

The RCPCH care pathway for children with drug allergies: an evidence and consensus based national approach

George du Toit,¹ Kate Lloyd,² Louise Sinnott,³ Debra Forster,⁴ Moira Austin,⁵ Christine Clark,⁶ David Tuthill,⁷ Jane S Lucas,⁸ Nicola Brathwaite,⁹ John Warner¹⁰; on behalf of the Science and Research Department, Royal College of Paediatrics and Child Health

► An additional supplementary appendix is published online only. To view this file please visit the journal online (http://adc.bmj.com/content/96/Suppl_2.toc)

¹Paediatric Allergy, Guy's and St Thomas' NHS Foundation Trust, London, UK

²Science and Research Department, Royal College of Paediatrics and Child Health, London, UK

³North West Specialised Commissioning Team, Warrington, UK

⁴Children's Clinic (South), RCN Nurses Allergy Group, Nottingham Children's Hospital, London, UK

⁵Anaphylaxis Campaign, Farnborough, UK

⁶Pharmacist, London, UK

⁷Department of Paediatrics, Children's Hospital for Wales, Cardiff, UK

⁸Division of Infection, Inflammation and Immunity, NIHR Respiratory Biomedical Research Unit, Sir Henry Wellcome Laboratories, University of Southampton, Southampton, UK

⁹Paediatric Allergy, King's College Hospital NHS Foundation Trust, London, UK

¹⁰Department of Paediatrics, Imperial College, St Mary's Hospital Campus, London, UK

Correspondence to

Dr George du Toit, Paediatric Allergy, Guy's and St Thomas' NHS Foundation Trust, Westminster Bridge Road, London SE1 7EH, UK; georgedutoit@gmail.com

Accepted 25 April 2011

ABSTRACT

Aims The Royal College of Paediatrics and Child Health (RCPCH) was commissioned by the Department of Health to develop a drug allergy pathway. It focuses on defining the competences to improve the equity of care received by children.

Method The drug pathway was developed by a multidisciplinary working group and was based on a comprehensive review of evidence. The team decided to focus on IgE-mediated reactions as these have the greatest potential to be life-threatening.

Results The results are presented in four parts: evidence review, pathway mapping, external review and core knowledge documents. The evidence review found a high percentage of putative penicillin allergy is not confirmed by objective testing and that re-sensitisation to β -lactam drugs was infrequent. It also highlighted the importance of a detailed history and accurate diagnosis along with clear communication of test results to both family and primary care.

Conclusions This pathway demonstrates the spectrum of drug allergy is varied and may differ for young children compared with older children and adults. The authors highlight the paucity of evidence to support allergy testing for most drugs, in children, other than supervised incremental provocation tests (when indicated). Acute presentations require emergency health professionals to address underlying allergic issues, including recognition and avoidance of potential drug allergy triggers. Non-acute presentations may include multi-system symptoms which may have a broad differential diagnosis; this document signposts to the relevant partners in the RCPCH care pathway portfolio. Management combines a care package including a definitive diagnosis, initiating treatments and ongoing education.

INTRODUCTION

Adverse drug reactions (ADRs) are defined by the WHO as any noxious, unintended and undesired effect of a drug that occurs at doses used for prevention, diagnosis or treatment. ADRs are commonly encountered in both inpatient and outpatient settings, and reactions can be severe in nature.^{1 2} ADRs are categorised into predictable (type A) and unpredictable (type B) reactions. Unpredictable reactions are further subdivided into drug intolerance (an undesirable pharmacological effect that occurs at low and sometimes

What is known about this topic

- Drug-induced allergic reactions can affect numerous organ systems and may present with a variety of clinical reactions.
- Drug-induced allergic reactions can have more than one mechanistic pathway.

What this study adds

- This is the first attempt to map the patient care pathway for children with drug allergy.
- The pathway identifies a paucity of evidence to support allergy testing for many drugs, with some notable exceptions, in children, other than supervised incremental provocation tests (when indicated).

subtherapeutic doses of the drug without underlying abnormalities of metabolism, excretion or bioavailability of the drug), drug idiosyncrasy (abnormal and unexpected effect, usually caused by underlying abnormalities of metabolism, excretion or bioavailability), drug allergy (immunologically mediated ADRs, including IgE-mediated drug allergy) and pseudoallergic reactions (also called anaphylactoid reactions, which are due to direct release of mediators from mast cells and basophils rather than IgE antibodies). However, other than in relation to diagnostic tests, anaphylactic and anaphylactoid reactions should be treated identically. This Royal College of Paediatrics and Child Health (RCPCH) national care pathway for drug allergy deals mostly with ADRs that arise due to IgE-mediated (immediate onset) reactions. While such reactions form a minority of ADRs, they are potentially life-threatening and therefore warrant a detailed care plan in order to facilitate a correct and safe diagnosis.

Drug-induced allergic reactions can affect numerous organ systems and may present with a variety of clinical reactions. Further complicating the diagnosis of drug allergy in children is the fact that drug-induced allergic reactions can have more than one mechanistic pathway. While cutaneous

Original article

manifestations are the most frequent clinical manifestation of drug-induced allergic reactions, many other organ systems can be involved, resulting in haematological abnormalities, nephritis, hepatitis, pneumonitis, lymphadenopathy or arthralgias.

The Gell and Coombs classification of hypersensitivity remains the most common method of classifying immunologically mediated ADRs, and an understanding of this classification is necessary to guide diagnostic and therapeutic modalities. In this pathway we make an evidence-based assessment of the diagnostic tools available for the diagnosis of specific-IgE to drugs and acknowledge that complex skin and intradermal testing is not always acceptable to young children. Such testing is time consuming but safe, and benefits to the patient include a valid diagnosis of the allergy; the confirmation of an allergy allows for the safe use of selected drugs in the future, while a diagnosis of tolerance allows the patient to safely receive the drug. In most circumstances there are significant health and cost advantages associated with a diagnosis of drug allergy.

METHOD

The pathway was developed by a multidisciplinary Drug, Venom and Latex Allergy Working Group (DVLWG), chaired by GdT who reported to the RCPCH Allergy Care Pathways Project Board. The DVLWG included health professionals with expertise in paediatric allergy, immunology, allergy nursing, secondary care and a parent/carer representative. Attempts to recruit additional health professionals from primary care were unsuccessful. The full methodology is outlined separately in this supplement.³

RESULTS

The pathway results are presented in four parts: evidence review, mapping, external review and core knowledge documents. The full pathway document can be downloaded from <http://www.rcpch.ac.uk/allergy/drugallergy>.

Evidence review

A total of 162 titles and abstracts were screened by the project manager and DVLWG chair (figure 1). Thirty-two systematic reviews and/or primary papers and 12 guidelines were identified for appraisal; handsearching the reference lists of appraised papers identified a further two papers. The full critical appraisal resulted in the inclusion of 12 systematic reviews and/or primary papers and five clinical practice guidelines.

The evidence review found that the prevalence of true penicillin allergy is much less common than perceived allergy and that re-sensitisation to β -lactam drugs was infrequent.^{4–6} A detailed history is required for an accurate diagnosis of a drug-induced reaction and skin prick tests should not be used to screen for drug allergy in the absence of a clinical history compatible with IgE-mediated drug allergy.⁷ The research also clearly showed the value of serial dilutions for skin tests where the patient has a history of serious reaction,⁸ although skin tests for patients with drug allergies were shown to be safe.⁸ The research highlighted that the mean antibiotic cost for patients with a β -lactam allergy was significantly higher compared with those without a β -lactam allergy, but that more research was needed to investigate cost effectiveness.⁹ As alternative antibiotics are cheap, this raised the health economics question as to whether it is cost-effective to conduct detailed tests to exclude penicillin allergy in the absence of other underlying disease predisposing to infection. The

research also highlighted the value of clear communication of test results to both family and primary care in the management for patients with drug allergy.^{7 10} A full evidence table can be obtained from the RCPCH Science and Research Department.

MAPPING

The RCPCH national care pathway for drug allergy is presented in online supplemental appendix 1. For the purposes of this pathway, drug allergy is defined as an immune-mediated hypersensitivity reaction to a drug (medicinal product) and may be divided into IgE-mediated (immediate onset) reactions and non-IgE-mediated (delayed onset) reactions.

The DVLWG acknowledges a wide range of adverse reactions occur to medicinal products, and this pathway does not cover the treatment of these reactions.

External review

This pathway was made available with the latex allergy and venom allergy pathways on the RCPCH website and emailed to a general allergy stakeholder list. Nine of 57 (16%) invited organisations responded, providing 32 comments.

Core knowledge documents

The working group did not identify key guidelines (core knowledge documents) supporting the skills required to deliver this pathway. Helpful reviews are available but these are not specific for drug allergy in childhood.

DISCUSSION

To our knowledge this is a novel care pathway for children with drug allergies in the UK. A fundamental aim of this drug allergy pathway is to demonstrate that the spectrum of drug allergy is varied and may be different for young children where age-specific pharmacodynamic and pharmacokinetic properties may result in unique clinical reactions, at different doses, and to different drugs. We highlight the paucity of evidence to support allergy testing for most drugs, in children, other than supervised incremental provocation tests (when indicated). The points of entry to the drug allergy pathway are therefore defined by symptoms and signs at presentation; recognition of these symptom complexes will be required in many community settings (including self-care), hospital emergency departments, general paediatric settings and specialist allergy clinics. The challenge for this pathway was to formulate a joined-up approach for the diagnosis and investigation of drug allergy while recognising that drug-induced clinical presentations vary in severity, with some reactions being more severe in nature and therefore requiring a higher level of medical expertise. The competences have, however, intentionally not been assigned to health professionals. This should allow for flexibility of service delivery at the local level. Individual health professionals must decide when they possess the appropriate competence to care for children with drug allergies and refer them to appropriate local services. The importance of delivering care across a network for children with allergies is made clear as is the need for intermittent review of established diagnoses.

Acute presentations

Severe or life-threatening drug reactions represent a medical emergency that requires treatment in accordance with evidence-based guidelines; accordingly, the management of such presentations is outlined separately in the anaphylaxis

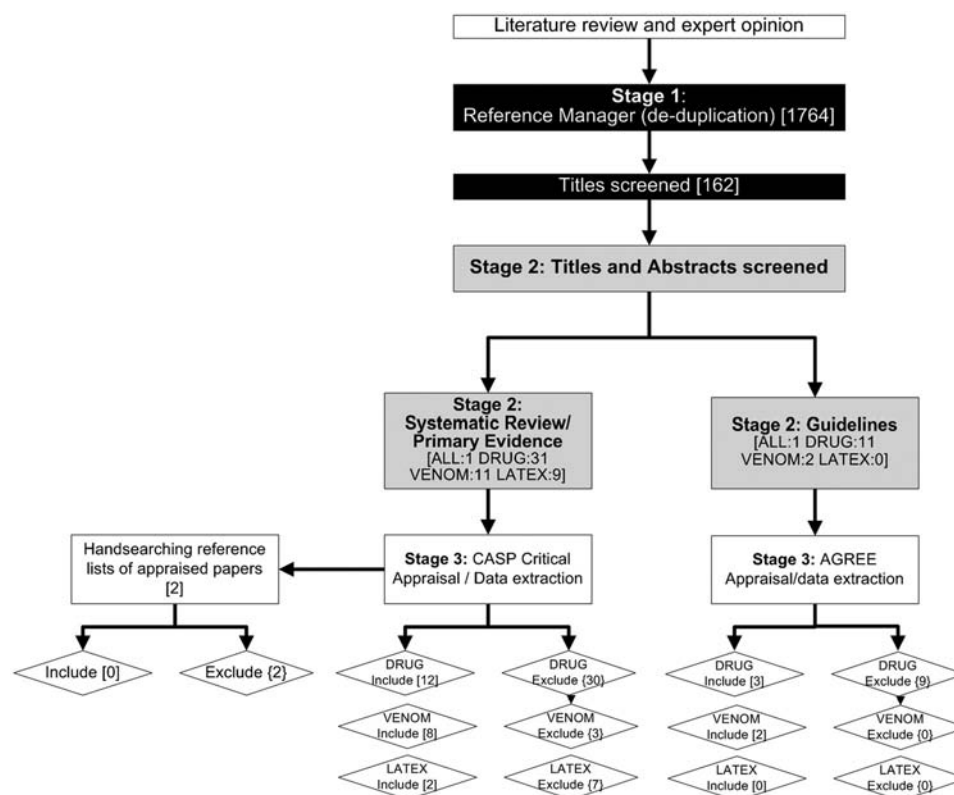


Figure 1 Methodology of evidence review.

pathway. While drug-induced reactions that are systemic and/or result in significant mucosal membrane and cutaneous desquamation, may result in significant morbidity and even mortality, this presentation was outside the scope of this drug allergy pathway (although such patients are commonly also referred to specialist allergy centres).

Once the seriously unwell child is stable, a review of their complete ‘drug allergy picture’ is indicated, as reflected by a single pathway from this point. This places a responsibility on the emergency care practitioner to address underlying allergic issues at that time, where possible including recognition and avoidance of potential ongoing, or related, drug allergy triggers.

Non-acute presentations

Drug allergy may present with multi-system symptoms and signs for which there may be a broad differential diagnosis. Thus, this document signposts the user to the relevant partners in the RCPCH care pathway portfolio. Patient management is characterised by a package of care that broadly includes steps to establish a definitive diagnosis, initiate appropriate treatments and provide ongoing education. A history of suspected drug allergy is common among children in the UK. If correct, this ensures a safe selection of medications in the future; however, an incomplete or incorrect diagnosis may have far-reaching consequences for a child’s general health, for example, future medication choices may be compromised, possibly leading to an inferior medication choice or medications that have significant side effects. The pathway therefore accommodates entry for those with a ‘history of suspected drug allergy’ as well as those with ‘non-life threatening reactions’. The pathway therefore emphasises the pressing need for ‘initial recognition’, as this is

the first step on the ideal patient care journey. The pathway also highlights the financial burden associated with drug allergy.

Patient–health professional partnership

A particular strength of this pathway is that input was collated from a large multi-disciplinary team that also included a representative from a national patient support charity. The pathway emphasises that all treatment and management plans should be achieved in partnership between patients with allergies, their carers and health professionals (concordance). Effective communication between all is a key item on the pathway. Concordance, or the agreement between the patient/family and health professional to follow a particular management plan, should be clearly established at the outset and the health professional should continue to review adherence to the joint agreed plan.

Clinical implications

The drug allergy pathway does not define where (or by whom) care should be provided, but rather describes the competences required by the relevant health professional(s) to deliver optimal care. Thus, for example, ‘further assessment and management’ may require specialised investigation and treatment skills. It is independent of conventional ‘primary’ versus ‘secondary’ versus ‘tertiary’ care terminology, although practically some specific treatments (example, desensitisation therapies) are likely to be restricted to specialist centres.

These competences utilise an evidence base to summarise the required knowledge and skills for the particular pathway step. While the competency-based model offers improved flexibility for high quality allergy care provision, it has a number of implications for clinical services. The pathway

Original article

emphasises the importance of a detailed clinical history; health professionals require time for these detailed appointments. Health professionals must be able to demonstrate competence at the levels outlined in the pathway steps; this will require input to, and revision of, training programmes for the diagnosis and management of drug allergy in childhood. Moreover, at the heart of a successful pathway is effective communication between all involved health professionals, and between health professionals, patients, carers and community services (schools, colleges, early years settings). Opportunities for training, as well as systems to address communication and patient follow-up (including transitional care) needs will require broader National Health Service support and resources if we are to provide the ideal pathway of care our children deserve.

CONCLUSION

The drug allergy pathway describes the steps in ideal care for children presenting with acute 'severe life-threatening' reactions, 'non-life threatening reactions' and those with a 'history of suspected drug allergy'. This represents an opportunity to improve the lives of children with drug allergy. The major limitation to the development of this pathway was the paucity of good quality evidence, particularly with respect to children. Further studies that make use of rigorous study methodologies that investigate the prevention, treatment and diagnosis of drug allergy in childhood are required. Research recommendations identified by the DVLWG are currently the subject of a Delphi consensus.

Acknowledgements We thank Ms Hilary Whitworth, a PhD Student at the University of Southampton, who provided assistance for the evidence review, the Royal College of Paediatrics and Child Health (RCPCH) Allergy Care

Pathways Project Board who provided guidance and assistance, and the RCPCH Clinical Standards team for their hard work on the approval process, in particular Ms Katie Jones.

Funding This project was funded by the Department of Health.

Competing interests GdT: Allergy Therapeutics, ALK, Phadia, Danone, Nutrition SHS; DT: Nutricia, SMA; CC: Stiefel, Galderma, Almirall, Leo, JL: ALK; JW: Novartis, Danone, Airsonette, Merck, Allergy Therapeutics, Phadia Research, GSK, AstraZeneca, Merck, Allergy Therapeutics, ALK.

Provenance and peer review Not commissioned; internally peer reviewed.

REFERENCES

1. **Gandhi TK**, Weingart SN, Borus J, *et al*. Adverse drug events in ambulatory care. *N Engl J Med* 2003;**348**:1556–64.
2. **Lazarou J**, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA* 1998;**279**:1200–5.
3. **Warner JO**, Lloyd K. Shared learning for chronic conditions: a methodology for developing the Royal College of Paediatrics and Child Health (RCPCH) care pathways for children with allergies. *Arch Dis Child* 2011;**96**(Suppl 2):i1–i6.
4. **Hershkovich J**, Broides A, Kirjner L, *et al*. Beta lactam allergy and resensitization in children with suspected beta lactam allergy. *Clin Exp Allergy* 2009;**39**:726–30.
5. **Ponvert C**, Weilenmann C, Wassenberg J, *et al*. Allergy to betalactam antibiotics in children: a prospective follow-up study in retreated children after negative responses in skin and challenge tests. *Allergy* 2007;**62**:42–6.
6. **Rebello Gomes E**, Fonseca J, Araujo L, *et al*. Drug allergy claims in children: from self-reporting to confirmed diagnosis. *Clin Exp Allergy* 2008;**38**:191–8.
7. **Mirakian R**, Ewan PW, Durham SR, *et al*. BSACI guidelines for the management of drug allergy. *Clin Exp Allergy* 2009;**39**:43–61.
8. **Valyasevi MA**, Van Dellen RG. Frequency of systematic reactions to penicillin skin tests. *Ann Allergy Asthma Immunol* 2000;**85**:363–5.
9. **MacLaughlin EJ**, Saseen JJ, Malone DC. Costs of beta-lactam allergies: selection and costs of antibiotics for patients with a reported beta-lactam allergy. *Arch Fam Med* 2000;**9**:722–6.
10. **Langley JM**, Halperin SA, Bortolussi R. History of penicillin allergy and referral for skin testing: evaluation of a pediatric penicillin allergy testing program. *Clin Invest Med* 2002;**25**:181–4.



The RCPCH care pathway for children with drug allergies: an evidence and consensus based national approach

George du Toit, Kate Lloyd, Louise Sinnott, et al.

Arch Dis Child 2011 96: i15-i18

doi: 10.1136/archdischild-2011-300116

Updated information and services can be found at:

http://adc.bmj.com/content/96/Suppl_2/i15.full.html

These include:

Data Supplement

"Web Only Data"

<http://adc.bmj.com/content/suppl/2011/11/02/archdischild-2011-300116.DC2.html>

References

This article cites 10 articles, 3 of which can be accessed free at:

http://adc.bmj.com/content/96/Suppl_2/i15.full.html#ref-list-1

Article cited in:

http://adc.bmj.com/content/96/Suppl_2/i15.full.html#related-urls

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:

<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:

<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:

<http://group.bmj.com/subscribe/>