Appendix A: Summary of evidence from surveillance

2018 surveillance of Drug allergy: diagnosis and management (2014) NICE guideline CG183

Summary of evidence from surveillance

Studies identified in searches are summarised from the information presented in their abstracts.

Feedback from topic experts who advised us on the approach to this surveillance review, was considered alongside the evidence to reach a final decision on the need to update each section of the guideline.

Assessment

Recommendations in this section of the guideline

1.1.1 When assessing a person presenting with possible drug allergy, take a history and undertake a clinical examination. Use the following boxes as a guide when deciding whether to suspect drug allergy.

Boxes 1–3 Signs and allergic patterns of suspected drug allergy with timing of onset*

Box 1 Immediate, rapidly evolving reactions

Anaphylaxis – a severe multi-system reaction characterised by: • erythema, urticaria or angioedema **and** • hypotension and/or bronchospasm	Onset usually less than 1 hour after drug exposure (previous exposure not always confirmed)
Urticaria or angioedema without systemic features	
Exacerbation of asthma (for example, with non-steroidal anti-inflammatory drugs [NSAIDs])	

Box 2 Non-immediate reactions without systemic involvement

Widespread red macules or papules (exanthema-like)	Onset usually 6–10 days after first drug exposure or within 3 days of second exposure
Fixed drug eruption (localised inflamed skin)	

Box 3 Non-immediate reactions with systemic involvement

Drug reaction with eosinophilia and systemic symptoms (DRESS) or drug hypersensitivity syndrome (DHS) characterised by: • widespread red macules, papules or erythroderma • fever • lymphadenopathy • liver dysfunction • eosinophilia	Onset usually 2–6 weeks after first drug exposure or within 3 days of second exposure
Toxic epidermal necrolysis or Stevens–Johnson syndrome characterised by: • painful rash and fever (often early signs) • mucosal or cutaneous erosions • vesicles, blistering or epidermal detachment • red purpuric macules or erythema multiforme	Onset usually 7–14 days after first drug exposure or within 3 days of second exposure
Acute generalised exanthematous pustulosis (AGEP) characterised by: • widespread pustules • fever • neutrophilia	Onset usually 3–5 days after first drug exposure

Common disorders caused, rarely, by drug allergy: • eczema • hepatitis • nephritis • photosensitivity • vasculitis	Time of onset variable

* Note that these boxes describe common and important presenting features of drug allergy but other presentations are also recognised

1.1.2 Be aware that the reaction is more likely to be caused by drug allergy if it occurred during or after use of the drug and:

- the drug is known to cause that type or reaction **or**
- the person has previously had a similar reaction to that drug or drug class.

1.1.3 Be aware that the reaction is less likely to be caused by drug allergy if:

- there is a possible non-drug cause for the person's symptoms (for example, they have had similar symptoms when not taking the drug) **or**
- the person has gastrointestinal symptoms only.

Measuring serum tryptase after suspected anaphylaxis

1.1.4 After a suspected drug-related anaphylactic reaction, take 2 blood samples for mast cell tryptase in line with recommendations in Anaphylaxis (NICE clinical guideline 134).

1.1.5 Record the exact timing of both blood samples taken for mast cell tryptase:

- in the person's medical records **and**
- on the pathology request form.

1.1.6 Ensure that tryptase sampling tubes are included in emergency anaphylaxis kits.

Measuring serum specific immunoglobulin E

1.1.7 Do not use blood testing for serum specific immunoglobulin E (IgE) to diagnose drug allergy in a non-specialist setting.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

Skin tests

A systematic review included 76 studies assessing the diagnostic utility of first line drug provocation testing (DPT) in children with suspected antibiotic allergy. The review included 4 studies which used DPT-based protocols to determine suspected antibiotic allergy, with 2 studies performing intradermal tests and DPTs in all subjects. Beta-lactam intradermal testing yielded a sensitivity of 66.7% and positive predictive value (PPV) of 36% and clarithromycin intradermal testing yielded a sensitivity of 75% and PPV of 33% when compared with DPT. (1)

A cohort study assessed the diagnostic value and safety of penicillin skin testing in children under the age of 18 (n=778) with a history of penicillin allergy. The results found that 703 children had a negative penicillin skin test, 66 had a positive test and 9 children had an uncertain result. A proportion of patients with negative skin test (369/703) were orally challenged with penicillin with 14 patients experiencing an adverse drug reaction (ADR) to penicillin, whilst no cases of adverse reactions to penicillin skin testing were reported. (2)

An observational study in children aged ≤ 18 years old (n=126) with a history of beta-lactam hypersensitivity assessed the diagnostic value of skin testing. Patients underwent skin testing (skin prick test and intradermal test) with penicillin G, ampicillin, amoxicillin-clavulanic acid, and the suspect beta-lactam antibiotic. Those with a negative skin test result underwent a DPT in a 3-dose-graded challenge. The results found that 22 patients were confirmed with a beta-lactam hypersensitivity with 12 of these confirmed by a skin test. Out of 104 patients with a negative skin test result, 10 patients showed reactions following a DPT, with skin testing yielding a negative predictive value (NPV) of 91.2%. No cases of systemic reactions were reported following skin testing for beta-lactam hypersensitivity. The authors concluded that skin testing alone did not yield a high sensitivity, therefore a DPT was required in order to confirm the diagnosis of beta-lactam hypersensitivity. (3)

An observational study assessed the safety and diagnostic performance of skin testing without penicilloyl-polylysine (PPL) using penicillin G followed by a 3-dose-graded challenge to penicillin (if a negative skin test result), in children (n=563) with a history of penicillin allergy. One hundred and eighty five patients had a positive skin test result, with subjects having a significantly shorter time period between the initial reaction and skin testing compared with those with a negative test result. Subjects with a negative skin test result (375/378) were challenged with 18 subjects showing a reaction resulting in a NPV of 95.2% (95% CI 92.5 to 97.1%). Subjects with a history of anaphylaxis (3/17) showing a negative skin test result reacted to oral challenge resulting in a NPV of 82.4% (95% CI, 59.0-93.8%). Reactions were reported as mild and treated without delay. (4)

An observational study in children (n=133) with a history of immediate or non-immediate reactions to amoxicillin assessed the utility of skin prick tests in the diagnosis of amoxicillin allergy. All

subjects underwent skin prick tests, followed by an oral graded challenge with amoxicillin. The results found that all children had a negative skin test result, and 3 children had an immediate reaction whilst 7 subjects had a non-immediate reaction. A family history of drug allergy (OR 0.12, 95% CI 0.026 to 0.613), asthma (OR 0.12, 95% CI 0.017 to 0.869) and older age at reaction (OR 0.837, 95% CI 0.699 to 1) were significantly associated with a lower likelihood of passing the oral challenge, along with angioedema (OR 0.22, 95% CI 0.043 to 1.12), however this was not statistically significant. (5)

Drug provocation test (DPT)

A cohort study assessed the diagnostic utility of graded drug provocation challenge in children (n=818) with suspected amoxicillin allergy. The results found that 770 children tolerated the provocation challenge, 17 developed mild immediate reactions and 31 developed non-immediate reactions. The graded drug provocation challenge yielded a specificity of 100.0% (95% CI, 90.9 to 100.0%), a NPV of 89.1% (95% CI, 77.1 to 95.5%), and a PPV of 100.0% (95% CI, 86.3 to 100.0%). Two hundred and fifty subjects responded during follow-up, with 49 out of 55 subjects reporting a tolerance to subsequent amoxicillin therapy whilst 6 subjects reported non-immediate cutaneous reactions. Immediate reactions to the drug provocation challenge was associated with a history of a reaction occurring within 5 minutes of exposure to amoxicillin (OR 9.6, 95% CI 1.5 to 64.0). Non-immediate reactions to the drug provocation challenge were associated with a rash present for more than 7 days (OR 4.8, 95% CI 1.4 to 16.4) and parental history of drug allergy (OR 3.0, 95% CI 1.3 to 6.8). (6)

An observational study assessed the diagnostic value of the drug provocation test (2-day protocol) in children with a history of non-immediate beta-lactam allergy. Subjects with a positive initial diagnostic drug provocation test (n=18) had a follow-up test after 3 years, with those subjects with a negative initial diagnostic test result completing a questionnaire to evaluate the tolerance of subsequent treatment with the implicated beta-lactam drug. Sixteen subjects with an initial positive diagnostic drug provocation test had a negative follow-up drug provocation test, with 2 cases of benign exanthema reported. Eleven out of 16 children were able to tolerate a subsequent treatment with the implicated beta-lactam drug without any reaction. The NPV of the 2-day protocol drug provocation test was 96.7%. (7)

An observational study assessed the value of direct DPT without prior skin testing in children (n=119) with non-immediate reactions to beta-lactam antibiotics. All subjects underwent a 5-dose-graded challenge continued for 5 days. The results found that amoxicillin-clavulanic acid was the most common culprit in 87 children, with maculopapular rash occurring in 74 subjects. During DPT, 4 children experienced an urticarial reaction. (8)

Multiple methods of allergy testing

An observational study assessed the diagnostic value of late-reading (48-72 hours) and hyper-late-reading (>=6-7 days) of skin tests and prolonged DPT (more than 3 days) in children (n=550) with non-immediate reactions to beta-lactam antibiotics. Children with a negative intradermal and patch tests (skin tests) were challenged with a prolonged DPT. The results found that non-immediate hypersensitivity to beta-lactam antibiotics was confirmed in 63 children (reporting 66 reactions), comprising 17 responses from skin tests (5 from intradermal testing, 8 to patch testing and 4 to both tests), 43 responses to DPT and 6 based on clinical history, including 3/9 subjects with severe cutaneous adverse reactions. A positive skin test was found after the 6-7th day in 14/17 children, whilst a positive DPT was observed after a median time of 3 days. No severe reactions were reported following skin testing or during prolonged DPT. (9)

Removing penicillin allergy label

An observational study assessed the effectiveness of penicillin allergy "de-labeling" in clinical practice in patients (n=401) aged ≥ 15 years with history of beta-lactam allergy. All subjects underwent skin testing (skin prick and intradermal testing) with immediate (n=151) and non-immediate reactions (n=250). The results found that 42/341 subjects were positive to ≥ 1 penicillin reagents, with this being significantly greater in immediate group (35/114) compared with non-immediate (7/227) reaction patients. Non-serious positive oral challenge reactions to single dose penicillin occurred in 3/355 patients from the immediate group, yielding a NPV of 99.2% for skin testing. Selective or unrestricted use of beta-lactam antibiotic was recommended in 238/250 (95.2%) in non-immediate reaction patients and 126/151 (83.4%) in the immediate group (p=0.0001). At follow-up 137/182 patients were complying with the allergy label modifications. (10)

Other investigations

An observational study assessed the diagnostic value of the basophil activation test (BAT) in the diagnosis of amoxicillin (AMX) or AMX-clavulanate (AMX-C) immunoglobulin E (IgE)-mediated hypersensitivity in children (n=18) and adults (n=21) with a history of immediate reactions to AMX or AMX-C. Subjects underwent skin prick and intradermal testing and BAT with AMX or AMX-C was completed within 6 months from the reaction. The results found that in children the concordance between skin prick/intradermal testing and BAT results was 83.3%, whilst reaction severity and skin test positivity did not correlate with BAT results. The authors concluded that "BAT does not seem to be a useful tool to increase the sensitivity of an allergy work-up to diagnose immediate hypersensitivity to AMX or AMX-C". (11)

Intelligence gathering

A topic expert commented that the recommendations state to take a history but do not provide further detail about next steps. NICE guideline CG183 does provide recommendations for documenting such information in medical records, sharing information with other healthcare professionals and lists criteria for referral to specialist services, therefore no impact on the guideline is anticipated.

Several topic experts highlighted that the recommendations should focus more on paediatric populations, particularly on antibiotic allergy and challenges without skin test in children. Although the guideline recommendations are applicable to children, young people and adults, one topic expert commented that children need different management compared with adult populations. As such, the evidence search approach for the surveillance review was focused on the diagnosis and management of drug allergy in children. An additional area of focus in the search approach included allergy to antibiotic drugs, whereby adverse drug reactions to antibiotics are common and often result in a lifelong drug allergy label in children.

Topic expert feedback focused on implementation of the guideline. One topic expert commented that the recommendations are difficult to implement in practice due to limited resources. Another topic expert commented that ongoing work is still required to implement the guideline recommendations, however NICE guideline CG183 has had widespread take-up and "has been read and analysed by many allergists and immunologist worldwide and recommendations very well received". The expert explained that their trust has developed an electronic system for documenting new drug allergy based on NICE guideline CG183. The expert also noted that this guideline "has had a wide-ranging effect and continues to do so therefore important not to amend yet as trusts are still getting to grips on how to implement".

A topic expert highlighted the Report and findings of the Royal College of Anaesthetists' 6th National Audit Project: Perioperative Anaphylaxis (2018) undertaken every 3 years, from which there are 7 publications in the pipeline. The audit recommendations support NICE guideline CG183 recommendations on documentation and referral of drug allergy.

A topic expert highlighted the British Society for Allergy and Clinical Immunology (BSACI) guidance on the Management of allergy to penicillins and other beta-lactams (2015) which is NICE accredited. The full guideline provides recommendations for UK specialists and clinicians practicing allergy including managing beta-lactam allergy in children.

Another expert highlighted the European Academy of Allergy and Clinical Immunology (EAACI) task force report: recognising the potential of the primary care physician in the diagnosis and management of drug hypersensitivity (2018), which broadly supports the recommendations in NICE guideline CG183.

Impact statement

As the evidence identified during this surveillance review did not include children presenting with signs and symptoms of drug allergy, the focus of this section is centred on people with a history of suspected drug allergy.

Skin tests

A small body of evidence (1 systematic review and 4 observational studies) was identified concerning skin tests (intradermal tests and skin prick tests) to diagnose antibiotic allergy in children. The evidence indicates that skin tests are generally safe in children, and yield high

negative predictive values. However, skin tests yielded low to moderate sensitivity values, and one study noted that a drug provocation test was needed to confirm drug hypersensitivity in children.

Whilst the evidence demonstrates that skin tests may have value in diagnosing antibiotic allergy in children, limited evidence was found supporting the reliability of the procedure. Therefore, it would not be feasible to develop specific recommendations on the use of this test in children.

Drug provocation test (DPT)

Three observational studies were identified which assessed the value of drug provocation tests (DPTs) in confirming beta-lactam allergy in children. Overall, the evidence supports the use of DPT in children, particularly in those with non-immediate reactions, however limited data was identified on the diagnostic performance of the test. Only 1 study reported that DPT yielded a high specificity and 2 studies reported that DPT yielded a high negative predictive value. The evidence indicates that drug provocation tests are generally safe in children, however length of oral challenges varied.

In addition insufficient evidence was identified on the effectiveness of direct oral antibiotic challenge without prior skin allergy testing, which was an area highlighted by topic experts. It would therefore be pertinent to wait for further evidence before considering this area for update.

Multiple methods of allergy testing

One observational study found that the sensitivity of skin tests was low despite additional hyper-late reading, whilst prolonged drug provocation test may improve the diagnostic accuracy of the test in the diagnosis of non-immediate hypersensitivity to beta-lactam antibiotics.

Although the evidence indicates that extended drug provocation tests may be favourable, an optimal time interval for provocation was not demonstrated in the evidence identified through surveillance. Therefore, it would be better to await further evidence synthesis in this area before considering for update.

Removing penicillin allergy label

One observational study indicated that penicillin allergy “de-labeling” in people with a history of beta-lactam allergy was effective by skin testing and oral challenge. This resulted in the majority of subjects being recommended either selective or unrestrictive use of beta-lactam antibiotics. However, the study found that not all subjects adhered to the allergy label modifications at follow-up.

Overall, the new evidence broadly supports existing recommendations to refer people with a suspected beta-lactam antibiotic for investigation if they specifically need treatment with a beta-lactam antibiotic, are likely to need beta-lactam antibiotics in the future or if they are not able to take beta-lactam antibiotics and at least 1 other class due to suspected allergy to these antibiotics.

Other investigations

One observational study was identified on the diagnostic value of the basophil activation test (BAT) in children with a history of beta-lactam hypersensitivity. The evidence indicated that BAT was not useful in the diagnosis of immediate

hypersensitivity to amoxicillin or amoxicillin-clavulanate. As such, no update in this area is anticipated.	New evidence is unlikely to change guideline recommendations.

Documenting and sharing information with other healthcare professionals

Recommendations in this section of the guideline

Recording drug allergy status

1.2.1 Document people's drug allergy status in their medical records using 1 of the following:

- 'drug allergy'
- 'none known'
- 'unable to ascertain' (document it as soon as the information is available).

1.2.2 If drug allergy status has been documented, record all of the following at a minimum:

- the drug name
- the signs, symptoms and severity of the reaction (see recommendation 1.1.1)
- the date when the reaction occurred.

Documenting new suspected drug allergic reactions

1.2.3 When a person presents with suspected drug allergy, document their reaction in a structured approach that includes:

- the generic and proprietary name of the drug or drugs suspected to have caused the reaction, including the strength and formulation
- a description of the reaction (see recommendation 1.1.1)
- the indication for the drug being taken (if there is no clinical diagnosis, describe the illness)
- the date and time of the reaction
- the number of doses taken or number of days on the drug before onset of the reaction
- the route of administration
- which drugs or drug classes to avoid in future.

Maintaining and sharing drug allergy information

1.2.4 Prescriptions (paper or electronic) issued in any healthcare setting should be standardised and redesigned to record information on which drugs or drug classes to avoid to reduce the risk of drug allergy.

1.2.5 Ensure that drug allergy status is documented separately from adverse drug reactions and that it is clearly visible to all healthcare professionals who are prescribing drugs.

1.2.6 Check a person's drug allergy status and confirm it with them (or their family members or carers as appropriate) before prescribing, dispensing or administering any drug (see also recommendation 1.3.4). Update the person's medical records or inform their GP if there is a change in drug allergy status.

1.2.7 Ensure that information about drug allergy status is updated and included in all:

- GP referral letters
- hospital discharge letters

1.2.8 Carry out medicines reconciliation for people admitted to hospital in line with recommendations in Technical patient safety solutions for medicines reconciliation on admission of adults to hospital (NICE patient safety solutions guidance 1).

Documenting information after specialist drug allergy investigations

For recommendations on referral to specialist services see section 1.4.

1.2.9 After specialist drug allergy investigations, allergy specialists should document:

- the diagnosis, drug name and whether the person had an allergic or non-allergic reaction
- the investigations used to confirm or exclude the diagnosis
- drugs or drug classes to avoid in future.

Surveillance decision

No new information was identified at any surveillance review.

Recommendation 1.2.8 should be amended to cross refer to the NICE guideline on Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes (NICE guideline NG5). The guideline number and hyperlink should be amended in the existing cross reference.

Providing information and support to patients

Recommendations in this section of the guideline

1.3.1 Discuss the person's suspected drug allergy with them (and their family members or carers as appropriate) and provide structured written information (see recommendation 1.2.3). Record who provided the information and when.

1.3.2 Provide information in line with the recommendations in Patient experience in adult NHS services (NICE clinical guideline 138).

1.3.3 Ensure that the person (and their family members or carers as appropriate) is aware of the drugs or drug classes that they need to avoid, and advise them to check with a pharmacist before taking any over-the-counter preparations.

1.3.4 Advise people (and their family members or carers as appropriate) to carry information they are given about their drug allergy at all times and to share this whenever they visit a healthcare professional or are prescribed, dispensed or are about to be administered a drug.

Providing information and support to people who have had specialist drug allergy investigations

For recommendations on referral to specialist services see section 1.4.

1.3.5 Allergy specialists should give the following written information to people who have undergone specialist drug allergy investigation:

- the diagnosis– whether they had an allergic or non-allergic reaction
- the drug name and a description of their reaction (see recommendation 1.1.1)
- the investigations used to confirm or exclude the diagnosis
- drugs or drug classes to avoid in future
- any safe alternative drugs that may be used.

1.3.6 Explain to people in whom allergy to a drug or drug class has been excluded by specialist investigation that they can now take this drug or drug class safely and ensure that their medical records are updated.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

No relevant evidence was identified.

Intelligence gathering

Expert advice emphasised it would be good practice to include recommendations on handling safeguarding concerns in relation to drug allergy in adults, whereas safeguarding in children is already covered in the guideline. The expert commented that recommendations about sharing advice on social care support if a person may have social care needs would be welcomed. In addition, the topic expert requested the guideline to detail how care workers should ensure that information on drug allergies is communicated when a person transfers to a new care setting, particularly if they lack capacity and clarification on who is responsible for sharing information with care workers.

Impact statement

Intelligence gathering highlighted topic expert feedback concerning management of drug allergy in people with social care needs.

Recommendation 1.3.2 of NICE guideline CG183 recommends to "provide information in line with the recommendations in Patient experience in adult NHS services" (NICE guideline CG138). NICE guideline CG138 includes recommendations on knowing the patient as an individual, tailoring healthcare services for each patient and essential requirements of care including consent and capacity. In addition, NICE guideline CG138 provides recommendations on continuity of care and relationships including recommendation 1.4.3 "to ensure clear and timely exchange of patient information between healthcare and social care professionals in line with the Health and Social Care Safety and Quality Act 2015".

NICE guideline CG183 includes recommendation 1.2.8 on carrying out medicines reconciliation which will be amended to include a cross referral to NICE guideline on Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes (NICE guideline NG5). NICE guideline NG5 details who is responsible for this process and how relevant information should be communicated about medicines when patients move from one care setting to another.

As such, the areas highlighted by the topic expert have been addressed by other NICE guidance referenced within existing recommendations. Therefore, no impact on the guideline is anticipated.

New evidence is unlikely to change guideline recommendations.

Non-specialist management and referral to specialist services

Recommendations in this section of the guideline

General

1.4.1 If drug allergy is suspected:

- consider stopping the drug suspected to have caused the allergic reaction and advising the person to avoid that drug in future
- treat the symptoms of the acute reaction if needed; send people with severe reactions to hospital
- document details of the suspected drug allergy in the person's medical records (see recommendations 1.2.3 and 1.2.6)
- provide the person with information (see section 1.3).

1.4.2 Refer people to a specialist drug allergy service if they have had:

- a suspected anaphylactic reaction (also see Anaphylaxis, NICE clinical guideline 134) or
- a severe non-immediate cutaneous reaction (for example, drug reaction with eosinophilia and systemic symptoms [DRESS], Stevens–Johnson Syndrome, toxic epidermal necrolysis).

Non-steroidal anti-inflammatory drugs (including selective cyclooxygenase 2 inhibitors)

1.4.3 Explain to people with a suspected allergy to a non-selective non-steroidal anti-inflammatory drug (NSAID) (and their family members or carers as appropriate) that in future they need to avoid all non-selective NSAIDs, including over-the-counter preparations.

1.4.4 For people who have had a mild allergic reaction to a non-selective NSAID but need an anti-inflammatory:

- discuss the benefits and risks of selective cyclooxygenase 2 (COX-2) inhibitors (including the low risk of drug allergy)
- consider introducing a selective COX-2 inhibitor at the lowest starting dose with only a single dose on the first day.

1.4.5 Do not offer a selective COX 2 inhibitor to people in a non-specialist setting if they have had a severe reaction, such as anaphylaxis, severe angioedema or an asthmatic reaction, to a non-selective NSAID.

1.4.6 Refer people who need treatment with an NSAID to a specialist drug allergy service if they have had a suspected allergic reaction to an NSAID with symptoms such as anaphylaxis, severe angioedema or an asthmatic reaction.

1.4.7 Be aware that people with asthma who also have nasal polyps are likely to have NSAID-sensitive asthma unless they are known to have tolerated NSAIDs in the last 12 months.

Beta-lactam antibiotics

1.4.8 Refer people with a suspected allergy to beta-lactam antibiotics to a specialist drug allergy service if they:

- need treatment for a disease or condition that can only be treated by a beta-lactam antibiotic **or**
- are likely to need beta-lactam antibiotics frequently in the future (for example, people with recurrent bacterial infections or immune deficiency).

1.4.9 Consider referring people to a specialist drug allergy service if they are not able to take beta-lactam antibiotics and at least 1 other class of antibiotic because of suspected allergy to these antibiotics.

Local anaesthetics

1.4.10 Refer people to a specialist drug allergy service if they need a procedure involving a local anaesthetic that they are unable to have because of suspected allergy to local anaesthetics.

General anaesthesia

1.4.11 Refer people to a specialist drug allergy service if they have had anaphylaxis or another suspected allergic reaction during or immediately after general anaesthesia.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

No relevant evidence was identified.

Intelligence gathering

A topic expert commented that the recommendations state to take a history but do not provide further detail about next steps. However, NICE guideline CG183 does provide recommendations for documenting such information in medical records, sharing information with other healthcare professionals and lists criteria for referral to specialist services, therefore no impact on the guideline is anticipated.

A topic expert highlighted the Report and findings of the Royal College of Anaesthetists' 6th National Audit Project: Perioperative Anaphylaxis (2018) undertaken every 3 years, from which there are 7 publications in the pipeline. The audit recommendations support NICE guideline CG183 recommendations on documentation and referral of drug allergy.

Impact statement

The absence of new evidence indicates that there is no need to update this section of the guideline.

New evidence is unlikely to change guideline recommendations.

Research recommendations

2.1 Designing systems for documenting drug allergy

Which documentation strategies would be most clinically and cost effective to minimise the number of people who are re-exposed to drugs to which they have a suspected or confirmed allergy, looking in particular at:

- electronic health records that include features specifically designed to record and alert clinicians to drug allergy information, compared with systems without such features **and**
- different formats for patient-held, structured drug allergy documentation?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.2 Communicating information about drug allergy

In people with suspected or confirmed drug allergies, are patient focused information strategies more effective than standard NHS practice in increasing people's likelihood of disclosing their drug allergy (or their suspected drug allergy) and therefore reducing the risk of being re-exposed to the affected drug?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.3 Using selective cyclooxygenase 2 inhibitors in people with previous severe allergic reactions to non-selective non-steroidal anti-inflammatory drugs

Should all patients who have experienced a severe allergic reaction to a non-selective non-steroidal anti-inflammatory drug (NSAID) be assessed by specialist drug allergy services or should they be advised to take a selective cyclooxygenase 2 (COX 2) inhibitor without further investigations if clinically appropriate?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.4 Oral antibiotic challenge for diagnosing antibiotic allergy in children

In children who have a suspected allergy to an antibiotic, is it clinically and cost effective to proceed directly (without prior skin or intradermal tests) to a diagnostic oral antibiotic challenge rather than referring them to specialist drug allergy services?

Summary of findings

Two studies were identified relevant to this research recommendation (see Drug provocation test). The new evidence indicates that direct oral antibiotic challenge may be of clinical value in confirming drug allergy without the need for prior allergy testing. However, during this surveillance review limited evidence was identified on the diagnostic value of direct provocation testing. In addition, no evidence was found on the cost-effectiveness of direct oral antibiotic challenge compared to referral for specialist services.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

References

1. Marrs T, Fox AT, Lack G, Toit du, G (2015) The diagnosis and management of antibiotic allergy in children: Systematic review to inform a contemporary approach. Archives of Disease in Childhood 100(6):583–8

2. Fox SJ, Park MA (2014) Penicillin skin testing is a safe and effective tool for evaluating penicillin allergy in the pediatric population. The Journal of Allergy & Clinical Immunology in Practice 2(4):439–44

3. Manuyakorn W, Singvijarn P, Benjaponpitak S, Kamchaisatian W, Rerkpattanapipat T, Sasisakulporn C, et al. (2016) Skin testing with beta-lactam antibiotics for diagnosis of beta-lactam hypersensitivity in children. Asian Pacific Journal of Allergy & Immunology 34(3):242–7

4. Picard M, Paradis L, Begin P, Paradis J, Roches D, A (2014) Skin testing only with penicillin G in children with a history of penicillin allergy. Annals of Allergy, Asthma, & Immunology 113(1):75–81

5. Faitelson Y, Boaz M, Dalal I (2018) Asthma, Family History of Drug Allergy, and Age Predict Amoxicillin Allergy in Children. Journal of Allergy and Clinical Immunology: In Practice 6(4):1363–7

6. Mill C, Primeau MN, Medoff E, Lejtenyi C, O'Keefe A, Netchiporouk E, et al. (2016) Assessing the Diagnostic Properties of a Graded Oral Provocation Challenge for the Diagnosis of Immediate and Nonimmediate Reactions to Amoxicillin in Children. JAMA Pediatrics 170(6):e160033

7. Tour T la, Aude, Marine M, A EP, Jean-Christoph C (2018) Natural History of Benign Nonimmediate Allergy to Beta-Lactams in Children: A Prospective Study in Retreated Patients After a Positive and a Negative Provocation Test. The Journal of Allergy & Clinical Immunology in Practice 6(4):1321–6

8. Vezir E, Dibek Misirlioglu E, Civelek E, Capanoglu M, Guvenir H, Ginis T, et al. (2015) Direct oral provocation tests in non-immediate mild cutaneous reactions related to beta-lactam antibiotics. Pediatric Allergy and Immunology 27(1):50–4

9. Lezmi G, Alrowaishdi F, Bados-Albiero A, Scheinmann P, Blic de, J, et al. (2018) Non-immediate-reading skin tests and prolonged challenges in non-immediate hypersensitivity to beta-lactams in children. Pediatric Allergy and Immunology 29(1):84–9

10. Bourke J, Pavlos R, James I, Phillips E (2015) Improving the Effectiveness of Penicillin Allergy De-labeling. The Journal of Allergy and Clinical Immunology: In Practice 3(3):365–374.e1

11. Barni S, Mori F, Valleriani C, Mangone G, Testi S, Saretta F, et al. (2017) The utility of the basophil activation test in the diagnosis of immediate amoxicillin or amoxicillin-clavulanate hypersensitivity in children and adults. Italian Journal of Pediatrics 43 (1) (no(42)