Editorial

Penicillin Allergy; Re-moulding Practice

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Penicillin allergy is the most commonly recorded drug allergy and is documented in 10% of medical records (Fact 1)[1]**.** However up to 95% of hospitalised patients with penicillin allergy documented in their notes are found to be non-allergic on skin testing or oral challenge testing (Fact 2)[2]. Restricting antibiotic use due to an unsubstantiated allergy is associated with adverse outcomes, including longer hospital stays, increased admissions to intensive care, emergence of resistant infections and a higher risk of mortality during hospitalization (Fact 3)[3]. SARI's Guidelines for Antimicrobial Stewardship in Hospitals In Ireland tantalizingly suggest annual savings of €34million with antibiotic stewardship but they do not even mention the well-established practice of testing for penicillin allergy to de-label such patients (Fact 4)[4]. We will make the case that these savings could be substantially higher if inpatient antibiotic allergy testing were included.

Most febrile illnesses in children are viral and viral infection is the most common cause of acute urticaria (via the complement pathway), not drug allergy or even food allergy (Fact 5)[5]. Parent-demanded and medically defensive prescription of antibiotics for simple febrile illnesses leads to lifelong defensive labelling of children as "allergic" to penicillin, partly so that a doctor or institution will not be blamed for a further exanthem if re-exposed to the antibiotic. That is clearly not good stewardship. An Irish study examining oral penicillin challenges in low risk children with suspected penicillin allergy in an outpatient setting found that 95% of patients had negative challenges, allowing the safe prescription of oral penicillins in the future. Adults who report penicillin allergy are often reciting family folklore about similar

rashes in their distant childhood, so it is likely the same reassuring statistics apply to them. In fact this is precisely the case as penicillin skin testing in this population is positive in just 1.7%, which is comparable to that for the general population (Fact 6)[6].

Take a history, take a history, take a history. A detailed history of the “allergy” episode is the critical first step (Fact 7)[7]. Important points to note include the interval between drug administration and the occurrence of symptoms, the nature of those symptoms, history of atopy or hypersensitivity to other drugs, and the illness for which the patient took the medication. True penicillin allergy precluding the administration of beta lactam antibiotics is an IgE dependent acute allergic reaction, including anaphylaxis. Cell-mediated reactions may occur such as erythema muliforme / Stephen-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS). These reactions are clearly identifiable by routine medical history and examination (including smartphone images if available). These patients, with convincing findings, should be advised to avoid these and structurally related drugs[6]. Furthermore, an accurate history can identify drug reactions without an allergic basis, which can also result in the allergy label being removed such as vomiting and diarrhea (which is nearly routine after amoxicillin/clavulanate). Additionally, cross reactivity with other beta lactam antibiotics is overstated. Less than 5% of penicillin allergic individuals will have in vivo cross reactivity to a first generation cephalosporin, less than two percent to a second, third, or fourth generation and one percent for carbapenems (Fact 8)[6].

In vitro testing with specific IgE to penicillin correlates poorly with oral challenge positivity raising questions about its usefulness (Fact 9). Skin prick testing (SPT) using benzylpenicillin has a specificity of 97-100%, sensitivity of 70%, and a positive predictive value of 40-100%**.** The combination of SPT and oral challenge, for those in whom SPT is negative, is the gold standard for testing for IgE mediated reactions (Fact 10)[7]. SPT can be done at the bedside, even in critically ill patients in ICU, and an actionable result is available in less than 15 minutes. Inpatient penicillin SPT with or without oral dosing challenge leads to a change in antibiotic selection in 55-78% of patients, reduced prescription of vancomycin and fluoroquinolones, and reduced healthcare associated costs. With this approach adverse outcomes were reported in less than one percent of cases (Fact 11)[2]. Accurate documentation and effective communication of a negative challenge and its results are crucial to ensure inappropriate prescribing practices are discontinued and the patient is “de-labelled”. Intradermal testing is a more specialized activity and should only be done by trained allergists.

Antibiotic desensitisation therapy is needed only by patients who are high risk for penicillin allergy (such as cystic fibrosis patients) in whom a beta lactam is unavoidable for urgent, lifesaving antibiotic therapy. It

is performed by administering increasing doses of the medication and induces a temporary tolerant state, which can only be maintained by continuous administration of the drug (Fact 12)[8].

Incorrect and even casual documentation of penicillin “allergy” represents a significant challenge for antimicrobial stewardship, which the SARI guidelines do not address. The only mention of drug allergy is in an appendix addressing preoperative prophylaxis and the scenario given is a very simple one, that should cause no confusion to any junior doctor[4]. Better antimicrobial guidelines and reduced prescribing for viral infections will reduce both unnecessary antibiotic exposure and the potential for real penicillin allergy but more importantly will also reduce mislabelling. Access to penicillin skin testing is very limited in Irish hospitals, confined mainly to referred outpatients, with no hospital, to our knowledge, offering such a service to inpatients. In the absence of allergy services in all but a tiny handful of Irish hospitals, other healthcare providers must be empowered to assess and safely rule out penicillin allergy through guidelines and stewardship initiatives that MUST include elimination of false diagnoses of drug allergies and the development of medical or allied health expertise on the ground to do the testing.

Addressing penicillin allergy must become an integral component of antimicrobial stewardship in order to reduce the unnecessary use of broad-spectrum and second and third line antibiotics. It will pay for itself and foster better medical care.

Conflict of interest

KMC none, JO’BH is President of the Irish Association of Allergy and Immunology.

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