culprit medication had been discontinued. The high frequency of drug-induced exanthems in the study mirrors the findings in other reports<sup>5-6,8-9</sup>. In our series, the drugs most commonly implicated in causing exanthems were the penicillins and carbopenams. Although investigations did not show evidence of herpes simplex or mycoplasma, one patient was felt to have erythema multiforme major based on clinical presentation.

NICE guidance recommends a structured approach to the assessment of drug allergy. Our study demonstrates that dermatologists are central both to the validation of allergic drug eruptions and to subsequent diagnostic categorisation. In three-quarters of patients, implication of a single culprit drug was achieved using drug administration time-lines, recognised notoriety, and known patient drug allergies.

For most aspects of a patient's admission episode the discharge summary is the principal document for disseminating current clinical issues. However, a cutaneous ADR occurring during the patient's admission was mentioned in only one-fifth of discharge summaries. This flaw can be easily corrected to improve communication of drug allergy information to all involved healthcare providers.

Dermatologists play a pivotal role in the diagnosis of ADRs, and thus in reducing length of in-patient stays and avoidance of future adverse events. The recognition of a cutaneous ADR, identification of culprit drug, and documentation in electronic medical records needs to be followed with a fail-safe system for relaying this information to the patient and other healthcare providers if inadvertent re-exposure is to be avoided.

### **References:**

1. World Health Organisation. International Drug Monitoring: the Role of the Hospital. Report of a WHO Meeting on International Drug Monitoring. Geneva: WHO, 1969.
2. Lazarou J, Pomeranz BH, and Corey PN. Incidence of Adverse Drug Reactions in Hospitalised Patients: A Meta-Analysis of Prospective Studies. JAMA 1998; 279(15):1200-1205
3. Drug Allergy. NICE Quality Standard (QS97) July 2015.
4. [http://www.who.int/medicines/areas/quality\\_safety/safety\\_efficacy/WHOcausalityassessment.pdf](http://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausalityassessment.pdf)
5. Chen CJ, Cheng CF, Lin HY et al. A Comprehensive 4-year Survey of Adverse Drug Reactions Using a Network-Based Hospital System. J Clin Pharm Ther 2012;37(6):647-51
6. Fiszenson-Albala F, Auzevie V, Mahe E et al. A 6-month Prospective Survey of cutaneous Drug Reactions in a Hospital Setting. Br J Dermatol 2003;149(5):1018-22
7. Tay LK, Lee Y, Thirumoorthy T et al. Dermatology Referrals in an East Asian Tertiary Hospital: A Need for Inpatient Medical Dermatology. Clin Exp Dermatol 2011;36(2):129-34
8. Luciane FF, Botelho MD, Adriana M et al. Adverse Cutaneous Drug Reactions in a Single Quaternary Referral Hospital. Int J Dermatol 2016;55(4):e198-203.
9. Hernandez-Salazar A, Rosales SP, Rangel-Frausto S et al. Epidemiology of Adverse Cutaneous Drug Reactions. A Prospective Study In Hospitalized Patients. Arch Med Res. 2006;37(7): 899-902.
10. Kardaun SH, Sidoroff A, Valeyrie-Allanore L et al. Variability in the Clinical Pattern of Cutaneous Side-Effects of Drugs with Systemic Symptoms: Does a DRESS Syndrome Really Exist? Br J Dermatol 2007;156(3):609-11.

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Table 1: Patient demographics and referral source of all in-patients diagnosed with cutaneous ADR over a 4-month period at a London Teaching Hospital

|                                  |             |
|----------------------------------|-------------|
| Adults                           | 29          |
| Children                         | 2           |
| Adults mean age (years); range   | 50.9; 17-88 |
| Children mean age (years); range | 4; 1-7      |
| Male (all patients)              | 16 (55.1)   |
| Female (all patients)            | 13 (44.9)   |
| Referrals                        |             |
| Medicine                         | 19 (61.2)   |
| Surgery                          | 2 (6.4)     |
| Intensive Care                   | 8 (26.0)    |
| Emergency Department             | 2 (6.4)     |

Values are n(%) unless stated otherwise

Table 2: Distribution of cutaneous adverse drug reactions and culprit medications

| Type of cADR                                                  | Numbers (%) | Culprit drug                                                                                                                     |
|---------------------------------------------------------------|-------------|----------------------------------------------------------------------------------------------------------------------------------|
| Drug-induced exanthem                                         | 18 (42.8)   | Penicillins x7<br>Meropenam x2<br>Alentuzumab x1<br>Idelalisib x1<br>Naproxen x1<br>Phenytoin x1<br>Probenecid x1<br>Ramipril x1 |
| Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) | 7 (16.6)    | Penicillins x3<br>Phenytoin x2<br>Carbamazepine x1<br>Anti-retrovirals (Darunavir, Ritonavir) x1                                 |
| Injection site reaction                                       | 1 (2.3)     | Azacitadine x1                                                                                                                   |
| Lichenoid drug reaction                                       | 1 (2.3)     | Allopurinol x1                                                                                                                   |
| Red man syndrome                                              | 1 (2.3)     | Vancomycin x1                                                                                                                    |
| Erythema multiforme major                                     | 1 (2.3)     | Meropenam x1                                                                                                                     |
| SDRIFE                                                        | 1 (2.3)     | Penicillin x1                                                                                                                    |
| Urticaria                                                     | 1 (2.3)     | Ibuprofen x1                                                                                                                     |